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Prize Lectures
Growth hormone (GH) secreted by the anterior pituitary gland regulates skeletal growth, metabolism and body composition. Although several of these actions are mediated by production of hepatic and local tissue IGF1, GH also acts independent of IGF1. GH is mainly produced from the pituitary as a systemic endocrine hormone, yet is also expressed in local tissues acting in an autocrine/paracrine/intracrine manner. Locally produced non-pituitary GH (npGH) signals the GHR to induce epithelial cell proliferation by suppressing p53, thereby enabling epithelial cell proliferation. Although endocrine GH levels drop markedly with aging, npGH increases with aging, blocking repair of age-associated DNA damage. Consistent with these findings, npGH is a component of the senescence-associated secretory phenotype thereby enabling a pro-proliferative epithelial milieu. As p53 is increased in vivo by blocking GHR signalling these mechanisms may explain the known cancer-protective effects of GH deficiency and GHR signalling disruption, as well as contributing to age-associated pathologies. Thus, GH is a powerful inducer of skeletal growth during childhood, and maintains body composition in the adult, after maturation and with aging. GHR actions are transformed to accumulate DNA damage. Unraveling these mechanisms supports a hypothesis whereby adverse age-related processes are in fact accelerated by GHR signalling. This notion supports the protective function of low circulating GH during aging, and also would call for vigilance against inappropriate adult GH abuse. This premise also supports the potential for trials designed to block GH action to enable extended healthspan. These insights point to pituitary and non-pituitary adult GH as a regulator of DNA damage contributing to the cellular micro-environment in addition to functioning as a promoter of skeletal growth.

DOI: 10.1530/endoabs.81.AP3
European Hormone Medal Award Lecture
AP5.1
Great impact in low quantities - thyroid hormones, trace elements and endocrine disruptors
Josef Köhrle
Institut für Experimentelle Endokrinologie, Charité Universitätsmedizin Berlin, Berlin, Germany

Thyroid hormones (TH) regulate (brain) development, growth, body temperature, most pathways involved in energy and structural metabolism as well as anabolic and catabolic reactions. Inadequate availability of essential trace elements (iodine, selenium, iron, zinc) limits TH biosynthesis, metabolism and action. Endocrine-disrupting chemicals (EDC), i.e., exogenous chemicals or their mixtures, can interfere with any aspect of TH synthesis, distribution, transport, metabolism, and action via (non-)canonical T3 receptor mediated signalling. Only a limited number of EDC exert their adverse effects by directly interfering with follicular TH production. Majority of EDC effects occurs by disruption of protein-protected TH distribution via bloodstream, specific TH transport across cellular membranes and/or intracellular (in-)activation and/or TH metabolism. This pre-receptor control of local T3 availability to intracellular T3 receptors, which act as ligand-modulated transcription factors for gene expression, represents the main operation field for EDC in the TH system (THS). Only few EDC modulate functions of T3 receptors, which contrasts adverse EDC actions on the sex steroid dependent reproductive processes, most of which are known to be associated with direct disruption of sex steroid receptor functions. Thus, individual blood TH concentrations only provide limited information about adverse action and consequences for EDC exposed individuals, e.g., mother-child pairs. TH, trace elements and EDC exert their direct and permissive effects in very low, locally regulated, physiological concentrations frequently not reflected at the systemic level as impressively illustrated during TH-regulated amphibian metamorphosis, embryonal development of fish or mammalian species, including humans. Considering that anthropogenic mass recently exceeded our blue planet’s biomass, we must minimize exposure to EDC, contained in and released from anthropogenic products, as EDC interfere already at very low concentrations with the THS. Concomitantly, the THS needs to be fortified and protected by globally adequate supply with those essential trace elements (I, Se, Fe) required for its proper function.

DOI: 10.1530/endoabs.81.AP5.1

AP5.2
Diabetic kidney disease: after years of darkness came light – finally new options for treatment!
Peter Rossing1,2
1Steno Diabetes Center Copenhagen, Gentofte, Denmark; 2Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Unfortunately diabetes is a growing problem with now more than 537 million people worldwide having diabetes according to International Diabetes Federation. Excess morbidity and mortality in diabetes is related to the development of diabetic kidney disease seen in 30-40%, which not only causes end stage kidney disease, but also increases risk for cardiovascular events and mortality, which is the leading cause of death. Treatment of diabetic kidney disease has been control of glucose, lipids, and blood pressure including blockade of the renin angiotensin system, but the residual risk on optimal treatment was large. Multiple interventions have been tested and failed in this condition, but in the past few years, we have suddenly been able to find new treatment options. First cardiovascular outcome trials in diabetes found the SGLT2 inhibitors reduced progression of kidney disease or heart failure, and GLP1 receptor agonists reduced cardiovascular events and maybe also improved kidney parameters. Then an endothelin receptor antagonist demonstrated reduced progression of kidney disease, and most recently the nonsteroidal mineralocorticoid receptor antagonist finerenone demonstrated reduction in progression of kidney and cardiovascular disease. Now we suddenly have the opportunity to improve on the most deadly complications to diabetes with several interventions, and as they work on different disease pathways (hemodynamic, metabolic, inflammatory) data suggest they can be combined with extra benefit for the person with diabetes. Now implementation is key, and quality monitoring systems should be in place to ensure this.

DOI: 10.1530/endoabs.81.AP5.2
Plenary Lectures
Genotype-phenotype analyses permit prediction of cure from Primary Aldosteronism
PL1

Abstract unavailable
DOI: 10.1530/endoabs.81.PL1

Cellular and molecular mechanisms regulating muscle regeneration in aging
PL2

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DOI: 10.1530/endoabs.81.PL2

Resilience Endocrinology
PL3

Abstract unavailable
DOI: 10.1530/endoabs.81.PL3

Fatty bone stem cells
PL4

Fatty bone stem cells
Clifford Rosen
Center for Clinical and Translational Research, Maine Medical Center Research Institute, Scarborough, United States

Bone marrow adipose tissue represents a unique depot surrounded by hematopoietic elements and trabecular bone. It expands during aging, and is dynamic in response to hormonal, nutritional and mechanical stimuli. The skeletal response to the increase in marrow adipocyte number and/or size is a relevant consideration, particularly since bone marrow adipose tissue is enhanced in states with low bone mass or rapid bone loss. Excess or deficient nutrient intake are powerful inducers of bone marrow adiposity in both humans and mice. We previously showed that 30% calorie restriction in mice stimulated bone marrow adiposity and drove bone loss. This led us to determine if fasting in humans also caused bone loss and expansion of marrow adipocytes. Volunteers were fasted for 10 days or given a high calorie diet for 10 days; bone marrow aspirates and skeletal quantitation was determined by uCT and MRI. Fasting induced a 10% increase in marrow fat, which was rapidly reversed by a 2 week return to a normal diet. In pathway analysis from marrow adipocytes using RNAseq, recruitment of progenitors (adipogenesis) was the major network activated, followed by the complement pathway. qRT-PCR demonstrated that adipin, complement factor D (CFD), was one of the most up-regulated genes in the marrow adipocytes. In vitro analysis of adipocytes from the marrow of 30% CR mice revealed increased CFU-F (CFD), was one of the most up-regulated genes in the marrow adipocytes. In vitro analysis of adipocytes from the marrow of 30% CR mice revealed increased CFU-F, which now is an extremely popular weight loss program, can cause bone loss and increased marrow adiposity. DOH: 10.1530/endoabs.81.PL4

Old dogmas and new players in puberty and reproduction
PL5

Old dogmas and new players in puberty and reproduction
Manuel Tena-Sempere
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Reproduction, as essential function for the perpetuation of species, is controlled by precise maturational programs and sophisticated regulatory circuits, which have been the subject of active research. Seminal findings in the last decades of the 20th century set basic dogmas in reproductive endocrinology, including the identification of gonadotropin-releasing hormone (GnRH), as the master hypothalamic signal controlling reproduction, and the initial description of complex networks of central transmitters and peripheral hormones, from glutamate and GABA to nitric oxide and leptin, as key modulators of puberty and fertility. In fact, by the turn of the Millennium, there was the perception that the fundamentals of the neuroendocrine systems governing the reproductive axis had been already exposed, thus leaving little room for major conceptual developments in this apparently exhausted field of contemporary Endocrinology. Reality, however, turned out to be much more exiting, so that in the last twenty years, we have witnessed groundbreaking findings in this area, epitomized by the discovery of the reproductive roles of kisspeptins. These have not only revolutionized our understanding of the mechanisms controlling puberty and reproduction, but have also boosted kind of a New-Age in reproductive research, where basic, translational and clinical studies have surfaced novel players, neuroendocrine circuits and molecular regulatory mechanisms responsible for the precise control of the reproductive axis along the lifespan. Some examples of these recent developments will be summarized in this lecture, which aims also to identify new avenues for further progress of this fertile area of modern Endocrinology.
DOI: 10.1530/endoabs.81.PL5

Thyroid Hormone Resistance, Diagnosis and Treatment
PL6

Thyroid hormone resistance, diagnosis and treatment
Carla Moran
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Resistance to Thyroid hormone (RTH) encompasses various disorders of Thyroid Hormone (TH) Action, including defective signalling through TH Receptors (RTH alpha, RTH Beta), abnormal TH metabolism (Selenoprotein deficiency) and altered cellular entry of TH (MCT8 defects). In this talk, I will focus on RTH alpha and beta. RTH beta is usually associated with mutations in the THRB gene and is often readily identified, due to the associated typical biochemical pattern of raised TH levels and non-suppressed TSH. Resistance to the action of TH occurs in tissues expressing the beta form of the TH receptor (hypothalamus, pituitary, liver), but TR alpha expressing tissues are exposed to elevated TH levels. Patients with Resistance to Thyroid Hormone alpha (RTH alpha; due to mutations in the THRA gene) are highly challenging to identify because many patients only have mildly abnormal (or even normal) thyroid hormone levels. Resistance to the action of TH occurs in tissues expressing the alpha form of the TH receptor (bone, skeletal muscle, brain and heart). The clinical features/phenotype of both RTHalpha and RTHbeta are highly variable; from mild developmental delay to severe learning impairment and disability in RTHalpha, and asymptomatic states to significant tissue specific thyrotoxicosis in RTHbeta. Treatment for RTHbeta is not always required, but beta-blockade and tri-iodothyroacetic acid (T3LAC) can be considered. Many patients with RTHalpha respond to thyroidine therapy, but optimal dosing schedules and treatment targets are not known.
DOI: 10.1530/endoabs.81.PL6
Endocrine-disrupting chemicals: scientific, economic, regulatory, and policy implications

Endocrine-disrupting chemicals: scientific, economic, regulatory, and policy implications
Leonardo Trasande,1,2,3
1NYU School of Medicine, New York, United States; 2NYU Wagner School of Public Service, New York, United States; 3NYU School of Global Public Health, New York, United States

Endocrine disrupting chemical (EDC) exposure contributes to disease and dysfunction, with annual costs >2% GDP in the US and >1% in Europe. Differences in policy explain differences in disease burden and cost. In Europe, general principles for EDCs call for minimization of human exposure, identification as substances of very high concern, and ban on use in pesticides. In the US, screening and testing programs are focused on estrogenic EDCs exclusively, and regulation is strictly risk-based. Since our reports describing 15 probable exposure-outcome associations due to EDCs, there has been a deepened understanding of their effects on human health. We have reviewed subsequent additions to the literature and identified new exposure-outcome associations with substantial human evidence. Although systematic evaluation is needed of their probability and strength, the growing evidence supports urgent action to reduce exposure. We suggest: expanded and comprehensive testing to conclusively identify EDCs, and a shift from a flawed, risk-based paradigm to one that proactively excludes chemicals with some evidence of hazardous properties. An international initiative on EDCs supported by the UN could address the weaknesses related to hazard identification and provide much-needed guidance for policies globally.

DOI: 10.1530/endoabs.81.PL7
Symposia
### Endocrine malignancies - update on rare tumours

**S1.1**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S1.1

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**S1.2**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S1.2

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**S1.3**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S1.3

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### Genetic and epigenetic basis of PCOS heritability

**S2.1**

**Prenatal androgen exposure causes transgenerational epigenetic transmission of PCOS**  
Elisabet Stener-Victorin  
Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

In a register-based and case-control studies it has been shown that daughters of women with or without PCOS have a five-fold increased risk of being diagnosed with the syndrome. Moreover, sons born to a mother with PCOS have two to three-fold increased risk of being obese. But how PCOS is inherited is unclear as PCOS loci identified by genome-wide association studies account for only 10% of the heritability. It has been suggested that epigenetic and developmental programming contributes to the inheritance of PCOS. In support for this, PCOS-like traits induced by androgen exposure during pregnancy in mice can be passed on from mothers (F0) to daughters (F1), granddaughters (F2), and even great-granddaughters (F3), and transcriptional and mitochondrial perturbations of oocytes accompany the transmission. Several of the oocyte gene signatures are detectable also in serum from daughters of women with PCOS and in adipose tissue of unrelated women with PCOS, indicating communication between germ cells, serum and somatic tissues/cells. Also, male offspring F1 to F3 of obese and androgen-exposed mothers develop aberrant reproductive and metabolic traits in adulthood. Small-noncoding (snc)RNA sequencing carried by the sperm contribute to a transgenerational epigenetic inheritance of phenotypic traits. As in females, several of sperm signatures are detectable in whole blood from sons of women with PCOS supporting the translational relevance of the mouse findings.  
DOI: 10.1530/endoabs.81.S2.1

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### Nutritional and Metabolics aspects of the Thyroid

**S3.1**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S3.1

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**S3.2**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S3.2

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**S3.3**

Abstract unavailable  
DOI: 10.1530/endoabs.81.S3.3

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### Parathyroid disorders clinical update (PARAT group)

**S4.1**

**Management of primary hyperparathyroidism (PHPT)**  
Neil Gittos  
Department of Endocrinology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

The European PARAT group have recently explored a number of practical management issues in parathyroid diseases. Herein, we present expert opinion on areas of controversy in the diagnosis and management of primary hyperparathyroidism (PHPT). Although PHPT is common, its differential diagnosis from familial hypocalciuric hypercalcaemia (FHH) poses practical problems. Proposed approaches to addressing this will be discussed. The definition and clinical course of normocalcemic PHPT remains controversial and there is particular emphasis...
on excluding causes of secondary hyperparathyroidism that can cause elevated PTH with normal blood calcium levels. An algorithm is presented to explore the approach to diagnosing normocalcaemic PHPT. Recurrent PHPT is rare but requires clear definition and approaches to reassessment and redo surgery should be performed at centres with great expertise in repeat surgery. Per- and post-operative management of patients with PHPT differs from centre to centre. We propose a structured approach to patient preparation for parathyroidectomy and review causes and management of post-operative hypocalcaemia. Longer term follow up and assessment of PHPT patients is also discussed. The recommendations on clinical management presented herein serve as background for further educational material aimed at a broad clinical audience and were developed with the focus on endocrinologists in training.

DOI: 10.1530/endoabs.81.S4.1

Organ crosstalk in metaflammation

**S5.1**

**Beta cells and inflammation in diabetes**

Thomas Mandrup-Poulsen
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Innate immunity contributes to inducing functional inhibition and apoptosis of pancreatic beta-cells in the pathogenesis of both Type 1 diabetes (T1D) and Type 2 diabetes (T2D). The past four decades has provided overwhelming circumstantial evidence from in vitro studies and animal models that innate immune cells and cytokines are key effectors in beta-cell killing. Pro-inflammatory cytokines activate signaling pathways that reprogram the beta-cell transcriptome and proteome, adversely affecting most functions of the cell and triggering death by the intrinsic (mitochondrial) death pathway. On the other hand, these signaling pathways also elicit numerous adaptive and protective responses that may guide development of preventive therapies. Researchers increasingly agree that environmental stressors that enhance insulin biosynthetic demand may lead to increased proinsulin misfolding, misprocessing and posttranslational modifications, triggering inflammation and neoepitope formation and presentation in the beta-cell. This novel concept attracts focus to beta-cell stress as an initiating event in the development of both T1D and T2D. There is clinical proof-of-concept that blocking the action of the pro-inflammatory cytokines interleukin-1 (IL-1) or tumor necrosis factor (TNF) improves glycaemia and beta-cell function in T2D and T1D, respectively, and meta-analyses on >2000 T2D patients substantiates the efficacy of IL-1 blockade. Yet, anti-cytokine biologics have not yet been adopted in clinical practice. This lecture will review key basic and clinical findings supporting the importance of inflammatory beta-cell damage in the pathogenesis of T1D and T2D, and will highlight central barriers that prevent clinical translation.

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Endocrine Abstracts (2022) Vol 81
S7.2
Cardiometabolic outcomes and mortality in patients with autonomous cortisol secretion
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Mild autonomous cortisol secretion (MACS) has been associated with cardiometabolic risk factors and cardiovascular disease in the 2000s and with increased mortality in the 2010s. Since the range of cortisol after dexamethasone suppression (cortisolDST) in MACS is wide, the associated risk may vary. To adequately decide treatment, the risk associated to the different levels of cortisolDST must be known. This year the ENSAT group published a study on cardiometabolic complications in MACS. Patients with cortisolDST 138 nmol/l or more had an increased adjusted prevalence ratio of hypertension 1.15 and more often had treatment with three or more antihypertensives. The adjusted prevalence ratios of dyslipidaemia and diabetes were similar, but insulin treatment was more common. Patients with cortisolDST 50 to 137 nmol/l had no increase in the prevalence of hypertension, diabetes, and dyslipidaemia. Last year our group published a study on 1048 patients with a median follow-up of 6.4 years. Patients with cortisolDST 83 to 137 nmol/l had a hazard ratio of 2.30 for mortality and patients with cortisolDST 138 nmol/l or more 3.04. Patients with cortisolDST 50 to 82 nmol/l had no significant increase in mortality. The increase in mortality was found to be linear up to cortisolDST levels of 200 nmol/l. The cardiovascular event rate was increased in patients with cortisolDST 138 nmol/l or more but unchanged at cortisolDST levels 50 to 137 nmol/l. The risk ratios for mortality seem larger than the relative prevalence of cardiometabolic complications. Therefore, improved medical treatment may not normalise the mortality risk in MACS. We suggest treatment of cardiovascular risk factors and incorporation of our results into the decision of which patients to recommend for adrenalectomy.

DOI: 10.1530/endoabs.81.S7.2

S7.3
Trace elements in endocrinology: too low or too high
S8.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S7.3

S8.2
Iron and the thyroid
Michael Zimmermann
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Despite significant progress, deficiencies of iron and iodine remain major public health problems affecting >30% of the global population. These deficiencies often coexist in populations. Iron deficiency has adverse effects on thyroid metabolism. Iron deficiency impairs thyroid hormone synthesis by reducing activity of heme-dependent thyroid peroxidase. Iron-deficiency anaemia blunts, and iron supplementation improves the efficacy of iodine supplementation. Studies have demonstrated that a high prevalence of iron deficiency among children in areas of endemic goiter may reduce the effectiveness of iodized salt programs. These findings argue strongly for improving iron status in areas of overlapping deficiency, not only to combat anaemia but also to increase the efficacy of iodine prophylaxis. Poor maternal iron status predicts both higher TSH and lower TT4 concentrations during pregnancy in an area of borderline iodine deficiency.

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S8.3
Genetics of adrenal endocrine tumors
S9.1
Genetic bases of pheochromocytoma and paraganglioma
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Pheochromocytoma and paraganglioma (PPGL) are rare tumours, whose genetic profile has gained complexity over the last two decades. The list of genes involved in the development of this disease has been steadily growing, and there are currently more than 20 driver genes capable of explaining either the hereditary or sporadic nature of the disease. Although genetic diagnosis is achieved in about 75-80% of cases, the genetic aetiology remains to be explained not only in patients with apparently sporadic PPGL, but also in patients with a family history or with multiple tumours, and who therefore meet the criteria to be considered as candidates for carrying mutations in as yet undiscovered genes. Taken together, the mutations in the known PPGL genes deregulate three distinct signalling pathways, which may be the starting point for personalised treatment of these patients. One of the most relevant features of PPGLs is that they show homogeneous genomic profiles according to the specific gene that is mutated in each case. This homogeneity is what is making it possible to identify new characteristics of PPGLs, including differential aspects of the tumour microenvironment, again dependent on the genetics of the tumour.

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S9.2
Trace elements in endocrinology: too low or too high
S9.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S9.2

S9.3
Iron and the thyroid
Michael Zimmermann
ETH Zürich, Switzerland

Endocrine Abstracts (2022) Vol 81
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<td>S12.2</td>
<td>Fructose but not glucose drives DNL</td>
<td>Philipp A Gerber</td>
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<td>Observational studies conducted during the past two decades provide evidence of an association of dietary fructose consumption with obesity and metabolic diseases as non-alcoholic fatty liver disease or insulin resistance / type 2 diabetes mellitus. However, these associations are challenged by the fact that it is difficult to adjust the results of such studies for excessive caloric intake, which often co-exists with high fructose intake, e.g., by consumption of sugar-sweetened beverages. Thus, there is a clear need for direct interventional studies exploring a possible causal role of fructose in the development of metabolic diseases, as compared to other sugars. To this aim, different controlled trials were conducted by our group as well as other investigators to assess this question. Such studies expose their participants to various amounts of different sugars for several weeks to months, and investigate different outcomes related to metabolic diseases as those outlined above. With these trials, it was possible to gain direct insights into the mechanisms by which different sugars may negatively influence metabolic health. In particular, latest research provides evidence of very distinct effects of fructose consumption on hepatic metabolism, in particular regarding a “metabolic switch” in hepatic tissue towards de novo lipogenesis. Furthermore, and in addition to the effects of fructose, the co-ingestion of fructose and glucose (which is very common due to their co-existence in the sucrose molecule) may have similar or even more deleterious effects than consumption of fructose alone. Thus, these results emphasize the importance of an overall reduction of added sugars in our diet, as suggested by the WHO and other organizations.</td>
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Molecular aspects of clinical management in liver/pancreatic cancer

Abstract unavailable
DOI: 10.1530/endoabs.81.S14.1

Bone microstructure - What techniques are there, what do they tell us
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Areal BMD from Dual energy X-Ray absorptiometry (DXA) accounts for approximately two-thirds of bone strength and is used as a surrogate for bone strength in clinical practice to predict fracture risk. Nevertheless, a more in-depth assessment of bone quality requires second level imaging techniques to assess bone quality parameters. Bone quality is a key parameter in determining bone strength. During time, several non-invasive high-resolution imaging techniques have been developed to visualise bone structure. As bony trabeculae measure 50–200 μm in thickness, the spatial resolution of imaging techniques applied to the non-invasive evaluation of bone microstructure must be higher than 200 μm to spatially solve the single trabeculae. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a low-dose technique that enable to image bone microarchitecture in vivo at peripheral skeletal sites, such as distal forearm and tibia. Differences and reference data exist for HR-pQCT by age and sex, race/ethnic origin and body composition. We will review the role of HR-pQCT in fractured patients, to highlight those parameters of bone microarchitecture and bone strength useful as predictors of incident fractures, as well as in subject with prevalent fractures. The role of HR-pQCT in monitoring response of anti-osteoporotic therapy will be addressed, as well as its role in patients with secondary osteoporosis and metabolic bone disorders. Finally, novel application of HR-pQCT will be briefly reviewed. The presentation will then deal with the evaluation and quantification of bone structure and microstructure with current available MRI techniques, also comparing the MRI performance with DXA and CT measurements. Limitation of each technique will be reviewed, as well as their current applicability in clinical practice.
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Tools for fracture risk assessment, and how to use them

Abstract unavailable
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Artificial intelligence in osteoporosis management
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Background
Osteoporosis is a systemic skeletal disease characterized by low bone mass, microarchitectural deterioration of bone tissue, and the consequence of an increased fracture risk. The term “artificial intelligence (AI)” denotes a field in computer science and related disciplines that enables computers to simulate different aspects of human intelligence, such as natural language understanding, pattern recognition or data driven learning. Machine Learning is a subset of AI, and within this field, Convolutional Neural Networks (CNN) play a key role particularly in relation to medical imaging.

Methods
Various AI applications as currently available for the management of osteoporosis are presented, including their strengths and pitfalls.

Results
One of the mainstays of AI supported applications in osteoporosis is imaging based detection of fractures. Almost any medical imaging technique including – but not limited to - plain radiography, computed tomography (CT) and MRT, is represented in an increasing number of studies. There is evidence that AI based technical support can improve fracture detection rate. Furthermore, AI supported algorithms are used not only to assess quantitative aspects of the bone, such as bone mineral density (BMD) at the lumbar spine, the hip and the total body, but also to assess qualitative properties, such as microarchitectue and even fracture load. However, it is of note that many of the clinical studies involving AI in the field of osteoporosis are short of scientific diligence. For example, algorithms behind specific diagnostic approaches are not always published in detail. Also, the logic behind a chosen approach is not always comprehensible. In general, there is a clear lack in standardized procedures.

Conclusion
There are aspects in support of integrating AI based tools into osteoporosis management workflows in daily clinical practice. However, there is also a clear need for high quality clinical research in this field. In this regard, implementation of, e.g., internationally consented quality standards could help to improve the relevance of study outcomes and also their credibility.

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Infections and endocrinology

S17.1
Sepsis as a pan-endocrine illness
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Sepsis is defined as “life-threatening organ dysfunction caused by a dysregulated host response to infection”. This response is expressed, inter alia, in the endocrine system and affects almost all endocrine axes. Endocrine dysfunction, in turn, may contribute to other aspects of dysregulated host response to infection, such as metabolism. Endocrine disorders in the course of sepsis are particularly noticeable in the area of the hypothalamic-pituitary-target tissue axis. Disorders of the hypothalamic-pituitary-adrenal axis manifest mainly by hypercortisolism in the acute phase. In the hypothalamic-pituitary-thyroid axis the most typical manifestation is a triiodothyronine concentration decrease and reverse triiodothyronine concentration increase. In terms of the somatotropic axis, a change in the secretion pattern of growth hormone and peripheral resistance to this hormone is characteristic. Hypothalamic-pituitary-gonadal axis disorders are expressed by the stress-induced amenorrhea in women and the reduction in testosterone level in men. Other changes include insulin resistance and catecholamine and ß-adrenergic stimulation disorders. It is also worth bearing in mind in that a patient’s endocrine profile is not the same for the entire duration of the disease, but changes over time, which is noticeable especially between the acute and the chronic phase. It is suggested that some of these changes are adaptive, but there is no doubt that all of them may have an impact on the patient’s clinical condition. Since the endocrine system is responsible for the homeostasis of the system, disturbances in its scope contribute to the dysregulation of other functions of the body, including metabolism, which, according to some authors, is one of the main pillars of the pathophysiology of sepsis. As stated by Singer et al., a more sophisticated understanding of the sequence, dynamics and interaction between the occurring metabolic, hormonal and immunological changes would provide a logical basis for patient-tailored therapeutic interventions, therefore this issue undoubtedly requires further researches.

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S17.2
Endocrine and metabolic aspects of COVID-19
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Coronavirus disease 19 (COVID-19) started to quickly spread worldwide in the end of 2019 and was declared by the WHO a pandemic on March 11, 2020. Prevailing signs and symptoms of COVID-19 comprise many organ systems and are very complex and variable and also even unpredictable and lead to tremendous increase in morbidity and mortality. Recently, there has been increasing evidence that COVID-19 affects in a complex way also the endocrine system. Renin-angiotensin-aldosterone system (RAAS) plays a crucial role at SARS-CoV-2 infection and pathogenesis. Angiotensin-converting enzyme 2 (ACE2) protein is crucial for the entry of the virus into the cells. However, it seems that overexpression of ACE2, which takes place also during the use of ACEi inhibitors, is not connected with higher susceptibility to SARS-CoV-2 infection. It is of note that the balance between ACE1 and ACE2 actions is disturbed during COVID-19 which favours proinflammatory pathways leading to tissue damage with that of lung tissue being critical for the course and prognosis of COVID-19. Thyroid gland disorders are frequently reported in relationship with COVID-19. During the severe course of COVID-19, the changes compatible with non-thyroidal illness syndrome are common. This, however, is a consequence of severe/critical illness rather than direct causal effect of COVID-19. Amongst thyroid disorders reported and studied in connection with either COVID-19 or vaccination, we can find autoimmune thyroid (AITD) disease manifestation and subacute thyroiditis. Several cases of adrenal insufficiency have been reported during or following COVID-19. These cases, however, are very likely a consequence of COVID-19 comorbidities such as antiphospholipide syndrome. It is necessary to point out that normal function of hypothalamic pituitary adrenal axis is necessary for the survival of patients mainly with severe course of the disease and proper replacement regimens in patients with adrenal insufficiency have to be introduced. Other conditions also possibly related to COVID-19 will be mentioned, mainly diabetes and obesity.

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S17.3
Endocrine and metabolic aspects of COVID-19
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Coronavirus disease 19 (COVID-19) started to quickly spread worldwide in the end of 2019 and was declared by the WHO a pandemic on March 11, 2020. Prevailing signs and symptoms of COVID-19 comprise many organ systems and are very complex and variable and also even unpredictable and lead to tremendous increase in morbidity and mortality. Recently, there has been increasing evidence that COVID-19 affects in a complex way also the endocrine system. Renin-angiotensin-aldosterone system (RAAS) plays a crucial role at SARS-CoV-2 infection and pathogenesis. Angiotensin-converting enzyme 2 (ACE2) protein is crucial for the entry of the virus into the cells. However, it seems that overexpression of ACE2, which takes place also during the use of ACEi inhibitors, is not connected with higher susceptibility to SARS-CoV-2 infection. It is of note that the balance between ACE1 and ACE2 actions is disturbed during COVID-19 which favours proinflammatory pathways leading to tissue damage with that of lung tissue being critical for the course and prognosis of COVID-19. Thyroid gland disorders are frequently reported in relationship with COVID-19. During the severe course of COVID-19, the changes compatible with non-thyroidal illness syndrome are common. This, however, is a consequence of severe/critical illness rather than direct causal effect of COVID-19. Amongst thyroid disorders reported and studied in connection with either COVID-19 or vaccination, we can find autoimmune thyroid (AITD) disease manifestation and subacute thyroiditis. Several cases of adrenal insufficiency have been reported during or following COVID-19. These cases, however, are very likely a consequence of COVID-19 comorbidities such as antiphospholipide syndrome. It is necessary to point out that normal function of hypothalamic pituitary adrenal axis is necessary for the survival of patients mainly with severe course of the disease and proper replacement regimens in patients with adrenal insufficiency have to be introduced. Other conditions also possibly related to COVID-19 will be mentioned, mainly diabetes and obesity.

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The aperitif: The neurobiology of appetite and hunger

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Environmental cues recalling palatable foods motivate eating beyond metabolic need, yet the timing of this response and whether it can develop towards a less palatable but readily available food remain elusive. Increasing evidence indicates that external stimuli in the olfactory modality communicate with the major hub in the feeding neurocircuitry, namely the hypothalamic arcuate nucleus (Arc), but the neural substrates involved have been only partially uncovered. By means of a home-cage hidden palatable food paradigm, aiming to mimic ubiquitous exposure to olfactory food cues in Western societies, we investigated whether the latter could drive the overeating of plain chow in non-food-deprived male rats and explored the neural mechanisms involved, including the possible engagement of the orexigenic ghrelin system. The olfactory detection of a familiar, palatable food impacted upon meal patterns, by increasing meal frequency, to cause the persistent overconsumption of chow. In line with the orexigenic response observed, sensing the palatable food in the environment stimulated food-seeking and risk-taking behavior, which are intrinsic components of food acquisition, and caused active ghrelin release. Our results suggest that olfactory food cues recruited intermingled populations of cells embedded within the feeding circuitry within the Arc, including, notably, those containing the ghrelin receptor. These data demonstrate the leverage of ubiquitous food cues, not only for palatable food searching, but also to powerfully drive food consumption in ways that resonate with heightened hunger, for which the orexigenic ghrelin system is implicated.

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Central impact of growth hormone GH-axis negative feedback and metabolic function

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Growth hormone (GH) responsive cells are extensively distributed in the brain, including in neurons of the arcuate nucleus (ARH) and ventromedial nucleus (VMH) of the hypothalamus, areas that control food intake, energy expenditure and blood glucose levels. However, the functional role of central GH signaling for energy and glucose homeostasis has not been unveiled yet. We generated mice lacking GH receptor (GHR) in multiple neuronal populations to investigate whether central GHR signaling modulates energy and glucose homeostasis during normal conditions or during situations of metabolic stress. GHR ablation in AgRP neurons did not affect the body weight, food intake, energy expenditure, glucose tolerance and leptin sensitivity, compared to control animals. However, fasting induced a lower c-Fos expression, a marker of neuronal activation, in the ARH of AgRP GHR KO, suggesting that AgRP neurons are unable to appropriately sense food deprivation without GH signaling. Remarkably, GHR ablation in AgRP cells mitigated highly characteristic hypothalamic and neuroendocrine adaptations induced by weight loss. Thus, while control mice adapted to a 60% food deprivation by progressively saving energy, AgRP GHR KO mice exhibited a higher T4 and testosterone concentrations as well as an increased energy expenditure and UCP-1 mRNA expression in the brown adipose tissue, compared to control animals. These effects led to a higher rate of weight loss, which was predominantly due to fat. In contrast, GHR ablation in steroidogenic factor-1 (SF1) cells, which include VMH neurons, did not affect the responses to food restriction in comparison with control group. However, a blunted counter-regulatory response to hypoglycemia was observed in SF1 GHR KO mice, indicating that GH signaling in VMH neurons helps the organism to recover from hypoglycemia. These findings indicate a previously unidentified function of GH to induce appropriate metabolic responses that ensure survival via its action on specific neuronal populations.

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Central impact of growth hormone GH-axis negative feedback and metabolic function

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Growth hormone (GH) responsive cells are extensively distributed in the brain, including in neurons of the arcuate nucleus (ARH) and ventromedial nucleus (VMH) of the hypothalamus, areas that control food intake, energy expenditure and blood glucose levels. However, the functional role of central GH signaling for energy and glucose homeostasis has not been unveiled yet. We generated mice lacking GH receptor (GHR) in multiple neuronal populations to investigate whether central GHR signaling modulates energy and glucose homeostasis during normal conditions or during situations of metabolic stress. GHR ablation in AgRP neurons did not affect the body weight, food intake, energy expenditure, glucose tolerance and leptin sensitivity, compared to control animals. However, fasting induced a lower c-Fos expression, a marker of neuronal activation, in the ARH of AgRP GHR KO, suggesting that AgRP neurons are unable to appropriately sense food deprivation without GH signaling. Remarkably, GHR ablation in AgRP cells mitigated highly characteristic hypothalamic and neuroendocrine adaptations induced by weight loss. Thus, while control mice adapted to a 60% food deprivation by progressively saving energy, AgRP GHR KO mice exhibited a higher T4 and testosterone concentrations as well as an increased energy expenditure and UCP-1 mRNA expression in the brown adipose tissue, compared to control animals. These effects led to a higher rate of weight loss, which was predominantly due to fat. In contrast, GHR ablation in steroidogenic factor-1 (SF1) cells, which include VMH neurons, did not affect the responses to food restriction in comparison with control group. However, a blunted counter-regulatory response to hypoglycemia was observed in SF1 GHR KO mice, indicating that GH signaling in VMH neurons helps the organism to recover from hypoglycemia. These findings indicate a previously unidentified function of GH to induce appropriate metabolic responses that ensure survival via its action on specific neuronal populations.

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Osteoporosis treatment

S20.1

Abstract unavailable

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Osteoporosis treatment

S20.2

Abstract unavailable

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Endocrine Abstracts (2022) Vol 81
Autoimmune polyendocrine syndromes

S21.1

Autoimmunity in families with Addison’s disease
Marta Fichna
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Since individuals with autoimmune Addison’s disease (AD) present considerable co-occurrence of other autoimmune conditions, clustering of autoimmunity was also predicted among their relatives. We aimed to evaluate the burden of autoimmunity in families of patients with AD by means of a survey, serum autoantibody testing and correlating these data with the established genetic risk factors. PTPN22 rs2476601, CTLA4 rs231775, and RAC12 rs3757247. 74.1% patients reported relative(s) with autoimmunity, and, inversely, 11.9% surveyed relatives, especially first-degree female family members, declared an autoimmune disease, most frequently Hashimoto’s thyroiditis, followed by Graves’ disease, vitiligo, and type 1 diabetes. Psoriasis, rheumatoid arthritis, pernicious anaemia, multiple sclerosis, and premature menopause were also quite common, while AD, alopecia, and celiac disease – less frequent. Significant correlation was noticed between the number of autoimmune conditions in AD proband and the number of affected relatives (P=0.031). Endocrine gland-specific serum autoantibodies were detectable in 39.8% first-degree relatives of patients with AD, including asymptomatic subjects. Antibodies to 21-hydroxylase were found in 6.2% relatives, thyroid peroxidase in 28.3%, thyroglobulin in 19.5%, glutamic acid decarboxylase in 8.0%, zinc transporter-8 in 7.1%, and islet antigen-2 in 2.6%. Autoantibodies were significantly more frequent in families of male patients (P=0.008; OR 3.31; 95% CI 1.334-8.234) and patients with polyglandular autoimmunity (P=0.009; OR 3.545; 95%CI 1.313-9.573). Autoimmunity-related genetic polymorphisms occurred more frequently among Addison’s families vs controls (all P<0.05), and PTPN22 rs2476601 was associated with all autoantibody prevalence, except for IA-2. In conclusion, there is convincing evidence of increased susceptibility for autoimmune endocrine conditions, especially thyroid disease, in the relatives of patients with AD, predominantly in females. Relatives of the male AD patients and of those with polyendocrine autoimmune AD are at particular risk and should undergo periodic screening for autoimmune endocrine disorders.

DOI: 10.1530/endoabs.81.S21.1

S21.2

Autoimmune regulator mutations and autoimmunity
Bergithe Ofstedal
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The autoimmune regulator (AIRE) gene is crucial for establishing central immunological tolerance and preventing autoimmunity. Mutations in AIRE cause a rare autosomal-recessive disease, autoimmune polyendocrine syndrome type 1 (APS-1). The clinical picture is highly variable, however, most patients present severe chronic mucocutaneous candidiasis and organ-specific autoimmunity from early childhood and have high levels of autoantibodies against interferon alpha and omega. Recently, it has become evident that AIRE variants also associate with more common organ-specific autoimmune diseases such as autoimmune adrenal insufficiency, gastritis, and type 1 diabetes. We have identified multiple patients with heterozygous variants in AIRE and investigated their dominant negative effect on AIRE’s gene regulation. We find that dominant negative AIRE variants cluster within the PHD1 and PHD2 domains and have a varying effect on AIRE’s transcriptional activity. As a group, these patients have fewer and milder manifestations masquerading as “common” organ-specific autoimmunity where enteropathy was the most frequent manifestation. Interestingly, a few of these patients have autoantibodies against interferon omega. By scrutiny of our national registry, we identified two female and two male APS-1 patients from three different families with late-onset APS-1 sharing a homozygous or compound heterozygous splice mutation in AIRE’s exon 7. In addition to the late onset, they also presented with a milder phenotype compared to classical APS-1. Both normal AIRE mRNA splicing and an altered splicing pattern including skipping of exon 7 were found in the patients and in the corresponding mouse model, indicating leaky rather than abolished mRNA splicing. Further, a moderately inhibited AIRE-regulated transcriptome was found in the mouse thymus. Our results underline the dose-effect of AIRE. Taken together, our results highlight the importance of functional validation of AIRE variants and suggest a dose-dependent function of AIRE.

DOI: 10.1530/endoabs.81.S21.3

S22.1

Male infertility

Abstract unavailable
DOI: 10.1530/endoabs.81.S22.1

S22.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S22.2

S22.3

Thyroid autoimmunity

Abstract unavailable
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Severe thyroid dysfunction may lead to menstrual disorders and subfertility via direct and indirect interactions with the hypothalamo–pituitary–ovarian axis and the reproductive organs. However, the exact prevalence of subfertility in women with thyroid disorders remains unknown. Fertility problems may persist after restoring normal thyroid function, and then surgery and/or an assisted reproductive technology (ART) may be necessary to obtain a pregnancy. The initial step in an ART treatment is the ovarian stimulation, putting strain on the thyroid gland, potentially leading to (permanent) hypothyroidism in women with thyroid autoimmunity (TAI) or when already treated with thyroid hormones (LT4). Moreover, women with ovarian and unexplained causes of subfertility have a higher prevalence of TAI. In women with TSH levels $>4.0$ mIU/l, fertilisation rates, embryo quality and live birth rates may be impaired and improved with LT4 therapy. The increased use of intracytoplasmic sperm injection (ICSI) as a type of ART on pregnancy outcomes in women with TAI deserves more attention as a therapeutic tool. In euthyroid women with TAI, LT4 should not be given systematically, but on a case-by-case basis if serum TSH is $>2.5$ mIU/l. Women already treated with LT4 should target a serum TSH level $<2.5$ mIU/l before ART. For all of the above reasons, women of subfertile couples should be screened systematically for the presence of thyroid disorders, and especially serum TSH and TPOAb. In this symposium, we will present the current state of art, discuss the gaps in the knowledge, and finally, make proposals for future investigations.

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Type 1 diabetes (T1D) is a chronic disease of childhood that also presents in adults, resulting from the destruction of insulin-producing $\beta$-cells by auto-reactive $T$ cells that have escaped central and peripheral immune tolerance. It is now well established that T1D is characterised by a wide heterogeneity especially in terms of age at onset, representing a major barrier for both pathogenesis and translational efforts aimed to develop novel therapeutic approaches. This concept represents a key factor in defining who should be treated with an intervention capable of inducing disease remission. The insulin secretory capacity assessed by the residual $\beta$-cell function (measurement of C-peptide) at the time of diagnosis and during the first few years after T1D diagnosis is a crucial factor to define when and how to intervene with the aim of modifying the natural history of the disease on the short and long term. We have to remember that in the vast majority of T1D patients at diagnosis a significant mass of functional islets has been destroyed by the autoimmune attack, thus lacking the chance to be either preserved or rescued by a therapeutic approach able to reverse the course of disease onset. However, some T1D patients show a substantial residual $\beta$-cell function at diagnosis and also in the first year after disease manifestation, thus representing an interesting population to target for an intervention able to protect endogenous insulin secretion. Furthermore, some patients may be overweight and become insulin resistant, thus implying that also this pathophysiological condition should be tackled. Patients with T1D and substantial residual $\beta$-cell function with or without signs of insulin resistance identify a specific endotypes of T1D. These novel concepts pave the way for new and diverse therapeutic options which can be applied to well characterised patients accordingly.

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Abstract unavailable

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Joint Sessions
JS1.1

Abstract unavailable
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JS2.1

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JS2.3

Abstract unavailable
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JS3.1

Is familial hypercholesterolemia an underdiagnosed and undertreated disease?
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Familial Hypercholesterolemia (FH) is a monogenic disease, associated with variants in the LDLR, APOB, and PCSK9 genes. The initial diagnosis is based on clinical criteria like the DLCN criteria. A score $\geq 8$ points qualifies the patient as "definite" for the diagnosis of FH. It is characterized by lifelong elevations in plasma low-density lipoprotein cholesterol (LDL-C) levels and premature coronary heart disease (CHD). FH is an underdiagnosed and undertreated genetic disorder, which affects 1 in 200 to 250 people worldwide of all races and ethnicities. The general lack of awareness about FH among the public and the medical community has resulted in only 10% of the FH population being diagnosed and adequately treated. It is recommended that children, adults, and families should be screened for FH if an individual or family member has FH, an adult plasma cholesterol level $\geq 8$ mmol/l ($\geq 310$ mg/dl) or in a child $\geq 6$ mmol/l ($\geq 230$ mg/dl), premature CHD, tendon xanthomas, or sudden premature cardiac death. In FH, low-density lipoprotein cholesterol goals are $< 3.5$ mmol/l ($< 135$ mg/dl) for children, $< 2.5$ mmol/l ($< 100$ mg/dl) for adults, and $< 1.8$ mmol/l ($< 70$ mg/dl) for adults with known CHD or diabetes. In addition to lifestyle and dietary advice, priority treatments are (i) in children, statins, ezetimibe, and bile acid-binding resins, and (ii) in adults, maximal potent statin dose, ezetimibe, bile acid-binding resins, and monoclonal antibodies directed against PCSK9. Lipoprotein apheresis can be offered in homozygotes with CHD refractory to treatment. FH is usually diagnosed late. Guidelines-recommended LDL cholesterol concentrations are rarely achieved with single-agent therapy. Cardiovascular risk factors and the presence of CHD were lower among non-index cases, who were diagnosed earlier. Earlier detection and an increase in the use of combination therapies are required to reduce the global burden of FH.
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JS3.3

Abstract unavailable
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JS4.1

Abstract unavailable
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ESE-EASO & ESPE Joint Session: Challenges in obesity care from childhood to adulthood

JS4.2

Abstract unavailable
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JS4.3

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EYES Symposium
How artificial intelligence could change our vision on assisted reproduction. Is it time to change the view?

Abstract unavailable
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The challenges in male infertility research. Which are the future topics of research?

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Infertility affects 15%–25% of couples, and male reproductive issues related primarily to semen quality play a role in many cases. Furthermore, impaired semen quality has been linked to adverse long-term health outcomes. A key pillar in the evaluation of men from infertile couples is the traditional semen analysis, which by and large has remained unchanged for decades, including assessment of semen volume, sperm concentration, motility and morphology. Though, the process of fertilization (in vivo) is much more complex that what is covered with these parameters. At present, most treatment options bypass natural reproduction barriers by enhancing ovulation and/or increasing the chance of oocyte/sperm interaction, whereas only few treatments target the underlying cause of infertility. The causes of male infertility are multifactorial involving both genetic factors and exposures in fetal life and adulthood. However, the interplay between and relative contributions of health behavior, psychosocial, environmental, genetic, endocrine, metabolic, immunologic, and epigenetic factors as well as pathogenic processes at different stages of life are still poorly understood. Despite the availability of increasingly advanced diagnostic and therapeutic techniques, approximately 30% of infertile couples do not obtain a live birth after fertility treatment. Reaching beyond the traditional semen analysis and implementing artificial intelligence methods is essential to further improve our ability to a) study risk factors for male (and female) infertility, b) identify new biomarkers to diagnose subfertility and predict fecundity and response to treatment, and c) identify subgroups of infertility patients at risk of long-term health impairment. With the establishment of the ReproUnion Biobank and Infertility Cohort (RUBIC), including 5000 well-characterized infertile Danish and Swedish couples, we hope to create a framework for this approach in a multidisciplinary research environment. An unresolved issue is, however, how to apply the artificial intelligence methods and develop the new interdisciplinary collaborations needed.

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ECAS Symposium
Europe needs more endocrinology

ECAS1.1

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ECAS1.2

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ECAS1.4

Laboratory chaos diverted – the case of the in vitro diagnostics regulation
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In vitro diagnostics (IVD) in the European Union are facing a fundamental change with the introduction of a new regulation, the so-called In Vitro Diagnostics Regulation (IVDR). Originally, the IVDR was scheduled to enter into force in May 2022, however, in January 2022, the EU legislator made a differentiated partial postponement of the application of important parts of the IVDR. The major innovation and achievement of the IVDR is that most commercially manufactured IVD products must now be certified by independent (albeit commercial) notified bodies - replacing the system of self-certification by manufacturers. Notified bodies are under surveillance by member states. Because key regulatory processes have not been implemented in time, the entry into force of the IVDR for commercial IVDs has been delayed to 2025 or 2027, depending on the risk class. For the IVD industry, the product certification process requires significant additional resources for compliance. This may result in niche products being phased out of the market by some manufacturers. In addition to commercial products, some elements of the IVDR are also mandatory for in-house manufactured products, particularly Annex I (general safety and performance requirements), starting as early as May 2022, particularly for calibration and control materials and reagents manufactured in-house. The definition of in-house products in Article 2 (IVDR) does not include measurement methods, and the term LDT (laboratory developed test) is not used by the IVDR. Compliance with this regulation is not assessed at EU level, but is the responsibility of the Member States.
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ECAS1.5

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ECAS1.6

Fighting endocrine disruption - Are we getting somewhere?
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The Daily Tolerable Intake (DTI) was reduced by BPA (bisphenol A) 100,000 fold. This is an unprecedented action to protect consumers and the environment from the most commonly used plasticizer. However, one problem identified was the fact that regrettable substitutes, such as BPS and BPF, were not included in the recommendation. There will be a fight to ensure that this passes into the European legislation. In the meantime, BP-B (4′-methylpropyliden) bisphenol (a substitute for BPA) and a sunscreen agent 4-MBC were proposed to be endocrine disruptors. Resorcinol was identified as a Substance of Very High Concern (SVHC). This was primarily due to its effects on the thyroid and other endocrine systems. GenX produced by Chemours lost their suit. Chemours had taken the EU Chemicals Agency (ECHA) to court over the inclusion of GenX chemicals in the SVHC list under REACH – the main EU law used to stop chemical pollution. Already, a multitude of other PFAS, per (and poly) fluoralkyl substances are classed as SVHCs, mainly due to their mobility and persistence. Next, the question of mixtures. As we showed in our paper ‘From Cohorts to Molecules’ (https://www.science.org/doi/epdf/10.1126/science.abe8244) the thyroid gland was among those endocrine systems affected. We showed the mixture of 8 chemicals affected language delay in children at 30 months and at 7 years of age. Given that in the US current figures for autism spectrum disorder have reached 1 in 44 children and the thyroid axis is needed for brain development the two could be linked.
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ECAS1.7

Hormones and public awareness – the need for better estimates of hormonal exposure
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Hormones are key regulators of numerous physiological processes. While most hormones are produced in select organs, their effects are felt throughout the body. Hormonal exposure is not only mediated by hormone production, but also by circulating binding proteins, and by local metabolism. Although we still heavily rely on total serum levels for the diagnosis of endocrine disorders and abnormalities, it is increasingly clear that total serum hormone levels do not always accurately reflect true exposure. Patients with binding protein defects presenting with low total hormone levels - but no profound clinical features - are a key example of this. Free serum hormone levels, the minor fractions of circulating non-protein bound (steroid) hormones, are recognized as superior markers of hormonal exposure and are increasingly used in the clinic. For example, using free testosterone is now recommended in the diagnosis of male hypogonadism and female hyperandrogenism. However, free serum hormone levels are mostly estimated using calculators, as access to direct measurements is limited because it is technically demanding and laborious. Also, alternative measurements in different matrices such as saliva and hair are being explored. Advantages of these measurements include more accurate reflections of hormonal exposure, over longer periods of time, minimizing patient discomfort, and the ability to collect samples ambulatory. Despite recent advances, further insight is necessary for a broader adaption of these new markers. In the BEED-ED project, we want to improve the clinical applicability of free steroid hormone concentrations in patients with specific conditions. As the number of available tests increases, so too does the need to educate both healthcare providers and patients. Increasing public awareness about the importance, implication and interpretation of these novel measures of hormonal exposure is key to advancing both the immediate care for patients and the utility of these novel estimates of hormonal exposure.
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New Scientific Approaches
Human gonadal development at single-cell resolution
NSA1

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Scaling down the study of pituitary tumours for better understanding their behaviour and intra-tumoral heterogeneity
NSA2

Scaling down the study of pituitary tumours for better understanding their behaviour and intra-tumoral heterogeneity
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Gonadotroph tumours (GoTs) are frequent intracranial neoplasms that represent 30% of all pituitary tumours (PiTs). While GoTs are responsible of an important morbidity, their tumorigenesis is not yet understood, and their treatment is limited to surgical resection and radiotherapy. The absence of identified driver-genes combined with their heterogeneity and silent behaviour (i.e. lack of hormone hypersecretion) limit the development of medical treatment. The current lack of relevant preclinical animal-models and patient-derived cell-lines has further slowed the study of the biological and molecular mechanism underlying gonadotroph tumorigenesis. Here we questioned whether we could scale down the culture and the functional analysis of tumour-cells derived from resected gonadotroph tumour to improve our knowledge of GoTs behaviour and intra-tumoral heterogeneity. We developed a series of approaches combining custom-made agarose-based micro-culture inserts and computerized-analyses of 3D-images to: i) characterize GoT intra-tumoral heterogeneity and ii) screen molecules to develop new therapeutics. The feasibility of these approaches was first addressed through the analysis of pituispheres obtained from rodent-pituitary cell-lines. Subsequently pituispheres obtained from GoT-patients were analyzed. Parameters such a size and percentage of tumor cells (CHGA+) vs non tumor-cells (i.e. Microenvironment, TME) and response to candidate therapeutic molecule were addresses in a 3D semi-high throughput manner (30-50 spheroids acquired through confocal scanning). Magnetic sort based on surface expressing-markers was also performed on surgically-resected gonadotroph tumours to compare the growing capabilities of different tumour-cell-populations isolated from single patients. In conclusion, we have built and validated custom-made micro-culture inserts for growing, imaging and analyzing pituitary rodent cell-lines and patient-derived cells. This work confirms that scaling down the analysis of patient-derived pituispheres could overcome the lack of patient-derived cell lines and could serve the screening of novel therapeutics for personalized medicine.
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How liquid biopsies can change clinical practice in oncology
NSA3

Abstract unavailable
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Debate Sessions
PRRT or targeted molecular therapies as preferred line of treatment

D1.1

For: PRRT or targeted molecular therapies as preferred line of treatment

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Purpose

Bronchopulmonary (BP) and gastroenteropancreatic (GEP) neuroendocrine neoplasms (NEN) are slow-growing tumors, which frequently express somatostatin receptors on their cell membranes. These receptors are targets for therapy with 177Lutetium-labeled somatostatin analogues.

Experimental Design

Patients receive four treatments of 177Lu-DOTATATE at a dose of 7.4 GBq every 8 weeks

An objective response rate of 39% was found for all BP & GEP NEN. Stable disease was reached in 43% of patients. Progression-free survival (PFS) and overall survival (OS) for all NET patients were 29 months (95% confidence interval (CI), 26–33) and 63 months (95% CI, 55–72). Long-term toxicity included acute leukemia (0.7%) and myelodysplastic syndrome (1.5%). No therapy-related long-term renal or hepatic failure occurred. The NETTER-1 study was the first randomized phase III study of 177Lu-DOTATATE and evaluated patients with midgut NENs who had progressed on standard doses of octreotide LAR. Patients were randomized to receive 177Lu-DOTATATE in combination with standard-dose octreotide or high-dose octreotide (60 mg/4 weeks) alone. Median OS was 48 months (95% CI, 37–55) in the 177Lu-DOTATATE group and 36 months (95% CI, 26–52) in the control group.

Conclusions

PRRT with 177Lu-DOTATATE is a favorable therapeutic option in patients with metastatic bronchial and gastroenteropancreatic NETs that express somatostatin receptors. PRRT with 177Lu-DOTATATE is safe with few side-effects and shows good response rates.

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Adjuvant Radioactive Iodine Therapy for low to intermediate risk differentiated thyroid cancer patients

D3.1

For: Adjuvant radioactive iodine therapy for low to intermediate risk differentiated thyroid cancer patients

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Current indications for adjuvant Radioactive Iodine (RAI) in low- and intermediate-risk differentiated thyroid cancer (DTC) are controversial. At the same time, there is universal consensus for personalized DTC management according to individual patient needs, as there does not appear to be a “right” way to treat patients with DTC. According to the Martinique Principles1, adjuvant RAI treatment has many goals, including: initial staging of the disease, facilitate follow-up, improve disease-specific survival, decrease recurrence, improve progression-free survival and, in some cases, curative intent. The same principles state that the key elements in adjuvant treatment decision-making are post-op risk assessment, impact on outcomes of interest, side effect profile, patient values and preferences, improved initial staging, and facilitate sensitive follow-up. In addition, other factors must be considered such as the availability and quality of pre- and post-op ultrasound, the quality of RAI imaging, thyroglobulin assay accuracy, the access to an experienced thyroid surgeon, the presence of anti-thyroglobulin antibodies and preferences of local disease management multidisciplinary team. All these factors (or a combination of them) could tip the balance for or against adjuvant RAI administration in DTC. There are fresh retrospective data showing that a decrease in the administration of adjuvant RAI in low- to intermediate-risk DTC individuals generates a substantial number of patients stranded in a misleading status labeled as “gray zone”. These patients are those appropriately identified as indeterminate or biochemical incomplete response to treatment when ablative RAI is administered. A large number of patients in a broad “gray zone” could likely complicate their follow-up, with more diagnostic tests that will lead to increasing costs and raise the anxiety level of both patient and attending physician. A very recent European Thyroid Association Consensus Statement2, recommends adjuvant RAI in intermediate-risk DTC patients who meet any of the following frequent conditions: advanced age (>45), aggressive histology, increase volume of nodal disease, extranodal extension, multiple lymph node or lymph node outside the central neck. In this conundrum we should bear in mind that changes that downgrade the intensity in the treatment of oncologic patients are normally based on the results emerging from large tertiary academic hospitals (those which are most often published). However, these results may not accurately reflect real-life outcomes. In other words, broad recommendations are not always applicable to individual cases. Finally, any proposal for change in the practice of medicine must be considered in light of both its ethical aspects and the precautionary principle, the latter emphasizes caution, pausing and review before embracing innovations that may in time prove disastrous.

References


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Meet The Expert Basic Scientist Sessions
Extracellular vesicles as theranostic tools in metabolic and cardiovascular diseases

MTEBS1

Extracellular vesicles in cardiometabolic disorders: from waste product to reliable disease biomarkers
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Circulating extracellular vesicles (EVs) are nano-sized bilayer membrane particles mainly released by platelets, inflammatory, endothelial cells and cancer cells, which play a pivotal role in inter-cellular communication. EV cargo, which consists of RNAs, proteins, DNA, and lipids, reflects the cell of origin and its activation state and the microenvironment; for this reason, it can be used as source of potential biomarkers in several conditions related to tumour development/progression, inflammation, atherosclerosis, thrombosis, and endothelial dysfunction. Therefore, cardiometabolic diseases can advantage of EVs for diagnostic/prognostic (theranostic) purposes. Recent advances in -omics technologies combined with artificial intelligence approaches allow high-throughput analysis, with the possibility to generate a biomolecular signature featuring a specific pathophysiological condition. An increase of specific EV sub-populations may even anticipate the rise of conventional biomarkers which usually require cell death or tissue necrosis (i.e., the rise of hs-troponin after cardiomyocyte death in cardiac ischemic disease). A change in EV secretome is expected in suffering, but still alive cells, thus providing great advantage for early diagnosis. Data on the impact of EV for diagnostic and therapeutic purposes in cardiometabolic settings will be discussed.
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How to assess hazard of EDC mixtures?

MTEBS2

Abstract unavailable
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The role of macrophages in the endocrine system

MTEBS3

Purinergic targeting of macrophages in obesity and diabetes
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The purinergic signaling complex comprising extracellular nucleotides and nucleosides, and their receptors, the P2 and P1 purinergic receptors, respectively, as well as catabolic enzymes and nucleoside transporters is a major regulatory system in the body. Macrophages are cells of the innate immune system that play myriad roles in the body. Macrophages are subject to regulation by the purinergic signaling complex. Macrophages are known to reside in endocrine glands and a body of evidence now suggests that these cells interact closely with endocrine cells and play important roles in both physiological and pathophysiological states. In the realm of inflammatory and auto-immune diseases, endocrine organs are known to be a frequent target, possibly due to the expression of a high density of major histocompatibility complex (MHC)-II molecules on resident macrophages. This implicates a key role of macrophages in the pathogenesis of auto-immune endocrine diseases and making them attractive targets for pharmacotherapy. Here I summarize the diverse roles played by the purinergic signaling complex in regulating macrophages in the endocrine system and identify potential targets for pharmacotherapy in endocrine diseases.
DOI: 10.1530/endoabs.81.MTEBS3
Meet The Expert Sessions
Personalized therapy in acromegaly
MTE1

Personalized therapy in acromegaly
Maria Chiara Zatelli
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Personalized medicine aims at providing indications concerning the management of each patient according to her/his specific needs and disease characteristics. Acromegaly, although a rare disease, has a profound impact on patients’ quality and expectancy of life, due to increased morbidity and mortality as compared to the general population in correlation mainly due to cardiovascular disease and cancer. Several clinical variables have been investigated as predictors of response to treatment (either surgical or medical) and as prognostic factors. Tumor diameter, invasiveness, genetic predisposition are recognized as the main predictors for surgical success. Adenoma granulation at electron microscopy, somatostatin receptor status, T2-intensity at MRI, age, and AIP mutation status have been indicated as predictive of response to treatment with somatostatin receptor ligands (SRLs). If resistance to SRL is foreseen, treatment with the growth hormone receptor antagonist pegvisomant or second-generation SRL pasireotide can be proposed, with the possibility of a combination therapy. In addition to tumor characteristics, a very important issue is represented by assessment of symptoms and of quality of life (Qol.). Several questionnaires have been developed to specifically evaluate Qol. in patients with acromegaly. The patient-assessed acromegaly symptom questionnaire consists of 5 acromegaly-related symptoms (soft-tissue swelling, arthralgia, headache, excessive perspiration, and fatigue) has not yet been clinically validated. The acromegaly quality of life questionnaire is used to assess the disease-specific physical and psychologic aspects. The acromegaly treatment satisfaction questionnaire is clinically validated to assess patient satisfaction with monthly injectable SRLs. Therefore, several items are available to clinicians to aid the best therapeutic managements of acromegaly and its complications on the basis of patient characteristics, but also (and mainly) on the basis of patient’s choice and specific health issues.

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Ultrasound-based approach in the management of thyroid nodules/ Does AI improve the accuracy of the current risk stratification systems
MTE2

Abstract unavailable
DOI: 10.1530/endoabs.81.MTE2

24h steroid measurements as new tools for the diagnosis of adrenal disease
MTE3

Abstract unavailable
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MicroRNA in Bone OR MicroRNA in bone diagnostics and treatment looking into the future
MTE4

MicroRNA in bone diagnostics and treatment looking into the future
Matthias Hackl
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MicroRNAs (miRNAs) are non-coding RNAs that control the expression of 70% of the protein-coding genes. Since their discovery in the late 1990s, the function of miRNAs in the context of biological pathways that are essential to bone homeostasis has been investigated. This has expanded our understanding of the mechanisms underlying bone health and disease and led to the identification of novel drug and biomarker candidates. From a diagnostic viewpoint the seminal finding that miRNAs can be actively or passively released from cells into biofluids such as serum or urine (“circulating miRNAs”), motivated researchers to investigate circulating miRNAs in several pathologic conditions, including bone diseases. Thus, several exploratory studies in cohorts representing various types of bone diseases have been performed. In this meet-the-expert session, the important molecular basics of intracellular miRNA function and extracellular release will be discussed, including recommendations for best (pre-)analytical practices and documentation standards for circulating miRNA research. In the second part evidence from pre-clinical and clinical studies that have investigated the utility of microRNAs as biomarkers and drug targets in musculoskeletal disorders will be presented, with a specific focus on type-2 diabetic osteopathy.

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Artificial pancreas to treat type 1 diabetes
MTE5

Abstract unavailable
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State of the art of clinical studies in the OMICS age
MTE6

Abstract unavailable
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What an endocrinologist should know about in vitro fertilization treatment and egg storage
MTE7

What an endocrinologist should know about in vitro fertilization treatment and egg storage
Sophie Catteaux-Jonard
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Achieving pregnancy through in vitro fertilization requires a minimum number of oocytes recovered during egg retrieval. These oocytes come from ovarian hyperstimulation that allows the entire oocyte cohort to mature. In physiology in a natural cycle, a dozen follicles are recruited at the beginning of the menstrual cycle under the action of the elevation of the FSH (the « FSH window »). Then, follicles secrete estradiol through aromatase under the action of FSH. By negative feedback, FSH levels decrease (the FSH window closes) and only the follicle most independent of FSH will continue to grow until ovulation: the dominant follicle. The other follicles of the cohort attenuate allowing mono-ovulation. On the contrary, it is very important in the process of in vitro fertilization to have a multifollicular development, in order to increase the chances of pregnancy. Indeed, there are still many stages before pregnancy: puncture and selection of oocytes, obtaining fertilization and then a quality embryo to be transferred. The goal of the treatment is therefore to continue the administration of FSH to avoid the closing of the window and thus allow the maturation of all the follicles of the cohort. The other very important aspect of stimulation treatment during IVF is to control the exact time of ovulation. GnRH agonists or antagonists are used but the use of simple progestins is also possible! Finally, the triggering of ovulation is achieved through the administration of either hCG (with an LH like action) or a GnRH agonist in cycles slowed down by GnRH antagonists. Completely artificial cycles are also possible to transfer devitriified embryos.

DOI: 10.1530/endoabs.81.MTE7
Management of panpNENs in MEN1 and vHHL
MTE8
Management of pancreatic neuroendocrine tumors in Multiple Endocrine Neoplasia Type 1 and the von Hippel Lindau syndrome
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Multiple Endocrine Neoplasia Type 1 (MEN1) and the von Hippel Lindau syndrome (VHL) are hereditary disease with an autosomal dominant inheritance. Among a wide variety of manifestations, both syndromes predispose patients to pancreatic neuro-endocrine neoplasms (PanNENs). Screening for presumptomatic diagnosis of PanNENs enables timely intervention with the intention to prevent metastasized disease and premature death. MEN1 and VHL lead to different manifestations and there are also distinct differences in occurrence and clinical course of PanNEN. Therefore the management of PanNEN occurring in both syndromes is different with consequences for the required multidisciplinary team. For both tumor syndromes screening for PanNEN should be based on general planning of screening and surveillance, utility of biochemical markers, the optimal choice for imaging modality, and risk stratification for individual patients. Recent research gives more insight into the main aspects of MEN1 and VHL-related pancreatic manifestations and their management. For care tailored to the needs of the individual patient and improving outcomes on an individual basis, studies are now needed to define predictors of tumor behavior and effects of more individualized interventions. Patients with MEN1 and VHL are therefore preferably treated in centers with specific expertise and dedication to collaborative research.

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Endocrine treatment in transgenders - when, who and how?
MTE11
Endocrine treatment in transgenders - when, who and how?
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Treatment of transgender patients has gained increasing importance in outpatient endocrinological care due to a steadily rising influx of patients in recent years. Many gaps in knowledge regarding hormonal therapy have been filled in recent years thanks to a growing body of literature based on larger cohort studies. Nowadays therapy can be regarded as safe and effective. While puberty arrest and peripubertal hormone treatment in transgender youth has gained growing acceptance in recent years, some questions still remain unresolved but will hopefully be answered in years to come, following the steadily growing knowledge and experience in this area. This talk summarizes the current knowledge on risks and benefits of endocrine treatment in transgender individuals and should open discussion based on patient cases on questions such as optimal treatment monitoring, the use of progestins/progesterone, fertility preservation, relevant comorbidities and ideal hormone treatment across the lifespan.

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Changing spectrum of hypophysitis
MTE9

Abstract unavailable
DOI: 10.1530/endoabs.81.MTE9

How do we have to treat patients with CAH to avoid complications for under-and over-treatment?
MTE10
How do we have to treat patients with CAH to avoid complications for under- and over-treatment?
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The management of adults with congenital adrenal hyperplasia due to classic 21-hydroxylase deficiency (21OHD) is a challenging balance of hormone replacement, disease control, and avoidance of adverse effects. The approach should emphasize the clinical evaluation and patient goals, and laboratory tests are used secondarily as ancillary data. Upon transition from pediatric to adult care, the concerns shift from growth and pubertal development to fertility, neoplasia formation, and long-term complications. Each visit requires a thorough physical exam to assess for cushingoid features such as skin thinning, bruising, muscle weakness, fat redistribution, and purple striae – much of this exam can be done via telemedicine. The most useful biomarkers to aid in glucocorticoid titration are androstenedione, the androstenedione/testosterone ratio in men, and follicular-phase progesterone in women attempting pregnancy. The major androgens in most 21OHD patients are the 11-oxygenated androgens, and these steroids appear to be useful analytes of disease control as well. Hydrocortisone remains the most effective glucocorticoid for cortisol replacement therapy. More potent synthetic glucocorticoids have narrower therapeutic indices and greater the risk of adverse effects than hydrocortisone. Attention to mineralocorticoid replacement is also important, and under-replacement is a common cause of chronic fatigue. Standing blood pressure, serum potassium, and plasma renin are used to titrate the fluorocortisone acetate dose in that order. Conceptually, the endocrinologist should distinguish doses used to replace the cortisol deficiency (first priority) and then additional doses to achieve adequate disease control. New treatments are under study to improve disease control while avoiding excessive glucocorticoid exposure.

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Diagnostic approach and clinical management of hypophosphatemia: Is it really an endocrine disorder?
MTE12
Diagnostic approach and clinical management of hypophosphatemia: Is it really an endocrine disorder?
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Phosphorus is involved in energy storage, metabolism, nucleic acids, cell membrane function, cell signaling; it is a fundamental constituent of skeleton and teeth. Homeostasis is regulated mainly by three hormones, namely parathyroid hormone (PTH), vitamin D and Fibroblast Growth Factor 23 (FGF23). Additionally, sex hormones are known to decrease circulating Pi levels, by reducing renal tubular reabsorption through direct and indirect effects on renal phosphate channels and likely stimulating FGF23 release. Though some patients may complain of muscle weakness, mild hypophosphatemia (HP) is usually asymptomatic, and, consequently, often overlooked, so that its prevalence in the general population is not known. Indeed, HP is not a rare feature in patients with osteoporosis. On the other hand, severe and chronic HP causes muscle weakness, bone pain and deformity, fragility fractures (osteomalacia), rhabdomyolysis, impaired mental status, heart failure. Several mechanisms can be involved, and reduced Pi intestinal absorption, internal redistribution or urinary loss must be differentiated. Once urinary loss has been established, differential diagnosis includes FGF23-dependent conditions [renal transplantation, tumor induced osteomalacia (TIO), hereditary hypophosphatemic rickets] and FGF23-independent ones (primary and secondary hyperparathyroidism, renal tubular defects, diuretics, glucocorticoid therapy, hereditary hypophosphatemic rickets with hypercalcemia). Diagnostic workup is complex and often unrewarding, and the cause of chronic HP can remain unexplained in a number of patients. Finally, in patients affected with osteoporosis, HP may occur as an adverse effect of the anti-osteoporotic drugs (bisphosphonates, denosumab, teriparatide), though most studies show that HP is rare and generally self-limiting in this context. Indeed, a subset of osteoporotic patients developing chronic HP on anti-osteoporotic treatment can be observed in clinical practice, but frequency and implications of this condition are not known. Lastly, it should be considered that recently a specific anti-FGF23 treatment is available implying the need to correctly diagnose FGF23-related HP.

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Oral Communications
Diabetes, Obesity, Metabolism and Nutrition 1

OC1.1
Clinical characteristics and outcomes in hospitalized COVID-19 patients with and without diabetes at Vilnius University Hospital Santaros Klinikos (VUHK)

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Background
Studies suggest that diabetes mellitus (DM) is associated with greater risk of developing severe forms of COVID-19 and mortality.

Aims
To compare clinical characteristics and outcomes in hospitalized COVID-19 patients with and without DM.

Methods
A single-center, retrospective, observational study included adult patients with laboratory-confirmed COVID-19 treated at VUHK between 2020-01-01 and 2021-03-31. Patients were allocated to DM and non-DM group. The demographic, laboratory and outcomes data were compared. Disease severity was described as requirement of either high flow oxygen, intubation or inotropic support.

Results
A total of 2559 patients (median age 60 years, 1424 (55.6%) men) were included. Compared with the non-DM group (n = 2058, 80.4%), patients with DM (n = 501, 19.6%) were older, had more co-morbidities: hypertension, coronary artery disease, heart failure, dyslipidemia, obesity, chronic kidney disease (P < 0.05). Serum glucose, CRP, procalcitonin, D-dimer, creatinine and lactate were significantly higher (P < 0.05), eGFR and LYM count - significantly lower (P < 0.05) in the DM group compared to non-DM. Patients with DM were more likely to develop acute respiratory failure (31.3 vs 20.9%; OR 1.57, 95% CI 1.391-2.146), sepsis or septic shock (9.2 vs 6.3%, OR 1.512, CI 1.063-2.149) acute kidney failure (18.4 vs 11.6%, OR 1.712, CI 1.316-2.228), to require high flow oxygen (18.4 vs 11.6%, OR 1.712, CI 1.316-2.228), to require high flow oxygen, intubation or inotropic support (12.2 vs 8.1%, P = 0.004), stayed longer at the hospital (median 11 vs 13 days, P = 0.000), had higher prevalence of severe disease (23.0 vs 14.7%, OR 1.732, CI 1.361-2.205) and mortality rate compared to non-DM patients (19.6 vs 12.7%, OR 1.674, CI 1.296-2.163). After matching for age and gender, DM remained significant risk factor for developing respiratory failure (OR 1.533, CI 1.157-2.031) and severe disease (OR 1.569, CI 1.142-2.154), but not death (19.4 vs 15.4%, OR 1.322, CI 0.952-1.837; P = 0.095).

Conclusions
Diabetes was prevalent in one fifth of patients hospitalized with COVID-19. It was associated with longer hospitalization, greater risk of severe COVID-19 disease and death. Further investigation of the relationship between COVID-19 severity and diabetes is warranted.

Keywords: coronavirus disease 2019 (COVID-19); diabetes; mortality; outcome.

DOI: 10.1530/endoabs.81.OC1.1

OC1.2
Glucose control and mortality in critically ill patients, based on real world evidence

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Objective
Published results of reduced morbidity and mortality with tight Glycemic Control of critical patients could not be reproduced in large prospective trials. Glycemic goals according to current respective guidelines include a target blood glucose range 140-180 mg/dl, while lower blood glucose targets may be appropriate for some patients. This study aims to provide real world evidence to this field.

Methods
We performed a retrospective study using the Medical Information Mart for Intensive Care Units (ICU) IV open access, anonymized database (MIMIC-IV) based on 15619 ICU admissions between 2008 and 2019 at Beth Israel Deaconess Medical Center, USA. Logistic regression was performed, using age, sex, SOFA, OASIS and proportion of time in glucose bands per ICU stay as predictors, and death in ICU as the target. Glucose bands and time proportions were defined as in

Table 1 Relationship between ICU mortality and proportion of time spent in each glucose band, controlling for age (< 0.001), gender, SOFA score (< 0.001), and OASIS score (< 0.001). Odds Ratios correspond to 1 unit increase

<table>
<thead>
<tr>
<th>Glucose Band</th>
<th>ICU Mortality</th>
<th>CI (95%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemic</td>
<td>4.583</td>
<td>(1.12, 18.69)</td>
<td>0.034</td>
</tr>
<tr>
<td>Stringent</td>
<td>0.111</td>
<td>(0.06, 0.19)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Normal</td>
<td>0.096</td>
<td>(0.06, 0.16)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Intermediate</td>
<td>5.050</td>
<td>(2.69, 9.48)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Liberal</td>
<td>254.094</td>
<td>(73.46, 876.95)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hyperglycemic</td>
<td>28.657</td>
<td>(17.18, 47.8)</td>
<td>&lt; 0.001</td>
</tr>
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</table>

Conclusion
Overall, increased time in the hypoglycemic, intermediate, liberal and hyperglycemic bands is related to increased ICU mortality, while increased time in the stringent and normal bands is related to decreased mortality. However, in medical ICUs, these results are not statistically significant with the available data, e.g. the OR for the "normal" band being around 1.

References

DOI: 10.1530/endoabs.81.OC1.2

OC1.3
Canakinumab patients with COVID-19 and type 2 diabetes (CanCoVdia) – a multicentric, randomised, double-blind, placebo-controlled phase 3 trial

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Finney et al.1 (hypoglycemic: blood glucose level <80 mg/dl, stringent: 80-110 mg/dl, normal: 111-144 mg/dl, intermediate: 145-180 mg/dl, liberal: 181-200 mg/dl, hyperglycemic: ≥ 201 mg/dl), where proportions were time-weighted to cope with variable measurement frequency. The study protocol was approved by the respective Institutional Review Boards.

Table 1 Results of reduced morbidity and mortality with tight Glycemic Control of critical patients could not be reproduced in large prospective trials. Glycemic goals according to current respective guidelines include a target blood glucose range 140-180 mg/dl, while lower blood glucose targets may be appropriate for some patients. This study aims to provide real world evidence to this field.

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Conclusion
Overall, increased time in the hypoglycemic, intermediate, liberal and hyperglycemic bands is related to increased ICU mortality, while increased time in the stringent and normal bands is related to decreased mortality. However, in medical ICUs, these results are not statistically significant with the available data, e.g. the OR for the “normal” band being around 1.

References

DOI: 10.1530/endoabs.81.OC1.2

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Patients with type 2 diabetes and overweight have a chronic activation of the innate immune system possibly explaining the increased risk of a hyperinflammatory response and severe COVID-19. We aimed to test whether blockade of interleukin-1β (IL-1β) using canakinumab improves clinical outcome.

**Methods**

CanCovDia was a multicenter, randomised, double-blind, placebo-controlled trial to assess the efficacy of canakinumab plus standard-of-care compared with placebo plus standard-of-care in patients with type 2 diabetes and a BMI ≥ 25 kg/m² hospitalised with SARS-CoV-2 infection. Patients were randomly assigned 1:1 to a single dose of canakinumab (body weight-adjusted dose of 450-750 mg) or placebo intravenously. Canakinumab and placebo were compared on the basis of an unmatched win-ratio approach consisting of length of survival, ventilation, ICU stay and hospitalization. This study is registered with ClinicalTrials.gov, NCT04510493.

**Findings**

Between October 23, 2020, and May 12, 2021, 116 patients were randomly assigned with 58 in each group. The win-ratio analysis between canakinumab vs placebo was 0.8 (95% CI 0.69-1.08; P = 0.72). After four weeks, in the canakinumab group 4 people died (7%), 12 were hospitalized for more than 5 weeks (23.5%), and 11 were on ICU (20%). vs 7 (12.3%), 19 (38.5%) and 11 patients (21.6%) respectively. Median ventilation time at 29 days was 10 days [IQR 6.0, 16.5] in the canakinumab group and 16 days [IQR 14.0, 23.0] in the placebo group. Placebo plus canakinumab (B B(A)Sc) in the canakinumab group vs placebo after four weeks was 7 [4-6, 8-30] vs 7.5 in the placebo group [6-18, 8-33] P = 0.955) despite a lower number of antidiabetics administered in patients treated with canakinumab vs placebo (OR 0.47 [95% CI 0.23-0.95] P = 0.03).

Median ratio to baseline of endogenous Insulin (pmol/l) at four weeks was 0.94 (0.59, 1.66) in the canakinumab group vs placebo 0.64 [0.29, 1.44] (OR 2.21 [1.09, 4.48] P = 0.029). Serious adverse events were reported in 13 (11.4%) patients in each group treated with canakinumab and placebo, respectively.

**Interpretation**

In patients with type 2 diabetes who were hospitalised with COVID-19, treatment with canakinumab in addition to standard-of-care did not result in a significant improvement of the primary composite outcome despite a numerical benefit in survival, ICU and ventilation time. Patients treated with canakinumab required significantly less antidiabetic drugs to achieve similar glycaemic control, possibly survival, ICU and ventilation time. Patients treated with canakinumab required improvement of the primary composite outcome despite a numerical benefit in patients in each group treated with canakinumab and placebo, respectively. [1.09, 4.48] (placebo was 1 assigned with 58 in each group. The win-ratio analysis between canakinumab vs placebo was 0.8 (95% CI 0.69-1.08; P = 0.72). After four weeks, in the canakinumab group 4 people died (7%), 12 were hospitalized for more than 5 weeks (23.5%), and 11 were on ICU (20%). vs 7 (12.3%), 19 (38.5%) and 11 patients (21.6%) respectively. Median ventilation time at 29 days was 10 days [IQR 6.0, 16.5] in the canakinumab group and 16 days [IQR 14.0, 23.0] in the placebo group. Placebo plus canakinumab (B B(A)Sc) in the canakinumab group vs placebo after four weeks was 7 [4-6, 8-30] vs 7.5 in the placebo group [6-18, 8-33] P = 0.955) despite a lower number of antidiabetics administered in patients treated with canakinumab vs placebo (OR 0.47 [95% CI 0.23-0.95] P = 0.03).

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**Conclusion**

These results suggest that activation of CB2 receptors by BCP alleviated diabetic cardiomyopathy by attenuating hyperglycemia/hyperlipidemia-induced cardiac fibrosis and remodeling via TGF-β/SMA signaling pathway. DOI: 10.1530/endoabs.81.OC1.4

### OC1.4

**β-Caryophyllene, a dietary CB2 receptor selective cannabinoid mitigates myocardial fibrosis in a mice model of diabetic cardiomyopathy**

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**β-Caryophyllene, a dietary CB2 receptor selective cannabinoid mitigates myocardial fibrosis in a mice model of diabetic cardiomyopathy**

**Background and aim**

Diabetic cardiomyopathy (DCM), a cardiac complication in diabetes is characterized by abnormal cardiac function accompanied with myocardial fibrosis. In recent years, the cannabinoid type 2 receptors (CB2) emerged as a crucial therapeutic target for diabetes and its complications. The downregulation of CB2 receptors has been documented in various cardiovascular diseases and diabetes, that supports the concepts that activation of CB2 receptors may protect against diabetic cardiomyopathy. The present study was designed to investigate the effect of a selective CB2 receptor agonist β-Caryophyllene (BCP), a dietary natural cannabinoid compound and chemically a bicyclic sesquiterpene on myocardial fibrosis in DCM mice.

**Methods**

Experimental DCM was developed in Male C57/Bl6 mice by feeding a high-fat diet for 4 weeks followed by a low dose of streptozotocin (100 mg/kg) injection. Both DCM and control mice were then treated with or without BCP (50 mg/kg, orally) for 12 weeks by continuous feeding of a high fat or normal diet. At the end of this period, hemodynamic parameters (systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate), and heart weight/body weight were evaluated. Fasting blood glucose, oral glucose tolerance test, insulin level, lipid parameters (triglyceride, total cholesterol, low-density lipoprotein, very-low-density lipoprotein, high-density lipoprotein), and lactate dehydrogenase in serum were detected. Hematoxylin-eosin and picrosirius red were used to determine heart morphological changes and cardiac fibrosis, respectively. Immunohistochemistry of collagen I and III and western blotting were taken to determine the expression levels of cardiac-fibrosis markers (TGF-β, SMAD, α-SMA).

**Results**

DCM mice exhibited hyperglycemia, insulin resistance, hyperlipidemia, hemodynamic abnormalities, significantly increased serum lactate dehydrogenase along with increased myocardial fibrosis, and hypertrophy. Oral administration of BCP significantly decreased the levels of blood glucose, serum lipids, while increased serum insulin level with improving the insulin resistance. Additionally, the myocardial enzyme (lactate dehydrogenase) was significantly decreased. Furthermore, BCP significantly improved hemodynamic changes and attenuated the abnormal morphologic change in DCM hearts. Moreover, BCP treatment decreased the expression of TGF-β, SMAD, α-SMA and reduced collagen deposition in the heart of DCM mice. Most importantly, pre-administration of the CB2 receptor antagonist AM630, abrogated the protective effects of BCP in DCM mice.

**Conclusion**

These results suggest that activation of CB2 receptors by BCP alleviated diabetic cardiomyopathy by attenuating hyperglycemia/hyperlipidemia-induced cardiac fibrosis and remodeling via TGF-β/SMA signaling pathway. DOI: 10.1530/endoabs.81.OC1.4
Adrenal and Cardiovascular Endocrinology 1

OC2.1

DLK1 expressing cells mark a population of progenitor cells in the adrenal cortex and contribute to the zonation of the adrenal gland

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The adrenal cortex is a dynamic organ that undergoes self-renewal. In the mouse it is divided into two concentric layers, the outer zona glomerulosa (ZG) and the inner zona fasciculata (ZF), that secrete aldosterone and corticosterone, respectively. Capsular and subcapsular stem/progenitor cells differentiate and migrate in a centripetal fashion to repopulate the gland until they reach the juxtednadillary region where they undergo senescence and apoptosis. Cell fate mapping studies have shown that the maintenance of the cortex relies on a pool of two interconnected cell populations, subcapsular undifferentiated cells secreting the morphogen Sonic Hedgehog (Shh) and capsular GLI1+ cells, which can transduce the Shh signal. Our lab has shown that Delta like non-canonical Notch ligand 1 (DLK1) is expressed in partially undifferentiated cells of the subcapsular region in rat and human adrenals, whilst it is mostly expressed in capsular cells in mice. Our recent line tracing analyses used a tamoxifen inducible DLK1CreERT2 mouse model carrying the R26tdTom reporter. Injection of pregnant dames at embryonic day (e) 12.5 and analysis of tdTomato expression at postnatal day (p) 10 and p38 showed that 35% (p10) and 24% (p38) of Steroidogenic Factor 1(SF1)+ cortical cells were tdTomato+. On the other hand, postnatal tamoxifen injections showed tdTomato+/Sf1+ cells only in 1-2% in cortical cells. This data indicates that capsular DLK1 marks a population of adrenocortical progenitor cells, that are mostly active during embryonic development and near-dormant postnatally. However, postnatal DLK1+ cells could be reactivated and contribute to the regeneration of the ZF after dexamethasone-induced atrophy. Mice were administered tamoxifen followed by 7 days of dexamethasone which resulted in ZF atrophy. Two weeks after removal of dexamethasone, regrowth of the ZF occurred and tdTomato+ cells were visible in the cortex suggesting that near-dormant capsular DLK1+ cells are re-activated during ZF regeneration to become steroidsogenic cells. Taken together, our results provide evidence for a role of DLK1+ cells as contributors to the development and zonation of the adrenal cortex.

DO: 10.1530/endoabs.81.OC2.1

OC2.2

Loss of SUMO-specific protease 2 leads to adrenal insufficiency limited to gluocorticoids

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The adrenal gland produces corticosteroids essential for hydromineral and metabolic homeostasis. It is organized, in mice, in two concentric layers. The zona glomerulosa (ZG) and fasciculata (ZF), renewed from progenitors located in the capsular periphery. Centripetal renewal and maintenance of cortical zonation are dependent of a balance between WNT/I beta-catenin and ACTH/PKA signalling pathways. They provide recruitment and consecutive differentiation of progenitors into ZG and ZF. SUMOylation is a reversible post-translational modification that helps embryonic development. It consists of the serial reactions of activation, conjugation and ligation that will enables SUMOylation of a specific target protein. The presence of deSUMOylases mainly represented by SENPs makes SUMOylation particularly dynamic. In the adrenal cortex, it follows a centripetal decreasing gradient whose function is unknown. Moreover, chronic and acute PAKa signalling stimulation leads to a decrease in SUMOylation in the adrenal cortex. In order to study the impact of hyperSUMOylation in the adrenal differentiation, we have chosen to delete the deSUMOylase SENP2 since it is positively regulated by ACTH/PKA signalling. Hence, we developed a model of Senp2 deficiency targeting specifically the adrenal cortex thanks to cre/loxP technology. Senp2 loss induces, as soon as 4 weeks of age, a glucocorticoids deficiency caused by ZF hypoplasia without any defect in ZG physiology. Even though, mice manage to normalise glucocorticoid levels throughout time, they still fail to respond properly to ACTH stimulation. We demonstrate, by biochemical and genetic experiments, that this lack of response was neither due to signalling upstream of PAKa nor downstream, pointing toward a direct change in intracrine PAKa catalytic activity. The hypoplasia is associated with a stimulation of apoptosis at the ZG/ZF boundary. We show that this apoptosis was linked to a lack of PKA dependant phosphorylation of DRP1, whose phosphorylation state can induce either apoptosis or steroidogenesis. Finally, beta-catenin, which is supposed to be limited to ZG cell membrane, is found in the ZF nuclei in Senp2 mutant adrenals. Moreover, this is associated with an increase in SUMOylation of beta-catenin and mild activation of the WNT signalling pathway. In conclusion, we show that HyperSUMOylation affects ZF homeostatic renewal by altering the balance between ACTH/PKA and WNT/beta-catenin signalling pathways and by stimulating early apoptosis of the ZF cells. SUMOylation is a central mechanism of adaptive cellular responses to stress. Our results suggest that it is a fundamental pathway in the processes of functional maintenance of the adrenal cortex.

DO: 10.1530/endoabs.81.OC2.2

Loss of lysine demethylase KDM1A in GIP-dependent bilateral macronodular adrenal hyperplasia with Cushing’s syndrome

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**Context**
Primary bilateral macronodular adrenal hyperplasia (PBMAH) with glucose-dependent insulinotopic polypeptide (GIP)-dependent Cushing’s syndrome is caused by ectopic expression of GIP receptor in the adrenal tissue. The bilateral nature of this adrenal disease suggests germline genetic predisposition. We aimed to identify the molecular driver event responsible for ectopic GIP receptor expression in PBMAH.

**Methods**
We conducted an international, multicenter, retrospective, cohort study to collect blood and adrenal samples from patients who had undergone unilateral or bilateral adrenalectomy for familial or sporadic GIP-dependent PBMAH with Cushing’s syndrome. We performed sequencing and copy-number analyses of blood and adrenal DNA. Adrenal samples from patients with PBMAH and Cushing’s syndrome without food-dependent cortisol production were used as controls. RNA-sequencing on adrenal samples was performed to study gene expression in GIP-dependent Cushing’s syndrome and in control samples. Functional in vitro studies were performed to study the impact of the genetic event identified in human adrenocortical H295R cells.

**Results**
17 patients with familial or sporadic GIP-dependent PBMAH with Cushing’s syndrome were studied. We identified germline heterozygous pathogenic or likely pathogenic variants in the lysine demethylase 1A (KDM1A, or LSD1) gene in all 17 patients. We further identified a recurrent deletion of the short arm of chromosome 1 harboring the KDM1A locus in the adrenal lesions of affected patients. None of the 25 patients in the control group had KDM1A germline or somatic alterations. Concomitant genetic inactivation of both KDM1A alleles resulted in loss of KDM1A expression in the adrenal lesions. Transcriptome analysis of adrenals from affected patients revealed the global effect of KDM1A loss in adrenal tissue on gene transcription and identified differentially regulated genes, including those encoding for GIP receptor and some other G protein-coupled receptors involved in adrenal tumorigenesis and regulation of steroidogenesis. 

**Discussion**
We found that familial and sporadic GIP-dependent PBMAH is a genetic disease caused in 100% of cases studied by germline inactivating pathogenic variants of the KDM1A gene with a loss of heterozygosity of the second KDM1A locus in the adrenal lesions. This stepwise inactivation of KDM1A is suggestive of a tumour suppressor gene model of tumorigenesis. Uncovering of a common genetic mechanism of GIP-dependent PBMAH will enable genetic testing and counselling of affected patients and earlier detection of the disease in their relatives.

**Conclusions**
Familial and sporadic GIP-dependent PBMAH is a genetic disease caused in 100% of cases studied by germline inactivating pathogenic variants of the KDM1A gene with a loss of heterozygosity of the second KDM1A locus in the adrenal lesions. This stepwise inactivation of KDM1A is suggestive of a tumour suppressor gene model of tumorigenesis. Uncovering of a common genetic mechanism of GIP-dependent PBMAH will enable genetic testing and counselling of affected patients and earlier detection of the disease in their relatives.

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**OC2.4**
**Autonomous cortisol secretion in adrenal incidentalomas and risk of fragility fractures: a large cross-sectional study**
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**Context**
Autonomous cortisol secretion (ACS) has been associated with a higher prevalence of osteoporosis and fragility fractures in several studies. However, the data rely on heterogeneous studies and criteria for osteoporosis screening in this population are still debated.

**Objective**
To assess the prevalence of fragility fractures and contributing factors in a large cohort of patients with adrenal incidentalomas.

**Methods**
We reviewed medical records of 1023 patients with adrenal incidentalomas from 1990 to 2019. Of these, 756 patients were selected after exclusion of confounders such as concomitant diseases or treatments, or missing data. Clinically-obtained electronic radiological images closest to the date of clinical evaluation, such as lateral views of spine X-rays or CT thoraco-abdominal scans, were reviewed by two experts blinded to clinical data to screen for asymptomatic or lytic vertebral fractures. Clinical fragility fractures were also recorded. 491 patients had non-secreting (NS) adrenal incidentalomas, 240 had ACS and 25 Cushing Syndrome (CS). Diagnosis of NS and ACS was based on cortisol after 1-mg dexamethasone suppression test (1 mgDST) (<50 and > 50 nmol/l, respectively). Biochemical parameters of bone metabolism and hormonal data were recorded.

**Results**
ACS were older than NS patients (65.5 vs 60.5 years, P < 0.001). Prevalence of fragility fractures was different (P = 0.021) between groups, respectively 18.9% (NS), 27.1% (ACS) and 32% (CS), with significant difference between NS and ACS (P = 0.012). When analyzed separately by sex and menopausal status, this difference remained significant in post-menopausal women (P = 0.003), with a prevalence of 16.7% (NS), 28.2% (ACS) and 50% (CS). By contrast, prevalence of fractures was similar in males, even when analysis was adjusted for low testosterone levels (<3 nmol/l). Women with ACS aged ≥65 years reported a 40% prevalence of fragility fractures, as compared with 23.6% in NS (P = 0.016).

In younger women and in males with cut-off age set at 65 years, prevalence of fractures was similar between groups. Following logistic regression analysis including biochemistries and clinical data of the overall population, fragility fractures were predicted independently by age (OR = 1.04, P < 0.001) and post-1 mgDST cortisol (OR = 2.07, P = 0.001). After sex and menopausal status sub-analysis, an independent contributor effect from age (OR = 1.07, P < 0.001) and 1 mgDST (OR = 4.49, P = 0.001) remained significant only in post-menopausal women.

**Conclusions**
Post-menopausal women aged 65 or older with adrenal incidentalomas and ACS showed higher risk of fragility fractures than NS, with ACS likely playing an independent major pathogenic role.

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**OC2.5 Elevated serum free cortisol is a strong predictor of mortality in hospitalized patients with Covid-19 irrespective of dexamethasone treatment**
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Serum total cortisol has been linked to increased mortality in patients with Covid-19, but its reliability in critically ill patients is limited. We examined the association between serum free cortisol (SFC) levels and clinical outcomes in patients hospitalized with Covid-19 between 5/5/2020 and 1/3/2021 in our institution.

**Methods**
SFC was measured in blood samples collected at patient’s admission, prior to any medical treatment. Patients’ files were reviewed retrospectively.

**Results**
There were 241 patients (78% female), mean (SD) age 67.4 (18.5), of whom 47.3% received dexamethasone treatment (DT). According to the NIH severity index, 46.9% had asymptomatic or mild disease, 17.4% moderate, and 35.7% had severe or critical disease. The in-hospital mortality, 30-day mortality and the need for assisted ventilation were 8.7%, 14.9% and 18.3% respectively. SFC levels were higher in patients who died in hospital (3.3 (2.8) vs 1.4 (0.8) μg/dl, P < 0.0001), or within 30 days (3.0 (2.3) vs 1.3 (0.77) μg/dl, P < 0.0001) or who required assisted ventilation [2.77 (2.4) vs 1.4 (0.8) μg/dl, P < 0.0001]. SFC levels were significantly higher in patients with diabetes, hypertension, cardiovascular disease and chronic renal failure. There was a positive correlation between SFC and IL-6, CRP, ferritin, LDH, D-dimers, neutrophil/lymphocyte ratio (NLR) and a negative correlation with GFR and oxygen saturation at admission (P < 0.0001 for all pair comparisons). The area under the ROC curve (AUC) to discriminate 30-day mortality was significantly higher for SFC (0.837) compared with IL-6 (0.733, P = 0.012), CRP (0.634, P = 0.0001), ferritin (0.618, P < 0.0001), LDH (0.667, P = 0.001) and NLR (0.759, P = 0.039). The AUC to discriminate in-hospital mortality for SFC (0.837) was similar to IL-6 (0.811), LDH (0.790) and ferritin (0.716), but higher than CRP (0.665, P = 0.004) and NLR (0.715, P = 0.006). The SFC AUC for the need for assisted ventilation was 0.723, not significantly different from the other parameters. Among patients who received...
Introduction

The 2015 American Thyroid Association (ATA) guidelines on the management of thyroid nodules and cancer recommend specific size cut-offs for fine needle aspiration (FNA) cytology. We assessed the correlation between sonographic and cytological stratification as per the guidelines, with emphasis on the size cut-offs.

Methods

In a ‘real world’ prospective study, we sonographically stratified 562 thyroid nodules prior to performing ultrasound-guided FNA as cysts (1.4%), very low (3.9%), low (54.8%), intermediate (19.9%), or high (19.9%) risk. Their Bethesda cytological classification was B1, B2, B3, B4, B5 and B6 in 3.6%, 77.9%, 3.9%, 5%, 2.8% and 6.8% of nodules, respectively. Strong sonographic-cytological correlation was observed \( (P<0.0001) \); for example, B2 (benign) cytology was reported in 100% of very low, 91.2% of low, 81.3% of intermediate and 32% of high risk nodules. Excluding B1 (non-diagnostic) results and nodules without size data, the diagnostic performance of ATA-proposed cut-offs for FNA based on sonographic appearance was compared to higher cut-offs. Increasing the size threshold for sonographically low and intermediate risk thyroid nodules would spare FNAs at the expense of missing a small proportion of B3–B6 cytological nodules and differentiated thyroid carcinomas (DTCs). The size cut-offs are compared against the cytological result of B2 (‘negative outcome’) or B3–B6 (‘positive outcome’). \( ^\dagger \) relative to number of available histopathology results. PPV, positive predictive value. NPV, negative predictive value.

Discussion

By increasing the size cut-off for low-risk nodules, the NPV value retains its excellent performance, whereas PPV remains unaffected with poor performance. By using a higher cut-off in intermediate-risk nodules, NPV and PPV performance remain unchanged. In high-risk nodules, both NPV and PPV perform poorly regardless of the size cut-off. The 20 and 40 mm cut-offs may have greater clinical significance in case of carcinoma, as they correspond to higher tumour grades \( (\geq T2 \text{ and } \geq T3) \), altering the clinical management.

Conclusion

Our results suggest that increasing the ATA size cut-off from 15 mm to 20 mm in sonographically low-risk nodules is clinically safe whilst reducing FNAs.

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Thyroid 1

OG3.1

Real world prospective application of ATA guidelines in over 500 aspirated thyroid nodules: Is it time for changing the size cut-offs for FNA?

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Introduction

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Conclusion

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OC2.6

Activity of abiraterone acetate in the management of cushing syndrome associated to advanced adrenocortical carcinoma: results of the ABACUS trial

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Background

More than 50% of adrenocortical carcinomas (ACC) in adults are associated with cortisol excess that makes tumor management challenging and has a negative impact on patient outcome. Abiraterone acetate (AA) is an irreversible inhibitor of the 17α-hydroxylase/C17, 20-lyase (CYP17 enzyme) that is used in patients with prostate cancer, in whom it leads to suppression of cortisol and androgens. The aim of this study was to assess the activity of AA to control cortisol excess in patients with advanced ACC and overt Cushing syndrome.

Methods

We designed the phase II trial ABACUS (NCT 03145285) whose primary endpoint was normalization of 24-h urinary free cortisol (UFC) excretion within 1 month from treatment start. Inclusion criteria were histologically proven ACC, locally advanced or metastatic disease, and Cushing syndrome confirmed by two measurements of UFC > 1.5 times the upper normal limit with suppressed ACTH. No concomitant treatment with mitotane or chemotherapy was allowed for the first 4 months. AA was able to control rapidly cortisol excess in most patients with a good safety profile. The results of this proof-of-concept study show that AA looks promising and may be viewed as an additional weapon to manage Cushing syndrome in patients with ACC. These findings pose the basis for power calculation and implementation of a prospective long-term study to establish AA efficacy in patients with a steroid-secreting ACC.

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OC3.2

Cabozantinib versus placebo in patients with radioiodine-refractory differentiated thyroid cancer (DTC) who have progressed after prior VEGFR-Targeted therapy: updated results from the phase 3 COSMIC-311 trial and prespecified subgroup analyses based on prior therapy Cosimo Durante1, Marcia Brose2, Bruce Robinson3, Steven I Sherman4, David S Hilsenrath5, Steven I Sherman6, Steven I Sherman7, Bruce Robinson8, Steven I Sherman9, Steven I Sherman10, Steven I Sherman11, Steven I Sherman12, Steven I Sherman13, Steven I Sherman14

Background
At a planned interim analysis (median follow-up 6.2 months) of the double-blind, phase 3 COSMIC-311 trial (NCT03690388), cabozantinib significantly improved progression-free survival (PFS) vs placebo (HR 0.22, 95% CI 0.13-0.36; P < 0.0001) in 187 patients with previously treated radioiodine-refractory DTC (Brose, Lancet Oncol; 2021). Patients must have received lenvatinib or sorafenib and progressed during or after 1-2 prior VEGFR inhibitors. We present the final analysis with an extended dataset of all randomized patients (ITT population) and for prespecified subgroups who received prior lenvatinib, sorafenib, or both.

Methods
Patients were randomized 2:1 to cabozantinib (60 mg QD) or placebo. Placebo patients could cross over to open-label cabozantinib upon disease progression per blinded independent radiology committee (BIRC). PFS (ITT) and objective response rate (ORR, first 100 randomized patients) per RECIST v1.1 by BIRC were the primary endpoints.

Results
At final analysis 258 patients (170 cabozantinib, 88 placebo) were randomized at data cut (8 Feb 2021); 96 had received prior sorafenib/lenvatinib, 102 prior lenvatinib/sorafenib, and 60 prior sorafenib and lenvatinib. Median follow-up was 11 months for cabozantinib vs 1.9 months for placebo in the ITT population (HR = 0.22, 95% CI 0.15-0.31; P < 0.0001). For subgroups, median PFS was 16.6 vs 3.2 months for prior sorafenib/lenvatinib (HR = 0.13, 95% CI 0.06-0.26); 5.8 vs 1.9 months for prior lenvatinib/sorafenib (HR = 0.28, 95% CI 0.17-0.48); and 7.6 vs 1.9 months for prior sorafenib and lenvatinib (HR = 0.27, 95% CI 0.13-0.54). In the ITT population, ORR was 11% for cabozantinib vs 0% for placebo & overall survival HR = 0.76 (95% CI 0.45-1.31). Grade 3/4 treatment emergent adverse events (TEAEs) were 62% in the cabozantinib arm vs 28% in placebo with treatment-related grade 5 events; 67% vs 5% required dose reductions due to TEAEs; 8.8% vs 0% discontinued treatment due to TEAEs not causally related to disease.

Conclusion
In the final analysis of COSMIC-311 with longer follow-up, cabozantinib maintained its superior efficacy vs placebo. The PFS-HR was consistent with the interim analysis, in patients with previously treated radioiodine-refractory DTC irrespective of prior treatment, with no unexpected toxicities.

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OC3.3

Adaptive approach reveals emerging risk factors for recurrent and persistent differentiated thyroid cancer Michele Gentili, Giorgio Grani & Federico Siciliano on behalf of Italian Thyroid Cancer Observatory, Italy

Background
The appropriate risk stratification of patients with differentiated thyroid cancer (DTC) is crucial because most cases have an indolent behavior and need a conservative approach. One of the most widely used tools is included in the American Thyroid Association (ATA) Guidelines, based on heterogeneous literature data derived by different populations, settings, and timeframes. Recent research focused on the inclusion of other features not included in the ATA system has allowed the identification of the clinical relevance of some of the included ones. In this prospective cohort study, we analyzed data of DTCs managed in 40 Italian clinical centers. The aims were to develop comprehensive, data-driven prediction models, able to capture all available features and to determine the weight of the potential predictors.

Methods
The Italian Thyroid Cancer Observatory (ITCO) web-based database (NCT04031339) now includes prospectively collected data of 10000 patients with histologically confirmed thyroid cancer. Each record contains information on patient demographics and biometrics, circumstances of the diagnosis, tumor pathology, treatments, and periodic follow-up examinations. We selected consecutive cases with DTC (n=4773) and at least early follow-up data. We built a decision tree, a relatively simple prediction model, to assign a risk index to each patient. The model allows to investigate the impact of different variables in the prediction of the risk level. Results. 2492 patients (52.2%) are classified as low, 1873 (39.2%) as intermediate, and 408 as high risk, according to the ATA risk estimation. Their response to treatment during their whole follow-up is excellent response in 2188 (45.8%), indeterminate in 1957 (41%), biochemical incomplete response in 250 (5.2%), and structural incomplete response in 378 (7.9%). The decision-tree model outperformed the ATA risk stratification system: the sensitivity of high-risk classification for structural disease increased from 37% to 49%, and the negative predictive value for low-risk patients also slightly increased by 3%, even without including information derived from radioiodine treatment (performed only in a subgroup of patients). The feature importance was estimated: several variables not included in the ATA system significantly impact the prediction of disease persistence/recurrence: age at diagnosis, gender, body mass index, cytology, family history of thyroid cancer, surgical approach, pre-surgical cytology, and circumstances of the diagnosis.

Conclusion
The current risk stratification systems may be complemented by the inclusion of other demographic, clinical and anthropometric data, to improve the prediction of disease persistence/recurrence. The use of a complete set of variables allows for a more precise clustering of patients, to predict their responses to treatment.

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OC3.4

Effect of age on efficacy and safety of cabozantinib vs placebo in patients with radioiodine refractory (RAI-R)-differentiated thyroid cancer (DTC) with progression after VEGFR-targeted therapy: subgroup analysis from phase 3 COSMIC 311 study Cosimo Durante1, Bruce Robinson2, Steven I Sherman3, Jolanta Krajewska4, Chia-Chi Lin5, Feranda Vaisman6, Ana O Hoff7, Erika Hite8, Daniel W Bowles9, Jorge Hernando10, Kamalika Banerjee11, Roman M Levitsky12, Jennifer W Oliver13, Bhumsuk Keam14 & Jaume Capdevila14

Background
Effect of age on efficacy and safety of cabozantinib vs placebo in patients with radioiodine refractory differentiated thyroid cancer (DTC) with progression after VEGFR-targeted therapy: subgroup analysis from Phase 3 COSMIC 311 study Cosimo Durante1, Bruce Robinson2, Steven I Sherman3, Jolanta Krajewska4, Chia-Chi Lin5, Feranda Vaisman6, Ana O Hoff7, Erika Hite8, Daniel W Bowles9, Jorge Hernando10, Kamalika Banerjee11, Roman M Levitsky12, Jennifer W Oliver13, Bhumsuk Keam14 & Jaume Capdevila14

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Results
In the younger subgroup, 49% patients had papillary thyroid cancer (PTC) in the
cazobatinib arm vs 66% in placebo, whereas 53% vs 36% had follicular thyroid
cancer (FTC). In the older subgroup, 64% had PTC in the cazobatinib arm vs
57% in placebo, whereas 38% vs 43% had FTC. In the younger subgroup, 65%
received prior sorafenib and 61% prior lenvatinib whereas in the older subgroup
55% received prior sorafenib and 65% prior lenvatinib. Median PFS for the
cazobatinib arm was 11.1 months (95% CI:7.2-NE) with HR 0.19 (95% CI:0.12-
0.32) for the younger subgroup and 11.1 months (95% CI:5.9-13.8) with HR 0.27
(95% CI:0.16-0.50) for the older subgroup. ORR with cazobatinib was 10%
(95% CI:4.9%-18.9%) for the younger and 12% (95% CI:5.9%-20.8%) for the
older subgroup vs 0% (95% CI:0.0-8.0) for both placebo subgroups. The
discontinuation rate of cazobatinib due to AE related to study treatment was 6%
both in the younger and the older subgroup and the percentage of patients with
any dose reduction was 65% vs 69%. The safety profile in both age groups was
similar and consistent with that of the overall population. No treatment-related
grade 5 adverse events were observed.

Conclusion
This subgroup analysis demonstrates that clinical benefit with cazobatinib is
maintained irrespective of age in previously treated RAIR DTC patients.

Keywords
Cazobatinib; COSMIC-311; DTC; VEGFR; age; differentiated thyroid

DOI: 10.1530/endoabs.81.OC3.3
Objective Hypothalamic obesity results in severe weight-gain and increased risk of cardiovascular and metabolic mortality. We aimed to assess the safety and efficacy of Tesomet (tesofensine plus metoprolol), and ongoing requirements in pituitary hormone replacement adjustments in adults with acquired hypothalamic obesity, a rare disease with no approved therapy.

Research design, patients and methods Twenty-one adults with hypothalamic obesity (16 females, 5 males, mean(SD) age 46(14.6) years; 90% with a BMI ≥ 30 kg/m²) were randomized to Tesomet (0.5 mg tesofensine/50 mg metoprolol) or placebo during a 24-week double-blind treatment period. Seventeen subjects (11 Tesomet; 6 placebo) continued in 24-week open-label extension, all treated with Tesomet. Primary endpoint was safety; secondary endpoints included body weight and waist circumference. Almost half had a craniofaryngioma, 86% had undergone pituitary/hypothalamic surgery, 52% irradiation. All received one or more anterior pituitary hormone replacements.

Trial NCT03845075.

Results Most common adverse events were sleep disorders, dizziness, dry mouth, and headache; mostly of mild to moderate severity. No clinically meaningful changes in blood pressure, heart rate or blood pressure were observed. On completion of the double-blind period, mean change in body weight from baseline was -7.84 kg for the Tesomet group vs -0.34 kg for placebo (P=0.03), and at the end of the open-label extension period it was -6.34 kg for the Tesomet-Tesomet group and -0.03 kg for the placebo-Tesomet group. Mean change in waist circumference from baseline was -7.1 cm for the Tesomet group vs -1.2 cm for the placebo group at the end of the double-blind period, and -5.7 cm for the Tesomet-Tesomet group and -3.0 cm for the placebo-Tesomet group at the end of the open-label extension period. Most subjects (65%) had Levothyroxine reduced; adjustments in pituitary-replacement and diabetic medications were otherwise few and did not differ significantly from baseline. Mean (SD) change in levothyroxine daily dose from baseline was -6.6% (6.1) and -6.4% (9.1) in Tesomet and placebo, respectively. In both groups, change in Levothyroxine correlated with weight-loss at time of adjustment (r² =0.37, P=0.006). This tendency was maintained during the extension period and implementing the reduction of levothyroxine in the management stabilised thyroid function.

Conclusion Tesomet was generally well tolerated after 48 weeks of treatment, did not affect heart rate or blood pressure, and resulted in significant reductions in body weight in this cohort of hypopituitary patients with hypothalamic obesity. Weight-loss necessitated reductions in levothyroxine dose in most subjects to maintain stable thyroid function.

DOI: 10.1530/endoabs.81.OC4.1

OC4.3

Long-term efficacy and safety data for oral octreotide capsules in acromegaly: mpowered trial open-label extension phase

Background

Oral octreotide capsules (OOC) are a treatment option for patients with acromegaly in the United States. The mpowered trial (NCT02685709) showed that OOC were noninferior to injectable somatostatin receptor ligands (sRLs; octreotide or lanreotide) in maintenance of biochemical control in patients previously responding to both treatments, as well as demonstrated improvements in patient-reported outcomes among patients receiving OOC.

Objective

Report long-term safety and efficacy outcomes with OOC from the open-label extension (OLE) of mpowered.

Methods

Patients were eligible for and could voluntarily enroll into the OLE if they had completed the 15-month core treatment phase of mpowered (6-month Run-in phase, followed by 9-month randomized controlled treatment [RCT] phase or, for OOC nonresponders during/at end of Run-in at participating sites, combination sub-study evaluating OOC in combination with cabergoline) and were adequately biochemically controlled per investigator assessment. Maintenance of response

First, to provide solid reference values for GH concentrations in term newborns, by means of a non-invasive procedure (GH from screening cards), using a current ultrasensitive GH assay. Secondly, to investigate eventual maternal and neonatal predictors of GH concentrations.

Methods

Using Immutte 2000 assay, GH was measured simultaneously from 200 dried blood spots (DBS) and serum samples of controls, thus validating this method for DBS. With the same assay, GH concentrations were measured in 444 filter papers of term newborns after 48 hours of life. Maternal and neonatal anamnestic data were collected from recorded clinical data.

Results

In our cohort (444 neonates, 212 males and 232 females), the auxological parameters were spread according with the reference neonatal anthropometric charts of Italian population (median length -0.05 SDS, median head circumference -0.07 SDS, median weight -0.12 SDS). Median GH value was 16.9 μg/L (IQR 11.2 - 23.1 μg/L), with no significant gender difference. We defined a lower limit of 6.5 μg/L as 5% centile through Harrell-Davis' method with a confidence interval at 90% between 5.9 and 7 μg/L by bootstrap BCA method. Considering our lower limit of GH < 6.5 μg/L, at logistic regression analysis, jaundice presented the greater association with GH concentrations (P<0.001). Indeed, neonates with jaundice had 5-fold increased risk of presenting a GH < 6.5 μg/L. No other significant correlation was found between GH and maternal or neonatal characteristics. Yet, the association between neonatal hypoglycaemia and lower GH concentrations was suggestive, though not significant (P=0.077).

Conclusions

We defined the lower limit of reference values for GH in term healthy newborns independently from sex, gestational age and auxological parameters using for the first time a widely available assay. The relationship found between symptoms/signs suggestive for cGHD and lower GH concentrations, even in healthy subjects, confirmed the crucial role of clinical presentation in the diagnosis of cGHD. Providing solid reference values in term newborns, we put the basis for further studies aiming at defining a reliable diagnostic cut-off of cGHD.

DOI: 10.1530/endoabs.81.OC4.2

OC4.4

Measurements of growth hormone in neonatal screening cards as a non-invasive and feasible tool: reference values in healthy term newborns

Background

Growth hormone (GH) is the main growth determinant of term newborns after 48 hours of life. Maternal and neonatal anamnestic data were collected from recorded clinical data. The auxological predictors of GH concentrations.

OC4.4.2

Measurements of growth hormone in neonatal screening cards as a non-invasive and feasible tool: reference values in healthy term newborns

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DOI: 10.1530/endoabs.81.OC4.2
OC4.4

Recurrent in acromegaly: a two tertiary centers experience
Elisa Sala1, Arianna Cremaschi1,2, Giulia Carosi1,3, Nazarena Betella4, Onnita Del Sindaco1,2, Alessandra Mangone1,2, Roberta Muniri1, Angela Pagano1,2, Rita Indirli1, Emanuele Ferrante1, Gherardo Mazzotti1,2, Marco Locatelli2, Davide Milani4,A, Andrea Gerardo Lana1,2, Maura Arosio2 & Giovanna Mantovani2,1

1Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; 2Department of Clinical Sciences and Community Health University of Milan, Milan, Italy; 3Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; 4Endocrinology, Diabetology and Medical Andrology Unit, Humanitas Clinical and Research Hospital, Rozzano, Italy; 5Department of Biomedical Sciences, Humanitas University, Rozzano, Italy; 6Neurosurgery Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy; 7Department of Pathology, Biopathology, Oncology and Transplantation, University of Milan, Milan, Italy; 8Neurosurgery Unit, Humanitas Clinical and Research Hospital, Rozzano, Italy

The aim of this study was to evaluate in a long follow-up time patients with acromegaly successfully treated by transphenoidal surgery (TPS) in order to establish the recurrence rate and the need of subsequent follow up.

Methods
We retrospectively analyzed data of 283 acromegalic patients (168 females, mean age: 44.2 ± 12.9 years) who underwent TNS for a GH secreting pituitary adenoma between 1980 and 2020, on regular follow-up at two Pituitary Units in the city of Milan (Fondazione IRCCS Ospedale Maggiore Policlinico and IRCCS Humanitas). Diagnosis of acromegaly was defined by the presence of clinical signs and symptoms, an elevated serum IGF-I level, age and sex matched, and lack of GH suppression based on appropriated criteria for the assay used at the time of diagnosis (GH < 2 µg/l using aRIA, 1 µg/l with a modern IRMA or < 0.4 µg/l with chemiluminescent assays, CLIA). For recurrence the same biochemical parameters were used.

Results
All patients had operative confirmation of acromegaly (mean IGF1: +13.7 ± 9.2 SDS, mean GH nadir: 15.9 ± 26 µg/l). MRI confirmed the presence of a pituitary adenoma in all patients (192 macro) and all patients underwent TNS. At the first follow-up after surgery (mean distance: 3.63 ± 2.5 months) we defined as not cured 143 patients (50%), as cured 132 (47%) and as “partially cured”, i.e. with normalization of only one parameter between GH suppression and IGF-1 levels, 8 patients (3%). Considering the group of cured patients, at the last follow-up (mean: 109 months after surgery) 51/32 (3.7%) patients needed medical therapy for recurrence. In particular, only 1 patient (0.7%) after 15 months form surgery showed a biochemical status of active acromegaly (IGF1 > 5.6I SDS, and GH nadir 1.27 µg/l assessed with CLIA). Four additional patients (3%), after a mean follow-up of 81 months, started therapy for an isolated increase in IGF1 levels (mean IGF1/SDS + 3.65). In the “partially cured” group, 26/85 (25%) patients showed after 12 and 37 months from surgery a biochemical status of active acromegaly (IGF1 SDS > 2.75 and > 3.62; GH nadir 0.6 and 0.5 µg/l respectively assessed with CLIA).

Conclusions
Recurrent of acromegaly occurred in less than 1% of patients successfully treated with surgery. More frequently (25%), recurrence occurred in patients with incomplete normalization of either IGF1 or GH after surgery. Our data suggest that most acromegalic patients with complete remission after surgery may be considered as definitely cured, while those in partial remission need a strict endocrinological follow-up.

DOI: 10.1530/endoabs.81.OC4.4

OC4.5

Real-world injection experience and use of independent injection among patients using lanreotide autogel/depot (LAN) prefilled syringe or octreotide long-acting release (OCT) to treat acromegaly or neuroendocrine tumors (NETs): international PRESTO 2 survey
Susan Webb1,2, Dermot O’Toole1, Pamela Kunz3, Aude Houchard4, Sandra Brazin5, Antonio Ribeiro-Oliveira6 & Ally Prebtani7

Aim
To compare the injection experience of patients with acromegaly or NETs who were receiving treatment with LAN prefilled syringe vs OCT syringe.

Methods
A 2021 e-survey of adults with acromegaly or NETs from Canada, USA, UK and Ireland who had received ≥3 months’ treatment with LAN or OCT (planned sample size, 304 [min 76/cohort]; 50:50 ratio [LAN, excluding patients in the USA, where LAN independent injection is not in the approved labelling.

Results
There were 304 respondents (acromegaly, n = 85; NETs, n = 219; LAN, n = 168; OCT, n = 136; 69.2% female; mean age 59.6 years). Fewer patients had injection-site pain lasting > 2 days after last dose with LAN (60.0%) vs OCT (22.8%); the odds of pain lasting > 2 days were significantly lower for LAN vs OCT, adjusted for disease group and occurrence of injection-site reaction (OR 0.13 [95% CI 0.06-0.30]; P < 0.0001). Secondary endpoints are summarized in the table. In the LAN group (excluding USA), 40.7% (n = 11) of patients with acromegaly and 38.7% (n = 29) with NETs received their last treatment via independent injection and indicated they chose this for flexibility (80.0%), time saved (70.0%) and it was easy to do (60.0%).

Conclusions

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>LAN (%)</th>
<th>OCT (%)</th>
</tr>
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<tbody>
<tr>
<td>Interference with daily life due to injection-site pain, %</td>
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<td>42.9</td>
</tr>
<tr>
<td>Not at all</td>
<td>59.0</td>
<td>40.0</td>
</tr>
<tr>
<td>A little bit</td>
<td>37.2</td>
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<tr>
<td>Quite a bit</td>
<td>3.8</td>
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<tr>
<td>Very much</td>
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*Patients with pain at last injection **Patients with > 6 months’ experience with current SSA

Introduction
Long-acting (LA) somatostatin analog (SSA) therapy is a common first-line medical treatment for acromegaly and NETs. There are limited real-world data on patients’ injection experience with the latest LA SSA devices/formulations.

Aims
To evaluate the injection experience of patients with acromegaly or NETs who were receiving treatment with LAN prefilled syringe vs OCT syringe.

Methods
A 2021 e-survey of adults with acromegaly or NETs from Canada, USA, UK and Ireland who had received ≥3 months’ treatment with LAN or OCT (planned sample size, 304 [min 76/cohort]; 50:50 ratio [LAN, excluding patients in the USA, where LAN independent injection is not in the approved labelling.

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*Patients with pain at last injection **Patients with > 6 months’ experience with current SSA

Endocrine Abstracts (2022) Vol 81

24th European Congress of Endocrinology
In this e-survey, LAN was associated with advantages relative to OCT beyond improvements in the occurrence of technical problems, especially regarding duration of pain at injection site and its interference with daily life. A substantial proportion of LAN patients had received independent injection, demonstrating the value of this treatment option.

**OC5.1**

**Pdgfrα-driven Alms1 deletion in mice recapitulates the obesity and insulin resistance of Alms1 global knockout**

Eleanor McKay, Ineke Luijten, Dominique McCormick, Adrian Thomson, Gillian Gray & Robert Semple

University of Edinburgh, Centre for Cardiovascular Science, Edinburgh, United Kingdom

**Background**

Alström Syndrome (AS) is a rare autosomal recessive disease featuring highly accelerated insulin resistance, fatty liver, diabetes and heart failure among other syndromic features. Heart failure leads to significant early mortality, but is complex and likely multifactorial, with developmental defects, accelerated atherosclerosis, and fibrosis all implicated. These cardiometabolic complications occur in the face of only moderate obesity in many patients. AS is caused by biallelic loss-of-function mutations in the Alms1 gene, encoding a large centrosomal protein. The precise derangement of centrosomal and/or primary ciliary function caused by loss of Alms1 is unknown. There is currently no specific treatment for AS. Further research is needed to address this unmet clinical need. Several global knockout (KO) mouse models have been described to recapitulate key metabolic components of AS, but none have characterised cardiac function in-vivo, and tissue-specific KO approaches have not yet been used to tease out contributions of different cell types to pathology.

**Hypothesis**

The metabolic profile of AS closely resembles that of lipidodystrophy. We thus hypothesised that loss of Alms1 function in mesenchymal stem cell populations, such as adipose precursor cells, would recapitulate the metabolic derangement in AS. We secondarily hypothesised that this would mitigate some but not all cardiac complications.

**Methods**

A novel global KO mouse was generated by crossing the EUCOMM Tm1Alms1 line with the global CAG-Cre driver. A Pdgfrα-Cre driver was used to abrogate Alms1 function only in mesenchymal progenitor cells and their descendants including preadipocytes and adipocytes. We undertook metabolic phenotyping and echocardiography of global and Pdgfrα+ Alms1-KO mouse models in both sexes on a 45% high-fat diet.

**Results**

Consistent with previous models and the human disease, global Alms1 KO mice were hyperphagic, obese, insulin resistant, and had severe hepatosteatosis. AS is caused by biallelic loss-of-function mutations in the Alms1 gene, encoding a large centrosomal protein. The precise derangement of centrosomal and/or primary ciliary function caused by loss of Alms1 is unknown. There is currently no specific treatment for AS. Further research is needed to address this unmet clinical need. Several global knockout (KO) mouse models have been described to recapitulate key metabolic components of AS, but none have characterised cardiac function in-vivo, and tissue-specific KO approaches have not yet been used to tease out contributions of different cell types to pathology.

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without late phase retention. Notably, those conclusions were made by an indirect method of estimation of GE through ingestion, absorption and determination of plasma level of paracetamol. Furthermore, in previous studies GE has been evaluated as a part of the composite outcome. The indirect method with paracetamol was shown to be appropriate for evaluation of kinetics of liquid meals, whereas it might lead to inaccurate estimation of late phase GE. Scintigraphic evaluation is considered as a reference method for the purpose.

This is the first study that evaluates the effect of once weekly subcutaneous semaglutide on late phase GE of a solid meal by scintigraphy as a primary outcome in obese women with PCOS without other comorbidities.

Materials and Methods
A single-blind, placebo-controlled trial was conducted in 20 women with PCOS and obesity, without diabetes and other comorbidities, randomized to once weekly subcutaneous semaglutide 1.0 mg (S) or placebo (P) for 8 weeks. Gastric emptying was assessed by scintigraphy after ingestion of 99mTc colloid in pancake labelled with radiopharmaceutical that maintained a stable binding within gastric environment by scintigraphy using sequential static imaging and dynamic acquisition. Estimation of GE was obtained by repeated imaging of remaining 99mTc activity (RA) at fixed time intervals over 4 hours and the half time (T1/2) of gastric emptying had been calculated. Additionally, we evaluated anthropometric, metabolic, hormonal and appetite parameters.

Results
At 30 min after ingestion significant difference in RA was observed between semaglutide group and placebo (92.5% in S vs 89% in P (P = 0.05)) and persisted throughout the observation period up to 4 hour (37% in S vs 0% in P (P = 0.002)). T1/2 was significantly longer in S as compared to P (171 min vs 118 min, respectively (P < 0.001)). In addition, semaglutide led to significant decrease in waist, hip and mid-thigh circumference. BMI and androgen levels. Subjective ratings of appetite suppression correlated with T1/2.

Conclusion
Semaglutide 1.0 mg resulted in a significant late-phase retention of solid meal measured by repeated scintigraphic imaging. This effect correlated with appetite suppression and likely contributed to weight loss.

DOI: 10.1530/endoabs.81.OC5.2

OC5.3 Weight loss attempts and weight perception in women with polycystic ovary syndrome (PCOS) - a 15-year follow-up in a population-based cohort study

Emilia Pesonen1,2, Meri-Maja Ollila1, Laure Morin-Papunen1, Juha S Tapainen1, Timo Jämsä1, Raija Korpela-Olari2,5, Mäisa Niemelä4, Marjukka Nurkka1,5,6, & Terhi T Piltonen1

1University of Oulu and Oulu University Hospital, Department of Obstetrics and Gynaecology, PEDEGO Research Unit, Medical Research Center, Oulu, Finland; 2Oulu Deaconess Institute Foundation sr., Department of Sports and Exercise Medicine, Oulu, Finland; 3University of Helsinki, Department of Obstetrics and Gynaecology, Helsinki, Finland; 4University of Oulu and Oulu University Hospital, Research Unit of Medical Imaging, Physics and Technology, Medical Research Center, Oulu, Finland; 5University of Oulu and Oulu University Hospital, The Center for Life Course Health Research (CLCHR), Faculty of Medicine; 6University of Oulu and Oulu University Hospital, Medical Research Center

Background
Women with polycystic ovary syndrome (PCOS) experience increased weight gain during life, thus weight management and preventing weight gain should be the first line treatment. Weight loss is usually self-initiated because practical support for weight management is often limited or even lacking. Perception of overweight is considered an important prerequisite for weight loss attempts, although there is no prior research regarding women with PCOS. The main aim of the study was to investigate whether women with PCOS are more likely to have multiple weight loss attempts compared to non-PCOS controls regardless of weight. In addition, we evaluated women’s weight perception in relation to weight loss attempts.

Methods
The study is part of Northern Finland Birth Cohort 1966 including women with PCOS (n = 280) and non-PCOS controls (n = 1573) examined at ages 31 and 46 years. Multiple weight loss attempts, weight perception, body mass index (BMI), and psychological distress were analyzed along with sociodemographic factors at both time points. Binary logistic regression analysis was performed, and the results were reported as odds ratios (ORs) with 95% confidence intervals. A P-value < 0.05 was considered statistically significant.

Results
Women with PCOS had higher prevalence of multiple weight loss attempts by age 31 and 46 years compared to controls (P < 0.001). Despite this, women with PCOS had significantly higher BMI at both time points (P < 0.001). PCOS was independently associated with multiple weight loss attempts at age 46 when adjusted for psychological distress and BMI (OR 1.44 [95% CI, 1.01–2.05]) or perception of overweight (OR 1.45 [95% CI, 1.03–2.03]). Perception of overweight was the most significant factor contributing to multiple weight loss attempts at both time points. Perception of overweight was more prevalent in PCOS compared to controls, and interestingly, perception of overweight was more common even among normal weight women with PCOS at age 31 (P = 0.004) and age 46 (P < 0.001) years. Indeed, PCOS was independently associated with perception of overweight at age 31 when adjusted for BMI and leisure-time physical activity (OR 1.69 [95% CI, 1.01–2.85]), and at age 46 when adjusted for BMI and psychological distress (OR 2.65 [95% CI, 1.37–5.13]).

Conclusions
Women with PCOS are more likely to experience multiple weight loss attempts as well as perception of overweight independent of BMI until late fertile age compared to non-PCOS controls. In clinical practice, adequate support and resources should be offered to reduce inefficient weight loss attempts and stress.

DOI: 10.1530/endoabs.81.OC5.3

OC5.4 Body composition during childhood, adolescence and adulthood influences the odds of developing polycystic ovary syndrome: a mendelian randomisation study with a systematic review and meta-analysis

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Background
Observational and genetic Mendelian randomisation (MR) data has demonstrated the association of adulthood overweight/obesity with development of polycystic ovary syndrome (PCOS). However, the contribution of early life (i.e. childhood/adolescence) body composition on incident PCOS is unclear. This study determines the influence of body composition on the likelihood of developing PCOS.

Methods
We conducted a 2-sample Mendelian randomisation study to determine the impact of body composition (using metabolic parameters: fasting serum insulin or sex-hormone binding globulin) on the odds of PCOS. PCOS genome-wide association study meta-analysis data (from 10,074 people with PCOS, 103,164 controls) was interrogated using the inverse-variance weighted method. Furthermore, we conducted a systematic review (71 studies) and meta-analysis (63 studies) of the role of overweight, obesity and central obesity (defined via waist circumference / waist-hip ratio) on odds of PCOS in adults and adolescents.

Results
From Mendelian randomisation, significant associations were shown between body composition and odds of PCOS. For every standard deviation increase in BMI (a BMI increase of 4.8 kg/m²), odds of PCOS increased significantly (OR: 2.76, 2.27 - 3.35). Similar associations were demonstrated between body fat percentage (OR: 3.05 per 8.5%, 2.24 - 4.15), whole-body fat mass (OR: 2.53 per 9.6 kg, 2.04 - 3.14), fasting insulin (OR: 6.98 per 7.99 pmol/L, 2.02 - 24.15) and sex-hormone binding globulin (OR: 0.74 per 28 nmol/L, 0.64 - 0.87). Genetically determined childhood body size increased odds of PCOS after adjusting for adult body size (PCOS: 2.56, 1.57 - 4.20). From meta-analysis, women with overweight (OR 3.80, 2.87 - 5.03), obesity (OR 4.99, 3.74 – 6.67) and central obesity (OR 2.93, 2.08 – 4.12) had increased odds of PCOS. For adolescents with overweight and/or obesity the PCOS odds were greater than for adults (adult vs adolescent: overweight: OR 3.57 and 5.32; Obese: OR 4.66 and 7.86).

Conclusions
Using two complementary epidemiological techniques we demonstrate a clear relationship between markers of body composition, indicative of excess body fat accumulation, and odds of developing PCOS, especially in childhood and adolescence. MR reports that genetically determined childhood body composition increases PCOS likelihood independent of adult body composition. From meta-analysis, women with overweight, obesity and central obesity had increased odds of PCOS, with odds even higher in adolescents with overweight and obesity.
Overall, this study has implications for the prevention and treatment of obesity and the importance of effective weight maintenance from early years and beyond.

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OC5.5

The glucocorticoid transporter ATP-binding cassette subfamily C member 1 (ABCC1) influences adiposity, glucose homeostasis and insulin sensitivity in male mice

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Background
Glucocorticoids (GCs) modulate glucose homeostasis by acting on metabolic tissues including liver, adipose and skeletal muscle. GC access to corticosteroid receptors in these tissues is regulated e.g. by pre-receptor metabolism. We recently identified a role for ABCC1, a transmembrane ‘drug-resistance’ transporter, as a GC exporter which limits intracellular GC concentrations and action in adipose tissue. Here, we tested the hypothesis that ABCC1, which is also highly expressed in skeletal muscle, influences glucose metabolism and insulin sensitivity, through regulation of tissue GC action.

Methods
Male global Abcc1 knockout (Abcc1-/-) and wild-type (WT) littermate mice were fed chow diet or high-fat diet (HFD - 58% fat and sucrose) for 9 weeks, starting at 8-12 weeks of age (n=10-13 each group). Glucose and insulin tolerance tests were performed (week 7-8), all procedures were done with ethical approval. Plasma and tissue GC concentrations were measured by Liquid Chromatography Elisa and by RT-qPCR and Western blot.

Results
Our findings show that on chow diet, Abcc1-/- mice have similar body weight, despite reduced fat mass (subcutaneous, gonadal and brown adipose tissue), normal glucose tolerance in the presence of reduced fasting insulin levels, and increased levels of corticosterone in plasma, subcutaneous adipose tissue (sWAT) and gastrocnemius muscle compared to WT mice. By contrast, on HFD, Abcc1-/- mice had similar body weight gain and fat mass to WT mice, but impaired glucose and insulin tolerance and fasting hyperinsulinemia, without measurable alterations in plasma or tissue GC levels. Interestingly, on HFD, WT mice protein levels of ABCC1 were upregulated in sWAT but not in skeletal muscle. Further, we investigated a number of genes and pathways that might be affected by the changes in insulin e.g. GSK-3β. We identified upregulation of the levels of pGSK-3β in skeletal muscle, but not in adipose tissue from Abcc1-/- mice on chow diet. By contrast, on HFD, the levels of pGSK-3β were upregulated in skeletal muscle from WT mice but not in Abcc1-/-. These changes were absent in adipose tissue.

Conclusions
Abcc1 influences adiposity, insulin sensitivity and glucose homeostasis differently according to diet and obesity, and by mechanisms which likely be only in part GC-dependent. Further dissection of the substrates for ABCC1 which mediate these effects may reveal new avenues for therapy in metabolic disease.

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OC5.6

Fetal sex predicts perinatal outcomes in women with gestational diabetes

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Background
Gestational diabetes (GD) is a known risk factor for delivery, fetal and perinatal complications. Fetal male sex is known to be associated with worse perinatal outcomes, such as macrosomia, neonatal hypoglycaemia, low Apgar scores, birth defects and mortality. However, studies evaluating the impact of fetal sex on perinatal outcomes in women with GD are scarce.

Objectives
We aimed to study whether male newborn sex is associated with neonatal outcomes, in women with GD.

Methods and Methods
Retrospective study based on the national register of GD. Included women with live-born singleton pregnancies followed between 2012 and 2017. Excluded women without data on variables of interest. Primary endpoint: Neonatal hypoglycaemia, neonatal macrosomia, respiratory distress syndrome (RDS) and neonatal intensive care unit admission (NICUA). BMI as pregestational weight divided by squared height. Female and male newborns were compared. Multivariate logistic regression models were built and included variables with different distribution between groups and with known association with the endpoint under analysis.

Results and Conclusions
We studied a total of 10768 newborns in mothers with GD, 5635 (52.5%) male, 438 (4.1%) had neonatal hypoglycaemia, 406 (3.8%) were macrosomic, 671 (6.2%) had RDS, and 671 (6.2%) had a NICUA. Male sex newborns were heavier, more frequently small and large for gestational age. No differences were observed on maternal age, BMI, HbA1c, anti-hyperglycaemic treatment, pregnancy complications or gestational age at delivery. In the multivariate regression analysis, male sex was independently associated with neonatal hypoglycaemia [OR 1.27 (IC 95%:1.04-1.55), P=0.02], neonatal macrosomia [1.98 (1.58-2.48), P=0.01], NICUA [1.27 (1.00-1.55), P =0.03] and RDS [1.33 (1.03-1.71), P=0.03]. Male newborns from mothers with GD have a 27% higher risk of neonatal hypoglycaemia, almost 2-fold higher risk of macrosomia, 33% higher risk of RDS and 27% higher risk of NICUA.

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Endocrine-Related Cancer

OC6.1

Recurrent disease in patients with sporadic pheochromocytoma and paraganglioma

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Background
It is well established that life-long follow-up is required for patients with hereditary pheochromocytomas and paragangliomas (PPGLs), due to the potential of developing recurrent disease. However, whether follow-up of patients with sporadic PPGLs is necessary, remains unclear.

Aims
To examine the prevalence and predictors of recurrent disease in patients with sporadic PPGLs. Materials and method: This multicenter study included retrospective clinical data of 528 patients with PPGLs. Recurrent disease was defined as presence of new tumor and/or locoregional recurrence and/or metastases one year after initial tumor diagnosis. Patients with sporadic PPGLs were defined as
those without germline mutations in known genes associated with hypoxia (cluster 1) or kinase (cluster 2) signaling pathways.

Results

Fifty-three percent of the patients had sporadic PPGLs and presented with a recurrence rate of 17.3%, which mainly reflected metastatic disease (10%). This was significantly lower than those with cluster 1 (54.3%), but similar to those with cluster 2 mutations (14.1%). Among patients with sporadic PPGLs and recurrent disease, 70.7% demonstrated recurrence within 10 years from initial tumor diagnosis. Multivariable Cox regression analysis showed that larger (> 4.5 cm) size (HR 1.8, 95% CI 1.1-3.3, P = 0.015) and extra-adrenal location (HR 2.4, 95% CI 1.4-4.1, P = 0.001) of the primary tumor, were independent predictors of recurrence in patients with sporadic PPGLs. Indeed, patients with small (<4.5 cm) sporadic pheochromocytomas presented with the lowest (7.8%) rate of recurrent disease (P < 0.001).

Conclusion

Among patients with sporadic PPGLs, prevalence of recurrence was mainly due to metastases and high enough to mandate long-term follow-up. Importantly, our findings indicate that size and tumor location are important to consider for further stratification and management of patients with sporadic PPGLs.

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OC6.2

Translational evidence for splicing factor RBM22 as a novel prognostic biomarker and therapeutic target in prostate cancer

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Prostate cancer (PCa) is one the leading causes of cancer-related deaths among men in developed countries. Therefore, identification of novel molecular and therapeutic approaches to tackle this pathology are urgently needed. In this scenario, our group has recently reported that elements of the cellular machinery controlling alternative splicing processes might be used as potential novel therapeutic tools against PCa and castration-resistant PCa (CRPC). In this context, RBM22 has been identified as a key spliceosome component, playing a crucial role for normal development; however, the potential dysregulation and functional role of RBM22 in cancer still remain unknown. Here, we identify for the first time that RBM22 plays a critical functional role in prostate cancer (PCa) (i.e. extraprostatic extension and perineural invasion). These results were corroborated using the TRAMP mouse model, wherein gradual formation, etc.), and drastically decreased tumor development and progression in vitro (using a preclinical mouse model), which would underlie a relevant direct and indirect antitumor activity of lower RBM22 levels with enhanced tumor progression. These results were corroborated using the TRAMP mouse model, wherein gradual reduction of RBM22 from prostatic intraepithelial neoplasia to moderately differentiated PCa and to poorly differentiated PCa was observed. These actions are likely mediated through the modulation of key signaling pathways (i.e. cycle, apoptosis, PI3K pathways, etc.) and critical molecular regulators (i.e. MYC, MCY and E2F), and may also involve the alteration of alternative splicing events of key genes involved in these pathways. Therefore, our study demonstrates for the first time that RBM22 plays a critical functional role in the pathophysiology of PCa and suggests that targeting negative regulators of RBM22 could represent a novel therapeutic strategy to tackle this devastating pathology.

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OC6.3

Systematic detection of mosaicism by using digital NGS in a cohort of 119 unresolved MEN1 cases reveals 3 new MEN1 mosaics

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Context

Mosaicism is a feature of several inherited tumor syndromes but is rarely systematically looked for in routine. MEN1 is an autosomal dominant hereditary syndrome characterized by several endocrine tumors affecting parathyroid glands, pancreas, and anterior pituitary most of the time, due to inactivating mutations in the MEN1 gene. Few cases of mosaicism in Multiple Endocrine Neoplasia type 1 (MEN1) have been described. MEN1 mosaicism is probably under-diagnosed because it is not routinely investigated. At present, Next generation sequencing (NGS) offers new possibilities to detect mosaicism. The challenge is to distinguish true mosaicism from sequencing artifacts. We reported the first study systematically looking for MEN1 mosaicism in MEN1 suspected patient but without MEN1 pathogenic variants (PV) at heterozygote state.

Methods

For that, we set up in routine a digital targeted NGS including unique molecular identifiers (UMIs). UMIs are tools for improving molecular detection of rare events in somatic DNA. We established the analytic performance of such method. Next MEN1 mosaicism was then looked for in a cohort of unresolved MEN1 cases addressed in the molecular biology laboratory between 2017 and 2019.

Results

For MEN1, sensitivity was 100% for detecting the variants up to an allelic frequency (AF) of 1%. By using UMIs, false positives were reduced by 98.4% for MEN1. Among a cohort of 119 patients harboring from 2 to 5 MEN1 lesions, we identified 3 patients with MEN1 mosaic PVs. The allelic frequencies ranged from 2.3 to 9.5%. The detection rate of MEN1 mosaicism in patients bearing at least 3 MEN1 lesions was 17% (3/18). No cases are detected in patients with 2 lesions.

Conclusion

we reported here 3 new cases with MEN1 mosaicism. This study deciphered the performances of UMI in MEN1 mosaic diagnosis in routine and underlined that the frequency of mosaicism is probably underestimated in MEN1 suspected patients.

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OC6.4

Clinical correlates of a large Israeli cohort of Cys 618 Arg RET mutation

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Introduction

A syndrome of MEN2A and Hirschsprung’s disease described in Israeli Jews of Moroccan descent is caused by Cys 618 Arg mutation, one of the less common causes of MEN2A. We aimed to define the clinical characteristics of a large cohort with this mutation from a multi-center Israeli registry.

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Methods
The Israeli MTC registry including 8 centers was searched retrospectively for results of RET mutational analysis. Patients with a Cys 618 Arg mutation belonging to a single large extended family were included in the study, as were their first-degree family members with MTC without available genetic test results. Clinical, laboratory and pathological data, as well as long-term surveillance data were retrieved.

Results
Of the 274 patients in the Israeli registry, 53 (19.3%) had documented RET mutations, and 29/53 (54.7%) had the Cys 618 Arg mutation. Through development of a family tree spanning five generations, a familial connection was determined for 28/29 patients, descendants of one large family of Moroccan Jewish descent. Another 4 patients from the MTC registry without available genetic test results belonged to this extended family. Clinical and pathological data pertaining to these 32 patients was analyzed. Nineteen patients (59%) were female; mean age at surgery was 26.6 ± 12.8 years. Tumor size was 10.8 ± 9.3 mm. Extrathyroidal extension was described in 4/19 (21.0%); vascular invasion in 5/18 (27.8%); multifocality in 17/21 (81.0%) and bilateral lesions in 17/22 (77.3%). Ki67 was mentioned for only one patient and was 3%. Lymph nodes were removed in 8 patients, and metastases found in 3. Extraneural extension was found in 1 case. Three patients had distant metastases at diagnosis. Of 22 patients with one-year follow-up, 11 were cured, 10 had persistent disease and 1 suffered disease-related mortality. Of those with persistent disease, 6 were biochemical, 2 structural and 2 unknown. Surveillance duration was 9.3 ± 12.9 years. Recurrence occurred in 4/19 patients (21.2%), 3 with distant metastases. Seven patients had additional therapy: 4 surgery, 2 radiotherapy and 1 tyrosine kinase inhibitors. One more patient died during follow-up; whether his death was disease-related is unclear. Comorbidities included pheochromocytoma in 2 patients, Hirschsprung disease in 2 and primary hyperparathyroidism in 1 patient.

Conclusion
The prevalent RET mutation in Israel is Cys 618 Arg, and almost all cases are linked to one large family of Moroccan Jewish descent. Genotype-phenotype correlation are similar to that described previously with cases of pheochromocytoma and Hirschsprung disease, arising from pleural mesothelial cells, generally due exposure to asbestos. Of note, different growth factors and their receptors are involved in the pathogenesis of MPM and resistance to therapy. Chemotherapy with cisplatin (cis/PEM) remain to be elucidated. Thus, in the present study, we assessed the antitumor effect of chemotherapy in human malignant pleural mesothelioma.

Glioblastoma (GBM; grade iv astrocytoma) is one of the most devastating endocrine-related cancer worldwide based on its locally aggressive behavior and because it cannot be cured by current therapies. Therefore, the identification of novel diagnostic and prognostic biomarkers, and especially efficient therapeutic targets is urgently needed. In this sense, defects in alternative splicing process are associated with poor survival and high aggressiveness in cancer, including GBM. Specifically, splicing factor SF3B1 (splicing factor-3b-subunit 1) is an essential and druggable component of spliceosome (machinery responsible for splicing process), has been identified as a key dysregulated factor in some endocrine-related cancer (e.g. prolactinomas and breast cancer); however, the oncogenic association with molecular features and clinical parameters have not been characterized in GBM, nor its putative therapeutic potential. Therefore, different human cohorts and dataset from different glioma mouse models were analyzed to determine the mutation frequency as well as the gene and protein expression levels between tumor and control samples of SF3B1. SF3B1 expression was also explored at the single cell level across all cell subpopulation and transcriptomic programs. The association of SF3B1 expression with relevant clinical data in different human cohorts was also analyzed. Moreover, different functional (proliferation/migration/tumorspheres-formation/ VEGF-secretion/apoptosis) and molecular/mechanistic (gene expression/signaling-pathways) assays were performed in different glioblastoma cells models (human primary-cultures and cell-lines) in response to SF3B1 blockade (using pladienolide B treatment). Additionally, tumor onset, formation and progression were monitored in response to SF3B1 inhibition in a preclinical model. Our data provide novel evidence demonstrating that SF3B1 is low-frequency mutated in human gliomas (1%) but widely overexpressed in glioblastoma compared with control samples from different human glioma models through which we characterized SF3B1 levels are associated with key molecular and clinical features (e.g., overall survival, poor prognosis and/or drug-resistance). Remarkably, in vitro and in vivo blockade of SF3B1 activity with pladienolide B drastically altered multiple glioblastoma pathophysiological processes (i.e.; reduction in proliferation, migration, tumorspheres-formation, VEGF-secretion, tumor initiation and increase in apoptosis) likely by suppressing Akt/mTOR/catenin pathways, causing an imbalance of BCL2L1 splicing. Together, we highlight...
Somatic mutations in splicing factor 3 subunit B1 (SF3B1) were found in about 20% of PRL-secreting PitNETs. SF3B1 is involved in pre-mRNA splicing and required for assembly of the U2 complex, which is critical for branch site recognition and the early stages of spliceosome assembly. Patients with mutant prolactinomas showed higher PRL levels and shorter progression-free survival compared to wild-type patients. Aims of the present study were: 1) to characterize the genetic profile of a cohort of 14 patients with PRL-secreting PitNETs, searching for somatic mutations in SF3B1 hotspot region; 2) to test the effects of SF3B1 inhibitor pladienolide-B on tumoral lactotroph cells; 3) to investigate dopamine receptor type 2 (DRD2) agonist effects in tumoral lactotroph cells silenced for SF3B1. We found no SF3B1 mutated patients in our cohort. In rat PRL-secreting pituitary tumoral cells MMQ, pladienolide-B was effective in reducing cell proliferation (-40 ± 10% at 20 μM, P < 0.001 vs basal), viability (-42 ± 7% at 10 nM, P < 0.05 vs basal) and in promoting apoptosis (6-fold increase at 50 nM, P < 0.05 vs basal). In primary cultured cells from one PRL-secreting PitNET, bearing wild-type SF3B1, pladienolide-B reduced cell proliferation and cyclin D3 expression and increased cell apoptosis. SF3B1 silencing in MMQ cells induced a reduction of DRD2 expression (-51 ± 13.2%, P < 0.001 vs control cells). Moreover, in MMQ cells lacking SF3B1, cabergoline completely lost its ability to reduce cell proliferation (-22 ± 4.8%, P < 0.001 vs basal), AKT phosphorylation (-31 ± 24.6%, P < 0.01 vs basal), cyclin D3 expression (23 ± 7.6%, P < 0.05 vs basal) and to increase p27 (+20 ± 8.6%, P < 0.05 vs basal). Interestingly, cabergoline treatment reduced SF3B1 protein expression levels in MMQ cells (-60 ± 40%, P < 0.05 vs control cells) and in primary cultured cells from 2 PRL-secreting PitNETs (-43 ± 6.4%, P < 0.01). In conclusion, our data demonstrated that SF3B1 inhibitor pladienolide-B exerts antitumoral actions in PRL-secreting PitNET cells bearing wild-type SF3B1. In MMQ cells, SF3B1 silencing reduced DRD2 expression and signaling, and cabergoline negatively regulated SF3B1 expression.
Background
Osilodrostat is a potent oral inhibitor of the adrenal enzymes aldosterone synthase and 11b-hydroxylase and decreases glucocorticoid and mineralocorticoid production and secretion. Phase 2 and 3 studies from the osilodrostat clinical trial program have demonstrated the drug’s efficacy and safety in patients with Cushing’s disease. Osilodrostat received European Marketing Authorization (MA) for the treatment of Cushing’s syndrome (CS) in adults.

Objective
Evaluate the use of osilodrostat for the treatment of CS in clinical practice in France (Autorisation Temporaire d’Utilisation [ATU], post-ATU, post-MA, authorization IDRCB2021A0140140).

Methods
This multicentre analysis included patients with CS who were treated with osilodrostat between 2019 and 2021. Causes of CS, therapeutic approaches, dosages, and efficacy and safety of osilodrostat were analysed in patients where data was available.

Results
Patients (n = 107) with CS aged 11–85 years were analysed; 68 patients were female and 39 were male. At diagnosis, urinary free cortisol (UFC; median ± standard deviation (SD) [range; n]) was 135 µg/24 h ± 1703 (10–27188; n = 79). Causes of CS in these patients include ACTH-dependent (Cushing’s disease [n = 57]; ectopic [n = 28]; uncertain [n = 5]) and ACTH-independent (adrenocortical carcinoma [n = 9]; macronodular adenocortical hyperplasia [n = 5]; adrenocortical adenoma [n = 2]). UFC levels (median ± SD [range; n]) at the time of initiating osilodrostat therapy were 135 µg/24 h ± 1703 (5–10000; n = 78). Regarding therapeutic approaches (n/N, %), 17/87 patients (20%) received osilodrostat as first-line therapy, whereas 36 patients (41%) received it as second-line therapy. Methods of osilodrostat administration included: titration (59/95, 62%), block and replace (9/84, 11%) and titration followed by block and replace (33/95, 35%). The initial osilodrostat dose (median ± SD [range; n]) was 4.0 mg/day ± 8.7 (1–60; n = 96), whereas the maximum dose was 12.0 mg/day ± 18 (1–80; n = 103). UFC normalization with osilodrostat was achieved in 64/78 patients (82%). Improvements of clinical signs and symptoms were reported in 67/95 patients (75%), and improvement of comorbidities with osilodrostat was reported in 39/62 patients (63%). In terms of safety in patients treated with osilodrostat, adrenal insufficiency was reported in 30/91 patients (33%) and hyperandrogenism was reported in 6/54 patients (11%).

Conclusion
These findings from clinical practice confirm the efficacy of osilodrostat in patients with various aetiologies of CS, in agreement with the European MA. These findings from clinical practice confirm the efficacy of osilodrostat in patients with various aetiologies of CS, in agreement with the European MA. The study also suggests that osilodrostat is a safe and effective treatment option for CS in clinical practice.

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See also: OC7.5

OC7.5
Epigenetic and somatic mutation profile of pituitary adenomas (PAs)/pituitary neuroendocrine tumors (PinNETs)
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Background
Pituitary adenomas (PAs)/pituitary neuroendocrine tumors (PinNETs) are a complex and heterogeneous group of lesions. Genetic and epigenetic studies have been performed to identify predictors of treatment outcome.

Study aim
To profile clinically non-aggressive (NA) and aggressive (A) PAs/PinNETs, and carcinomas for somatic mutations and epigenetic alterations of genes involved in cell proliferation/differentiation, miRNA/incRNA-post-transcriptional regulators, and therapy targets.

Patients and Methods
64 NA and 41 A PAs/PinNETs (40 males; 21 ACTH-, 50 FSH-/LH-, 16 GH-, 3 GH/PRL-, 12 PRL-secreting; 1 null cell; 2 plthromurmal PTT-1+) and 6 carcinomas (3 males; 3 ACTH-, 2 PRL- and 1 FSH/H-secreting) treated by endoscopic surgery from 2003 to 2017, with ≥ 1-year follow-up were included. Clinicoradiological and histological data were collected. Somatic mutations of 17, and DNA methylation of 22 genes were assessed in fresh frozen and/or formalin-fixed paraffin-embedded tumor tissue (20% VAF and 100x coverage in both strands). Ten normal pituitaries were used as control.
OC8.1 Effectiveness of anti-resorptive drugs on risk of vertebral fractures in women receiving aromatase inhibitors: a prospective study in real-life clinical practice

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Bone loss is a frequent complication of aromatase inhibitors (AIs) therapy in women with breast cancer. Bone-active drugs are effective in protecting the skeleton from detrimental actions of AIs. However, bone mineral density (BMD) was the primary end-point in most of published studies, whereas data on fractures were scant and mainly limited to denosumab. In this prospective study, we investigated the effects of denosumab, oral bisphosphonates and intravenous zoledronate on risk of morphometric vertebral fractures (VFs; primary end-point) and BMD at lumbar spine, femoral neck and total hip (explanatory end-point). To address these aims, 567 consecutive women (median age 62 years, range 28- 83) were evaluated for BMD and clinical outcomes at baseline and after 18-24 months of follow-up. The inclusion criteria were: 1) hormone receptor-positive breast cancer with morphometric VFs at baseline and after 18-24 months of follow-up. The primary end-point was defined as the occurrence of new fractures.

The efficacy of anti-osteoporotic medications, risk of VFs resulted to be significantly decreased by denosumab (odds ratio (OR) 0.22, 95% confidence interval (CI) 0.11-0.46; P<0.001) and zoledronate (OR 0.27, 95% CI 0.10-0.73; P=0.001), but not by oral BPs (95% CI 0.64; P=0.89-0.91). Stratifying women for type of anti-osteoporotic medications, risk of VFs resulted to be significantly decreased by denosumab [odds ratio (OR) 0.22, 95% confidence interval (CI) 0.11-0.46; P<0.001] and zoledronate (OR 0.27, 95% CI 0.10-0.73; P=0.001). Stratifying women for type of anti-osteoporotic medications, risk of VFs resulted to be significantly decreased by denosumab [odds ratio (OR) 0.22, 95% confidence interval (CI) 0.11-0.46; P<0.001] and zoledronate (OR 0.27, 95% CI 0.10-0.73; P=0.001). All anti-osteoporotic medications induced significant increase in median BMD at any skeletal site, whereas BMD decreased significantly in women who were not treated with bone-active drugs. In conclusion, this prospective study, reflecting the real-life clinical practice, shows that in women exposed to AI therapy, denosumab and zoledronate are more effective than oral BPs in decreasing the risk of VFs during the first 24 months of treatment. Future prospective studies will clarify whether in the long-term also oral BPs
could reduce the risk of fractures in women exposed to estrogen-deprivation therapies.

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OC8.2

SGLT2 inhibitor treatment does not increase risk of osteoporotic fractures compared to GLP-1 receptor agonists: a Danish population-based cohort study

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Background
Type 2 diabetes mellitus (T2D) is associated with an increased risk of fractures. Research on the effects of sodium-glucose cotransporter 2 (SGLT-2) inhibitors is scarce and unsettled. We aimed to investigate the risk of major osteoporotic fractures (MOF) – i.e., hip, vertebral, humerus, and forearm fractures – with SGLT2 inhibitors compared to glucagon-like peptide 1 (GLP-1) receptor agonists when either is used in combination with metformin.

Methods
We conducted a population-based cohort study using discharge diagnosis codes from the Danish National Patient Registry and data on all redeemed drug prescriptions from the Danish National Prescription Registry. Subjects treated with metformin in combination with either SGLT2 inhibitors or GLP-1 receptor agonists between 2012 and 2018 were identified. Subjects were then propensity-score matched 1:1 based on age, sex, and index date. Survival curves were plotted using the Kaplan-Meier estimator. A Cox proportional hazards model was utilized to estimate crude and adjusted hazard rate ratios (HR) for MOF. Finally, Aalen’s Additive Regression (AAR) model was used to examine a possible additive rather than multiplicative effect of SGLT2 inhibitors on fracture hazard while allowing time-varying covariate effects.

Results
We identified 27,543 individuals treated with either combination. After matching, 18,390 individuals were included in the main analysis (9,190 in each group). Median follow-up times were 355 [interquartile range (IQR) 126-780] and 372 [IQR 136-766] days in the SGLT2 inhibitor and GLP-1 receptor agonist group, respectively. The crude HR for MOPF was 0.77 [95% CI 0.56-1.04] with SGLT2 inhibitors compared to GLP-1 receptor agonists. The fully adjusted model yielded a lower HR of 0.76 [95% CI 0.56-1.04]. Results were similar across subgroup and sensitivity analyses. Similarly, the multivariate AAR model yielded a non-significant difference between the two exposure groups.

Conclusion
These results suggest that SGLT2 inhibitors have no effect on fracture risk when compared to GLP-1 receptor agonists. This is in line with results from previous studies.

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OC8.3

Impact of preoperative zoledronic acid on hungry bone syndrome and bone health indices in patients with primary hyperparathyroidism after curative parathyroidectomy: a randomized controlled trial

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Background
In individuals with primary hyperparathyroidism (PHPT), the utility of preoperative bisphosphonate administration in prevention of post-curative-parathyroidectomy hungry bone syndrome (HBS) and effects on long-term bone accrual are uncertain.

Objectives
To estimate the effect of preoperative administration of single infusion of zoledronic acid (ZA) on occurrence of HBS and gain in bone mineral density (BMD) at one year in individuals with PHPT undergoing curative parathyroidectomy.

Methods
In this single-centre, randomized (1:1), single-blind, placebo-controlled study (CTRI/2019/10/021762), a total of 48 adults (age > 18 years) with PHPT (serum Calcium ≥ 11 mg/dl) were enrolled. Prior to parathyroidectomy (≤ 2 weeks), participants received either a single intravenous infusion of 5 mg ZA (n = 24) or placebo (n = 24). Post-curative-parathyroidectomy, participants were monitored for occurrence of HBS until discharge. HBS was defined by the presence of hypocalcemia (Ca < 8.5 mg/dl) and hypophosphatemia (P < 2.7 mg/dl) with rise in alkaline phosphatase (ALP) (> 5%) on any day after surgery. BMD (Hologic Discovery 4500) and trabecular bone score (TBS) were assessed at baseline and one year after surgery. In addition, bone turnover markers (CTX, PINP) were assessed at baseline, first week, 3-, 9- and 12-months post-surgery. Occurrence of HBS was assessed using binary logistic regression model. Changes in BMD and BTM were assessed using linear mixed model for repeated measures.

Results
Forty five out of 48 participants had successful curative parathyroidectomy. HBS occurred in 6 (27.3%) individuals in ZA and in 0 (26.1%) in placebo group (OR: 1.06 (0.28 - 3.98); P = 0.928). The odds for developing HBS were comparable after adjusting for baseline severity and serum 25(OH)D levels (P = 0.075). Individuals in ZA group had a higher gain in BMD at lumbar spine (7.54%; 95% CI, 0.06 to 15.02; P = 0.048), comparable gain at neck of femur (9.74%; 95% CI, 5.005 to 24.49; P = 0.190) and a fall in BMD at distal radius (3.29%; 95% CI, -10.17 to 2.31; P = 0.008). Rise in TBS was comparable between the two groups (P = 0.396). The higher gain in BMD at lumbar spine was paralleled by a higher decline in CTX (27.8%; 95% CI, -48.44 to -7.12; P = 0.009) in ZA group while ALP (10.9%; 95% CI, -23.39 to 1.44; P = 0.082) and PINP levels remained comparable (9.50%; 95% CI, -22.36 to 41.37; P = 0.360).

Conclusion
In PHPT, preoperative administration of single infusion of ZA is associated with increased bone mineral accrual at lumbar spine without significant effect on occurrence of HBS.

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OC8.4

Is the “rebound phenomenon” following Denosumab discontinuation a risk factor for Zoledronic acid acute phase adverse reactions? 

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Background
Zoledronic acid (ZOL) administration may cause acute phase adverse reactions (APR), which manifest with fever, malaise, bone and muscular pain, headache

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Conclusions
1.002, 95% CI 1.000-1.003, significantly associated with an increased risk of moderate-severe APR post ZOL in patients. In our cohort of VitD sufficient patients, CTX seems to be the only factor associated with APR.

Methods
we retrospectively evaluated 112 patients (56 postDmab and 56 naïve) treated with ZOL 5 mg intravenously for osteoporosis in our center during the last 24 months. Bisphosphonates treatment preceding ZOL administration, including previous ZOL infusions, was considered an exclusion criterion. All patients were taking vitamin D and calcium. In all patients we evaluated femoral neck (FN) and lumbar spine (LS) bone mineral density (BMD), C-terminal telopeptide (CTX) and VitD levels.

Results
PostDmab patients were older (71.4 ± 8.7 vs 65.1 ± 11.4 years, P=0.001), had higher BMD (LS T-score -2.3 ± 0.8 vs -3.1 ± 1.2, P=0.0001, FN T-score -2.0 ± 0.8 vs -2.4 ± 0.8, P=0.011) and lower CTX levels (452 ± 350 vs 630 ± 307 ng/ml P=0.0088) as compared to naïve patients, while the prevalence of fractures (56.3 vs 43.8% P=0.333; respectively postDmab and naïve) and the VitD levels (40.4 ± 13.9 vs 42.8 ± 23.1 ng/ml P=0.509; respectively postDmab and naïve) were comparable in the two groups. No difference was found in the overall APR rate (65.3 vs 58%, P=0.156; respectively postDmab and naïve) or in the moderate-severe APR rate (34.7% vs 42%, P=0.156 respectively postDmab and naïve) between the two groups. The logistic regression analysis showed a significant association between CTX levels and the occurrence of moderate-severe APR, regardless of age, group (naïve or postDmab) and VitD levels (OR 1.002, 95% CI 1.000-1.003, P=0.027).

Conclusions
In our cohort of ZOL treated patients we found a higher incidence of APR than reported in literature without significant differences between postDmab and naïve patients. In our cohort of VitD sufficient patients, CTX seems to be the only factor significantly associated with an increased risk of moderate-severe APR post ZOL infusion.

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OC8.6
Dose-range analysis of the effects of the long-acting parathyroid hormone analog AZP-3601 versus PTH(1-34) delivered by daily injection or continuous infusion on blood calcium levels and bone metabolism in thyroparathyroidectomized (TPTX) rats

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AZP-3601, a long-acting PTH/PTHrP(1-36) analog, is a candidate new treatment option for hypoparathyroidism (HP). As compared to conventional PTH(1-34), AZP-3601 binds with higher affinity to the R0 conformation of the PTH-1 receptor, resulting in prolonged signaling and sustained elevations in blood calcium (Ca$^{2+}$) in vivo, despite a very short circulating half-life. We assessed whether repeated injection of AZP-3601 into TPTX rats at doses aimed to normalize serum Ca$^{2+}$ levels would produce different effects on bone than PTH(1-34) administered either intermittently or continuously.

Methods
Male S-D rats at age 9 weeks and 2 weeks after TPTX surgery received either a daily sc injection of AZP-3601 at doses of 1.0, 2.0 or 4.0 nmol/kg, daily sc injection of PTH(1-34) at 307 pg/ml, 350 vs 630 nmoI/kg daily sc injection of PTH(1-34) at 50, 100 or 150 nmol/kg, or continuous infusion of PTH(1-34) via ALZET mini pump at 1.5, 2.0 or 3.0 nmol/kg/day (n=8/group) for 16 days, TPTX controls received vehicle injections or infusion. Tail vein blood Ca$^{2+}$ was analyzed on days 7 and 14 at 6 h post-injection. Rats were euthanized on day 16 (24 h post injection) and blood and femurs collected for analysis.

Results
Each treatment modality resulted in dose-dependent increases in blood Ca$^{2+}$ levels. Optimal doses for raising blood Ca$^{2+}$ to normal range (1.2-1.4 mM vs 0.9-1.1 mM in TPTX-vehicle controls, P<0.001) on days 7 and 14 were identified as 1.0 nmol/kg for AZP-3601 daily injection, 50 nmol/kg for PTH(1-34) daily injection and 3.0 nmol/kg/day for PTH(1-34) continuous infusion. Effects on bone markers and uCT parameters at these optimal doses were as follows: Continuous infusion of PTH(1-34) significantly increased serum levels of the bone formation marker PINP (P=0.03) and the bone resorption markers CTX1 (P=0.02) and TRAP-5b (P=0.03), and decreased distal femur trabecular (Tb) bone volume relative to tissue volume (BV/TV, P=0.002), as well as mid-femur cortical thickness (Ct.Th P=0.01). Daily injection of PTH(1-34) significantly increased serum PINP (P<0.001) and TRAP-5b (P=0.001), and increased distal femur trabecular BV/TV (P=0.01) as well as mid-femur cortical thickness (P=0.02). Daily injection of AZP-3601 caused no significant change in these bone turnover and structural parameters.

Conclusion
At doses that similarly normalized blood Ca$^{2+}$ levels in TPTX rats, continuous infusion of PTH(1-34) was bone-catabolic, daily injection of PTH(1-34) was bone-anabolic and daily injection of AZP-3601 was bone-neutral. The distinct mechanism used by AZP-3601 may lead to less impact on bone, as compared to either daily injection or sustained, continuous delivery of PTH(1-34), when used as chronic treatments for HP.

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OC8.5
Key4OI: Development and implementation of a standard set of outcome measures for osteogenesis imperfecta
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Key4OI : Development and implementation of a Standard set of Outcome measures for Osteogenesis Imperfecta. Osteogenesis Imperfecta (OI) is a genetic disorder also known as ‘brittle bone disease’. The clinical manifestation of OI shows a wide variation. Therefore, care for patients with OI requires an interdisciplinary approach. The effectiveness of particular interventional and treatment protocols of interdisciplinary teams is not clear due to a non-standardized and wide variation of patient outcomes thus making the comparison of outcome measures available in the literature difficult. In 2018 the Key4OI project was started, an international interdisciplinary working group of 27 experts used a consensus-driven modified Delphi approach to develop a set of global outcome measures for patients with OI. More than 400 different outcome measures were identified in our literature search. After three Delphi rounds, 24 domains were selected. After the focus group sessions with members from OI community, the number of domains were reduced to 15. A consensus was reached on the measuring instruments to cover these domains for both children and adults. The entire approach was in line with the International Consortium for Health Outcomes Measurement (ICHOM) methodology. The Key4OI project resulted in a standard set of outcome measures focused on the needs and wishes of individuals with OI and their families. This outcome set will enable healthcare teams and systems to compare and to improve their care pathways and quality of care world. Implementation was started in 5 different countries (6 hospitals): China, Norway, USA, Canada and the Netherlands (Isala Zwolle and UMC Utrecht). Various other countries will start implementation in 2022. Anton Franken, D. Mekking on behalf of the international Key4OI expertgroup.

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OC9.1
Higher free thyroxine associated with PFAS exposure in first trimester. The odense child cohort
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Background
Perfluoroalkyl substances (PFAS) are endocrine disrupting chemicals, with elimination half-lives ranging from four to eight years. Experimental studies found PFAS able to interfere with thyroid hormone-binding proteins. During the first 20 weeks of gestation (GW), the fetus is reliant on placental transfer of maternal thyroid hormones, mainly free thyroxine (FT4). However, previous studies investigating associations between exposure to PFAS and thyroid hormone status mainly focused on blood samples from late pregnancy or umbilical cord with mixed findings.

Objectives
To investigate associations between concentrations of PFAS and FT4 and thyroid stimulating hormone (TSH) in early pregnancy.

Methods
In Odense Child Cohort (OCC), a single-center study, we measured maternal pregnancy serum concentrations of five PFAS: perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA); and FT4 and TSH in 1,048 pregnant women at median gestational week 12 (25th, 75th percentiles: 10, 15). Multivariate linear regression models were performed to estimate associations between concentrations of PFAS and FT4 and TSH.

Results
included women had a mean age of 30.2 (± 4.5 SD) years and median pre-pregnancy BMI of 23.5 (5th, 95th percentiles: 19.2, 32.5) kg/m², and 58.7% were nulliparous. A doubling in PFOS, PFOA, and PFNA concentrations was associated with an increment in FT4 concentration by 1.85% (95% CI: 0.66%, 3.05%), 1.29% (95% CI: 0.21%, 2.39%), and 1.70% (95% CI: 0.48%, 2.94%), respectively, in adjusted analyses. A statistically significant dose-response relationship was observed across exposure quartiles for PFOS, PFOA, and PFNA in the association with FT4. No association was found between concentrations of PFAS and TSH in adjusted analyses.

Conclusion and perspectives
Exposure to PFOS, PFOA, and PFNA was associated with higher FT4 concentrations in women during early pregnancy. Our observed associations between exposure to PFAS and FT4 concentrations were small in magnitude, nonetheless, the effects may be greater in populations with higher concentrations of PFAS exposure. The clinical significance of these findings remains to be elucidated. At population level, the demonstrated potential disruption of maternal thyroid hormone status in response to PFAS exposure during early pregnancy may affect offspring neurodevelopment. Hence, the findings are of general public interest, which supports the necessity of a follow-up of offspring in the OCC to assess putative long-term implications on neurodevelopment.

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OC9.2
Effect of legacy and new generation PFAS on thyrocyte function
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OC9.3
Transcriptional profiling of developing male rat perineum and phallus following exposure to the anti-androgenic fungicide triticonazole
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Perfluoroalkyl substances (PFASs) have been claimed as thyroid disrupting chemicals since the exposure to several PFASs was significantly associated with thyroid hormones derangements. Demographics such as sex, age, and disease status likely influence the associations between PFASs exposure and thyroid hormones since major hypothyroidism effects were observed among pregnant women and infants. This study aims to evaluate the possible impact of legacy and new-generation PFAS exposure on the thyroid stimulating hormone (TSH) receptor (TSHR)-mediated effects on available cell models of thyrocytes. Based on their surfactant properties, PFAS are supposed to interfere with the cell function through the alteration of the biophysical properties of plasma membrane. FRTL-5 normal rat thyroid follicular cell line was exposed to C6O4, perfluorooctanoic-acid (PFOA) or perfluoro-octan-sulphonate (PFOS) at a concentration ranging from 0 ng/ml (CTRL) to 100 ng/ml for 24 hours and the possible cell accumulation was evaluated by LC-MS/MS. The cell content of all tested PFAS was below the limit of detection and, accordingly, membrane fluidity evaluated by Merocyanin 540 (MC540) showed no obvious variation showed no variation compared to CTRL. The quantification of intracellular cAMP levels upon stimulation with 10 µM of TSH for 30 minutes showed a significant reduction, compared to CTRL sample, when cells were exposed for 24 hours exposure to PFAS. A dose-dependent effect detected for PFOA whilst, for C6O4 and PFOS, a sharp blunt of cAMP was observed at the lowest concentration tested. The possible interaction of TSHR with PFAS was evaluated by computational docking methods, addressing the possible binding of C6O4 or PFOA to TSHR extracellular domain. Molecular dynamics also showed that the receptor bound by C6O4 or PFOA displayed major conformational differences related to the unbound receptor. Specifically, the root-mean-square deviation (RMSF) profile of the atomic positions in LEU100-GLN170 range, the most involved in the binding to TSH, showed a modified flexibility than the unbound structure, particularly for PFOA. The cell iodide uptake upon 10 µM TSH stimulation was then evaluated with the Sandell-Kolthoff (SK) reaction. Stimulation with TSH was associated with a strong and significant increase of the intracellular iodide levels in CTRL conditions. Differently, the exposure to PFOA was associated with a significant reduction of iodide uptake at the highest concentration tested of 10 ng/ml, whilst C6O4 and PFOS were essentially unaffected. Further gene expression experiments are planned to clarify whether this effect is mediated by the down-regulation of downstream event related to TSHR-signaling.

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Androgen signaling is essential for male reproductive development and masculinization during fetal life. Developmental exposure to endocrine disrupting chemicals, not least those that disrupt androgen action, can lead to reproductive disorders such as cryptorchidism, hypospadias, and poor fertility. In rodent toxicity studies, as well as human epidemiological studies, a general biomarker for compromised fetal androgen signaling is a shorter
anogenital distance (AGD) in male offspring. Some outstanding questions, however, is if AGD is strictly sensitive to androgenic effects or if other signaling pathways are involved such as estrogen signaling. Similarly, penis development and hypospadias formation also involve additional signaling pathways, but which pathways that are vulnerable to developmental exposure to endocrine disruptors are not well characterized. Therefore, we need a better molecular understanding of how these tissues are regulated and vulnerable to chemical exposures. Trictonazo, an agricultural azole fungicide, inhibits androgen receptor activity in vitro and induces short AGD in male rat offspring following gestational exposure. Though trictonazo has anti-androgenic properties, we previously showed that intrauterine exposure does not affect the transcriptome of the fetal rat testes. We thus investigated the transcriptional effects in the androgen-sensitive fetal male rat perineum and phallus. Pregnant Sprague Dawley rats were exposed via oral gavage to trictonazo (450 mg/kg bw/day) or corn oil (control) from gestational day (GD) 7-21. Fetuses (n=11-12) were collected at GD17 or GD21 and perineum and phallus were isolated. Bulk RNA barcoding and sequencing (BRB-seq) was used to analyze the transcriptomes. The transcriptomes of the developing rat perineum and phallus changed significantly during late gestation, showing distinct regional differences between these adjacent tissues and revealing 2,703 differentially expressed genes (DEGs). The transcriptional changes induced by trictonazo exposure (100 DEGs) were different between perineum and phallus, but also between different stages of development. Interestingly, DEGs not only included several androgen receptor (AR) target genes, but also estrogen receptor (ER) target genes. Our results highlight the importance of considering chemical mode of action and spatiotemporal effects when using transcriptomics approaches in characterizing complex in vivo adverse outcomes in toxicity studies. These data furthermore constitute a rich resource for studying the spatiotemporal gene networks that are involved in the development of rat perineum and phallus and the regulatory networks that can be disrupted upon exposure to xenobiotics that prevent normal masculinization of the male fetus and lead to reproductive disorders.

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OC9.4

Morphostructural characterization of the testis in a large cohort of men living in highly polluted areas of Campania Region in south Italy: a focus on cadmium exposure

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Campania Region has been facing waste management crisis since 1980, characterized by urban, toxic and industrial waste illegal disposal, burning and incineration. Cadmium (Cd) is consistently shown to affect male reproductive function by multiple mechanisms, mostly elucidated in experimental models. The aim of the current single-center, observational, cross-sectional cohort study was to evaluate the prevalence of testis morphostructural alterations in a large cohort of men living in 3 municipalities of Campania Region (Acerra, Afragola, Giulianio) belonging to the high-environmental impact area “Land of Fires”, by addressing the potential association with seminal Cd (sCd) levels. Study cohort included 465 males (age range: 14-50 yrs mean: 29.5 ± 7.23 yrs). Morphostructural testis characteristics were assessed by ultrasound and sCd determination was performed in 385 samples by inductively coupled plasma-mass spectrometry. Prevalences of testis morphostructural alterations, unilateral or bilateral, included varicocele (35.4%), hydroscele (34.8%), parenchymal structure inhomogeneity (19%), hytoprotroky (14.6%), microthlipsisi (2.5%), solid lesions > 5 mm (0.2%). Participants with detectable sCd levels (n=128) displayed significantly reduced mean testicular volume (16.56 ± 4.68 vs 17.66 ± 4.34; P=0.0153) and higher prevalence of hytoprotroky (21% vs 10%; P=0.0059) and varicocele I-IV grade (47.5% vs 29.5%; P=0.0008), but not clinically relevant varicocele III-V grade (18% vs 11%; P=0.09), together with a slightly higher parenchymal structure prevalence of inhomogeneity (25.8% vs 16.7%; P=0.059) compared to participants with undetectable sCd levels (n=257). Furthermore, a significant difference in mean testicular volume was detected when comparing participants with sCd levels above (n=49) and below median value (n=79) and undetectable sCd levels, respectively (14.88 ± 3.79 vs 17.22 ± 5.03 vs 17.66 ± 4.34; P<0.001). sCd level was persistently correlated with mean testicular volume after correction for the presence of clinically relevant varicocele (r=-0.185; P=0.001). sCd levels was identified as the best predictor of mean testicular volume in linear regression analysis performed by setting sCd, smoking habit, age and BMI as independent variables. ROC curve analysis highlighted that a sCd level >0.76 µg/l correctly identified testicular hytoprotroky with a 60% sensitivity and 70% specificity. In conclusion, the current study demonstrated for the first time, in a large cohort of adult males living in high-environmental impact areas of Campania Region, an inverse relationship between sCd levels and mean testicular volume and prevalence of varicocele, independently from age, BMI and smoking habit, therefore further strengthening the concept of gonadal toxicity exerted by Cd, potentially explained by Cd-induced damage to testicular vascular endothelium.

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OC9.5

Decoding the role of environmental cadmium exposure in thyroid disorders

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As a ubiquitous present metal, cadmium (Cd) represents a matter of great concern, especially considering its potential thyroid disrupting capacity. The study evaluated the connection between this environmentally relevant metal exposure and thyroid hormone levels. The DecodExpo study enrolled 425 participants (207 males and 218 females) with various disorders (236 participants) and healthy controls (189 participants). Collected blood samples were digested, and Cd levels were determined by flame atomic absorption method (AAS GTA 120 graphite tube atomizer and FAAS, Agilent technologies, Santa Clara, CA, USA). In contrast, thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were measured in serum. The DecodExpo study evaluated the connection between this environmentally relevant metal exposure and thyroid hormone levels. The DecodExpo study enrolled 425 participants (207 males and 218 females) with various disorders (236 participants) and healthy controls (189 participants). Collected blood samples were digested, and Cd levels were determined by flame atomic absorption method (AAS GTA 120 graphite tube atomizer and FAAS, Agilent technologies, Santa Clara, CA, USA). In contrast, thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were measured in serum. The dose-response relationship between Cd in thyroid hormone disturbances was elucidated using a novel Benchmark dose (BMD) approach previously proposed as applicable to human data by the EFSA guidance. The Benchmark response (BMR) was set at 10% in the modeling procedure, expressed as an additional risk in% - an absolute change in response frequency divided by the benchmark (BMR) was set at 10% in the modeling procedure, expressed as an additional risk in% - an absolute change in response frequency divided by the additional risk in% - an absolute change in response frequency divided by the
Iodine nutrition among adolescent Faroese comply with recommen-
dations – are we home-safe?
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Introduction
Iodine nutrition is critical for human health. In recent years the main focus was on the developing brain during pregnancy. In addition, iodine nutrition is essential for growth and development during adolescence. Iodine nutrition was recently low within the recommended range among adult Faroese living on local, iodine-rich marine food items. Dietary habits among young generations are drifting away from local foods, and this raises a concern that led us to perform the first study of iodine nutrition among Faroese teenagers.

Method
We surveyed 14-year olds aiming for the number of participants recommended for a 90% precision of the estimated iodine nutrition level: Urin from one hundred twenty-nine girls (n = 65) and boys (n = 64) sampled in iodine-free containers. Iodine was measured using standard laboratory methods using the ceri/arsen method after alkaline ashing and creatinine. We calculated the iodine/creatinine ratio to adjust for dilution. A food frequency questionnaire recorded intake of iodine-rich foods.

Results
The median urinary iodine concentration was 166 μg/l, creatinine adjusted 124 μg/g. Iodine was in recommended range in 102 urine samples (79%), above the recommended range in 22 (17%), and in the range of insufficiency in 4%. No single sample suggested severe iodine deficiency. The urinary iodine concentration was markedly higher in those who reported higher “fish dinners per week” than those who reported limited or no fish intake.

Conclusion
Our nationwide study demonstrated Faroese teenagers to be iodine replete according to the WHO recommendations. However, the Faroese may have adapted to a high iodine intake from the formerly frequent intake of marine foods. Dietary habits change with new generations, and surveying iodine deficiency disorders is needed. In addition, the changing dietary habits emphasise the need for continuous monitoring of iodine nutrition.

Figure 1 Proportions of urinary iodine concentrations among 14-year-old Faroese boys and girls, from a population-based sample of 129 participants divided into the following groups: moderate (20-49), mild deficiency (50-99), adequate (100-199), slightly increased (200-299) and excess (300+).

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Diabetes, Obesity, Metabolism and Nutrition 3

OC10.1

Single-cell molecular and functional mapping of POMC neurons in obesity: a multi-modal approach
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The brain plays a crucial role in maintaining the body’s energy needs, a process involving the activity of a group of hypothalamic neurons that express the neuropeptidergic marker pro-opiomelanocortin (POMC). POMC neuronal dysfunction can cause obesity and its associated metabolic sequelae. However, this population of neurons is highly diverse at a molecular and functional level, and whether or not such heterogeneity is implicated in disease establishment or progression has yet to be elucidated. Here, using a lineage-tracing approach in combination with histological and electrophysiological tools, we have characterized POMC neuronal cells at a single-cell resolution in control of lean and diet-induced obese (DIO) mice. Thanks to this genetic strategy, we ‘traced’ with a reporter protein POMC neurons in adult mice, thus studying these neuronal cells independently from the expression of their main marker POMC. Different histological techniques, including immunohistochemistry, fluorescent in-situ hybridization, and RNAscope, have been used to cluster genetically ‘traced’ POMC neuronal cells based on their expression of the main marker POMC. Different approaches consistently allowed the identification of a previously uncharacterized sub-population that expresses negligible POMC mRNA and protein levels, which we named Ghost-POMC neurons. We also observed that Ghost-POMC neurons are insensitive to acute nutritional cues (fasting and refeeding) relative to ‘classic’ POMC positive neurons. Intriguingly, DIO mice presented an increased number of Ghost-POMC neurons relative to control animals. Furthermore, we developed an approach that combines whole-cell patch-clamp of traced POMC neurons with the subsequent molecular profiling of the patched cell by single-cell qPCR. Thanks to this approach, we observed that DIO leads to electrical alterations only in a fraction of POMC neurons expressing undetectable levels of POMC mRNA, which is reminiscent of the Ghost population previously identified by histological techniques. Thus, Ghost-POMC neurons might constitute a novel subpopulation of POMC neurons that undergo dysfunction in response to prolonged dietary cues, perhaps contributing to obesity establishment or progression.

Keywords: POMC neurons; heterogeneity; neuroanatomy; electrophysiology.

DOI: 10.1530/endobubs.81.OC10.1
OC10.2
Success in implementing changes in macronutrients intake in a high-protein and high-unsaturated fatty acids dietary intervention: 36-months results of the NutriAct randomized controlled multi-center trial
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Background & Aims
NutriAct is a 36-month randomized controlled multi-center trial aiming to analyze the effects of a dietary pattern focusing on a high-protein and high-unsaturated fatty acids (UFA) intake on healthy aging. We aimed to explore changes in intake of macronutrients and determine factors associated with a successful modulation of dietary pattern after 36 months in elderly community dwelling participants.

Methods
502 participants were randomized into a usual care control group including dietary recommendations of the German Nutrition Society or an intervention group, which used supplementation of rapeseed oil and specifically designed foods as well as repetitive advice to implement a food pattern based on high intake of predominantly plant proteins and UFA. Food intake was repeatedly assessed by 3-day food records at months 0, 3, 6, 12, 24 and 36 months. Linear regression models were carried out to investigate differences in changes in macronutrients intake between the intervention arms and determinants of modulation of dietary pattern during the intervention in 36 months.

Results
148 intervention and 164 control participants (median age 66 y, 36% males) with available food records at baseline and at month 36 were included. The intervention resulted in higher intake of protein, mono- and polysaturated fatty acids (MUFA and PUFAs) and fiber, and lower carbohydrate and saturated fat consumption (all P < 0.05). While individuals who were already at baseline closer to the NutriAct pattern also achieved a diet closer to the proposed pattern at month 36, the strongest relative changes of dietary behavior were seen in those with dietary patterns further away from the proposed pattern at baseline. Sex, age, baseline BMI, education, comorbidities, smoking, cognitive status and shared household were not associated to a higher implementation of the proposed diet.

Conclusions
A successfully modification of dietary pattern was achieved by the intervention within 36 months. Baseline dietary habits were substantial determinants predicting change in dietary pattern.

Table. Changes in macronutrients intake between baseline and month 36 between intervention and control groups

<table>
<thead>
<tr>
<th>Macronutrient</th>
<th>Beta coefficient (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (%E)</td>
<td>2.35 (1.44, 3.25)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Total fat (%E)</td>
<td>2.70 (1.00, 4.39)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Carbohydrate (%E)</td>
<td>-4.83 (-6.60, -3.05)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Sat. Fatty acids (%E)</td>
<td>-2.30 (-3.24, -1.32)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PUFAs (%E)</td>
<td>3.67 (2.70, 4.44)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>MUFA (%E)</td>
<td>0.82 (0.08, 1.60)</td>
<td>0.03</td>
</tr>
<tr>
<td>Fiber (%E)</td>
<td>3.64 (1.72, 5.56)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

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OC10.4
Variants in obesity-related genes in a population with early-onset obesity
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Introduction
Genetic testing can improve the diagnosis of rare genetic diseases of obesity and identify patients who may benefit from targeted therapeutic intervention. For example, patients with genetic defects in the melanocortin-4 (MC4R) pathway may present with severe early-onset obesity and hyperphagia. Historically, however, genetic testing in patients with obesity has been limited. The Uncovering Rare Obesity® diagnostic genetic testing program aims to enhance access to genetic testing for these patients. The frequency of rare genetic variants in this clinical patient population is currently unknown.

Methods
We sequenced 8599 individuals with severe, early-onset obesity as part of the US-based Uncovering Rare Obesity® program. Genes selected include those with well-established associations with obesity, as well as genes associated with the MC4R pathway. In this program, we sequenced 7811 individuals for 40 genes, and recently expanded the gene panel to include an additional 39 genes and the 16p11.2 chromosomal region; 788 individuals have been sequenced on the broader panel. Yield estimates were weighted by the number of individuals sequenced for each gene.

Results
Integrating across the two panels using weighted yield estimates, 54.6% of sequenced individuals had variants that may qualify them for commercial or institutional treatment with setmelanotide. An additional 9.9% of individuals had variants not eligible for setmelanotide treatment, but that may support a genetic diagnosis of obesity. Overall, 2.7% of individuals carried pathogenic or likely pathogenic variants that also met mode of inheritance criteria (2 or more alleles in autosomal recessive conditions and 1 or more alleles in autosomal dominant conditions).

Conclusions
In this selected cohort of individuals with severe, early-onset obesity, 64.5% carried potentially clinically relevant variants. As additional data become available about the investigational genes and obesity, and/or as new obesity-related genes are identified, these estimates may change. Genetic testing of patients with severe obesity, particularly those with a history of early-onset
Liver-expressed antimicrobial peptide 2 (LEAP-2) has been recently characterized as an endogenous GHSLR1a antagonist. LEAP-2 is produced mainly in the liver, and it was described that an acute ghrelin administration blocks food intake, GH release and normalizes glucose levels during chronic caloric restriction. For this reason, it could be considered as a key endocrine factor in the regulation of systemic energy metabolism. Nevertheless, the exact mechanism of action is still unknown. Our aim was to investigate the central LEAP-2 effects in energy homeostasis in mice with standard diet and in a ghrelin resistance mice model induced by diet. We used male C57BL/6 mice fed standard or high fat diet (60% fat, 12 weeks). We performed an acute or chronic ICV administration of vehicle, ghrelin, LEAP-2 or ghrelin and LEAP-2. Food intake, body weight and circulating cholesterol and leptin plasma levels were measured. Human HEK293 cells treated with oleic acid were used and they were co-treated with LEAP-2. Hepatic fat accumulation was analysed using oil red-O staining. Genes related to glucose and lipid metabolism were studied by qPCR. Statistical analysis conducted through t-student and ANOVA. The results obtained showed that LEAP-2 inhibits food intake, and body weight and in all the mice models studied and in an acute and chronic treatment. Moreover, chronic treatment is able to decrease the orexigenic response of ghrelin when they are co-administered. Furthermore, LEAP-2 decreases leptin and cholesterol plasma levels, and decreases the liver lipid content. When we analysed human hepatocytes treated with LEAP-2, they exhibit a lower lipid accumulation with a reduction in the expression of genes of gluconeogenesis and de novo lipogenesis in standard conditions and under oleic acid effect. As a conclusion, chronic central administration of LEAP-2 in mice antagonizes the major effects of ghrelin in vivo and the co-administration with ghrelin attenuates the ghrelin orexigenic and obesogenic effects, in a diet independent manner. Moreover, it decreases fat accumulation directly in human hepatic cells. These novel results place LEAP-2 as a counter-regulatory hormone in the ghrelin system, and as a promising therapeutic target in the treatment of obesity, MAFLD and other metabolic diseases.

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Thyroid 2

OC11.1

Thr92Ala polymorphism of the type 2 deiodinase (DIO2) is associated with higher risk of iatrogenic thyrotoxicosis in thyroidectomized subjects treated with levothyroxine and liothyronine

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Introduction

Hypothyroidism treatment is classically based on levothyroxine (LT4). However, 10% of hypothyroid patients treated with LT4 complain of hypothyroidism symptoms, despite normal thyroid stimulating hormone (TSH) serum levels. This “peripheral hypothyroidism” has been linked to decreased availability of free triiodothyronine (FT3), likely related to single nucleotide polymorphisms (SNP) in deiodinase genes (DIO), reducing enzymatic activity. Since Thr92Ala-DIO2 was associated to altered responsiveness to LT4, combined levothyroxine/liothyronine (LT4/LT3) therapy was suggested to improve quality of life in hypothyroid patients encoding Thr92Ala-DIO2.

Aims

To evaluate the influence of Thr92Ala-DIO2 variant on thyroid therapeutic compensation in thyroidectomized subjects treated with LT4 or LT4/LT3.

Methods

An interim analysis of a prospective, randomized, placebo-controlled, double-blind clinical trial was performed. Totally thyroidectomized patients treated with LT4 and with TSH levels within reference range in the previous 3 months were enrolled. Subjects were randomized in two groups: personalized-combined-twice-daily therapy with LT4/LT3 at 1:3:2:1 ratio (study group) and LT4 plus placebo (control group). Subjects were evaluated three times during the 6-month treatment. Iatrogenic thyrotoxicosis and hypothyroidism rates were assessed at each visit, measuring serum levels of TSH, FT4 and FT3. DNA was extracted from blood samples and the DIO2 genotype was analysed by Sanger’s sequencing. The Thr92Ala-DIO2 rate was calculated in both groups.

Results

A total of 139 patients (age 55.6±15; 12.1 years, TSH 1.3±15; 10.9 years) were enrolled, 70 in the study (age 55.1±15; 10.9 years) and 69
OC1.1

What you choose makes the difference: the first medical therapy for amiodarone-induced thyrotoxicosis has significant implications on cardiovascular events and hospitalizations

Danielle Cappellani1, Gia Cosentino1, Riccardo Morganti2, Luca Manetti1, Sileo1,2, Joris Osinga3,4, Edward Visser3,4, Arash Derakhshan3,4, Ferrari1, Anna Roux1, Alessandro Piovesan1

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Context
Amiodarone is a widely used anti-arrhythmic medication, however associated with a 15-29% rate of thyroid adverse effects. Amiodarone-induced thyrotoxicosis (AIT) is a rare disease due to diagnostic difficulties and therapeutic challenges. AIT patients often receive initial therapy for thyrotoxicosis before admission to a referral center. Whether the first-line medical therapy (i.e. therapies for thyrotoxicosis at first diagnosis of AIT) may affect the outcome of AIT patients is unknown.

Study design
Single-center historical-prospective cohort study of 313 AIT patients admitted to our university referral center for amiodarone-induced thyroid disorders.

Methods
Clinical and biochemical data at first diagnosis, at a referral center, and during the course of AIT were collected. The medical figure responsible for the first approach to the disease were recorded. Primary outcomes were cardiovascular (CV) events and hospitalizations. First-line therapies were appropriate when included glucocorticoids for type 2 AIT and methimazole for type 1 AIT at the approved dosage, either alone (optimal medical therapy, OMT) or in combination (right-dose combination therapy, RTC).

Results
34.5% patients received appropriate therapy (28.1% OMT and 6.4% RTC), whereas inappropriate therapies accounted for 65.6% of cases: specifically most patients initially approached by general practitioners and cardiologists received no therapy at all (56.9% and 30% respectively), whereas inappropriate therapies for the AIT-type (i.e. glucocorticoids for type 1 AIT and methimazole for type 2 AIT) was the most common therapy for patients originally approached by endocrinologists outside the referral center. CV events, and hospitalizations were more frequent in patients who received non-appropriate therapies (33.2% vs 4.5%, and 24.9% vs 6.5%, respectively; P < 0.0001 for both). Appropriate therapies reduced serum thyroid hormone concentrations (P = 0.018) at variance with non-appropriate therapies. The duration of exposure to thyrotoxicosis was longer in patients receiving non-appropriate therapies and was a risk factor for arrhythmias (HR 1.004, P = 0.0008), MACEs (HR 1.004, P = 0.020) and hospitalizations (HR 1.006, P < 0.0001).

Conclusions
The first medical therapy of AIT influences the exposure to thyrotoxicosis and the occurrence of cardiovascular events and hospitalizations.

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OC1.1.2

in the control group (age 56.0±18.3 years). Thr92Ala-DIO2 frequency (11.4%) was similar to general population (12.36%). Drop-out rate did not differ between groups (11.4 vs 14.5%, respectively, P = 0.591) and no difference was found for biochemical thyroid function examinations (considering also FT4/FT3 ratio) and LT4 pro-Kg dosage comparing study and control groups at baseline. Combined LT4/IT3 therapy resulted in more frequent iatrogenic thyrotoxicosis than LT4 monotherapy (9.8% vs 2.2%; P < 0.05), with a significantly higher incidence in Thr92Ala-DIO2 carriers. More frequent dose adjustments were required in the study group compared to controls (44.5% vs 22.5%; P = 0.001) and, among cases, in those with Thr92Ala-DIO2 compared to wild-type (52.0% vs 37.6%; P < 0.05).

Conclusion
Thr92Ala-DIO2 variant seems to have no influence on LT4 monotherapy effectiveness. In our interim analysis, carriers of Thr92Ala-DIO2 are at higher risk of iatrogenic thyrotoxicosis when treated with LT4/IT3: this result surprisingly suggests an increased enzymatic activity in SNPs carriers. Accordingly, the management of these patients is more challenging, requiring more frequent dose adjustments in the first six months of therapy.

DOI: 10.1530/endoabs.81.DC1.1.2

OC1.1.3

PD-1/PD-L1 inhibitors and immune-related thyroid toxicity according to pre-existing thyroid dysfunction and TPO antibody levels: a single centre experience

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Background
Immune checkpoint inhibitors (ICIs) have modified the outcome of several advanced malignancies. Thyroid dysfunctions (DYSTHYR) are the most common endocrine immune-related adverse events (IRAEs) during treatment with the programmed cell death protein-1 (PD-1) and its ligand (PD-L1) inhibitors. Data regarding predictive biomarkers enabling stratification of DYSTHYR risk are still limited.

Patients and methods
We retrospectively analyzed patients who started treatment with PD-1/PD-L1 inhibitors between 2017 and 2020 at Città della Salute e della Scienza Hospital (Department of Oncology). Both the onset of new DYSTHYR during ICI and the worsening of pre-existing DYSTHYR were recorded; patients with central hypothyroidism were excluded. In subjects without pre-existing hormonal thyroid alterations, it was evaluated the relationship between thyroid peroxidase antibody (Ab-TPO) level before the start of ICI and the onset of DYSTHYR during treatment. These patients were divided into two groups (MED-TPO+ and MED-TPO-) using the median Ab-TPO titer of the population as a cut-off value.

Results
In our cohort (median age 67 years, 70.7% males, 40.4% lung cancer, 95.4% anti PD-1 therapy), we observed a high frequency of DYSTHYR (80 out of 324 patients; 24.7%); thyrotoxicosis was detected in 7.7% of the population, while hypothyroidism occurred in 21% of subjects (after a median time of 1.8 and 3.7 months, respectively). Among cases with pre-existing thyroid hormonal alterations (14.5% of the sample), the worsening of DYSTHYR was found in 42.6% of cases after the start of ICI; the risk of DYSTHYR was significantly higher in comparison to patients without a thyroid disease history (OR 2.68 at univariate analysis, P = 0.03). Baseline Ab-TPO levels were available for 97 patients (Ab-TPO median value 12 UI/ml). Mean Ab-TPO level in the group with DYSTHYR during ICI (42.5 U/ml) was significantly higher than Ab-TPO titer in patients without DYSTHYR (16.1 U/ml, P = 0.0003). DYSTHYR after the start of ICI occurred in 33.9% of MED-TPO+ patients vs 7.9% of MED-TPO- subjects (P = 0.003); a significantly increased risk of developing DYSTHYR was observed in MED-TPO+ patients when compared to MED-TPO- cases (OR 5.98 at univariate analysis; P = 0.007).

Conclusion
Our data confirm the high frequency of DYSTHYR (mostly hypothyroidism) during PD1/PD-L1 inhibitors. We observed a greater risk of DYSTHYR during ICI in patients with pre-existing thyroid function alterations and in cases of higher baseline Ab-TPO level. These results may help the oncologist to identify the patients who are most likely to require an endocrinologist consultation during ICIs.

DOI: 10.1530/endoabs.81.DC1.1.3

OC1.1.4

Association of thyroid function and TPO positivity with the risk of postpartum depression: a population-based cohort study and systematic review

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Background
Postpartum depression (PPD) is a common mental health disorder with a major impact on maternal health and wellbeing and offspring development. Thyroperoxidase antibody (TPOAb) positivity is a major risk factor for
postpartum thyroiditis and via this link, it is hypothesized that TPOAb positivity is a risk factor for PPD. However, the results of currently available single center studies are heterogeneous and affected by major study limitations.

Objectives
To examine the association of TPOAb and thyroid function with the risk of PPD.

Methods
In the Generation R Study, a population-based prospective birth cohort in Rotterdam, the Netherlands, we measured TSH, FT4 and TPOAb in blood samples collected between 8-18 weeks of pregnancy. Postpartum depressive symptoms were assessed with the Edinburgh Postpartum Depression Scale (EPDS) at 2 months postpartum and with the Brief Symptom Inventory (BSI) at 2, 6 and 36 months postpartum. In addition, we performed a systematic review of literature assessing the association of thyroid function and/or TPOAb positivity with risk of PPD.

Results
There was no association of TSH or FT4 levels with the risk of postpartum depression (log TSH OR: 0.79, 95% CI: 0.56-1.13, P = 0.20; FT4 OR: 1.02, 95% CI: 0.96-1.08, P = 0.57). There was also no association of TPOAb positivity with PPD (OR: 0.79, 95% CI: 0.39-1.19, P = 0.39). Additional analyses assessed an impaired thyroidal response to TSH stimulation and defined the combined effects of a high TSH or low FT4 as an alternative marker of TPOAb positivity. We identified that an impaired thyroidal response to TSH stimulation was associated with a lower risk of PPD (P for interaction TSH = 0.04 and FT4 = 0.06). In our systematic review, ten out of 1219 identified articles were included: four studies showed an association of TPOAb positivity with PPD, two showed an association of thyroid function with PPD, the remaining studies showed no association of either thyroid function or autoimmunity with PPD.

Conclusions
Our original study is by far the largest study on this topic showing that neither TPOAb positivity nor TSH or FT4 were associated with PPD. Our systematic review revealed high heterogeneity and suboptimal methodological quality in the current literature, but overall does not support a link with PPD. Although TPOAb positive women should be monitored for postpartum thyroiditis, there does not seem to be an indication to screen for postpartum thyroiditis.


OC11.6
A new grading system for medullary thyroid cancer
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Introduction
Medullary thyroid carcinoma (MTC) is a neuroendocrine thyroidal cancer. World Health Organization recognizes a grading system for almost all neuroendocrine tumors; however, a shared grading system for MTC is still lacking. We performed a clinical and pathological review of 257 MTCs to evaluate which histologic features have an impact on the disease specific survival and to propose a new grading system.

Method
We retrospectively reviewed clinical data of 257 consecutive patients with sporadic MTC, surgically treated at the Endocrine Surgery Unit and followed at the University of the University Hospital of Pisa, from 2000 to 2018. In this cohort, MTC histopathologic variants (classical, follicular, papillary, oncocytic, clear cell, small cell and spindle cell), desmoplastic reaction (fibrosis ≥ 10%), number of mitosis for 10 high-power field (x10HPF), Ki67 percentage and necrosis were evaluated.

Results
Patients were followed for a median time of 9.3 years. The MTC variants were distributed as follows: 164/257 (63.3%) classical variant, 50/257 (19.3%) spindle cell variant and 43/257 (17.4%) other variants with a frequency <5% each. Desmoplastic reaction was present in 159/257 (61.9%). Number of mitosis and Ki-67 percentage higher than 2 were present in 57/257 (22.2%) and 97/257 (37.7%), respectively. Necrosis was present in 19/257 samples (7.4%). According to Kaplan-Meier analysis, MTC with desmoplastic reaction, mitosis number > 2, Ki-67 > 2% or necrosis had lower disease specific survival (P < 0.001). After preliminary analysis, we proposed the following grading system composed by desmoplastic reaction and Ki-67 percentage: high grade (presence of desmoplastic reaction and Ki-67 > 2%) and low grade (all other combinations). At Kaplan-Meier analysis, high grade MTC had lower disease specific survival compared to low grade (74.7% vs 98.6%, P < 0.001). Intriguingly, this grading system was able to predict DSM, both in intrathyroidal (stage I-II) (P = 0.034) and extrathyroidal (stage III-IV) MTCs (P < 0.001).

Conclusions
In our large MTC series, presence of desmoplastic reaction and necrosis, mitosis number x10HPF > 2, and Ki-67 > 2% were negative prognostic factors for DSM. Grading system composed by Ki-67 > 2% and desmoplastic reaction was able to identify the MTCs with the worst prognosis, both in low (I-II) than in more advanced (III-IV) stages.

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Reproductive and Developmental Endocrinology
OC12.1
The European Registries for Rare Endocrine Conditions (EuRRECa): the use of a core registry for collecting common data elements and clinician and patient reported outcomes
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Objectives
Despite the increasing role of molecular profiling, the association between mutation expression and pre-operative cytology for thyroid nodules has not been established.

Methods
We collected data on patients who underwent molecular profiling of thyroid nodules in Bethesda categories III to VI from two tertiary academic hospitals and via systematic literature review. We tested the associations between Bethesda categories and molecular mutation stratified by risk levels, according to the 2015 ATA guidelines. When thyroidectomy was preformed, we also evaluated association with postoperative diagnosis and aggressivity of disease based on histopathological variants, nodal metastasis or extra-thyroidal extension.

Results
We analyzed data from 452 nodules in our institutional cohort and 3912 nodules from the systematic literature review. A significant positive correlation was found between Bethesda categories and mutations, demonstrated by an increase in the intermediate to high-risk mutation rate in the higher BSRTC categories (Rs = 0.660, P ≤ 0.001). In the institutional cohort malignancy rate for BSRTC III and IV was 56.7% and 75.7%, respectively. The most common mutation was BRAFV600E with 95.9% (93/97) of those patients in Bethesda category V or VI (P < 0.001). All had confirmed thyroid cancer on pathology, with aggressive tumor behavior in most (60%). Patients with low-risk mutation, as H, K or N RAS alleles, showed association with Bethesda categories III and IV (P ≤ 0.01). In mutation-negative nodules of BSATC III to VI who underwent surgery, we found a lower incidence of aggressive thyroid cancer compared to those with an identified mutation (12.6% vs 44.3%, P < 0.01).

Conclusion
We found positive correlation between cytology results and molecular testing. These findings may provide clinicians with better interpretation for BSRTC results and may contribute to the identification of aggressive thyroid nodules associated with indeterminate Bethesda categories.

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Introduction
The European Registries for Rare Endocrine Conditions (EuRRECa) was created in collaboration with the European Reference Network on Rare Endocrine Conditions (Endo-ERN), the European Society for Paediatric Endocrinology and the European Society of Endocrinology to support the needs of the endocrine community.

Objectives

To describe the patient population and data entered in the EuRRECa Core Registry between June 2019 and December 2021.

Materials and Methods

Core Registry clinical contributors are invited to register new and existing cases of endocrine conditions seen in their centres. Diseases are organized in eight main condition groups. A core data set and a condition-specific data set collect information regarding demographics and diagnosis. Generic Patient-Reported Outcome Measures (PROMs) are available for clinicians and patients to complete. Patients can access the platform, view their data and complete outcomes.

Results

Twenty centres from 12 countries have registered cases. To date, a total of 644 cases have been added to the registry, 238 (36%) in the sex development and maturation condition group, 160 (24%) in the pituitary group, 153 (23%) in the calcium and phosphate group, 51 (8%) in the adrenal group, 24 (4%) in the thyroid group, 23 (3%) in the genetic endocrine tumour syndrome group, 10 (1%) in the growth and obesity group and 5 (0.7%) in the disorders of glucose and insulin metabolism. Of 664 cases, 183 (28%) were within the age range 0-9 years, 140 (22%) within 10-17 years and 321 (51%) over 18 years. The median age was 19 (0, 88) years with 341 (52%) cases over 18 years. Of these, 26 (4%) have been completed by clinicians and 2 by patients.

Conclusion

The EuRRECa Core Registry has shown its ability to collect information on a wide range of endocrine conditions in patients of all ages. The additional information for collecting patient reported and clinician reported outcomes has now been tested and can be used for studying long-term clinical outcomes for rare endocrine conditions.

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OC12.2

Genetic cause of POI are common, the case for next generation sequencing?

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Context

Premature ovarian insufficiency (POI) affects approximately 1-3% of women. Clinical presentations are heterogeneous and the underlying etiologies remain unknown in the majority of cases. The precise development of the Gonadotropin Releasing Hormone (GnRH) neurons is essential for the proper function of the hypothalamic-pituitary-gonadal axis, as GnRH is the master regulator of reproductive functions in vertebrates. Mutations in genes involved in the development of GnRH neurons are associated with Congenital Hypogonadotropic Hypogonadism (CHH), a heterogeneous genetic disorder characterized by hypogonadism, lack of puberty onset, and infertility, which is named Kallmann Syndrome (KS) when the disease associates with anosmia. In this study, we identified in two European cohorts of CHH/KS patients rare nonsense variants in the NOTCH1 ligand gene JAG1. It is already reported in the literature the key role of the Notch signaling in the development of the olfactory system in both mouse and drosophila; therefore, considering the intimate connection between the olfactory and GnRH systems we studied its possible role in the development of the GnRH system. We first performed multiple fluorescence in situ hybridization combined with immunofluorescence to assess the expression pattern of JAG1 and its receptors NOTCH1, NOTCH2, NOTCH3 and NOTCH4 in human fetal sections of the nasal compartment during the first trimester of gestation. We showed that those molecules were expressed along the GnRH migratory pathway as well as by GnRH neurons, suggesting a paracrine and/or autocrine mechanism. Taking advantage of the zebrafish model, we observed that jag1a, jag1b, notch1a, and GnRH3 (homologous of the mammalian GnRH) were expressed in the olfactory placodes of early zebrafish embryos. Moreover, we reported that genetic inhibition of jag1b altered the development of the GnRH3 neurons and the olfactory scaffold used for their migratory process. Functional in vitro validation of the JAG1 variants identified in CHH patients revealed that some were retained into the cytoplasm and did not reach the cell membrane. We also showed that some variants

OC12.3

Defective Notch1/Jag1 signaling impacts GnRH development and contributes to hypogonadotropic hypogonadism

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The precise development of the Gonadotropin Releasing Hormone (GnRH) neurons is essential for the proper function of the hypothalamic-pituitary-gonadal axis, as GnRH is the master regulator of reproductive functions in vertebrates. Mutations in genes involved in the development of GnRH neurons are associated with Congenital Hypogonadotropic Hypogonadism (CHH), a heterogeneous genetic disorder characterized by hypogonadism, lack of puberty onset, and infertility, which is named Kallmann Syndrome (KS) when the disease associates with anosmia. In this study, we identified in two European cohorts of CHH/KS patients rare nonsense variants in the NOTCH1 ligand gene JAG1. It is already reported in the literature the key role of the Notch signaling in the development of the olfactory system in both mouse and drosophila; therefore, considering the intimate connection between the olfactory and GnRH systems we studied its possible role in the development of the GnRH system. We first performed multiple fluorescence in situ hybridization combined with immunofluorescence to assess the expression pattern of JAG1 and its receptors NOTCH1, NOTCH2, NOTCH3 and NOTCH4 in human fetal sections of the nasal compartment during the first trimester of gestation. We showed that those molecules were expressed along the GnRH migratory pathway as well as by GnRH neurons, suggesting a paracrine and/or autocrine mechanism. Taking advantage of the zebrafish model, we observed that jag1a, jag1b, notch1a, and GnRH3 (homologous of the mammalian GnRH) were expressed in the olfactory placodes of early zebrafish embryos. Moreover, we reported that genetic inhibition of jag1b altered the development of the GnRH3 neurons and the olfactory scaffold used for their migratory process. Functional in vitro validation of the JAG1 variants identified in CHH patients revealed that some were retained into the cytoplasm and did not reach the cell membrane. We also showed that some variants

Objectives/aim

To characterize presentations of POI and to evaluate the distribution of underlying etiologies in women with newly diagnosed POI of unknown cause.

Design

Prospective study of 100 women with newly diagnosed POI. Autoimmunity was examined by radio immune assays of autoantibodies associated with POI, i.e. 21-hydroxylase (21 OH), cholesterol side-chain cleavage enzyme (SCC), 17α-hydroxylase (17 OH), and NALP5. Extensive chromosomal and genetic analyses were performed in all, including FMR-1 premutation sequencing and next generation sequencing (NGS) of 100 POI associated genes.

Results

Three percent had autoimmune POI based on the presence of 21OH and SCC autoantibodies. Copy number profiling or chromosome analysis revealed X-chromosome abnormalities in 5%, and a large deletion on chromosome 8 in one patient. FMR-1 premutations were identified in 3%. NGS analysis found genetic variants classified as likely causes of POI in approximately one third of cases. These included genes SOHLH2, STAG3 and EPI6ENF1. Furthermore, several patients carried highly suspicious variants of unknown significance (VUS) in genes such as SOX8, BUB1B and C14ORF39. One patient with primary amenorrhea was homozygous for a rare missense variant in MCM8. A family history of POI was less common (10% vs 26% vs P 0.040) and fewer women reported previous pregnancies (38% vs 61%, P 0.041), in genetic compared to idiopathic POI. FSH levels were higher in genetic compared with idiopathic POI (53.4 ± 40.9 vs 37.3 ± 16.0 IU/l, P 0.043). There were no significant differences between the groups in frequency of primary amenorrhea (15%), timing of menarche (13 [9-17] years) or age at secondary amenorrhea (33 [12-3] years). A larger proportion of women with African heritage carried a VUS (9/17).

Conclusion

In women with newly diagnosed POI, screening for chromosomal abnormalities and FMR mutations identified genetic etiology in 8%, whereas the extensive NGS panel revealed a possible underlying genetic etiology in more than one third, actualizing the discussion of which tests should be a part of diagnostic screening in clinical practice.

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did not properly activate the Notch Responsive Element, suggesting that they are loss-of-function mutations. Combining morphological analysis in vivo, together with genetic manipulation in zebrafish and human genetic analysis, we provide compelling evidence that Notch1/Jag1 signaling plays a role in the development of GnRH neurons and propose that Notch1/Jag1 signaling insufficiency may contribute to the pathogenesis of CHH in humans.

Key words: CHH, KS, GnRH. Notch signaling, Reproduction

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OC12.4

Sex-chromosome dosage effects on circular RNA: A circular trans- 
scriptome-wide study of Turner and Klinefelter syndrome across 
different tissues

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Background

Turner syndrome (45,X; TS) and Klinefelter syndrome (47,XXY; KS) present with a range of clinical features due to copy number aberrations of the X chromosome. The underlying genetics of these syndromes have revealed karyotype-dependent transcription and methylation patterns, and implicated genes that escape X chromosome inactivation (XCI). Alterations in the expression pattern of non-coding RNAs has previously been reported in TS and KS, yet the landscape of circular RNAs (circRNAs) has never been investigated. These endogenous circularized RNAs have the potential to facilitate regulatory processes, thereby affecting transcription, translation and epigenetics, and may contribute to the TS and KS phenotype.

Methods

Primary samples of blood, muscle and adipose tissue were collected from individuals with TS (n = 33) and KS (n = 22) and from males (n = 16) and females (n = 44) of normal karyotype. The circRNAs were identified and quantified from RNAseq data from these samples, using a combination of three different circRNA identification pipelines (CIRI2, CIRCexplorer2 and circRNA_finder). CircRNA differential expression, interaction prediction and functional enrichment analysis was carried out to describe the nature of the circRNA profile in KS and TS.

Results

Differential expression was observed throughout the genome in all tested tissues. The host-genes of these circRNAs were associated with known phenotypic traits. Furthermore, several differentially expressed circRNAs had the potential to sponge certain miRNAs and these miRNAs were predicted to interact with genes that were differentially expressed between TS and females and KS and males. CircRNAs arising specifically from the PAR-genes, displayed a general pattern of opposing expression with up-regulation in TS and down-regulation in KS, which was similar to that of their respective host-genes. Furthermore, we observed that CircRNA-miRNA-mRNA networks may compensate for altered X-chromosome dosage of the PAR-genes.

Conclusion

The present study shows pervasive changes in the circRNA transcriptome throughout three different relevant tissues in Turner and Klinefelter syndrome. It extends our understanding of TS and KS genomics, being not only limited to changes in the miRNA transcription and methylation. The conceptual picture of these syndromes is clearly much more complex than hitherto thought and future studies will need to include multiple tissues, more components of the endogenous crRNA complex, as well as the epigenome. We propose that the phenotype of these syndromes shall be seen through a lens of a complicated multi-tissue framework with multiple genomic mechanisms causing, regulating and compensating the resultant output – the patient.

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OC12.5

Luteinizing hormone (LH)- and choriongonadotropin (hCG)-induced 
internalization of the receptor (LHCGR) is responsible for hormone-

specific signaling

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Introduction

Luteinizing hormone (LH) and human choriongonadotropin (hCG) regulate reproduction through binding the same receptor (LHCGR). They act via activation of G protein- and β-arrestin-dependent signals, resulting in ligand-specific pattern of signaling cascades and LHCGR internalization into endosomes/early endosomes.

Previous studies differentiated the action of these two hormones in LH-related proliferative signals and hCG-related steroidogenic signals. Aim: We compared the role of LHCGR internalization in determining LH- and hCG-specific signals.

Methods

Ligand-specific patterns of LHCGR trafficking and signaling were evaluated in HEK293 cells overexpressing the receptor and specific bioluminescence resonance energy transfer (BRET) biosensors, with or without internalization blockade by Dynasore. LH- and hCG-induced LHCGR internalization and trafficking were evaluated over 30 min, determining the interaction between receptor and endosomal type-specific markers Rab-GTPases (Rab) 5, 7, and 11, as well as β-arrestin 2. Ligand-specific receptor coupling to Gs, Gi, and Gq protein, and related cAMP, extracellularly-regulated kinases 1 and 2 (ERK1/2), and intracellular Ca2+ increase were evaluated as well. Results were compared by Kruskal Wallis test and Dunn’s post-test; P < 0.05; n ≥ 4-8.

Results

The interaction between LHCGR and markers of internalization/localization into early endosome, i.e. β-arrestin 2 and Rab5, is markedly more induced upon cell treatment with hCG, than with LH (P < 0.05; n = 4). Conversely, LH induces preferential LHCGR-Rab11 interaction, indicating the routing of the receptor toward recycling in cell membrane (P < 0.05; n = 4), while no hormone-specific LHCGR-Rab7 interaction was found (P > 0.05; n = 4). Interestingly, LHCGR trafficking is modulated by the blockade of internalization with Dynasore. Under this condition, hCG-induced LHCGR-β-arrestin 2/Rab5, as well as LH-induced LHCGR-Rab11 interactions were lost (P > 0.05; n = 4), suggesting missing ligand-specific receptor trafficking. Moreover, Dynasore treatment increases LH-, but not hCG-induced LHCGR-Rab7 interaction, indicating ligand-specific routing toward the degradation pathway. Hormone-specific trafficking reflects the downstream signaling pattern. hCG has higher efficacy than LH in inducing Gi- and Gq coupling to LHCGR (P < 0.05; n = 8), reflecting more pronounced activation of cAMP and intracellular Ca2+ increase (P < 0.05; n = 4), as two molecules upregulating the synthesis of gonadal steroids. Cell treatment with Dynasore did neither change the hCG-related G protein coupling to LHCGR, nor cAMP production, while it decreased intracellular Ca2+ increase. Conversely, LH was more effective than hCG in inducing LHCGR coupling to Gi protein (P < 0.05; n = 8), preferentially activating proliferation-related ERK1/2 downstream signaling (P < 0.05; n = 4). However, LH-induced LHCGR-Gi coupling and ERK1/2 activation were inhibited by Dynasore (P > 0.05; n = 4).

Conclusion

We conclude that LH-related proliferative and hCG-linked steroidogenic signals require hormone-specific trafficking of the receptor.

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OC12.6

Analysis of cardiovascular comorbidities and events in a cohort of 
three cohorts of patients with GAHT

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Introduction

According to the DSM-5, gender dysphoria (GD) is defined as a distress that results from an incongruence between one’s sex assigned at birth and one’s gender identity. This condition may require gender-affirming hormone therapy (GAHT), in order to reduce distress. GAHT, however, is not free from side effects and it could increase the risk of onset of new pathological conditions.

Aim of the study

To evaluate cardiovascular comorbidities and events in a cohort of patients with GD taking GAHT.

Subjects and methods

We enrolled subjects with GD [assigned male at birth (AMAB) and assigned female at birth (AFAB)] who were regularly followed by the local gender team in Molinette Hospital, Turin (Italy), between February 2007 and July 2021. For each
patient, at each access anthropometric parameters, smoking habit and a cardiovascular assessment (arterial hypertension, diabetes, dyslipidaemia, ACS, stroke, DVT) were recorded. A baseline analysis of the whole cohort was carried out subsequently an evaluation of cumulative incidence of comorbidities during GAHT was performed. Finally, mortality was assessed in terms of SMR (standardized mortality ratio - ratio between observed and expected death).

Results
We enrolled 613 patients, 380 transgender-AMAB with a median age of 33.9 years [22.04-45.85] and 233 transgender-AFAB, aged 27.4 years old [22.01-39.54], observed for a median follow-up time of 43.50 [17.72-25] and 41.50 [19-74] months, respectively. Only transgender-AMAB showed a significant weight gain (+2.4 kg after 24 months). At baseline, 39% of transgender-AMAB and 39.1% of transgender-AFAB were active smokers; no significant difference during follow-up was recorded. During observation time, new cases of arterial hypertension (n = 12), diabetes (n = 4) and dyslipidaemia (n = 28) were recorded in transgender-AMAB, while 12 new cases of arterial hypertension, 2 of diabetes and 21 of dyslipidaemia were reported in transgender-AFAB. Three cases of DVT were registered within transgender-AMAB. One case of ACS and one stroke were described in transgender-AFAB group. Finally, 4 deaths were recorded in the transgender-AMAB group (1.04%) and 1 in the transgender-AFAB group (0.42%). In both groups, SMR was higher than age-matched cisgender women [AMAB SMR: 1.32 (IC 95% 0.42-3.19); AFAB SMR: 1.26 (IC 95% 0.04-3.91)].

Conclusions
Although trans-AMAB and AMAB enrolled were relatively young and not fully representative of the general transgender population, during GAHT an increase of main cardiovascular comorbidities was observed. Thus, our data highlight the need of a proper follow-up and medical monitoring to manage these new conditions and to prevent the onset of major cardiovascular events.

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Adrenal and Cardiovascular Endocrinology 2

OC13.1

Development of [18F]AldoView as the first highly selective aldosterone synthase PET tracer for imaging of patients with primary hyperaldosteronism
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Background
Inappropriately high aldosterone in patients with primary hyperaldosteronism (PHA) is due to increased aldosterone synthase (CYP11B2) activity. Selective in vivo imaging of overexpressed CYP11B2 in adrenals with positron emission tomography (PET) has not yet been achieved due to close homology of enzymes involved in aldosterone and cortisol (CYP11B1) synthesis.

Aim
Synthesise a fluorine-18 labelled highly selective CYP11B2 inhibitor, [18F] A AldoView, and assess its potential for the detection of aldosterone producing adrenomas (APAs) and aldosterone producing cell clusters (APCCs) with PET in patients with PHA.

Methods
[18F]AldoView was synthesised in high radiochemical yields using a proprietary radiochemistry platform. Dynamic PET/CT imaging, biodistribution studies and metabolite analysis was performed in wild type female BALB/c mice. [18F]AldoView binding to CYP11B2 was characterised by quantitative phosphorimaging in tissue sections prepared from adrenalectomy specimens of patients with PHA. Cushing, phaeochromocytoma and incidentaloma. CYP11B2 specific immunohistochemistry (IHC) was performed in directly adjacent sections.

Results
In mice, [18F]AldoView showed a favourable pharmacokinetic profile, including rapid distribution and clearance. In tissue sections, [18F]AldoView binding was visually consistent with CYP11B2 IHC staining. Specific tracer binding to CYP11B2 positive areas ranged from 8.6 to 19.1 kBq/cm² and was evenly distributed across tissue identified as APA, in contrast to cortex, which had diffuse patches with hot spots in keepings with APCCs. There was no evidence of elevated tracer uptake in CYP11B2 negative areas in patients with or without PHA (3.2±1.1 kBq/cm² and 2.6±1.8 kBq/cm², respectively).

Conclusion
Our results strongly suggest that [18F]AldoView can image CYP11B2 expression in human adrenals and could become first highly selective radio tracer to be used to identify patients with PHA for adrenalectomy.

OC13.2

Early post-operative ACTH-stimulated aldosterone predicts long-term biochemical outcome in primary aldosteronism
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Introduction
Primary aldosteronism (PA) is the most commonly surgically curable cause for endocrine hypertension. Patients with unilateral aldosterone-producing adenoma undergo adrenalectomy (ADX). Clinical and biochemical outcome is assessed 6-12 months after ADX according to PASO consensus. To reduce unnecessary follow-up visits and change in medication for diagnostic purposes for potentially cured patients after ADX, a prediction tool is needed. Previous research had shown greater ACTH-responsiveness in unilateral disease. Thus, we analyzed if early post-operative ACTH-stimulated aldosterone can predict PASO outcomes.

Methods
We prospectively included 100 patients of the German Conns’s registry from 2015-2021, who underwent ADX and post-operative ACTH stimulation tests. 6-12 months after ADX we assessed blood pressure and biochemical remission according to PASO criteria. In addition, serum cortisol and plasma aldosterone concentrations (PAC) were measured before and 30 minutes after the application of 250 μg Synacthen® within the first week after ADX. We used ROC (receiver operating curve) analysis and paired baseline and stimulated PAC and serum cortisol to PASO outcomes.

Results
81% of the patients had complete, 13% partial and 6% absent biochemical remission at 6-12 months after ADX. Complete clinical remission was observed in 28%. There was a significant correlation between biochemical outcome and ACTH-stimulated PAC values (P=0.01, r=0.53). Using 58.5 pg/ml as a cut off, post-operative stimulated PAC had high specificity (95%) and reasonable specificity (74%) for predicting partial or absent biochemical remission at 6-12 months after ADX. Additionally, stimulated PAC AUC (area under the curve) values (0.89; CI 0.82-0.96) were significantly higher (P=0.03) than baseline PAC AUC (P=0.28). In contrast, baseline and stimulated serum cortisol levels were less useful (baseline cortisol AUC 0.60; CI 0.45-0.74), stimulated cortisol AUC 0.67; CI 0.54-0.80, (P=0.01; P=0.01). Blood pressure outcome AUC for baseline and stimulated serum cortisol and PAC ranged from 0.56-0.66, indicating a low predictive value.

Conclusions
In our series, low post-operative ACTH-stimulated PAC was predictive of biochemical remission after ADX. As post-operative ACTH stimulation tests are used to detect adrenal insufficiency, concurrent stimulated PAC measurements should be included in routine care. If confirmed, this approach could reduce follow-up visits to assess biochemical outcome.

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OC13.3

11-oxygenated C19 steroids are the predominant androgens responsible for hyperandrogenemia in Cushing’s disease
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Background
Symptoms of hyperandrogenism are common in patients with Cushing’s disease (CD), but they cannot be sufficiently explained by measured concentrations of circulating androgens. In this study we analyzed the contribution of 11-oxygenated (11o×C19) androgens to hyperandrogenemia in female patients with CD as well as the influence of treatment with steroidogenesis inhibitors osilodrostat and metyrapone on 11o×C19 and classic androgens.

Methods
In this single-center study, we assessed saliva day profiles of 23 females with treatment naive CD, 26 female controls, 5 females with CD treated with metyrapone and 5 treated with osilodrostat for cortisol, cortisone, androsterone (A4), 11-hydroxyandrostenedione (11OHA4), testosterone (T) and 11-ketotestosterone (11KT) by liquid chromatography tandem mass spectrometry as well as morning baseline levels of gonadotropins and estradiol, sex hormone-binding globulin, cortisol and dehydroepiandrosterone sulfate (DHEAS) in serum and adrenocorticotropic hormone in plasma.

Results
Treatment naive females with CD showed significantly elevated areas under the curve (AUC) of 11OHA4 and 11KT throughout the day compared to controls (11OHA4 mean rank difference (mrd) 18.13, P=0.0002; 11KT mrd 17.42, P=0.0005) whereas A4, T and DHEAS were comparable to controls. Patients with more symptoms of hyperandrogenism displayed higher concentrations of 11o×C19 androgens and had significantly lower SHBG concentrations.

Concentration levels were within normal in all patients with CD (LH 7.18 U/l (SD 14.28 U/l); FSH 7.68 U/l (SD 12.0 U/l)) and did not correlate with any other parameters. Treatment with osilodrostat and metyrapone efficaciously blocked 11o×C19 androgen synthesis. In metyrapone but not in osilodrostat treatment a trend towards increased concentrations of T and significantly increased A4 concentrations were observed (A4 mrd 23.07, P=0.0119).

Conclusion
Hyperandrogenemia in CD is predominantly caused by excess of 11-oxygenated (11o×C19) androgens and had significantly lower SHBG concentrations. Concomitant levels were within normal in all patients with CD and did not correlate with any other parameters. Treatment with osilodrostat and metyrapone efficaciously blocked 11o×C19 androgen synthesis. In metyrapone but not in osilodrostat treatment a trend towards increased concentrations of T and significantly increased A4 concentrations were observed (A4 mrd 23.07, P=0.0119).

Impact of contraception: Women on hormonal contraceptives had lower T and 11- KT concentrations in saliva, but not in serum.

Conclusion
While classic androgens decline with age and are subject to menstrual cycle-dependent variation, 11-oxygenated androgens form a stable pool during adulthood. While all other measured androgens decreased after menopause, 11OHA4 and 11KT increased, which may have clinical implications for diagnostic work-up of hormonal pathologies.

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OC13.4

Classic and 11-oxygenated androgens in serum and saliva across adulthood and the menstrual cycle – a mass spectrometry-based cross-sectional study

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Objective
Quantify classic and 11-oxygenated androgens in serum and saliva and determine variations across age, sex, body mass index (BMI), menstruation and hormonal contraception use.

Methods
Morning serum samples were collected from 292 healthy volunteers (125 men, 22-95 years; 167 women, 21-91 years). Morning saliva was collected from 83 healthy volunteers (51 women, 32 men). 25 individuals (12 women, 13 men) also collected a 7-timepoint diurnal saliva profile; the 12 women also collected morning saliva on seven consecutive days during both follicular and luteal phase.

The following steroids were quantified by liquid chromatography-tandem mass spectrometry: classic androgens and their precursors (dehydroepiandrosterone sulfate [DHEAS], dehydroepiandrosterone [DHEA], androstenedione [A4], testosterone [T], dehydrotestosterone [DHT]), and 11-oxygenated androgens and their precursors (11-hydroxy androstenedione [11OHA4], 11-keto androstenedione [11KA4], 11-hydroxy testosterone [11OHT], 11-keto testosterone [11KT]). Data were pooled Descriptive statistics and non-parametric tools were used for each variable to obtain median, IQR and significance (p-values). Multiple linear regressions were performed to delineate the distinct effects of age and BMI in a sex-specific analysis.

Results
Age: In serum, DHEAS, DHEA, and A4 decreased with age in both men and women, while 11OHA4, 11KA4, 11OHT, 11KT remained stable. Sex: Serum concentrations of DHEA, A4, and 11-oxygenated androgens were similar in men and women while, as expected, T and DHT were higher in men. 11OHA4 levels were the highest of all 11-oxygenated androgens and were higher than A4 and similar to DHEA levels. BMI: There were no associations of DHEAS, DHEA, A4, 11OHA4 and 11KA4 with BMI. After adjusting for age, 11KT positively correlated with BMI in men (change/kg/m² (%5 CI) = 3.05(0.08, 6.03), P=0.044), while the relationship between 11OHT and BMI was not significant.

Menstrual status: Saliva classic and 11-oxygenated androgens showed a clear diurnal pattern in men and in the follicular phase in women, but in the luteal phase only 11-oxygenated androgens showed diurnal variation. Postmenopausal women had lower serum DHEAS, DHEA, A4, T, and 11KA4 (P<0.001) compared to premenopausal women (P<0.001 and P=0.005, respectively).

Impact of contraception: Women on hormonal contraceptives had lower T and 11KT concentrations in saliva, but not in serum.

Conclusion
While classic androgens decline with age and are subject to menstrual cycle-dependent variation, 11-oxygenated androgens form a stable pool during adulthood. While all other measured androgens decreased after menopause, 11OHA4 and 11KT increased, which may have clinical implications for diagnostic work-up of hormonal pathologies.

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OC13.5

Machine learning-based texture analysis in the characterization of cortisol secreting vs non secreting adrenocortical incidentalomas in CT scans

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Adrenal nodular disease is a frequently increasing in the general population with an incidence that reaches almost 10% in the seventh decade of life. More and more evidences show these lesions discovered through diagnostic imaging (CT, MRI) performed for other medical problems (incidentalomas). New radiomaging techniques, exploiting the quantitative variables of imaging, permit to identify an hypothetical pathological tissue. We have applied this potential in a retrospective series of 72 patients of both sexes with single adrenal lesion >1 cm in dimension with adrenal incidentalomas followed at our center. Patients were studied following ESE/ENSAT current criteria practice guideline in order to exclude any hormonal hypersecretion considering in this study only not secreting and cortisol secreting adrenal masses by dexamethasone-suppression test (DST). Based on cortisol value they were divided in two groups: functioning (32) and non-functioning (40) adrenal incidentalomas with cortisol values >50 nmol/l and <50 nmol/l respectively. Machine learning concept, through different algorithms offers the possibility to study several biological processes obtaining quantitative information from imaging and correlating it with outcomes. Radiomics is an emerging technique that translates radiological images into quantitative data to yield biological information and permits an in depth radiological characterization, thus improving diagnosis, decision support, and follow up monitoring. It is a multistage process in which features based on shape, pixel densities, and texture are extracted from CT or MR images. Each incidentaloma was studied in the preliminary non-contrast phase with a specific software (Mazda), surrounding a region of interest within each lesion. 314 features were extrapolated. Mean and standard deviations of features were obtained and the difference in means between the two groups was quantified statistically analyzed. ROC curves were used to identify an optimal cut off for each variable and a prediction model was constructed via multivariate logistic regression with backward and stepwise selection. A 11-variables prediction model was constructed and a ROC curve was used to

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OC13.6
Machine Learning models for the accurate prediction of malignant pheochromocytomas and paragangliomas
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Introduction
Pheochromocytomas and paragangliomas (PPGLs) exhibit an up to 20% malignancy rate. Various clinical, genetic, and pathological features have been proposed as predictors of malignancy. However, until present there are no robust indices to reliably predict metastatic PPGLs.

Aim
The aim of the present study was to prospectively validate the value of methoxytyramine as risk marker of metastatic disease and establish a machine learning (ML) model, based on clinical and biochemical features, to reliably predict malignancy in patients with PPGLs.

Methods
This study included retrospective data of 493 patients for the generation and training of ML models. Data of 295 patients prospectively enrolled in the multicenter international PMT-Study were used for the validation of the predictive value of methoxytyramine and the external validation of the selected ML model. The predefined features for selection analysis were sex, age at initial diagnosis, locations and size of tumor(s), previous history of PPGL, presence of SDHB mutation, plasma normetanephrine, metanephrine and methoxytyramine.

Results
Receiver operating characteristic curves indicated that plasma methoxytyramine as risk marker of metastatic disease and establish a machine learning (ML), based on clinical and biochemical features, to reliably predict malignancy in patients with PPGLs.

Conclusions
Our study confirms in a prospective series the value of methoxytyramine as a strong predictor of metastatic PPGLs. Importantly, we demonstrate predictive ML models, as the first effective, non-invasive and highly accurate approach to predict malignant disease in patients with PPGLs, providing immediate guidance to clinicians for individualized patient management and follow-up strategies.

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OC14.1
Expression of lutetizing hormone-chorionic gonadotrophin receptor in pheochromocytomas
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Pheochromocytomas and paragangliomas (PPGL) are catecholamine-producing neuroendocrine tumors that display the highest heritability rate among all human tumors. Genomic analyses revealed the existence of 2 main clusters of PPGL, i.e. cluster 1 containing SDHx- and VHL-mutated tumors which do not produce epinephrine, and cluster 2 including epinephrine-secreting PPGL related to RET, NF1, TME127 and MAX mutations. Early diagnosis and treatment of PPGL is crucial to prevent adrenergic crises, especially in pregnant patients with previously undiagnosed pheochromocytoma (PCC). In this context, PCC are associated with a high risk of maternal or fetal complications due to catecholamine excess triggered by tumor compression induced by fetus growth, or labor and delivery. However, it is known that surges in plasma catecholamines may also occur during early gestation suggesting that pregnancy may also activate the secretory activity of PPGL through the involvement of non-mechanical factors, such as gestational hormones. Herein, we report a case of silent PCC in a pregnant woman with the first symptoms of catecholamine excess appearing during the first trimester and a life-threatening adrenergic myocarditis occurring at 31 weeks of gestation. Genetic analysis revealed the presence of a heterozygous germline RET variant of uncertain significance. The fact that the first symptoms of catecholamine excess had occurred during the first trimester of pregnancy led us to conduct in vitro studies to investigate the effects of estradiol and human chorionic gonadotropin (hCG) on epinephrine secretion by cultured cells derived from the patient’s tumor. Expression of LH/hCG receptor (LHGR) was searched for in the tumor and an additional series of 12 PCC by RT-qPCR and immunohistochemistry. LHGR expression was also analyzed in silico in the PPGL cohorts of the COMETE network and The Cancer Genome Atlas (TCGA) databases. hCG stimulated epinephrine secretion by primary cultured PCC cells. The tumor expressed the LHGR receptor, which was colocalized with catecholamine-producing enzymes. LHGR expression was also detected in 5 out of a series of 12 PCCs. In silico studies revealed that PPGL display the highest expression levels of LHGR mRNA among the 32 solid tumor types of TCGA cohort. Interestingly, expression of LHGR was higher in cluster 2 than in cluster 1 PPGL. These data show that PCC can express functional LHGR receptor. Consequently, pregnancy may activate catecholamine production by previously silent PCC as early as the first trimester of gestation especially in women with gene mutations that predispose to cluster 2 epinephrine-secreting PCC.

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OC14.2
Peripheral facial paralysis as first manifestation of hypopharynx glioma: a case report
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Introduction
Low-grade pituitary gliomas are extremely rare neoplasms, originating from the pituitary cells of the posterior pituitary or infundibulum. The incidence of these tumors increases with age and peaks in the seventh decade of life. Gliomas are primary brain tumors of the supporting glial cells of the central nervous system, which derive from neuroglial stem cells or progenitor cells. They are responsible for nearly 30% of all primary brain tumors and 80% of all malignant tumors, as well as the majority of deaths from primary brain tumors. The clinical manifestation is mainly through visual impairment, due to optic nerve compression, headache, and pituitary deficits.

Case report
A 16-year-old female patient presented with left peripheral facial paralysis, with no change in the imaging tests, with spontaneous improvement. Evolved with progressive headache, severe nasal congestion, bilateral visual acuity alteration, and right peripheral facial paralysis, associated with findings of a tumor in the sellar topography, dilatation of the supratentorial ventricular system, and diffuse meningeal impregnation, suggestive of the spread of the pathology. She underwent a ventriculoperitoneal shunt and subsequent transphenoidal excision of the mass (4.9 × 2.6 × 2.5 cm) which was successfully performed. Anatomopathological analysis showed a low cell neoplasm with fibrillar background and low-grade hyalinized vessels, suggestive of glial neoplasm. In the early postoperative period, developed diabetes insipidus, treated with desmopressin acetate nasal spray 0.1 mg/ml twice a day, and
hypothalamic obesity. In the outpatient follow-up, a diagnosis of panhypopituitarism was made, consisting of hypogonadotropic hypogonadism, central adrenal insufficiency, and central hypothryoidism, and replacement of estradiol valerate 2 mg = levonorgestrel 0.25 mg, hydrocortisone 17.5 mg, and levotiroxine 123 mcg/day was initiated. The patient remains under outpatient follow-up, in good general condition, asymptomatic, and with good control of complications.

Conclusion

Although pituitary tumors are the most commonly found intracranial neoplasms, the low-grade pituitary glioma presented by the patient is an extremely rare pathology. As no other studies in the literature have mentioned such a condition, asymptomatic, and with good control of complications.

Are the neutrophil-to-lymphocyte ratio and large unstained cells (LUCs) different in hospitalized patients COVID-19 PCR positive with and without diabetes mellitus?

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OBJECTIVES

The novel coronavirus disease-2019 (COVID-19) is the fastest-spreading disease worldwide, with over 380 million cases and 5 million deaths. The presence of diabetes mellitus (DM) in patients with COVID-19 was associated with mortality, acute respiratory distress syndrome, disease progression. COVID-19 was progressed with some hematological disorders, especially lymphopenia. Studies implicated that neutrophil-to-lymphocyte ratio (NLR) level can be a reliable marker in showing the severity of COVID-19 disease. A routine hematology analyzer measures the percentage of large unstained cells (%LUCs), reflecting activated lymphocytes and peroxidase-negative cells. In previous studies, the %LUCs was found to be associated with disease progression in patients with COVID-19.

MATERIALS AND METHODS

The data of the patients hospitalized in the Infectious Diseases Service and Intensive Care Unit with a COVID-19 in Ankara City Hospital between 15.03.2020 and 15.07.2020 were collected in our retrospective study. This study included 656 patients with COVID-19, 131 with DM, and 525 with the DM-free control group. While blood cell (WBC) count, neutrophils, neutrophil percentage, lymphocytes, lymphocyte percentage, LUCs,%LUCs, NLR, platelets, hemoglobin which was taken within the first 24 hours after admission, and history of DM were noted from the records.

RESULTS

The mean age was 61.29 ± 13.81 years in the diabetic patient group and 44.37 ± 17.14 years in the non-diabetic control group with COVID-19, which was significantly higher in the diabetic group (P < 0.001). NLR, WBC count, neutrophils, and neutrophil percentage were statistically significantly higher in patients with DM (respectively, P < 0.001, P = 0.008, P = 0.008, and P = 0.049). There were more significant differences between the groups regarding lymphocyte, platelet, LUCs, and %LUCs values (P > 0.05).

CONCLUSION

There are studies in the literature that a decrease in %LUCs value and an increase in NLR are indicators of severe disease in COVID-19. Our study did not detect a difference in %LUCs value in diabetic patients, but our study is a preliminary study. Analysis of the data with clinical conclusions continues with more patients.

Keywords: COVID-19, Diabetes Mellitus, neutrophil-to-lymphocyte ratio, large unstained cells

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Discovery of microRNA biomarkers in circulation and bone tissue from a type-2 diabetes mellitus rat model under different anti-osteoporotic treatments

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Metabolic changes in Type-2 Diabetes-Mellitus (T2DM) make patients prone to develop osteoporosis and delayed bone healing. We hypothesize that microRNAs could be involved in the underlying mechanism and used as biomarkers in this context. To test this hypothesis, we analyzed microRNAs in samples from Zucker Diabetic Fatty (ZDF) rats, a T2DM model with reduced bone healing and bone mass. 11-week-old male ZDF and wildtype rats with a femur subcritical defect were treated with placebo, anti-sclerostin, PTH and insulin treatments for 12 weeks. After the treatment, metabolic and bone phenotype parameters of all the rats were measured and serum and ulna samples were obtained (n = 4-5 per group). RNA isolation and small RNA next generation sequencing (NGS) were performed using serum and ulna samples for untargeted genome-wide miRNA analysis. Significantly (adj. P < 0.05) regulated miRNAs identified by NGS were further analyzed with the online tool miRNet 2.0 for miRNA target network construction and with the PANTOM5 browser for cell-type enrichment analysis. Our results show that insulin induced a strong dysregulation of circulating miRNAs mainly involved in metabolism, and even rescued seven circulating miRNAs in the ZDF model (rno-miR-802-5p, rno-miR-122-3p, rno-miR-375-3p, rno-miR-27a-5p, rno-miR-31a-5p, rno-miR-192-5p, rno-miR-122-5p). Anti-sclerostin caused a less intense miRNA dysregulation in serum but affected miRNAs shown to be enriched in bone tissue, particularly one of those miRNAs (rno-miR-145-5p). PTH treatment did not produce any effect on circulating neither on bone miRNAs in the ZDF rats, most probably due to a blunting effect of diabetes over the PTH. Altogether, this study shows the enhancement effect on bone mass and bone regeneration potentially caused by dysregulation of bone miRNAs and of the rescue of circulating miRNAs in ZDF rats under the three analyzed treatments.

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THE EFFECT OF MULTIPLE PASSES TO THE SAME THYROID NODULE IN THE FINE NEEDLE ASPIRATION BIOPSY SESSION ON OBTAINING ADEQUATE AND/OR THE AUS/FLUS CYTLOGICAL RESULT

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AIM

To determine whether multiple fine needle passes to the same thyroid nodule in the fine needle aspiration biopsy (FNA) session affect sufficient and/or atypia of the cytological result.

MATERIALS AND METHODS

Ultrasoundography (US) and cyto-histopathology results of the nodules of patients who were diagnosed with thyroid nodules and underwent FNA between May-August 2021 were retrospectively analyzed. The nodules were divided into two groups according to the number of needle passes performed in the same FNA session as those with one pass (one-pass group) and those with two or three passes (multiple-passes group). The two groups were compared in terms of cytological adequacy and the rate of AUS/FLUS diagnosis as well as US features and TIRADS scores.

RESULTS

A total of 1500 thyroid nodules of 708 patients (575 female and 133 male) were included in the study. The mean age of the patients was 51.57 ± 12.51 years. 1409 (93.9%) nodules were performed one pass, and 91 (6.1%) were performed two (n = 85) or three passes (n = 8). While the cystic/mixed nodule ratio and macrocalcification rate were higher in the multiple-passes group, the rates of coalescent nodules and presence of halo were higher in the one-pass group (P = 0.001, P = 0.039, P = 0.006, and P = 0.040, respectively). TIRADS 3 score was higher in multiple-passes group (P = 0.001). The adequacy and AUS/FLUS ratios were similar in the two groups. When nodules with macrocalcifications and cystic/mixed structures were evaluated as two separate subgroups, the adequacy and AUS/FLUS ratios were similar in one-pass and multiple-passes groups.

CONCLUSION

Two or three passes to thyroid nodules have similar cytological adequacy and AUS/FLUS ratios compared to one pass. Although more passes are performed in
Young Investigator Awards

Y11

Excessive bilateral adrenal hyperplasia associated with aldosterone synthase (CYP11B2) deficiency

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Introduction

Congenital adrenal hyperplasia (CAH) encompasses a group of enzymatic defects in cortisol biosynthesis resulting in adrenal hyperplasia through chronic compensatory ACTH stimulation. Aldosterone synthase deficiency, however, is associated with normal cortisol secretion and there are no reports on whether it may be associated with adrenocortical hyperplasia.

Case Presentation

A 37-year-old, Greek female was referred for further investigation of excessive diffuse bilateral adrenal hyperplasia discovered during investigations for post-partum weight gain (25 kg), fatigue, hirsutism, easy bruising, and depression associated with borderline cortisol status abnormalities (cortisol post-1mg dexamethasone: 100 nmol/l, basal ACTH: 7.3 pg/ml and 24-h urinary free cortisol (UFC): 1.32×ULN; androgens, as well as 17-hydroxyprogesterone, were normal). In infancy, the patient was erroneously diagnosed with CAH when she presented with failure to thrive, hyponatremia and hyperkalemia. She was treated with methylprednisolone and fludrocortisone until the age of 2, when she was re-evaluated with a Cosyntropin Stimulation Test (CST) with normal basal and stimulated cortisol levels (0’/60’:6.3/6.9 ng/dl). Aldosterone was 13 ng/dl with PRA>40 ng/ml/h and 11-Deoxycorticost 2.2 ng/ml. On repeated testing, aldosterone was 15.6 ng/dl, PRA: 2.2 ng/ml/h, 17OHP: 0.2 ng/ml and the diagnosis of pseudo-hypoaldosteronism was made. Subsequently, the patient had normal growth and pubertal development; she had oligomenorrhea until pregnancy and subsequently normalization of menstrual cycles. The coding regions of CYP11B2, CYP21A2 and CYP11B1 genes underwent Sanger sequencing.

Results

On physical examination, she had no clinical stigmata of Cushing’s Syndrome. Cortisol post-dexamethasone was borderline (63 nmol/l) without any other features of hypercortisolism (normal midnight serum cortisol and UFC). Basal aldosterone levels were 5.44 ng/dl with marginally elevated renin levels (56.40 mcU/ml). Given her PMH we performed a CST, in which she had a normal cortisol response, a borderline increase of 17-OH PREG (0’/60’:730/2.2 nmol/l) but a remarkable lack of aldosterone response (0’/60’:6.3/6.9 ng/dl). We suspected CYP11B2 gene deficiency, which was confirmed by genetic testing, that revealed compound heterozygosity for two pathogenic variants (p.T185I and p.E255X). No mutations were identified in CYP21A2 and CYP11B1 genes.

Conclusion

To our knowledge, this is the first report that associates diffuse bilateral adrenal hyperplasia with CYP11B2 deficiency, a rare defect that is usually diagnosed during infancy and improves with age so that adults are asymptomatic. Our patient presented with impressively enlarged adrenals without discrete nodules and no other evident cause of adrenal hyperplasia.

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Y12

Single-nuclei transcriptome of adult human adrenal glands reveals novel insights into molecular mechanisms intrinsic to adrenocortical tumourigenesis and cortisol secretion

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Background
Molecular mechanisms underlying the pathogenesis of adrenocortical adenomas (ACAs) and autonomous cortisol secretion remains frequently unexplained despite previous comprehensive genomic studies. Aim To gain novel insights into molecular pathogenesis of adrenocortical tumours by investigating transcriptome profiles of ACAs at single-nucleus resolution (snRNA-Seq), using adult human normal adrenal glands (NAGs) as reference. Methods We isolated single nuclei from 6 NAGs and 12 ACAs, including 7 cortisol-producing adenomas (CPAs) and 5 endocrine inactive adenomas (EIAs) with different genetic background. snRNA-Seq was performed using inDrop1M technology. Data analysis, integration and exploration was performed using Seurat, Findings Pathway enrichment analysis was performed using pathwayR with KEGG pathways as reference. Transcriptome profile from ACA was integrated with NAG using anchor pairs between the two datasets. Identification of tumour- and mutation-specific cell subpopulations (i.e. clusters) was done by differential gene expression analysis. Results Within the NAGs, we identified different satellite clusters of immune, myeloid and vascular origin, in addition to main clusters representing the three adrenal cortex zones, medulla and capsule. We also identified two subpopulations potentially representing adrenocortical and adrenomedullary progenitor cells, located within and underneath the capsule. Comparative analysis of the transcriptional profiles of NAGs and ACAs revealed the presence of six ACA-specific clusters, namely four “tumour-specific” (TC1-4), “tumour microenvironment” (TME), and one cluster overexpressing genes of cholesterol pathway (Chol-upreg). Specifically, the TC1 was mostly found in 2 CTNBB1-mutated samples (one EIA and one CPA), where a significant overexpression of AFF3, FTO and ISMI, as well as genes of spliceosome (fold enrichment, FE = 7.6), ECM-receptor interaction (FE = 7.3) and Hippo signaling (FE = 2.8) pathways were observed. The TC2 cluster was more abundant in EIA and characterized by overexpression of genes like MMP26, SP100 and EIF4H, as well as genes of NOD-like receptor (FE = 3.6) and IL-17 signaling pathway (FE = 3.5) associated with tumour promotion. The Chol_upreg cluster was largely represented in CPAs and characterized by a very high expression of genes associated to steroid biosynthesis (FE = 34.2) and cortisol synthesis and secretion (FE = 9.5), including HMGCS1, SLC16A1 and P450. The remaining clusters (TME, TC3-4) were quite homogeneously distributed in all ACAs, independently from mutational status (2 PRKACA -, 1 GNAS-, 6 CTNBB1-, 3 no driver-mutation) and cortisol secretion. Conclusion Our human adult NAG single-cell atlas represents a unique source for investigations of adrenal diseases and allowed us to investigate the molecular heterogeneity of ACAs at single-cell level, showing the presence of specific cell populations associated with cortisol secretion and genetic background.

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Y13

Generalization of TSH and FT4 reference intervals in pregnancy: an individual participant data meta-analysis

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Objective Defining thyroid function test abnormalities in pregnancy is complicated by changes in maternal physiology. Ideally, reference intervals (RIs) should be population-based and pregnancy-specific. Large methodological differences between published reports limit the adoption of such RIs into clinical practice. Methods The study was performed in the Consortium on Thyroid and Pregnancy. In line with current consensus and the 2017 American Thyroid Association guidelines, cohort-specific RIs based on the 2.5th and 97.5th percentiles were calculated after exclusion of participants with pre-pregnancy thyroid disease, thyroid medication use and TPOAb positivity. Additional exclusions were also calculated using the above mentioned methods and eight different methodological approaches. Results The final study population comprised of n = 63,198 participants from 22 cohorts. Between cohorts, the upper limit for TSH calculated according to the current consensus ranged from 2.24 to 6.02 mIU/L in the first trimester, from 2.67 to 6.15 mIU/L in the second trimester and from 3.03 to 6.13 mIU/L in the third trimester. Not including TPOAb-positive participants led to a rise of the upper limits of TSH in all cohorts, especially in the first (+17.6% average, range +1.6 to +30.3%) and second (+9.8% average, range +0.6 to +32.3%) trimester. The use of the 95th percentile led to considerable changes in upper limits, varying from −10.8% to −21.8% for TSH and −1.2% to −13.2% for FT4 across all trimesters. All other additional exclusion criteria led to less than 3.5% variability around the 97.5th percentile, without a trend towards increase or decrease. Conclusion The large variability in reference limits between cohorts stress the importance of how to generalise RIs. Furthermore, we data emphasize the importance of excluding TPOAb-positive participants and the use of appropriate cut-offs. Additional exclusions frequently encountered in literature did not affect TSH or FT4 reference intervals during pregnancy, indicating that the majority of published studies can be implemented into clinical practice despite methodological differences and future studies can adapt simplified study setups to define valid RIs.

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Y14

The role of miR-335-5p in the differentiation of thyroid cancers with BRAF mutation

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The most frequent mutation in papillary thyroid carcinoma (PTC) is the p.V600E of the BRAF gene. This mutation leads to the aberrant activation of the RAS/BRAF/MEK/ERK pathway and consequently to the under-regulation of thyroid-specific genes, resulting in uncontrolled growth and de-differentiation of cancer cells. In this work, we analyzed the transcriptomics data produced by the TCGA project using a network approach. The analysis led to the identification of regulatory genes, called switch genes, involved in the network changes despite mutated BRAF papillary carcinomas and normal thyroid tissues. In particular, we identified 227 switch genes. Within the network generated by these genes, 63 were found to be targets of the same microRNA, the miR-335-5p. The role of this microRNA was then investigated through an in vitro study. We selected two primary cell lines and four immortalized lines of thyroid cancer, all of them carrying the BRAF mutation, which showed lower levels of miR-335-5p expression compared with normal control cells. A synthetic microRNA was transfected in all six cell lines. After transfection, the analyses showed an increase in TSHR, PAX8, and NIS expression in the two primary cell lines and in three out of four immortalized lines. Furthermore, all the studied lines showed an increased iodine uptake following treatment with mir-335-5p. Moreover, we obtained organoid cultures growing the transfected lines in a semi-solid culture medium. We studied the morphology of the 3D structures generated before and after the transfection of miR-335-5p, the interaction among organoid cells and extracellular matrix components, and the protein levels of thyroid-specific genes through immunofluorescence. Our results led us to conclude that the restoration of the intracellular levels of miR-335-5p could have a role in promoting the re-differentiation of thyroid tumors with BRAF mutation.

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Y15

Pseudohypoparathyroidism: focus on neonatal features, preliminary data from a retrospective analysis of a large cohort of patients
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Since the first description of pseudohypoparathyroidism (PHP), a remarkable clinical variability was observed. In 2016 a new classification of this group of diseases has been published by the European Network on PHP and related disorders, proposing “inactivating FTH1/PTHrP signaling disorder” (iPPSd) as a new term that encompasses all the clinical entities. PHP and related disorders vary in clinical presentation and disease severity, and clinical features usually develop during mid and late childhood. There are only few reports in literature about neonatal PHP, describing hypocalcemic seizures in late neonatal period. To our knowledge no other neonatal complications are described as associated to iPPSd.

The aim of this study is to analyze a large cohort of iPPSd patients and to investigate early history of the disease, with special focus on neonatal complications. We collected data from 136 patients diagnosed with iPPSd and in regular follow-up at the Endocrinology Unit of Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico (Milan, Italy) and at the Pediatric Endocrinology Unit of Hôpital Bicêtre (Paris, France). We have retrospectively collected data about birth, and we have then investigated the rate of neonatal complications occurring within the first month of life. Then, we have subdivided neonatal complications in several categories (respiratory, cardiac, neurological, gastrointestinal, metabolic, multiple districts, others) and we have assessed the number of complications for each patient. We analysed data from 83 children and 55 adults with diagnosis of iPPSd (mean age 18 ± 11 years).

In our cohort 55.9% of patients were diagnosed with iPPSd2 (PHP1A) and 17.6% with iPPSd3 (PHP1B). 11.8% of patients suffered from acrodysostosis type 1 or 2 and 2.2% had a mutation of KDM1A as the genetic cause of food-dependent Cushing syndrome.

Overall, 38.9% of iPPSd2 patients developed neonatal complications.

Methods

We could also identify recurrent complications at birth. We could also identify recurrent complications at birth. We could also identify recurrent complications at birth. We could also identify recurrent complications at birth.

Conclusion

This study reveals three distinct molecular groups of PHP with specific expression profiles of GPCR and identifies KDM1A inactivation as the genetic cause of iPPSds. Besides GPCR KDM1A inactivation helps to drive the overexpression of the LH/CG receptor, potentially responsible for Cushing syndrome associated with pregnancy and menopause. KDM1A tumors present specific pathologic aspects including a large proportion of eosinophilic cells. ARMC5 and KDM1A genetic screening can now be offered for all PBMAH cases, opening the way to earlier diagnosis and improved management.

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Y16

Integrated genomics reveals the molecular classification of Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH), correlating with specific profiles of illegitimate receptors expression and identities KDM1A as the genetic cause of food-dependent Cushing syndrome

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Introduction

In Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH), cortisol secretion may be consecutive to physiological stimuli, through the illegitimate expression of G-protein coupled receptors (GPCR) in adrenocortical cells. The most characterized is the overexpression of GIP receptor (GIPR) leading to food-dependent Cushing syndrome (FDCS) but it has not been associated with the consecutive inactivation of ARMC5 responsible for 25% of PBMAH. This work aimed to investigate the molecular heterogeneity of PBMAH and its genetic cause.

Methods

The integrative analysis revealed three molecular groups with different clinical features: G1, 16 patients with PBMAH due to ARMC5 inactivating variants; G2, 6 patients with FDCs; and G3, 14 patients with a less severe phenotype. Exome sequencing identified germline truncating variants of KDM1A in 5 G2 patients, constantly associated with a somatic loss of the KDM1A wild-type allele on 1p, leading to a loss of KDM1A expression both at mRNA and protein levels (P = 1.2 × 10-12 and P < 0.001, respectively). G2 tumors are characterized by a specific pathological aspect including a large proportion of eosinophilic cells compared to G1 and G3 (P < 0.001). The transcriptome analysis allowed to show specific expression profiles of GPCR: G1/ARMC5 tumors showed a relative overexpression of the vasopressin receptors AVPR1A and AVPR1B compared to the two other groups (fold-change [FC] = 7.39, P < 0.001 and 3.98, P < 0.001, respectively) but a lower expression of AVPR2 (FC = 0.43, P = 0.15); G2/KDM1A tumors showed a dramatic overexpression of GIPR compared to the two other groups (FC = 105.02, P < 0.001) but also of the adrenergic receptors ADRA1B and ADR2A and PFC = 2.93, P = 0.027 and 9.99, P < 0.001, respectively) and of the LH/CG receptor (LHCG) (FC = 12.20, P < 0.001); G3 tumors showed a slight overexpression of the adrenergic receptors ADRA1B (FC = 3.49, P = 0.001) and in few tumors ADRA1D, AVPR2 and LHCGR were highly expressed suggesting molecular heterogeneity in G3.

Conclusion

This study reveals three distinct molecular groups of PBMAH with specific expression profiles of GPCR and identifies KDM1A inactivation as the genetic cause of FDCS. Besides GPCR KDM1A inactivation seems to drive the overexpression of the LH/CG receptor, potentially responsible for Cushing syndrome associated with pregnancy and menopause. KDM1A tumors present specific pathologic aspects including a large proportion of eosinophilic cells. ARMC5 and KDM1A genetic screening can now be offered for all PBMAH cases, opening the way to earlier diagnosis and improved management.

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Background

The risk of a second brain tumour following radiotherapy for pituitary adenoma or craniopharyngioma in adults is currently unclear. Studies are methodologically limited by small patient sample size, few case events, selection biases or the use of inappropriate controls.

Objective

To ascertain whether radiotherapy delivered to adults with pituitary adenoma or craniopharyngioma is associated with an increased second brain tumour risk using appropriate methodology.

Design

Multicentre, retrospective cohort study involving six adult endocrine centres.

Methods

4,292 patients with pituitary adenoma or craniopharyngioma detected until 31st December 2013 were identified from departmental registries. Patients with one image, unknown radiotherapy exposure status, genetic predisposition, history of brain tumour prior to study entry, or aged < 18 years at the time of radiotherapy, were excluded (n = 598). Recipients of proton or stereotactic radiotherapy (n = 81) were also excluded from statistical analyses, such that data were explored for 930 patients exposed to conventional, 3D-CRT or IMRT and 2,683 controls. Follow-up was defined by imaging dates from the time of radiotherapy until last imaging in the exposure group, and from the time of pituitary tumour detection until last imaging in the control group.

Results

Over 43,887 patient-years (12,674 radiotherapy, 31,213 controls), second brain tumours were reported in 58 patients (27 radiotherapy, 31 controls): 6 were malignant (4 radiotherapy, 2 controls), and 52 benign (23 radiotherapy, 29 controls). Older age at pituitary tumour diagnosis and radiography exposure was associated with increased risk of second brain tumour (HR 1.036, 95% CI 1.018-1.055, P < 0.0001 and HR 1.744, 95% CI 1.040-2.927, P = 0.035, respectively), but tumour type and sex were not. After adjusting for age, radiotherapy exposure was associated with an increased risk of second brain tumour (HR 1.728, 95% CI 1.029-2.902, P = 0.031). Cumulative probability of second brain tumour at 20 years was 4.2% and 2.1%, for the radiotherapy group and control group, respectively. Incidence rate ratio of irradiated versus controls was 2.15 (95% CI 1.27-3.60, P = 0.005). Median latency after radiotherapy was 8.1 years (7.5-27.3) for malignant and 17.2 years (3.0-50.8) for benign tumours, respectively.

Conclusions

This is the first study assessing the risk of a second brain tumour in a cohort of non-selected irradiated adults and appropriate controls with confirmed long-term imaging surveillance. The risk of a second brain tumour following radiotherapy (conventional, 3D-CRT or IMRT) for pituitary tumours is increased, although less than previously reported. Our results inform clinical practice and provide data to be used when counselling patients on the risks of radiotherapy.

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Y18

AKR1D1 knockdown identifies 7α-hydroxy-3-oxo-4-cholestenolic acid (7-HOCA) as a driver of metabolic dysfunction and hepatocellular cancer risk in patients with non-alcoholic fatty liver disease (NAFLD)

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Introduction

Acute kidney injury (AKI) is highly prevalent during hospitalization of patients with type 2 diabetes (T2D), and has been associated with increased risk of hypoglycaemia in Intensive Care Units. However, this association in non-critically ill patients is less clear and evidence on the impact of AKI’s severity and duration on hypoglycaemia is lacking.

Objectives

To assess the impact of AKI and its severity and duration on the risk of hypoglycaemia during hospitalization of non-critically ill patients with T2D.

Methods

Retrospective cohort study of patients with T2D, hospitalized in Internal Medicine wards, from 01/01/2018 to 31/12/2019. AKI was defined as an increase in serum creatinine by ≥0.3 mg/dl in 48 hours or ≥1.5 times baseline within 7 days, and as hypoglycaemia as blood glucose concentration < 70mg/dl. Glomerular filtration rate (GFR) was calculated by CKD-EPI equation and patients with chronic kidney disease (CKD) stage ≥4 were excluded. 239 hospitalizations with AKI were obtained (Group 1) and an equivalent number without AKI was randomly selected (Group 2). Binary logistic regression was used to control for confounding factors and ROC curve analysis to determine cut-offs values for AKI’s duration.

Results

478 cases were analysed, with mean HbA1C of 7.4 ± 1.6%, 36.0% previously treated with insulin. Patients with AKI were older (82.7 ± 7.9 vs 80.3 ± 10.1 years, P = 0.004) and had lower basal GFR (59.0 ± 17.3 vs 70.7 ± 19.1, P < 0.001). The prevalence of hypoglycaemia was higher in Group 1 (40.2% vs 15.9%, P < 0.001) and the risk increase was sustained when adjusted for confounding factors (including previous insulin therapy and insulin therapy protocol during hospitalization), with a 4.5 times greater risk of hypoglycaemia in the presence of AKI (95% CI 1.9-10.3). AKI’s severity was associated with mortality but not with hypoglycaemia. In contrast, each day of AKI’s duration was associated with an increase of 15% on the risk of hypoglycaemia and 16% on the risk of 30-day mortality, independently of its severity. A cut-off of 5.5 days of AKI was obtained for increased risk of hypoglycaemia and mortality. Globally, patients with hypoglycaemia had 4.4 times greater risk of death in 30 days (95% CI: 2.4-8.1).

Conclusion

AKI was an important risk factor for hypoglycaemia in non-critically ill hospitalized patients with T2D, and its prevalence was superior in elderly patients with CKD. The duration of AKI was the main factor increasing the risk of hypoglycaemia and mortality. These results highlight the need to define specific protocols to avoid hypoglycaemia and its burden in patients with AKI.

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Lifelong thyroid health depends on establishment of thyroid gland structure and function during early life development. However, thyroid development can be disrupted and lead to early- or adult life thyroid disorders. Still, the molecular machinery underpinning thyroid gland development remains poorly understood, particularly after the onset of fetal thyroid function. Here we used bulk-RNA-barcoding and sequencing (BRB-seq) to map the thyroid gland transcriptome as it undergoes transcriptional reprogramming after the onset of fetal thyroid gland function. We found 1619 differentially expressed genes (DEGs) during rat thyroid gland development from gestation day 21 to postnatal days 3, 6, 16 and 22. The DEGs partitioned into 6 clusters that display distinct temporal transcriptional patterns. Highly expressed genes in fetuses and neonates were primarily related to cell division, development and morphogenesis. This immaturity of the thyroid gland, even after the onset of thyroid function, was verified histologically, as the fetal thyroids displayed a dense structure with very little follicular lumen. Later on in postnatal development, as thyroid hormone concentrations peak, thyroid gland structure was more mature with larger follicles. This was also reflected in the postnatal transcriptome where genes important for thyroid hormone synthesis, such as Tpo, Slc5a5(MS) and Nkx2-1, were upregulated. In addition to the temporal DEGs, we identified 205 DEGs between males and females. Some of these DEGs were related to DEG hierarchy, Tg, Duox1 and Duox2, but the enriched terms also showed that developmental processes as well as the immune system and response to hormones was different between males and females. Thus, it is possible that these differences mediate a sex-specific susceptibility to external stressors such as environmental chemicals. Our results show that, even after the onset of thyroid function, the thyroid gland is still developing with a distinct and sexually dimorphic transcriptional landscape. Disruptions to this transcriptional reprogramming could alter development and thus susceptibility to thyroid disorders in adult life.

Background

Pancreatic Neuroendocrine Tumors (PanNETs) are highly prevalent in Multiple Endocrine Neoplasia type 1 (MEN1) and one of the main causes of mortality. Conventional imaging is the mainstay of PanNET screening/surveillance in MEN1. This study aims to assess the diagnostic accuracy of conventional pancreatic imaging studies and to determine the added value of pancreatic fine needle aspirations (FNA) for the diagnosis of MEN1-related PanNETs.

Methods

Patients were included from the population-based MEN1 database of the DutchMEN Study Group from 1990–2017 (n = 445). Magnetic resonance imaging (MRI), computed tomography (CT), endoscopic ultrasound (EUS), FNA, and surgical resection were obtained. For diagnostic accuracy assessment, patients with a PanNET diagnosis >1900 were included if both index and reference test were available. To assess diagnostic accuracy, the first imaging (CT, MRI or EUS) of the pancreatic head and the first imaging of the pancreatic body/tail were considered the index test. For specific comparison of diagnostic accuracy between MRI and CT in the modern era, the first MRI or CT between 2010 and 2017 was the index test. The reference standard was a composite of surgical histopathology and if histopathology was unavailable radiological follow-up. Results

413 patients underwent 3477 imaging studies. Median radiological follow-up was 8.4 yrs. Time trends show an increasing number of scans/patient, and a preference for MRI in the last decade. Overall diagnostic accuracy of the combined imaging approach was good with a positive (PPV) and negative predictive value (NPV) of 88.9% (76.0-95.6) and 92.8% (89.4-95.1) for PanNET located in the pancreatic head and 92% (85.3-96.0) and 85.3% (80.5-89.1) in the body/tail. For comparison of MRI vs CT, PPV and NPV for tumors located in the head were 100% (76.0-100) and 87.1% (76.3-93.6) (MRI vs CT) (22.9-88.4) and 70.4% (51.3-84.3) (CT). PPV and NPV for tumors located in the body/tail were 91.3% (72.0-98.8) and 87.0% (75.3-93.9) (MRI) vs 100% (74.0-100) and 77.8% (54.3-91.5) (CT). FNA was performed of 34 lesions in 33 patients. FNA diagnosis was PanNET in 24 (all confirmed PanNET by histology (10) or follow-up (14)), normal/cyst/unrepresentative in 6 (all confirmed PanNET by follow-up), and adenocarcinoma in 4 (2 confirmed, 2 PanNET).

Conclusion

Diagnostic accuracy for the diagnosis of PanNET was higher for MRI compared to CT and should be the preferred non-invasive test. Perturbating modality for PanNET screening/surveillance in MEN1. The high diagnostic accuracy of pancreatic imaging and the sporadic occurrence of pancreatic adenocarcinoma question the need for routine (EUS-guided) FNA.

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Role of the transcription factor HHEX in inner adrenal cortex homeostasis and response to progesterone signaling

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The adrenal glands serve as central organs of the endocrine system by producing steroid hormone essential for organismal homeostasis. Mechanisms ensuring proper adrenal homeostasis and function are therefore crucial for maintaining human life. ACTH, released by the pituitary corticotropic, is required for the differentiation of the inner part of the adrenal cortex (the zona fasciculata) and the resultant stimulation of cortisol production. Perturbation of ACTH signaling can lead to diverse pathologic manifestations such as adrenal hyperplasia, hypertrophy, hormone overproduction or adrenal insufficiency. For example, elevated ACTH is a characteristic of patients suffering from Congenital Adrenal Hyperplasia (CAH), a set of defects in cortisol synthesis due to autosomal recessive mutations in genes encoding steroidogenic enzymes. To study the complexity of the ACTH-responsive cell population in the adrenal cortex, we performed single-cell RNAseq of the steroidogenic lineage in the adult mouse adrenal. We identified Hhex as a transcription factor with a restricted expression to the ACTH-responsive zona fasciculata. Although the role of HHEX in adrenal biology is completely unknown, a meta-analysis identified a germ-line variant of uncertain significance near the gene HHEX associated with increased adrenal androgens and introduction of human genes. Interestingly, we have also observed an increase in Hhex expression in a mouse model of CAH. Together with our scRNAseq data, we hypothesized that HHEX contributes to the unique function of the ACTH-responsive inner cortex. To define the role of HHEX in adrenal homeostasis, we generated Hhex knockout mouse models. KO mice exhibited progressive adrenomegaly by 15 weeks of age, accompanied by hypertrophy, most prominent in the inner cortex. Expression of the transcription factor Nr5a2/SF1 and steroidogenic enzymes involved in corticosterone production were significantly upregulated at 6 weeks old, prior to adrenomegaly. Interestingly, we found dramatic downregulation of members of the membranous progesterone receptor family (PAQR). PAQR signaling has been implicated in the downregulation of CAMP, a primary mediator of ACTH signaling. Thereby, we speculate that down-regulation of PAQR and subsequent increased ACTH sensitivity could drive the increase in steroidogenesis in Hhex KO mice. These findings suggest that HHEX provides a unique autocrine/paracrine intra-adrenal feedback to ACTH-driven CAMP signaling by upregulating PAQR in a unique progesterone-responsive cell population in the inner cortex. As a result, we are currently assessing the implication of HHEX in contributing to the hypertrophy and steroidogenic phenotype observed in CAH.

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Rapid Communications
Diabetes, Obesity, Metabolism and Nutrition 1

RC1.1 Predictors of missing postpartum reclassification OGTT in women with gestational diabetes
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Introduction
Women with gestational diabetes (GD) have an increased risk of developing future type 2 diabetes mellitus (T2DM). A reclassification oral glucose tolerance test (OGTT) is currently recommended in the postpartum period. However, most studies report a compliance rate below 50% and as low as 23%.

Objectives
We aimed to study predictors of missing postpartum OGTT in women with GD. Materials and Methods
Retrospective study based on the national register of GD. Included women followed between 2012 and 2017. Excluded women with fetal losses and missing data on age, educational level, BMI, previous history of GD, abortion or arterial hypertension, family history of T2DM, treatment, delivery and obstetric/neonatal complications. Women with and without OGTT were compared. A logistic regression model was used to study factors associated with absence of OGTT: variables with different distribution between groups were included in the analysis.

Results and Conclusions
We studied a total of 14081 women, 4324 (30.7%) had missed postpartum OGTT. Women without OGTT were younger, more frequently foreigners, had higher BMI and more often had previous GD, multiparity, twin pregnancies and preterm deliveries and they were less frequently diagnosed in the 1st trimester. Newborns from women without OGTT were more often macrosomic and had neonatal hypoglycemia. In the multivariate analysis, age (OR 0.96 (IC 95%: 0.95-0.96), P < 0.001), BMI ≥30 kg/m² (1.13 (1.04-1.23), P = 0.004), preterm delivery (1.35 (1.18-1.54), P < 0.001), foreign nationality (1.33 (1.18-1.49), P < 0.001), having a college degree (0.90 (0.83-0.97), P = 0.01), multiparity (0.91 (1.01-5.21, P < 0.001), twin pregnancy (1.19 (1.08-1.78), P = 0.09), pathological treatment (0.68 (0.63-0.73), P < 0.001), previous GD (1.16 (1.04-1.29), P = 0.01), previous abortion (1.21 (1.12-1.32), P = 0.001), diagnosis in the 1st trimester [0.86 (0.79-0.92), P < 0.001] and neonatal hypoglycemia [1.21 (1.01-1.45), P = 0.04] were associated with missing postpartum OGTT. Women with higher BMI, multiparity, foreigners, with twin pregnancies, previous history of GD, abortion, preterm delivery and neonatal hypoglycemia have an increased risk of missing OGTT. On the other hand, older women and those who needed pharmacological treatment, who have a college degree and who are diagnosed in the 1st trimester have lesser risk of missing OGTT.

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RC1.2 Glucose alterations, insulin resistance, hypertension, and activation of the renin-aldosterone system are strictly associated in pediatric obesity
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Background
The increase of global childhood obesity has led to an increase of associated co-morbidities also at a young age. The pro-inflammatory state and insulin resistance are two master regulators of several complications, including hypertension and pre-diabetes frequently connected in a complex cross-talk.

Aim
To evaluate the relationship between glucose alterations and blood pressure and the pathogenetic involvement of the renin-aldosterone system (RAAS) in pediatric obesity.

Methods
We retrospectively evaluated 800 paediatric subjects (11.4 ± 3.1 years) with overweight or obesity at the first visit with a complete clinical and metabolic screening (BMI, BMI-SDS, blood pressure, glucose, and insulin levels during an OGTT). Aldosterone and renin were measured with chemiluminescence, and their ratio (ARR) was calculated.

Results
774 patients had all the parameters. 11.5% of patients were with overweight and 88.5% with obesity. Blood pressure has been characterized following the last American Academy of Pediatrics guidelines: 679 patients (87.6% 88.0%) had hypertension (HTN). Of them, 38.5% had elevated blood pressure, 226 (29.2%) were classified as HTN stage 1, and 414 (53.4%) stage 2. Regarding glucose levels, 41 subjects had impaired glucose levels (IGF), 52 impaired glucose tolerance (IGT), 3 type 2 diabetes (T2DM), and a totally 80 subjects had one or more glucose alterations (IFG/IGT/T2DM). Patients with IGF (P < 0.01), IGT (P < 0.02), or T2DM/glucose alterations (P < 0.02) were more frequently with HTN. Blood pressure levels were higher in subjects with glucose alterations (P < 0.04) than those with normal glucose levels (NGT). OGTT glucose levels and HOMA-IR (P < 0.002) were higher in subjects with the three HTN stages than those with normal levels. Subjects with glucose levels > 155 mg/dl after 60′ at OGTT had more frequent HTN (P < 0.001) and higher diastolic blood pressure levels (P < 0.002) than NGT. We also found increased activation of the renin-angiotensin-aldosterone system (RAAS), positively correlated with BMI and female gender, that mainly characterized subjects in HTN stage 2. Aldosterone levels were higher in subjects with glucose levels > 155 mg/dl after 60′ at OGTT than without those it (P < 0.003).

Conclusions
Already in childhood obesity, there is a close relationship between insulin resistance, glucose alterations, hypertension, and RAAS. The identification of specific risk categories, such as the presence of altered glucose blood or hypertension, could provide risk indicators to close clinical surveillance for the prevention and identification of complications and follow-up of organ damage.

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RC1.3 Plasma amino acid profile in women with polycystic ovary syndrome and its correlation with metabolic disturbances
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Background
Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinopathy commonly diagnosed in reproductive age women, predisposing to the development of metabolic disturbances. However, the mechanisms underlying the connection between PCOS and metabolic disorders are still not well understood. The aim of the study was to investigate amino acid (AA) profile in women with PCOS and to assess its relation with metabolic disturbances.

Methods
326 women: 209 diagnosed with PCOS and 117 healthy controls participated in the study. Anthropometrical, biochemical and hormonal parameters were assessed. A subgroup of patients with abdominal obesity (defined as the waist circumference ≥ 80 cm) was separated and included 143 PCOS patients and 74 controls. The gas–liquid chromatography combined with tandem mass spectrometry was used to assess amino acids levels – branched chain amino acids (BCAAs); leucine, isoleucine, and valine, and the aromatic amino acids (AAAs); phenylalanine, typtophan and tyrosine.

Results
Statistical analysis showed significantly higher plasma levels of the BCAAs (540.4 ± 97.0 nmol/ml vs 501.2 ± 85.7 nmol/ml; P < 0.001) and AAAs (162.8 ± 22.6 nmol/ml vs 153.1 ± 20.5 nmol/ml; P < 0.001) in women with PCOS. Significant correlations (P < 0.05) were also found in PCOS patients between both BMI and HOMA-IR and BCAAs (rs = 0.34 for BMI and rs = 0.39 for HOMA-IR) and AAAs (rs = 0.15 for BMI and rs = 0.23 for HOMA-IR). In the analysis of women with abdominal obesity, there were significant differences between PCOS subjects and controls in BCAs (560.2 ± 99.2 nmol/ml vs 513.5 ± 78.1 nmol/ml; P < 0.001) and AAAs (163.1 ± 21.4 nmol/ml vs 156.7 ± 20.1 nmol/ml; P = 0.01).

Conclusions
Plasma amino acid profile is altered in women with PCOS and it is correlated with BMI and HOMA-IR. Additionally, in women with abdominal obesity BCAAs...
and AAAs concentrations are more severe altered in PCOS group. Derangement in the plasma amino acid profile might be an important connection between PCOS and metabolic disturbances, however, further studies are needed.

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RC1.4
Exploring the role of skeletal muscle Mineralocorticoid Receptor in glucose metabolism and insulin signaling

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Mineralocorticoid Receptor (MR) is able to regulate the transcription of a number of genes in the myotube, nevertheless the role of this steroid hormone receptor in skeletal muscle (SM) metabolism needs to be clarified. SM represents a major site for glucose uptake and local metabolic derangements play a pivotal role in the development of insulin resistance (IR). The aim of this study was to investigate the contribution of MR in mediating SM metabolic alterations in a mouse model of diet-induced obesity. We observed that mice fed a high fat diet (HFD mice), showed impaired glucose tolerance compared to mice fed a normal diet (ND mice). Mice fed a HFD treated with the MRA spironolactone (HFD + spiro mice) revealed an improvement in glucose tolerance, compared with HFD mice. In addition, MRA-treated obese mice showed brown adipose tissue activation, which was expected to contribute to the improved glucose metabolism. To investigate if MR blockade in SM could contribute to the observed MRA-mediated metabolic effects, we analyzed MR expression in gastrocnemius, observing that MR protein abundance was downregulated by HFD compared to ND mice, whereas administration of spiro was able to partially revert this effect in HFD + spiro mice. Interestingly, SM MR expression profile was opposite to that observed in adipose tissue (AT), showing increased protein abundance in HFD group, thus suggesting a different metabolic function of MR in AT and SM.

Upregulated levels of mineralocorticoids, as well as up-regulated MR activation, are associated with impaired glucose metabolism. In our experimental model, downregulated expression and function of MR in SM of HFD mice with altered glucose tolerance, suggests that SM MR has a completely different role in regulation of glucose metabolism. To confirm this hypothesis, we investigated the effect of MR blockade on insulin signalling in a cellular model of myocytes (C2C12) with IR, which was obtained by treatment with palmitate, in the presence of glucose metabolism. To confirm if MR blockade in SM could contribute to the observed MRA-mediated metabolic effects, we analyzed MR expression in gastrocnemius, observing that MR protein abundance was downregulated by HFD compared to ND mice, whereas administration of spiro was able to partially revert this effect in HFD + spiro mice. Interestingly, SM MR expression profile was opposite to that observed in adipose tissue (AT), showing increased protein abundance in HFD group, thus suggesting a different metabolic function of MR in AT and SM. Observed in adipose tissue (AT), showing increased protein abundance in HFD group, thus suggesting a different metabolic function of MR in AT and SM.

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RC1.6
Evidence for three superimposed components, via which metformin affects blood glucose in obese mice

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Introduction
Despite a plethora of suggested targets and pathways, the mechanism of anti-hyperglycaemic metformin action is still unknown. The present study critically re-analysed protocols broadly applied in preclinical rodent studies.

Methods
Obese male C57BL/6J mice on high fat diet were treated with metformin in the form of a single dose, daily intraperitoneal injections, admixture to drinking water, or continuous infusion via intraperitoneal minipumps. Glucose tolerance tests (GTT) were performed to evaluate effects on blood glucose homeostasis.

Results
Thirty min after intraperitoneal injection of 50mg/kg metformin, the plasma concentration of metformin was 56±22µM and glucose tolerance was improved (AUC, min*g/dl: 40.4±1.8 vs 34.0±1.2, P=0.008). The beneficial effect on glucose tolerance was gone 3 h after drug administration, when plasma metformin was down to 2.8±0.7µM (AUC, min*g/dl: 39.0±1.4 vs 36.4±1.7, n.s.). Rapid clearance of metformin accompanied by fading of its action suggests that mice under regular treatment, however, metformin also affected glucose tolerance indirectly via reduced appetite and weight-mediated actions were eliminated by restricted feeding water, or continuous infusion via intraperitoneal minipumps. Glucose tolerance tests (GTT) were performed to evaluate effects on blood glucose homeostasis.

Conclusions
Sex steroids regulate liver fat content and body fat distribution in both men and women: a study in transgender persons

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Objective
Visceral adipose tissue (VAT) and liver fat content are associated with insulin resistance and cardiovascular disease and show clear sex differences. Our objective is to determine the effect of estradiol and testosteron on VAT and liver fat content in trans women (assigned male at birth, identity as female) and trans men (assigned female at birth, identity as male).

Design
Open-label partly randomized intervention study in 8 trans women and 18 trans men, receiving hormone treatment.

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Adrenal and Cardiovascular Endocrinology 1

RC2.1

A rapid genetic diagnosis for >80% individuals with non-CAH Primary Adrenal Insufficiency is achievable by candidate gene sequencing combined with WES

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Primary adrenal insufficiency in children can be due to mutations in >20 genes, most commonly CYP21A2, giving rise to 21-hydroxylase deficiency. Phenotypically these disorders overlap and present with conditions ranging from isolated (or familial) glucocorticoid deficiency (FGD) to syndromic disorders involving multiple tissues. Distinguishing between them can be problematic, especially where biochemical testing is not possible or not undertaken. Over the last 30 years 400 individuals with suspected FGD, from 31 different countries, have been referred to our centre for genetic testing. All cases had low/undetectable serum cortisol and, where measured, elevated plasma ACTH levels. Using a combined, two-step protocol we have sequenced 369 of the 400 individuals. In the first step we sequenced the small, frequently mutated, candidate genes: MIRC2, MRAP, STAR and CYP11A1, by Sanger sequencing (CGS) before proceeding to whole exome sequencing (WES) if these were mutation free. For CGS, sequences were aligned to reference sequences using BioEdit software and WES variant call files were analysed using Ingenuity Variant Analysis package and/or examination of BAM files, using the Integrative Genomics Viewer, to detect exonic deletions. Rare, synonymous or predicted benign variants were subjected to an in vitro splicing assay using the pET01 vector (MoBiTec). In 308/369 individuals we found a definitive diagnosis in a causative gene for adrenal insufficiency, a success rate of 81%, and identified many novel mutations. The findings also highlighted a number of causal synonymous and predicted benign variants resulting in splice defects. The aetiologies of cases with a gene defect were as follows: MIRC2 (22%), MRAP (17%), NNT (15%), STAR (9%), CYP11A1 (7%), with the remaining 30% due to a further 13 genes. Previous founder effects were reinforced e.g. S74I in MIRC2 and ns6161 in CYP11A1 in the UK population, P24Rfs*4 in MCM4 in Ireland and R188C in STAR in Canada, with new associations being discovered for T731i in NNT in Sudan and R222Q in SGPL1 in Saudi Arabia. In contrast, common MRAP splice mutations seen at the exon 3/intron 3 junction were present in individuals from many countries. The use of CGS/WES now permits a rapid genetic diagnosis for >80% individuals and is an invaluable, cost-effective tool to improve tailored patient management. For patients without a genetic diagnosis, it is unclear whether they have unconventional mutations in known genes or if there are further gene defects to be discovered.

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RC2.2

FKBP5 methylation in adrenal insufficiency: looking at a new tool for assessing the quality of glucocorticoid replacement?

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Available glucocorticoid (GC) replacement regimens in adrenal insufficiency (AI) only roughly correspond to physiological steroid profiles. Control of subtherapeutic quality is therefore difficult but significant, as even mild under-compensation or under-replacement may be clinically relevant. FKBP5 regulates GC receptor sensitivity by reducing its affinity to cortisol when bound to the receptor complex. FKBP5 methylation has been inversely correlated with cortisol levels both in healthy controls and in patients with endogenous hypercortisolism. We analyzed FKBP5 gene methylation (DNAm) within introns containing GC responsive elements as well as promoter and proximal enhancer regions by bisulfite pyrosequencing in a cohort of 96 patients with primary (PAI, n = 57) and secondary (SAI, n = 29) AI. Results were correlated with GC dose, salivary and 24-hour urinary cortisol, prevalence of adrenal crises (AC) per patient-year and 24-hour blood pressure (BP) levels. GC dose and DNAm were negatively correlated for the majority of the investigated regions (intron 1: r = -0.45, P < 0.01, intron 5: r = -0.35 P < 0.01, intron 7: r = -0.23 P = 0.034, promoter A1: r = -0.35 P < 0.01). Intronic DNAm correlated negatively with 24-hour urinary cortisol (intron 2: r = -0.25, P = 0.032) and positively with bedtime salivary cortisol (intron 7: r = 0.3, P < 0.01). We observed a positive correlation between the prevalence of AC and intronic DNAm (intron 2 and 5: r = 0.29 P < 0.01 for each) and day-time BP, systolic and diastolic night-time BP and nocturnal dipping correlated negatively with DNAm within several intronic, promoter and proximal enhancer regions. GC replacement was higher, whereas intronic DNAm was lower in PAI compared to SAI: GCC 22 (10-60) vs 20 (10-37.5) ng P = 0.032, intron 5: 11% vs 15% P = 0.028). FKBP5 methylation analysis may provide helpful further insight regarding the evaluation of GC replacement and might help improving assessment of GC load in AI, as it correlates with replacement doses, cortisol levels and 24-hour BP. Our observations warrant further analyses in larger cohorts.

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limitation in the current COVID-19 pandemic and Synacthen test. We aimed to investigate the value of basal cortisol level for predicting AI in our selected cohort of patients at risk of secondary adrenal insufficiency from pituitary disease, pituitary surgery or pituitary irradiation.

Methods

A ten-year retrospective review was performed in our tertiary unit. SSTs were performed before midday. AI was defined as peak serum cortisol level of < 550 nmol/l on Roche Cortisol I assay or < 420 nmol/l on Roche Cortisol II assay. Conversion of baseline cortisol level from Roche I to Roche II equivalent measurement was done using validated regression equation. Diagnostic performance was evaluated by Receiver Operating Curve (ROC) analysis.

Results

595 SSTs performed from 2010 to 2020 were included. 51 (8.6%) were positive for AI. The ROC analysis showed an overall area under the curve (AUC) for basal cortisol of 0.975 (95% CI 0.959 to 0.986). If a basal cortisol level cut-off of ≤ 237 nmol/l was implemented to predict AI, no failed SST would be missed, hence the negative predictive value to rule-out AI was 100% (95% CI 93 to 100%). By using a cut-off value of 237 nmol/l, 399 out of 544 (73%) SSTs could be eliminated. With a lower basal cortisol cut-off of ≤ 165 nmol/l, 5 out of 51 failed SSTs would be missed but 503 out of 544 (92%) normal SSTs would be avoided.

Conclusion

In our cohort of patients at risk of secondary adrenal insufficiency, basal morning serum cortisol concentration can be utilised as a convenient screening test, with high diagnostic performance, to identify patients requiring confirmatory dynamic testing using SST. Further prospective studies are required to validate the cut-off values proposed.

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RC2.4

Diagnostic value of basal cortisol level to predict adrenal insufficiency in patients treated with glucocorticoids during COVID-19: a single centre observational cohort study

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Objective

During the current pandemic of COVID-19, many therapeutic protocols adopted high dose systemic glucocorticoids (GC) for treatment of moderate to severe respiratory insufficiency. The suppression of the hypothalamic–pituitary–adrenal axis by synthetic GC, even after a short treatment period, cannot be reliably predicted due to pathophysiological changes in cortisol dynamics in critically ill, inter-individual pharmacokinetic differences, and sensitivity variations in glucocorticoid receptors. Moreover, the revealed pathological adrenal changes in Covid-19 patients make prior estimates even less reliable.

Aim

We aimed to estimate percentage of patients with adrenal insufficiency (AI) at the end of acute phase of COVID-19 after tapering GC toward replacement dose of hydrocortisone for at least 1 week and to investigate for the first time the basal cortisol level for prediction of AI in this population.

Methods

We retrospectively analysed 287 consecutive patients (median 65 years, range 26-91 years); 113 (39.4%) female and 174 (60.6%) male) who had low-dose (1 mg) cosyntropin testing. Site-specific cut-off levels for AI were < 500 nmol/l. The overall potential of cortisol at baseline to classify patients into adrenal (in) sufficiency was assessed using receiver-operating-characteristic (ROC) curve analysis.

Results

The average cortisol level at baseline was 419 nmol/l (median 429, range 36-953 nmol/l), and at 30’ 617 nmol/l (median 623, range 114-1092 nmol/l); Overall, 65 (22.6%) showed an insufficient increase of cortisol and were categorized as AI. ROC showed an overall area under the curve (AUC) for basal cortisol of 0.84, with 95% confidence interval 0.79-0.89. If basal cortisol level was below 100 nmol/l, which was the case in 125 patients (43.6%), the negative predictive value (NPV) to predict no AI was 96.0%; if it was at least 400 nmol/l (158 patients, 55.1%), NPV was 93.0%; and if it was at least 460 nmol/l (113 patients, 39.4%), NPV was 99.1%. PPV sharply declines after the threshold of 100 nmol/l. On the other hand, PPV increases approximately linearly over the threshold range from 350 to 460 nmol/l, where it practically reaches 100%.

Conclusion

Basal cortisol levels ≤ 100 and ≥ 460 nmol/l in patients tested for possible AI were found in 41.2% and had sufficient diagnostic accuracy to safely abolish the need for cosyntropin testing. The data may help guide clinicians when testing for AI can be simplified.

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RC2.5

Treatment of adrenal insufficiency in the netherlands from a patient perspective in the recent past. Lessons learned for europe

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In 2015 AdrenalINET organized a roundtable conference with patient representatives, prescribers and pharmaceutical industry. The cause of this meeting was complaints of patients about the problematic hydrocortisone market in the Netherlands, characterized by frequent availability issues (shortage) of the hydrocortisone tablets/capsules and frequent changes in manufacturers (compounding companies) leading to quality issues. All parties at the roundtable meeting agreed to join forces to achieve hydrocortisone tablets with the following requirements:

1. Immediate release hydrocortisone tablets for both children and adults.
2. Conventional IR-released hydrocortisone remains the gold standard (EndoERN position paper 2021).
3. Various strengths ranging from 1 to 10 mg.
4. Colour coded tablets with no bad taste and no need for splitting anymore.
5. Permanent availability which will be increased by obtaining marketing authorization and by production of hydrocortisone tablets in the EU from preferable European raw materials. In 2018 one of our partners, a small Dutch pharmaceutical company, started the development of new hydrocortisone tablets based on the above requirements. Despite a lot of regulatory struggles, in March 2020 registration was approved in the Netherlands for the 1.5 and 10 mg tablets, followed by recent registration (2021) of the 2 and 5 mg hydrocortisone. The different strengths make it possible to mimic the individual patient’s cortisol pattern during the day most closely. The introduction of the new tablets was followed by a fast-uptake in the market. At the moment expansion of these hydrocortisone tablets to other European countries will take place. This project is a good example of fruitful collaboration between patients, doctors and pharmaceutical companies which deserves a roll-out over the rest of Europe. AdrenalINET and Endo-ERN may serve an important role in achieving this.

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therapy. We have examined whether MRHC can improve CAH control in patients receiving high dose standard treatment.

Methods
We reviewed the data of patients in the randomised study of standard treatment versus MRHC and selected those on >25 mg/day hydrocortisone dose equivalent (HDE = prednisolone dose 5 & dexamethasone 80) at study entry. Patients were assessed at 24 weeks after blinded dose titration aimed to bring 17OHP into the optimal range (<35 nmol/l) and A4 into the reference range. After 24 weeks, patients participated in an ongoing MRHC single arm extension study. Control of CAH was defined as 0900h 17OHP <36 nmol/l.

Results
At baseline 41% (n = 43/105) of patients were on >25 mg HDE/day standard treatment: 21/43 were female, mean baseline 0900h 17OHP was 106 nmol/l and 48% were uncontrolled. At 24 weeks 95% (n = 21/22) of patients on MRHC were controlled on median 40 mg/day (mean 17OHP 10 nmol/l) and for standard treatment 81% were controlled on median 40 mg HDE/day (mean 17OHP 49 nmol/l). In the full cohort, there were no adrenal crises in the MRHC group and three in the standard treatment group (10.7/100 patient years). After 24 weeks 27 of the 43 patients entered the clinician-titrated, MRHC single-arm extension study. At the 18-month interim analysis 76% patients were in control with a median dose of 25 mg (52% <25 mg/day) and mean 17OHP 24 nmol/l. In the ongoing extension study of all patients on MRHC (221 patient years), there were 12 adrenal crises in 5 patients (5.4/100 patient years).

Conclusions
It is common in CAH patients for the glucocorticoid dose to exceed the recommended adrenal replacement dose and stil~50% of patients remain uncontrolled. MRHC controlled 17OHP in 95% patients who were previously on high dose standard therapy and over time it was possible to reduce the MRHC dose to an adrenal replacement dose in ~50% of patients and retain control in 75%.

References

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RC2.7
Improved biochemical control with modified-release hydrocortisone overturns the impaired fludrocortisone effect in salt-wasting CAH patients

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Background
Patients with salt-wasting congenital adrenal hyperplasia (CAH) due to classic 21-hydroxylase deficiency require glucocorticoid (GC) and mineralocorticoid (MC) replacement therapy. Recently, it was shown that twice daily modified-release hydrocortisone hard capsules (MRHC, Efmody) improved biochemical control with most patients showing good disease control versus standard GC therapy. However, no data has been reported on the renin-angiotensin-aldosterone (RAA) system in these patients. This is of clinical relevance because 17-hydroxyprogesterone (17-OHP) is a known MC-receptor antagonist, and poorly controlled salt-wasting CAH patients often require higher fludrocortisone doses than patients with primary adrenal insufficiency. The aim of this study was to investigate the RAA system in patients on MRHC.

Methods
Data was analyzed from the 6-month, phase 3 study.1 Patients with salt-wasting CAH (5 excluded; 83 included; 34.9% male, median age 35.3 yrs) were randomized to either MRHC twice daily (n = 42) or standard GC (n = 41). 4.9% dexamethasone, 39% prednisolone, 56.1% HIC). MC replacement therapy with fludrocortisone remained stable and unchanged throughout the study. Blood pressure, potassium, sodium, plasma-renin-activity (PRA) serum androgen precursors 17-OHP and androstenedione were analysed at baseline, 4, 12 and 24 weeks.

Results
Both groups improved hormonal control (17-OHP and androstenedione) on intensive monitoring and with stable GC doses on MRHC (median 25.0 to 25.0 mg/d, P = 0.002) and increased doses on standard GC (25.0 to 31.3 mg/d, P = 0.001) at 24 weeks. However, the serum 17-OHP was significantly lower on MRHC compared to standard GC at 24 weeks (2.5 nmol/l vs 10.5 nmol/l, P = 0.001). PRA decreased significantly from baseline to 24 weeks in patients on MRHC (0.83 ng/l/s to 0.48 ng/l/s, P = 0.012) but not in patients on standard GC therapy (0.53 ng/l/s to 0.52 ng/l/s, P = 0.613). In line with these changes, serum sodium concentrations increased from baseline to 24 weeks in patients on MRHC (138.8 ± 1.9 mmol/l to 139.3 ± 1.8 mmol/l, P = 0.047), but remained unchanged on standard GC (139.8 ± 1.6 mmol/l to 139.3 ± 1.9 mmol/l, P = 0.135). No significant changes were seen in systolic and diastolic blood pressure and serum potassium levels.

Conclusion
Six months of MRHC therapy decreased PRA and increased sodium levels indicating a better MC effect of the unchanged fludrocortisone dose. This might be due to the significantly decreased levels of the MC-receptor antagonist 17-OHP owing to the improved control of precursor excess by MRHC, indicating lower fludrocortisone efficacy in poorly controlled salt-wasting CAH patients.

References
Merke DP. JCEM 2021 106 e2063-e2077.

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RC2.8
Fertility in congenital adrenal hyperplasia (CAH) patients on modified release hydrocortisone capsules (MRHC, Efmody)

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Background
Fertility in CAH women is impaired: 0.25 live births vs 1.8 in the UK population and 45% have irregular menses vs 13.6% in healthy women. Male fertility is also impaired in CAH with oligospermia reported in 48%. Treatment of infertility usually involves increasing the glucocorticoid dose to normalise adrenal androgens and progesterone to facilitate ovulation and implantation, respectively.

Modified-release hydrocortisone (MRHC) capsules, (Efmody, Diurnal Ltd, Cardiff, UK), replicate the physiological cortisol diurnal rhythm and improve CAH control compared to standard therapy. In the phase 3 randomised study of MRHC versus standard treatment,4 women had restoration of menses on MRHC versus 1 on standard treatment but seeking fertility was an exclusion criteria. We have examined fertility in the ongoing MRHC single arm extension study.

Methods
Review of fertility in the ongoing MRHC single arm extension study. Standard therapy dose is given as hydrocortisone dose equivalent (HDE = prednisolone dose 5 & dexamethasone 80).

Results
Twenty-seven of 49 premenopausal women were not using oral or intrauterine contraception. Of these women, 10/27 (37%) reported evidence of improved fertility: 5 reported menstrual regularisation and 5 women reported 6 pregnancies (3 healthy live births, 1 ongoing, 2 miscarriages). In these women the mean(SD) HDE on standard treatment before the study and pregnancy was 29(12) mg and then on MRHC at time of interim analysis or withdrawal due to positive pregnancy test the dose was 28(8) mg. In the 29 men (contraception data not collected), 4 pregnancies occurred in 3 female partners resulting in healthy live births.
Thyroid 1
RC3.1
Usefulness of the EU-TIRADS score on sparing thyroid nodules cytology: a retrospective study
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Introduction
Incidental diagnosis of thyroid nodules has increased in recent years, leading to thyroid cancer diagnosis inflation. Nonetheless, mortality rate for thyroid malignancies remains very low, suggesting that its treatment is unlikely to affect the overall prognosis in the majority of cases. Several thyroid imaging scores have been proposed to reduce unnecessary invasive diagnostic procedures. Our aim was to verify the usefulness of the EU-TIRADS score on sparing thyroid nodules cytology.

Methods
We conducted a retrospective and observational study of thyroid nodules submitted to fine-needle aspiration biopsy (FNAB) between January 2016 and October 2021 at our center. Each nodule was classified as whether having an indication for FNAB (group A) or not (group B) according to the EU-TIRADS score. We then compared cytology results between the two groups, using Bethesda diagnostic categories.

Results
FNAB were performed in 1935 thyroid nodules from 1308 patients. Using the EU-TIRADS score, 766 (39.6%) nodules had no cytology indication (group B). Of these, 40.2% (n = 308) were EU-TIRADS 2, 35.4% (n = 271) EU-TIRADS 3 ≤ 20 mm, 20.2% (n = 155) EU-TIRADS 4 ≤ 15 mm and 4.2% (n = 32) EU-TIRADS 5 ≤ 10 mm. In group B, a suspicious or malignant category was reported only in 7 (0.9%) nodules. Suspicious follicular neoplasm was reported in 13 (1.7%) nodules. Group A presented a higher prevalence of suspicious or malignant categories (2.8% vs 0.9%, P < 0.01), a higher prevalence of suspicious follicular neoplasm category (4.1% vs 1.7%, P < 0.01) and a higher prevalence of nondiagnostic categories (45.1% vs 36.5%, P < 0.01). Notably, nondiagnostic categories were found in 279 (36.5%) of nodules submitted to cytology in group B, leading to repetition of cytology and consequent avoidable visit to the clinic in 63 individuals. Interestingly, when comparing avoidable cytology rate per year, we observed a lower rate in the more recent year (26.8% vs 41.3%, P < 0.01), suggesting a greater adherence to the EU-TIRADS system for decision making.

Conclusion
In the context of a common disease, such as thyroid nodules, application of the EU-TIRADS system score can avoid unnecessary cytologies, reducing over-diagnosis and consequent overtreatment.

RC3.2
Performance of a raman fingerprint in thyroid nodules with indeterminate cytology: a prospective blinded monocentric study
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Background
Molecular analysis of thyroid fine-needle aspiration biopsy (FNA) was proposed to improve indeterminate nodules management. However, sensitivity and specificity as well as the cost of molecular diagnostics require to be improved to increase their cost-effectiveness for medical practice setting. Raman spectroscopy (RS) demonstrated ability in separating benign from malignant thyroid lesions in surgically removed tissues, based on specific RS profile. This study aimed to investigate the diagnostic performance of RS on cytological samples obtained by thyroid FNA.

Methods
In this prospective, blinded monocentric study, we enrolled 123 patients with indeterminate or worse cytological diagnosis, candidate to surgery according to international guidelines, and submitted to RS analysis of FNA samples. Cytology specimens were evaluated in agreement to Italian Reporting System for Thyroid Cytopathology1 as follows: TIR1 (non-diagnostic), TIR1C (non-diagnostic-cytostic), TIR2 (non-malignant/benign), TIR3A (low-risk indeterminate lesion), TIR3B (high-risk indeterminate lesion), TIR4 (suspicious of malignancy), or TIR 5 (malignant). As previously published2, the two diagnostic subcategories referred to indeterminate nodules with low (TIR3A) and high risk (TIR3B) of malignancy, may be respectively compared to the class III and Class IV of The Bethesda System for Reporting Thyroid Cytopathology. We compared RS, cytology and final histology, as reference standard, using various statistical approaches.

Findings
Our study population included 37 TIR3A, 32 TIR3B, 16 TIR4 and 38 TIR5; the 30.9% of patients had benign histological diagnosis after surgery. In particular, 72.9% of patients classified TIR3A and 31.5% TIR3B had benign histological diagnosis. RS analysis of FNA samples had overall specificity of 86.8% in predicting thyroid malignancy. In indeterminate cytological categories, RS specificity was 86.5%. In patients with TIR-RADS score four or five, the specificity of RS increased to 87.5% for TIR3A and reached 100% in TIR3B; if considering RS positive test, unequivocal surgical surgery was reduced to 7.4% in the whole sample, 33.3% in TIR3A, and 6.7% in TIR 3B.

Interpretation
We demonstrated for the first time that RS represents a valuable tool for thyroid cytology and a valid alternative to molecular analyses, able to improve management and reduce unnecessary surgery in indeterminate nodules.

Funding
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References

RC3.3
Tailoring the diagnostic indication to radioactive iodine treatment in differentia ted thyroid cancer- novel biomarkers
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Differentiated thyroid cancer (DTC) is the most common malignant neoplasm arising from the thyroid parenchymal cells. DTC incidence is steadily increasing worldwide and there are approximately 1700 new cases/year in Poland. The biopsy with subsequent thyroid resection plays a central role in the diagnosis and treatment of this malignancy. After surgery, radioactive iodine (RAI) treatment is recommended to eradicate potential residual disease and improve prognosis. Due to the fact that RAI application is associated with oxidative stress formation, this treatment may exert an important impact on homeostasis. From the other hand, it was proved that protein 53 (p53), nuclear factor kappa B (NF-κB), forkhead box protein 01 (FOXO) and sirtuin 1 (SIRT1) play a crucial role in oxidative stress as well as cancer progression. Therefore, the determination of their role may be useful in DTC clinical management. In our study, we evaluated the total oxidative status (TOS), total antioxidant capacity (TAC), and p53, NF-κB, FOXO, SIRT1 concentrations to assess diagnostic usefulness of these parameters as indication markers for RAI therapy. For the purpose of this study 60 patients diagnosed with different stages of DTC after total thyroidectomy with an indication to RAI therapy and 20 pT1a DTC patients after total thyroidectomy without any recommendation to RAI therapy were enrolled as study and control groups, respectively. Serum TOS status and SIRT1 concentration were significantly higher (both P <0.01), when TAC status and p53, NK-κB, FOXO concentrations were significantly lower (all P <0.05) in the study group
compared to the control group. All the parameters were tested for their diagnostic utility as indicators for RAI treatment. The diagnostic usefulness as RAI indication markers was demonstrated for TAC (AUC = 0.99), FOFOX (AUC = 0.78), TOC (AUC = 0.76), SIRT1 (AUC = 0.74), p53 (AUC = 0.71) and NK-κB (AUC = 0.68). Furthermore, our study revealed increased oxidative stress and decreased antioxidant capacity in DTC patients qualified for RAI treatment. This may indicate a worse prognosis and advanced neoplastic process.

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RC3.4
Are BRAF-TERT mutated differentiated thyroid cancers similar to other double mutated?
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Introduction
Differentiated thyroid cancers (DTCs) carrying BRAF and TERT mutations are associated with high-risk clinicopathological features and poor prognosis. However, there are currently no studies comparing BRAF-TERT tumors to other double mutated DTCs.

Aim
To verify whether BRAF-TERT mutated DTCs differ from other double mutated DTCs in terms of clinicopathological characteristics and outcome.

Materials and Methods
168 DTCs consecutively operated between 2017 and 2021 were analyzed by Next Generation Sequencing. Based on the number of mutant genes, patients were firstly classified into single or double mutated groups. Multiple mutated DTCs were further subclassified based on the presence of absence or BRAF-TERT mutation in two groups and finally compared each other regarding clinicopathological characteristics, persistent disease one year after the initial treatment and at the end of the follow-up, respectively.

Results
In our population 25/168 DTCs (14.8%) had a double mutation, which in more than 50% (14/25 – 56%) was BRAF-TERT positive. The other double mutated tumors were subdivided as: 5/25 RAS-TERT (20%), 2/25 BRAF-P53 (8%), 2/25 BRAF-PI3KCA (8%), 1/25 RAS-P53KCA (4%) and 1/25 TERT-P53KCA (4%). From the comparison of the single mutated DTCs, double mutated DTCs were more associated with older age, larger tumor, more advanced TNM stage (OR 8.88, 95% CI 2.12 to 39.36), greater risk of structural persistence (OR 13.39, 95% CI 5.06 to 35.41), increased progression of disease (OR 7.09, 95% CI 2.04 to 23.93) and death. Compared to other double mutated, BRAF-TERT DTCs do not differ in age, sex, aggressive histotype, tumor size, extrathyroidal extension, lymph node involvement, distant metastases, stage (AJCC 8 ed), ATA risk, post-therapeutic I-131 whole body scan and PET uptake (P-value > 0.05). Although 3 of the 14 patients carrying BRAF-TERT mutated DTC died from disease progression, this data was not statistically significant and no differences were observed in terms of disease persistence rates at 12 months and at the last follow-up. The two groups differ from each other only in the value of thyroglobulin at the time of ablation, which was statistically significant lower in the BRAF-TERT subgroup (median 2.2 ng/dl vs 54.10 ng/dl P-value 0.010).

Conclusions
Double mutated DTCs showed similar clinicopathological features, regardless the pair of gene involved. Furthermore, lower thyroglobulin at ablation in BRAF-TERT mutated DTCs should not be considered as a valid predictor of remission. Further prospective studies with longer follow-up and wider population are necessary to confirm our results.

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RC3.5
Impact of stimulated thyroglobulin and BRAF status in Stage I and ATA intermediate risk DTC
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Introduction
There is no clear indication for radioiodine treatment (RAI) in patients affected by differentiated thyroid cancer (DTC) in Stage I and ATA intermediate risk, according to American Thyroid Association (ATA) guidelines.

Purpose
Our aim is to evaluate whether integration of BRAF status and thyroglobulin TSH-stimulated at the time of RAI (A-HTg) could further improve accuracy of stratification, and therefore therapeutic management, in DTC patients with Stage I AICT and ATA intermediate risk.

Materials and Methods
This retrospective study involved 372 patients affected by DTC with Stage I AICT 8th ed. and ATA intermediate risk, followed at the Endocrinology and Diabetes Prevention and Treatment Department from 2000 to 2020. For each patient we analyzed persistence of the disease one year after the initial treatment and at the end of the follow up (median: 8 years), BRAF status and A-HTg levels, respectively. By ROC curve we calculated the A-HTg cutoff of 5.9 ng/ml (sensitivity 64%, specificity 75%, AUC 0.725).

Results
In our population, 265/372 (68.8%) patients had BRAFV600E mutation, 121/372 (32.5%) A-HTg levels > 5.9 ng/ml, 91/372 (24.4%) persistent disease after one year and 75/372 (20.2%) at the end of the follow up. The presence of A-HTg levels > 5.9 ng/ml, regardless of BRAF status, was associated with a higher risk of disease persistence after one year (BRAFwt: RR 7.615, p-value < 0.001; BRAFV600E: RR 5.353, p-value < 0.001) and at the end of the follow up (BRAFwt: RR 3.004, p-value 0.038; BRAFV600E: RR 4.776, p-value < 0.001).

Our population was further divided in 4 groups: A-HTg < 5.9 mg/ml and BRAFwt, A-HTg < 5.9 mg/ml and BRAFV600E, A-HTg > 5.9 mg/ml and BRAFwt, A-HTg > 5.9 mg/ml and BRAFV600E. In these subpopulations we observed a progressive increase of persistent disease after one year, respectively of 8.3%, 15.6%, 40.9% and 50.6% (P-value < 0.001), and at the end of the follow up, respectively of 9.7%, 15.1%, 24.4% and 46.2% (P-value < 0.001).

Conclusions
Among patients with Stage I and ATA intermediate risk DTC, those with high A-HTg and BRAFV600E had the maximum rate of persistent disease. Therefore, radioiodine treatment could be proposed only to this subpopulation, rather to the entire cohort of Stage I and ATA intermediate risk. Prospective studies with longer follow-up and wider population are necessary to confirm our results.

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RC3.6
The mRNA of fibronectin 1 and of the integrin subunit alpha V are powerful prognostic indicators in papillary thyroid carcinoma
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Integrins are cell-extracellular matrix adhesion molecules considered functionally related to the development of cancer metastasis. Starting from the dataset of

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mRNA-seq of papillary thyroid carcinoma (PTC) from the TCGA, we determined the expression of fibrotenclin 1 (FN1) and fibrotenclin-binding integrins in PTC. We then analyzed the association of the expression of these two genes with the disease progression, the stage of the disease and metastatic outcome. 355 PTCs and 58 normal thyroid (NT) tissues with the corresponding mutations of the driver genes, the pathological characteristics and the outcome of the disease entered the analysis. FN1 mRNA was increased 60-fold in PTC compared to NT. The integrin heterocomplex that bind FN1 are αvβ3, αvβ5, αvβ1, V and V6. The mRNA levels of those integrins were all overexpressed. Flow cytometric analysis with specific antibodies confirmed in two PTC cell lines (BCPAP and TPC1) that the integrins V1, V3 and V6 were highly expressed. BREFV600E positive PTC showed the greatest expression of FN1 and integrin subunits, while the RAS positive PTC expression profile was much lower and similar to that of NT. FN1 expression was positively correlated with lymph node metastases, advanced stage and extrathyroidal extension (P < 0.0001) and with poor disease outcome (odds ratio 8.2: P < 0.001). The expression of V mRNA also correlated positively with an advanced disease and a worse outcome (odds ratio 4.05; P < 0.002). In conclusion, PTCs with BREFV600E have a higher expression of FN1 and V mRNA. The expression of these genes correlates positively with an advanced disease and an unfavorable outcome, representing a powerful prognostic indicator.

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RC3.7
Immune-related thyroid dysfunctions during PD-1/PD-L1 inhibitors and their association to the oncological outcome: new evidence
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Background
Immune checkpoint inhibitors (ICIs) showed impressive results in several malignancies: however, a large spectrum of immune-related adverse events (IRAEs) may occur, including thyroid dysfunction (DYSTHYR). IRAEs seem to be associated with better cancer outcome; limited data suggested that thyroid toxicity could be a predictor of response to ICIs.

Patients and methods
We retrospectively evaluated all patients who started treatment with the programmed cell death protein-1 (PD-1) and its ligand (PD-L1) inhibitors between 2017 and 2020 at the Città della Salute e della Scienza Hospital (Department of Oncology). Patients with central hypothyroidism were excluded from the analysis. Both the new onset and the worsening of pre-existing DYSTHYR were recorded; hypothyroidism was categorized as grade (G) 1 or 2 according to TSH levels (< 10 mU/l) similarly to thyrotoxicosis (G1 or 2 in case of TSH > or ≤ 0.1 mU/l). Radiological tumor response was defined according to RECIST criteria. Progression free survival (PFS) and overall survival (OS) were assessed and compared among different groups.

Results
Among 324 patients (median age 67 years, 70.7% males, 95.4% treated with anti-PD-1, 49.4% affected by lung cancer), DYSTHYR was observed in 24.7% of the population, after a median time of 3.3 (1.8-6.2) months. The most recorded event was hypothyroidism (85%); DYSTHYR was G2 in 70% of cases. No statistically significant benefit in terms of PFS was observed in patients with DYSTHYR. However, the development of DYSTHYR was associated with a significantly longer OS (87.3% vs 73.5% at 12 months, P = 0.03) and lower mortality (HR 0.61; 95% CI 0.39-0.95). Considering only patients without pre-existing thyroid dysfunction at baseline (277, 85.5% of the sample), a better OS was observed in case of DYSTHYR G2 in comparison to cases with DYSTHYR G1 or without DYSTHYR (P = 0.03), with a decreased risk of death (HR 0.47; 95% CI 0.24-0.91).

Conclusions
DYSTHYR is a common IRAE during anti PD-1/PD-L1 treatment. We detected a better clinical outcome in patients with DYSTHYR during ICIs, in terms of improved OS and reduced mortality. In subjects without pre-existing thyroid alteration, the benefit was observed especially in case of detection of higher TSH levels during ICIs.

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Pituitary and Neuroendocrinology 1

RC4.1
Immunotherapy in a non-functioning metastatic pituitary neuroendocrine tumor. An encouraging case report
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Introduction
Metastatic pituitary neuroendocrine tumors (PitNETs) or pituitary carcinomas are rare and challenging conditions. We present a recent and encouraging observation of a temozolomide (TMZ)-resistant clinically non-functioning metastatic PitNET showing a remarkable response to the anti-PDL1 drug Pembrolizumab.

Case presentation
A 57-years-old man had transphenoidal surgery in November 2012 for a large non-functioning intra/suprasellar mass revealed by visual defects, and invasive into the left cavernous sinus. A diagnosis of “null cell” PitNET (Ki-67 10%; p53 5%) was made and in June 2013 the surgical resection was completed transcranially. One year later he received stereotactic radiotherapy on the left cavernous remnant with a good response. However, delayed infrasellar regrowth was observed, first presenting as nasal pseudopodlyps and leading to re-operation in March 2018. The pathological diagnosis was consistent with the aggressive clinical behavior (Ki67 20%; p53 10%) and two small pre-pontine nodules revealed metastatic progression. Further immunohistochemical characterization of the tumor indicated a PIT1 lineage. The patient started TMZ with a standard schedule for 5 cycles, followed by a metronomic schedule in association with stereotactic radiotherapy on pre-pontine nodules and additional small multiple asymptomatic brain and spinal metastases indicative of disease progression. The primary tumor also progressed with nasal obstruction and visual loss. Searching for alternative therapeutic options, a high expression of PDL-1 was found and suggested immunotherapy. TMZ was withdrawn and in March 2021 the patient started Pembrolizumab. Encouraging results were noticed after 4 cycles of treatment. After 8 cycles of treatment, a remarkable clinical, radiological and metabolic response was documented, with a significant shrinkage of the primary lesion, a regression of metastatic nodules, and a decrease of SUV values at 18-FDG PET-CT. Moderate cutaneous and renal toxicities (G1-G2) and mild eosinophilia were observed and successfully managed by systemic steroid therapy and transient drug withdrawal. Pembrolizumab is currently continued as a maintenance therapy.

Discussion
To the best of our knowledge, no such remarkable response to anti-PDL1 monotherapy in a Pit1-positive metastatic PitNET has been reported so far. Interestingly, in few reports of aggressive or metastatic PitNET treated by immunotherapy, PDL1 expression - if available - was low (<1%) or negative. This case supports recent data suggesting that PIT1-positive PitNETs may express more PDL-1 than other phenotypes.

Conclusion
This observation suggests a promising role of immunotherapy for metastatic PitNETs, refractory to standard therapy. In addition to the potential role of PDL-1 expression, further predictors of response should be searched for.

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RC4.2
Macro-GH – a novel clinical entity causing a diagnostic challenge – a case report
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Macro-GH is a rare and challenging condition. We present a recent and encouraging observation of a novel clinical entity causing a diagnostic challenge – a case report.
Hormone macromolecules are complexes of hormones with other compounds, most often with IgG immunoglobulin. They show variable immunoreactivity in immunochromatographic tests (IRM, ELISA, CLIA, ECLIA) and usually have a weak biological effect. They can interfere with immunological assays of various hormones. Some known hormone macromolecules are: BB-PRL (24% - 34%), macro-TSH (0.6% - 1.2%) and very rare macromolecules of various hormones: calcitonin, PTH, insulin (single reports). Presentation of a new hormone macromolecule – macro-GH (GH - growth hormone), that may interfere with different GH assays leading to false-high results in serum samples.

Methods and results

We found a different immunoreactivity (different results) in the determination of GH by routine immunochromatographic methods; ECLIA, CLIA and IRMA. A serial dilution test showed non-linearity. Rheumatoid factor (RF) was absent. The test for the presence of heterophile antibodies was performed. GH recovery after incubation was 95%, indicating no interference from heterophile antibodies. In the penultimate stage, a sample of the patient’s serum was incubated with the serum of an acromegalic patient with a high concentration of GH. The GH recovery after incubation was 98%. Next, the sample was precipitated with 25% PEG. The GH recovery was 12%, which means that 88% of growth hormone was in the form of macrocomplex (macro-GH). The last step in confirming the presence of the macrocomplex GH (macro-GH) was the use of the reference method - size-exclusion chromatography (SEC).

Conclusions

In the analyzed case, we confirmed a very rare type of interference - a presence of macro-GH. In each case of suspected inconsistency of laboratory test results with the clinical picture and other clinical tests, it is advisable to start the procedure of excluding/looking for various types of interference that may impede the diagnosis and/or treatment of patients with various endocrine diseases.

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Results

A total of 1868 patients were found, 938 reported in both registers and 930 patients only in one register (908 only in the NPR and 22 only in the SPR). Internal validation of the algorithm was performed in the SPR and captured 98.4% of the patients. All 22 patients only reported in the SPR were validated, and 14 patients were confirmed with acromegaly. Applying the diagnostic algorithm to the NPR-search reduced the number of patients only found in the NPR to 347, of which 85 have confirmed acromegaly after review of medical records. Thus, 1023 of the total 1846 patients with acromegaly codes in NPR was constructed from validated data and applied to the remaining four health care regions. The algorithm was based on at least two registrations in the NPR of diagnostic codes E220 or Z23A or the diagnostic code alone in combinations with codes for pituitary tumour and/or pituitary surgery, giving the highest functional diagnosis sensitivity and high positive predictive value (PPV).

Conclusion

By using the diagnostic code for acromegaly alone to identify patients with the disease in NPR is not sufficiently specific for epidemiological research. However, the use of an algorithm including combinations of diagnostic, tumour and surgical codes increased the probability of correct diagnosis and provided an improved estimate of the incidence of acromegaly in Sweden.

Background

Diabetes is an important risk factor for cardiovascular morbidity and mortality but its impact on outcome in acromegaly is unknown.

Methods

This was a nationwide, observational, matched-cohort study. Adult patients with acromegaly due to a pituitary adenoma were identified in the Swedish National Patient Registry between 1987 and 2020 and those with coexistent type 2 diabetes in the National Diabetes Registry and Drug Registry. Overall mortality, and cardiovascular mortality and morbidity were estimated in acromegalic patients with diabetes (ACRO-DM group) in comparison with those without diabetes (ACRO group) using Cox regression adjusted for multiple confounders with propensity score.

Results

The study included 786 patients with acromegaly, 254 in the ACRO-DM group and 532 in the ACRO group. Mean follow-up was 9.2 years. At baseline, mean age (SD) was 62.6 (11.4) and 60.0 (12.1) years (P=0.004) and mean duration of acromegaly was 6.8 (8.1) and 6.0 (6.2) years (P=0.096) in the ACRO-DM and ACRO group, respectively. Mean income and level of education were lower in patients with coexistent diabetes while the frequency of pre-existing cardiovascular diseases was higher (61% vs 37%, P<0.001). The use of pituitary surgery (71% vs 68%, P=0.062) and radiotherapy (16% vs 16%, P=1.00) was similar among the two groups. Overall, 466 (59%) patients received pharmacotherapy in the entire study cohort. The use of somatostatin analogues (37% vs 30%, P=0.055) and GH receptor antagonists (10% vs 6%, P=0.063) was somewhat more frequent in the ACRO-DM group. The unadjusted overall mortality rate per 1000 person-years was 35.1 (95% CI 27.2–44.7) for the ACRO-DM group and 20.1 (16.5–24.3) for the ACRO group, with a hazard ratio (HR) of 1.58 (1.12–2.23) after adjustment for multiple confounders. The ACRO-DM group had increased cardiovascular mortality (HR 2.11, 1.09–4.10) and increased risk of cardiovascular diseases (HR 1.49, 1.21–1.82). Risk factor for cardiovascular diseases were age (HR 1.03 (95% CI 1.02–1.04)), diabetes duration (HR 1.09 (1.05–1.15)), diastolic blood pressure (HR 1.02 (1.00–1.04)), body mass index (HR 1.05 (1.01–1.09)), and treatment with antihypertensive drugs (HR 2.1 (1.21–3.64)) or lipid-lowering medication (HR 1.60 (1.08–2.36)).

Conclusions

Diabetes in patients with acromegaly was associated with excess overall and cardiovascular mortality and increased risk of cardiovascular diseases. These findings are novel and emphasize the need of optimizing management of acromegaly to prevent the development of diabetes since it might improve survival.

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Diabetes, Obesity, Metabolism and Nutrition 2

RC5.1  
Vascular cellular adhesion molecules are high during one year after acute COVID-19 infection in patients with type 2 diabetes  
Anna Aliyeva, Feruza Khidayrova, Khurshida Sultonova, Khurshida Kamalova, Vasila Talenova & Iroda Tajeva  

Background  
Molecules of adhesion is a group of glycoproteins which expressed in cell surface and play pivotal role in inflammatory and oncological processes, and new studies show increasing of adhesion molecules within 6-12 hours after COVID-19 contamination, peaking in 24 hours. High level of adhesion molecules is a predictor of disease severity and mortality rate.  

Aim  
Our study was to evaluate the level of VCAM-1 in patients with type 2 diabetes mellitus in one year after COVID-19 infection.  

Materials and methods  
We studied 166 type 2 diabetes patients who had COVID-19 in 2020 in 3-15 months (average, one year) after the acute infection. VCAM-1 was tested using Human ELISA Kit assay (Elabscience) in the laboratory of the Republic of Centre of Endocrinology. Statistic analysis was performed using STATA v.16.0.  

Results  
The level of VCAM-1 stayed increased up to 15 months after the COVID-19 onset. It was significantly lower in patients regularly taking rivaroxaban (174.65, 95% CI 134.2-215.1 vs 618.12, 95% CI 542.04-694.19), beta-blockers (466.39, 95% CI 373.91-558.87 vs 676.35, 95% CI 578.15-774.56), ACE inhibitors (417.76, 95% CI 314.72-520.81 vs 674.82, 95% CI 586.86-762.77), statins (318.65, 95% CI 238.54-398.75 vs 717.02, 95% CI 630.12-803.91), and fibrates (235.35, 95% CI 133.96-336.75 vs 902.53, 95% CI 812.43-992.63) and had no difference depending on glucose lowering therapy, aspirin or clopidogrel, or coagulogram. Interestingly, VCAM-1 level was significantly lower in those patients who received dexamethasone (423.76, 95% CI 332.37-515.14 vs 664.26, 95% CI 572.79-755.72) and remdesivir (244.29, 95% CI 160.25-328.32 vs 666.07, 95% CI 586.89-745.25), but not favipiravir during the acute COVID-19. Patients who had arterial hypertension and did not take regular antihypertensive therapy had significantly higher levels of VCAM-1 (851.09, 95% CI 597.77-1104.42 vs 527.93, 95% CI 461.99-593.86).  

Conclusion  
Endothelial dysfunction may be preserved up to one year after COVID-19, and patients with type 2 diabetes should be monitored closely for post-COVID vascular complications.  

Key words: Diabetes, COVID-19, vascular adhesion molecules, endothelial dysfunction  
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RC5.2  
Association between lipoprotein(a) concentrations and atherosclerotic cardiovascular disease risk in patients with familial hypercholesterolaemia: an analysis from the HELLAS-FH  
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Aims  
Lipoprotein(a) [Lp(a)] is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD) in the general population. However, such a role in patients with familial hypercholesterolemia (FH) is less documented. The purpose of this study was to evaluate the association between Lp(a) concentrations and ASCVD prevalence in adult patients with FH.
RC5.3

Microvascular assessment of diabetes mellitus patients by nailfold capillaroscopy

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Introduction

Diabetes mellitus (DM) is frequently associated with vascular complications including diabetic microangiopathy. Nailfold capillaroscopy is a useful non-invasive diagnostic tool to identify changes in the microvascular architecture. Published literature hints at the presence of nailfold circulatory morphologic changes in diabetic patients.

Objective

The purpose of the study was to identify by nailfold capillaroscopy microvascular changes in patients with type II diabetes mellitus.

Materials and methods

Observational, descriptive and prospective study which included patients with diabetes type II. Capillaroscopy was performed in the fourth and fifth digit of the non-dominant hand, by a 200x magnification capillaroscope (Dino-Lite). Data was analyzed using SPSS v.23.

Results

We included 36 diabetic patients, 58% [21] male and 42% [15] female, with a mean age of 36.2 ± 18, race included hispanic 56% [20], white 39% [14], African American and asian in 5% respectively. The mean of years of diagnosis was 16 ± 10 [1-40] years. The mean of hemoglobin A1c was 7.96 ± .776 [6.2-10.6]. Total cholesterol was reduced 29% [14], very reduced in 6% [2], good in 42% [15] and very good in 14% [5]. The presence of giant capillaries was seen in 44% [16], avascular areas in 36% [13], ramified capillaries 25% [9], ectasia 67% [24], microhemorrhages 6% [2], tortuous capillaries 83% [30] and cross linked capillaries 83% [30]. SD pattern was seen in 11% [4]. The mean of apical capillary diameter was 41.52 ± 8.7 [32-71]. It was seen a significance correlation between the presence of decreased density and increased HgbA1c. Between groups of controlled and uncontrolled diabetes, it was seen that the architecture was more altered in the uncontrolled group than the controlled group. Density was reduced in 23% and 42% in the uncontrolled group.

Conclusion

The overall architecture was altered in 70%, the characteristic pattern was the presence of ectasias, tortuous and cross linked with increased presence of ramified capillaries and reduced density. It was evident that patients with uncontrolled diabetes had more capillaroscopic changes than the controlled disease group. Further studies will need to be performed to correlate these findings.

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RC5.4

Empagliflozin induces endocan expression and alleviates NAFLD through regulation of NF-kB pathway

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Conclusions

Prevalence of coronary artery disease (8.3%, 12.2% and 16.1%, respectively; P<0.001 and P<0.01 and P<0.05 among tertiles) was also observed. No difference in the prevalence of stroke and peripheral artery disease was found across tertiles.

Conclusions

Elevated Lp(a) concentrations are significantly associated with increased prevalence of ASCVD in patients with possible/probable/definite HeFH.

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RC5.5

Very Low Calorie Ketogenic Diet combined with interval training for preserving muscle mass during weight loss in sarcopenic obesity: a pilot study

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disorders. Endothelin is a novel molecule of endothelial dysfunction which is expressed in liver. SGLT2i have been reported to improve NAFLD through amelioration of inflammation. While there are contradictory results regarding the role of SGLT2i on NAFLD patients, data regarding endocan expression in liver tissue are limited.

Aim

Herein, we aimed to investigate the effect of SGLT2i empagliflozin on the expression of endocan in liver tissues as well as in hepatocyte cells and to delineate the underlying mechanism.

Material and methods

ApoE(-/-) mice fed a western high-fat diet were used as NAFLD model. At the age of 5 weeks, ApoE(-/-) male mice were switched from normal diet to HFD. After 5 weeks, mice were divided into two groups: Control-groups (HFD + vehicle), Empa-group (HFD + empagliflozin 10 mg/kg/day) for 5 further weeks. At the end of intervention, mice were sacrificed, whole blood was drawn by cardiac puncture and liver tissues were harvested. H&E staining was performed in all liver sections for histomorphometric analysis and IHC was performed to evaluate endocan levels. The mRNA levels of endocan, ICAM-1, VCAM-1, LFA-1, SGLT2, and IL-6 were measured by qRT-PCR and the protein levels of p65 and phospho-p65, were evaluated by immunoblotting. HepG2 cells were cultured in media supplemented with low(1 g/l), intermediate(2.25 g/l) and high(4.5 g/l) glucose concentrations. The expression of the abovementioned genes were evaluated after 24 and 48 h of treatment with empagliflozin (10-5, 2 × 10-5, 10-5 M).

Results

Biochemical tests revealed reduction in blood glucose, total cholesterol, LDL-cholesterol, and triglycerides after empagliflozin intervention for 5 weeks as compared to the Control-group. Additionally, empagliflozin administration resulted in reduced hepatic lipid accumulation and NA score (NAS). Empagliflozin significantly increased the endocan mRNA and protein levels while reduced IL-6 mRNA levels. Western blot analysis revealed that empagliflozin also regulated the NF-kB pathway through phosphorylation of p65 subunit. Moreover, our in vitro data confirmed the in vivo results since 48 hours incubation of HepG2 cells with empagliflozin (10-5M,2×10-5 M) at the presence of low and intermediate glucose levels, but not high glucose levels, increased endocan expression (P<0.01 and P<0.05, respectively). Interestingly, SGLT2i mRNA expression was detected in liver and HepG2 cells.

Conclusions

Our in vitro and animal study results indicate that empagliflozin ameliorates NAFLD through –among others- induction of endocan expression. Regulation of NF-kB pathway and IL-6 expression may mediate these effects.

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The prevalence of sarcopenic obesity (SO) is increasing worldwide, posing important challenges to public health and national health care systems, especially during the COVID pandemic. In subjects with SO, it is essential to reduce body weight preserving lean mass, in order to avoid a worsening of muscle function. Lifestyle modification with adequate nutrition and proper physical activity is essential to counteract SO progression. In accordance with the Position Statement of the Italian Society of Endocrinology, Very Low Calorie Ketogenic Diet (VLCKD), a well-established nutritional intervention in the context of obesity, has been promoted also for the treatment of SO. To date, the effects of physical training during VLCKD have not been studied.

Aim
This pilot study aims to determine the efficacy of VLCKD combined with interval training, compared to a VLCKD alone, on weight-loss, body composition and physical performance in patient with SO.

Materials and methods
Twenty-six patients with SO, aged between 50 and 70 years, who met the inclusion criteria, accepted to adhere to a VLCKD nutritional program (< 800 Kcal/die) and gave informed consent, were enrolled in the study. Thirteen patients followed a structured VLCKD protocol (VLCKD group) and thirteen patients followed a structured VLCKD protocol combined with interval training (IT), two times a week (VLCKD + IT group). Data were collected at baseline and after 45 days. Anthropometric indexes, body composition by Bioelectrical Impedance Analysis, muscle strength measurement by Chair Stand Test and physical performance analysis by Short Physical Performance Battery were assessed at baseline and at the end of treatment.

Results
At the end of the study, Body Mass Index, body weight and waist circumference were significantly reduced both in the VLCKD group and in the VLCKD + IT group. Moreover, significant improvement of muscle strength and physical performance was found in all groups. A significant reduction in hip circumference was observed only in the VLCKD + IT group. A multiple comparisons of delta variations in the measured parameters between groups was performed. No differences were observed for the majority of parameters, with the exception of FFM and FM: the individuals fed with VLCKD combined with IT preserved their FFM (P < 0.0001) and reduced their FM (P = 0.0006) to a greater extent than in the VLCKD group.

Conclusions
Our pilot study showed that a VLCKD was effective in terms of body weight reduction, particularly of FM; moreover, we conclude that the combination of VLCKD and interval training determines a better preservation of FFM.

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RC5.6
Effects of bariatric surgery and dietary intervention on changes in insulin resistance and appetite hormones over the period of 3 years
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Objectives
Little is known about the mechanisms responsible for improvement in insulin resistance after bariatric surgery. We examined the impact of three types of bariatric surgery, in comparison with dietary intervention (DIET) on concurrent changes in Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and appetite hormones over the period of 3 years. We also investigated the weight loss independent hormonal effects on insulin resistance.

Methods
Fifty-five adults undergoing weight-loss interventions, Roux-en-Y gastric bypass RYGB (n = 7), gastric sleeve GS (n = 21), laparoscopic adjustable gastric banding surgery LAGB (n = 11) and DIET (n = 16) were studied at baseline and at 1, 3, 6, 12, 24 and 36-months post intervention. Measurements of glucose (BSL), HbA1c, insulin levels, fasting and postprandial PY and GLP1, adiponectin, C-reactive protein (CRP), retinol-binding protein 4 (RBP4), fibroblast growth factor-21 (FGF21) and dual-Xray absorptiometry were performed throughout the study. Two separate, random, intercept mixed-effects models examined the HOMA-IR changes within individual groups and in comparison with DIET during the initial phase of rapid weight loss (0-12 months) and during the phase of weight stability (12-36 months).

Results
During the first 12 months, RYGB, GS and DIET, but not LAGB, led to significant reductions in HOMA-IR. However, after controlling for the lost weight, postoperative HOMA-IR values were not different to the DIET group. During the phase of weight stability, all three bariatric procedures, achieved significant reductions in HOMA-IR, with the greatest difference in the RYGB group (-3.7; 95% CI: -5.4, -2.1; P = 0.001). After controlling for the weight loss procedure, weight and body composition changes, HOMA-IR level decreased by 1.1 (95% CI: -2.1, -0.06; P = 0.045) for every 2-fold increase in baseline in postprandial PY. Fasting insulin declined by 3.4 μU/L (95% CI: -7.2, 0.09; P = 0.06) for every 2-fold increase in adiponectin level. Initial, non-sustained changes in RBP4 and FGF21 had no significant association with HOMA-IR values.

Conclusions
An initial rapid weight loss after bariatric surgery is a major contributing factor to the decline in HOMA-IR score. The exaggerated secretions of the FYY hormone and adiponectin are associated with weight-independent improvements in HOMA-IR during weight stability. The metabolic roles of RBP4 and FGF21 may be related to rapid fluctuations in weight or changes in nutritional intake. Further mechanistic studies involving larger numbers of subjects are needed to fully understand the complex neuroendocrine regulation of weight, appetite, and glucose homeostasis in bariatric patients.

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RC5.7
How do people with type 2 diabetes compare with type 1 diabetes in their outcomes of diabetes-related ketoacidosis?
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Introduction
Diabetes-related ketoacidosis (DKA) is an acute endocrine emergency requiring immediate diagnosis and management. Common misconception is that DKA is associated with type 1 diabetes only. We explored the proportion of people with type 2 diabetes, and compared the management, complications and outcome of DKA between people with type 1 and type 2 diabetes.

Methods
We conducted a retrospective study on people admitted with DKA across six hospitals in the United Kingdom from January to November 2021. DKA was diagnosed as serum glucose ≥ 11 mmol/l or known history of diabetes, ketones ≥ 3 mmol/l and pH ≤ 7.3 or bicarbonate ≤ 15 mmol/l. Data on demographics, use of exogenous insulin infusion (FRII) and intravenous fluid infusion (IVI), blood glucose and ketone monitoring, DKA duration and length of stay were collected. We also collected data on hypoglycaemia and potassium derangement during DKA treatment.

Results
A total of 418 people admitted during this period with biochemically-proven DKA were included. 287 (68.7%) of people had type 1 diabetes; 131 (31.3%) had type 2 diabetes. There was no significant difference in duration of DKA between people with type 1 vs type 2 diabetes (13.2 hours vs 15 hours, P = 0.137), however, those with type 2 diabetes had a significantly longer length of stay (3 days vs 8 days, P = 0.000). There was no significant difference in the proportion of hourly glucose (99.9% vs 98.6%, P = 0.633) and ketone measurement (71.5% vs 68.6%, P = 0.731), or use of FRII (100% vs 100%, P = 0.376) and IVI (100% vs 93.3%, P = 0.681) There was no significant difference in the prevalence of hypoglycaemia (12.2% vs 12.2%, P = 0.950), hypokalaemia (31.7% vs 36.6%, P = 0.36) or hyperkalaemia (33.4% vs 36.6%, P = 0.345).

Conclusions
Nearly a third of DKA cases are in people with type 2 diabetes, debunking the myth DKA is synonymous with type 1 diabetes. There was no significant difference in the complications or outcomes associated with DKA between people with type 1 vs type 2 diabetes mellitus, suggesting the current guidelines are appropriate for either type of diabetes. However, further research is needed to study if revised guidelines may result in better outcomes in DKA in type 2 diabetes. People with type 2 diabetes had significantly longer hospital stays; this

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Endocrine-Related Cancer
RC6.1
Clinical relevance of body composition measurement at L3 level in gastroenteropancreatic neuroendocrine tumors
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Introduction
Nutritional status in patients with neuroendocrine tumors (NETs), especially with gastroenteropancreatic origin, may be affected and have an impact on prognosis and survival. Different techniques are currently available to assess nutritional status, but not all of them are accessible in routine clinical practice. In this context, body composition of NET patients was calculated by computed tomography (CT) at L3 level to evaluate its importance on clinical prognosis.

Materials and Methods
We collected gastroenteropancreatic NET patients with L3 level CT images at diagnosis since 2004 at Hospital Universitario La Princesa (Madrid). L3 CT images were analyzed using NIH ImageJ protocol and R version 4.0. The following measurements were obtained: body area, visceral fat tissue, subcutaneous fat, total fat, intermuscular fat, very low density muscle, low density muscle, normal density muscle (NDM), high density muscle and total muscle. All of them were normalized by the squared height of each patient. We used normality Shapiro-Wilk test and Mann-Whitney-U or Kruskal-Wallis tests and one-way t test or ANOVA/ANCOVA for group differences in those with non-normal and normal distribution respectively. We applied Spearman correlation to establish possible relationships between age and biochemical parameters and body composition measures. All the statistical analysis was performed using R 4.0 version.

Results
The sample is composed of 61 gastroenteropancreatic NET patients classified according to: 1) their NET primary location in small intestine (44.26%), pancreatic (37.70%) and large intestine (24.59%); and 2) tumor type: non-functioning (70.49%), functioning carcinoid (24.59%), gastrinoma (4.92%) and insulinoma (6.56%). Patients' mean age was 63.19 +/- 10.97 years, and 53.73% were females. NDM was positively correlated with albumin (r = 0.3655, P = 0.0084) and lymphocyte number (r = 0.3749, P = 0.0100). On the other hand, NDM was inversely correlated with age (r = -0.5185, P = 0.0012), myosteatosis (r = -0.7065, P < 0.0001) and inflammation parameters such as ferritin (r = -0.3038, P = 0.0349) and fibrinogen (r = -0.3119, P = 0.0481). Low levels of NDM and total muscle were associated with any type (P = 0.0007, P = 0.0029) and tumor-specific mortality (P = 0.0149, P = 0.0113), regardless of sex and age in multivariable analysis. Patients with metastasis have less total fat (pvalue = 0.0187) and myosteatosis was more frequent in insulinoma (P < 0.05) than in non-functioning tumors, carcinoids and gastrinomas. There were no differences according to tumor location.

Conclusion
Body composition analysis is feasible using CT data acquired in routine clinical practice in patients with NETs. Low levels of NDM seem to be independently associated with a worse analytical profile and with mortality.

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Endocrine-Related Cancer
RC6.2
Reciprocal interactions between fibroblast and pancreatic neuroendocrine tumor cells: putative impact of the tumor microenvironment
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Introduction
Pancreatic neuroendocrine neoplasms (PEN) present with a fibrotic stroma which constitutes the tumor microenvironment (TME). The role played by stromal fibroblasts over the growth of PEN and their sensitivity to the mTOR inhibitors, RAD001, are as yet unestablished.

Methods
We investigated reciprocal interactions between 1) human PEN cell lines (BON-1,QGP-1) or primary cultures of human ileal neuroendocrine neoplasm (NEN) or PEN; and 2) human fibroblast cell lines (HPF/HFL-1). Proliferation was assessed in transwell co-culture (HFL-1, HPFw, BON-1w, QGPw) or in the presence of serum-free conditioned media (BON-1cm, QGP-1cm, HFL-1cm, HPFcm), with and without RAD001. Migration of BON-1/QGP-1 was evaluated when incubated with HPFcm.

Results
Proliferation of BON-1 and QGP-1 increased in the presence of HFL-1cm, HPFcm, HFL-1w and HPFw (BON-1: +46 to +70% and QGP-1: +42 to +46%); migration of BON-1/QGP-1 was increased in the presence of HFL-1cm, HPFcm, HFL-1w and HPFw (BON-1: +46 to +70% and QGP-1: +42 to +46%).

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+55% (P < 0.001 vs controls for both), whereas this stimulatory effect was reversed in presence of RAD001. Likewise, proliferation of human iNEN and PNEN primary cultures increased in presence of HFL-1 or HFP. Reciprocally, BON-1cm and BONtw stimulated the proliferation of HPF (1+90 ± 1/61% and +55 ± 6.47% respectively, P < 0.001 vs controls), an effect less pronounced with either QGP-1cm or QGPw (1+90 to + 27%, P < 0.05 vs controls) and unmodified by RAD001. RAD001 resulted in a decrease of colony number of BON-1 and QGP-1, while colony size remained the same in presence of the drug. Finally, a higher migration potential of BON-1 and QGP-1 occurred in presence of HPFcm (P < 0.001 vs basal).

Conclusions
Fibroblasts, in the TME of PNEN, represent a target of interest to control escape from mTOR inhibitors tumor growth and dissemination.

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RC6.3

New epigenetic and functional features in pheochromocytoma
Jacopo Manci1, Loris Bertazza1, Susi Barollo2, Simona Censi2, Alicja4 with either QGP-1cm or QGPtw (DOI: 10.1530/endoabs.81.RC6.2 from mTOR inhibitors tumor growth and dissemination.

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Conclusions
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RC6.5

Granin family peptides and INSM-1 (Insulinoma-associated protein 1) in the biochemical diagnosis of pheochromocytoma
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Introduction
Pheochromocytoma is a rare, usually benign tumor composed of neuroendocrine (chromaffin) cells of the adrenal medulla. It is the cause of secondary arterial hypertension. The biochemical diagnosis of a pheochromocytoma is based on the determination of concentration/excretion of catecholamine metabolites in blood or urine. The most sensitive biomarkers in the biochemical diagnosis of pheochromocytoma are plasma free methanephrines (metanephrine, normetanephrine and 3-methoxytyramine) assayed with chromatography tandem mass spectrometry (LC-MS/MS). Neuroendocrine cells have the ability to produce a variety of proteins and neuropeptides, which, together with catecholamines, are released into the blood and can be designated as so-called circulating tumor markers.

Purpose
The aim of the study was to assess the usefulness of the determination of levels of selected Granin family proteins and INSM-1 (Insulinoma-associated protein 1) in the diagnosis of patients with pheochromocytoma.

Material and methods
Patients were divided into 4 groups: patients with pheochromocytoma (n = 39), patients with incidentaloma (n = 20), patients with primary arterial hypertension (n = 20), and control group – healthy volunteers (n = 40).

The following biochemical determinations were performed in all patients: plasma levels of metanephrine, normetanephrine and 3-methoxytyramine, concentration of chromogranin B (CgB), proSAAS, INSM-1, chromogranin A (CgA) and other peptides: Pancreastatin/chromogranin A (250-301), Sematostatin/prepro-chromogranin A (429-454), WE-14/prepro-chromogranin A (342-355) and Catestatin. Biochemical determinations were made using the LC-MS/MS technique with various immunochemical techniques (RIA, IRMA, ELISA). Results
In patients with adrenal pheochromocytoma levels of CgA, WE-14 and Catestatin were significantly different (P < 0.001) compared to control groups (adenoma, hypertension and healthy subjects). The concentration of INSM-1 was significantly higher (P < 0.001) in patients with pheochromocytoma compared to...
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the group of healthy people. In the group of patients with pheochromocytoma, the following indicators of the diagnostic value of the analyzed biomarkers were obtained: CgA: 82% sensitivity and 100% specificity (AUC 0.930); CgB: 87% sensitivity and 77% specificity (AUC 0.885); WE-14: 90% sensitivity and 95% specificity (AUC 0.903); Cathepsin: 80% sensitivity and 95% specificity (AUC 0.913); proSAAS: 82% sensitivity and 67% specificity (AUC 0.760); INSM-1: 97% sensitivity and 100% specificity (AUC 0.976).

Conclusion

Determination of biomarkers: CgA, WE-14, Cathepsin and INSM-1 had the highest diagnostic value in patients with pheochromocytoma.

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RC6.6

The clinical and molecular evaluation of the GIP/GIPR axis in Medullary Thyroid Cancer (MTC)

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The glucose-dependent insulinotropic polypeptide receptor (GIPR) is a 7-transmembrane class B G-protein-coupled receptor that mediates the incretin response after nutrient stimulation. Although mostly involved in metabolic disorders, in the last years an improper activation of the GIP/GIPR axis has been increasingly recognized in endocrine tumors, with a potential diagnostic and prognostic value. In Medullary Thyroid Cancer (MTC), a neuroendocrine tumor of the parafollicular C cells, a high tumor-to-normal tissue ratio (T/N ratio) of GIPR was reported both in human and in rat. In this latter, a direct link between the neoplastic transformation and the mechanism of receptor overexpression has been proposed. In this work, we aimed at evaluating the potential diagnostic and prognostic significance of GIP expression in a large cohort of MTC by correlating GIPR mRNA steady-state level with patients' clinical features. Moreover, given the paucity of data on the GIP/GIPR axis in this tumor type, an additional aim of this study was to molecularly dissect the signaling pathways associated with GIPR stimulation in MTC-derived cells with particular attention to cell proliferation and calcitonin secretion. By Droplet Digital PCR pathways associated with GIPR stimulation in MTC-derived cells with particular attention to cell proliferation and calcitonin secretion. By Droplet Digital PCR technology, we observed a GIPR positive expression (GIPR+) of nearly 80% (36/45) of MTC tumor specimens and more frequently in larger, advanced-stage cancer with higher Ki-67 values and sporadic rather than familial manifestation. In MTC-derived cells (i.e., MZ-CRC-1, and a primary culture originating from a MTC patient), GIPR stimulation induced cAMP elevation - with the consequent activation of the PKA cascade - and a small but significant fluctuation in Ca2+ - both likely associated with increased calcitonin secretion. GIP has instead no effects on cell viability nor on P38-Akt and MAPK-ERK1/2 signalling pathways. The data emerging from this study confirmed the high T/N GIPR ratio in MTC tumors and demonstrate for the first time that it may represent an index of the degree of advancement of the malignant process. The observation that GIP stimulated the adenylyl cyclase and activate the downstream cAMP pathway in MTC-derived cellular models confirms the correct coupling of GIPR to Gas which was ultimately related to an increased CT secretion. Further studies with specific provocative tests, however, will be mandatory to establish the real involvement of GIP/GIPR axis in regulating calcitonin secretion in MTC.

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RC6.8

Unveiling the role and contribution of CELF4 to the malignant features of PanNETs

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Aim

To investigate the association of endocrine complications after ICIs immuno-therapy with progression free survival (PFS) and overall survival (OS) in a large single-center oncological cohort.

Patients and methods

In total, 351 patients were included in the analysis, 248 men (70.7%) and 103 women (29.3%). The median age was 66 years. Patients had a variety of cancer types, namely bladder cancer (131, 37.3%), renal cancer (89, 25.4%), lung cancer (74, 21.1%), ovarian cancer (22, 6.3%) and other types of cancer (35, 10%). The majority (314, 89.4%) were classified as stage IV, while 10.6% (37) were classified as stage III. Most of the patients received immunotherapy with anti-PD1 agents (262, 74.6%) and the rest with anti-PD-L1 agents (89, 25.4%). Kaplan-Meier estimates were used to describe and visualize the effect of categorical variables on OS and PFS. Survival analysis was performed by Kaplan-Meier curves and survival differences between groups were estimated using the log-rank test. The estimation of the prognostic value of several variables with patients’ survival was made by Cox regression models.

Results

In total, 68 (19.4%) of patients presented an endocrine complication after immunotherapy with ICIs. Specifically, 66 (18.8%) had thyroid dysfunction, 1 patient presented hypophysitis (0.3%) and 1 patient had combination of thyroid dysfunction and hypophysitis (0.3%). Patients with an endocrine complication had mPFS of 15 months (95% CI 11.0-18.9 months), while in those without endocrine complication mPFS was 7 months (95% CI 6.1-7.9 months, P < 0.001). Similarly, median OS (mOS) was statistically significant lower in the patients’ group without endocrine complication. In fact, mOS was 51 months (95% CI 39.3-62.7 months) for these patients. These results retained significance in terms of longer PFS (1.812, 95% CI 1.270-2.586) and OS (1.805, 95% CI 1.088-2.994) after multivariable analysis.

Conclusions

ICIs endocrinopathies may be a positive predictor of immunotherapy response.

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Pancreatic neuroendocrine tumors (PanNETs) are heterogeneous neoplasms with a relatively low but increasing incidence, mainly due to the difficulty in diagnosing this disease in its early stages. This notably complicates the treatment of this pathology and leads to a poor prognosis. One of the main reasons for this problem is the lack of suitable diagnostic biomarkers as well as effective therapeutic targets. In this sense, there is still a limited knowledge about alternative splicing, a key process emerging as a transversal hallmark of cancer, as its frequent dysregulation influences most tumor cell features. In a pilot study, we discovered that expression levels were determined using a microfluidic based technology, comparing tumor and adjacent non-tumor tissue,
in a cohort of 20 PanNETs patients. This revealed a clear overexpression of CELF4 in tumor tissue compared to adjacent non-tumoral tissue. Then, an RNA-seq dataset was used to investigate the associations between CELF4 expression, patient clinical parameters, and splicing event patterns. We observed that CELF4 is linked to critical features of malignancy, the expression of key genes in tumors (TP53 or CDKN2B) and different splicing events profiles. Likewise, the functional relevance of this factor was determined in vitro with several functional assays (cell proliferation and drug response) in two PanNETs cell models (BON-1 and GQ1-1), including an mTOR phospho-antibody array to determine the mechanism of action of CELF4. Remarkably, the modulation of CELF4 expression levels in the cell lines resulted in a significant change in proliferation as well as in the response of these cells to the mTOR inhibitor everolimus. In particular, CELF4 silencing resulted in a disruption of several crucial intermediaries in the mTOR signaling pathway. Finally, we carried out in vivo studies using BON-1-xenografted mice, observing a significant reduction of tumor growth by silencing CELF4. These results demonstrate that the splicing factor CELF4 is dysregulated in PanNETs, and it alteration can contribute to tumor development and a more aggressive phenotype, impacting the mTOR signaling pathway. Altogether, these findings provide original evidence that encourage further study of this factor as a novel potential target in PanNETs.

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**Pituitary and Neuroendocrinology 2**

**RC7.1**

**Does the postoperative dose of hydrocortisone influence the health-related quality of life in patients with cured Cushing syndrome?**

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Objective

Patients with Cushing syndrome (CS) have impaired health-related quality of life (HRQoL) before and after surgery. The data on the optimal hydrocortisone dose after surgical cure of CS is scarce. Therefore, we investigated the influence of hydrocortisone dose on HRQoL after surgical treatment of CS. We hypothesized that patients who receive higher hydrocortisone doses after surgery would have better HRQoL and fewer cortisol withdrawal symptoms.

Methods

The study population comprised 38 patients with CS, 18 with adrenal, and 20 with pituitary origin. After surgical remission of CS, patients were randomized to 15 mg or 30 mg of hydrocortisone. All patients completed the EQ-5D questionnaire at baseline, one month, and three months after surgery. In addition, data on symptoms related to cortisol withdrawal and the consequent need for hydrocortisone dose escalation were collected.

Results

The HRQoL did not differ between patients receiving 15 mg (22 patients) or 30 mg (16 patients) of hydrocortisone, at baseline, after one month, or three months after curative surgery. Total EQ-5D scores in patients on 15 mg and 30 mg of hydrocortisone were 60(1-90) vs 60(0-100), 70(3-85) vs 45(2-95), and 80(20-100) vs 52.5(20-100), respectively \((P=0.934, P=0.308, \text{and } P=0.544)\). Three patients needed a temporary increase of hydrocortisone dose during follow-up due to acute illness or worsening of symptoms.

Conclusions

This prospective randomized study showed no difference in HRQoL, between patients receiving 15 or 30 mg of hydrocortisone replacement therapy in the first three months after the surgical remission of CS.

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**RC7.2**

**Development and internal validation of a predictive score for the diagnosis of central adrenal insufficiency when morning cortisol is in the grey zone**

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Background

When evaluating a patient for central adrenal insufficiency (CAI), there is a wide range of morning cortisol values for which no final conclusion on hypothalamic-pituitary-adrenal (HPA) axis function can be drawn; in these cases, a stimulation test is required. Aim of this study was to develop an integrated model for the prediction of CAI when morning cortisol is in the grey zone, here defined as 40.0-160.0 µg/l.

Methods

Overall, 119 patients with history of sellar tumour which underwent insulin tolerance test (ITT) for the evaluation of HPA axis were enrolled; a peak cortisol value \(\geq 180.0 \mu\text{g/l} \) at ITT was adopted for the definition of CAI. Supervised regression techniques were used for model development. Model calibration was evaluated by the Hosmer-Lemeshow test. A ten-fold cross-validation algorithm was adopted for internal validation.

Results

After a stepwise backward selection, the variables retaining a statistically significant association with the outcome were morning cortisol values, the presence of \(\geq 3\) other pituitary deficits, and male sex. Based on these predictors, a multivariable predictive model was developed, and showed a significantly better diagnostic performance in the prediction of CAI than morning cortisol alone (AUC 0.811 vs 0.699, \(P=0.003\)). The Hosmer-Lemeshow test did not reveal any significant calibration \((P=0.54)\). At ten-fold cross-validation, the final estimation of the model performance on unseen data was equal to 0.769, thus reassuring about a small overfitting effect. In order to simplify the use of the model in clinical practice, a novel predictive score (CAI-score) is proposed, on a 5.5-point scale, by considering morning cortisol (0 points if 130.1-160.0 µg/l, 1 point if 100.1-130.0 µg/l, 1.5 points if 70.1-100.0 µg/l, 2.5 points if 40.0-70.0 µg/l), other pituitary deficits (2 points if \(\geq 3\) deficits), and sex (1 point if male). A diagnostic algorithm integrating CAI-score and ITT is finally presented, with an overall accuracy of 99.2%, and the possibility to avoid the execution of a stimulation test in 25.2% of patients.

Conclusion

This was the first study that formally proposed and internally validated a multivariable predictive score for the diagnosis of CAI when morning cortisol is in the grey zone. This score might be helpful to reduce the number of patients who need a stimulation test for the assessment of HPA axis function.

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**RC7.3**

**Pituitary microadenoma vs macroadenomas in cushing’s disease: does size matter?**

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Background

The majority of adrenocorticotropic hormone (ACTH)-secreting pituitary adenomas are less than 10 mm in diameter and are described as microadenomas, while corticotroph macroadenomas (≥10 mm) are a less common cause of Cushing’s disease. Prior reports on the differences of clinical and biochemical behavior of corticotroph microadenomas and macroadenomas were inconsistent. Objective

Describe the clinical and biochemical characteristics of patients with corticotroph macroadenomas and microadenomas.

Methods

Retrospective charts review of patients with Cushing’s disease treated at Rabin Medical Center between 2000 and 2017, or at Maccabi Healthcare Services in Israel between 2005 and 2017. Tumors in which the largest diameter was ≥10 mm were considered to be macroadenomas. When no visible tumor was seen on MRI, the tumor was considered to be a microadenoma. Epidemiologic, clinical and biochemical factors were compared between patients with corticotroph macroadenomas and microadenomas.

Results

The cohort included 105 patients (82 women, 78%; mean age ± SD, 41.5 ± 14.5 years), including 68 patients (64.8%) with a pituitary microadenoma (mean size, 5.2±2.2 mm), 25 patients (23.8%) with a macroadenoma (mean size, 18.0±7.7 mm), and 12 patients with no visible adenoma. Baseline characteristics were similar between the groups, including age, gender, body mass index, and comorbidities. Most common reasons for completing an investigation for Cushing’s syndrome among patients with microadenomas and macroadenomas were weight gain (46.3% vs 52.0%, \(P=\text{NS}\)) and Cushingsoid features (27.5% vs 20.0%, \(P=\text{NS}\)). While mean urinary free cortisol levels (5.2 ± 5.4 ULN vs 7.8

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RC7.4 Evaluation of the impact of covid-19 on the hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-thyroid axis
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Context
The long-term consequences of Covid-19 are unknown. Most patients experience persistent symptoms more than one month after the acute illness, including fatigue, dyspnea, memory loss, concentration disorder. The pituitary, the thyroid and the adrenal gland express the ACE-2 receptor, which is the cellular receptor for SARS-CoV-2, and could therefore be affected by the virus. However, the effect of Covid-19 on the hypothalamic-pituitary-adrenal axis and hypothalamic-pituitary-thyroid axis are unclear.

Objective
Our objective was to evaluate the impact of the SARS-CoV-2 infection on the hypothalamic-pituitary-adrenal axis and hypothalamic-pituitary-thyroid axis in the medium term.

Methods
A prospective, observational study conducted from May 2020 to March 2021 at Amiens University Hospital, including 318 adult patients hospitalized for Covid-19. Participants attended a medical consultation 3 month after hospital admission. They had serum cortisol, TSH and FT4 analyzed, and the persistence of symptoms after hospitalization was evaluated. Adrenal insufficiency was defined by a morning cortisol < 5 μg/dl. Possible central hypothyroidism was defined by FT4 below the laboratory range and low or normal TSH levels.

Results
The post-COVID-19 consultation took place 112 [97-144] days after hospital admission. Basal morning serum cortisol was available for 232 patients. 2 patients had secondary adrenal insufficiency, with basal cortisol levels respectively of 1.4 and 2.1 μg/dl, and adrenocorticotropin levels of 33.5 et 7.6 pg/ml. No patient had primary adrenal insufficiency. The median of basal cortisol level was 13.1 μg/dl [10.1-16.9] in the group of patients who received Dexamethasone during hospitalization, and 14.7 μg/dl [11.5-18.3] in the group of patients who didn’t receive Dexamethasone, there was no statistical difference between the two groups. TSH and FT4 were available for 219 patients. 8 patients had results compatible with central hypothyroidism. One patient had both central adrenal insufficiency and central hypothyroidism, due to a pituitary apoplexy following Covid-19 infection. 113 patients presented with persistent symptoms. There was no difference in basal cortisol level between patients who experienced persistent symptoms and those who didn’t, the median of cortisol levels were respectively 14.1 and 13.9 μg/dl. The FT4 levels were not different between patients with persisting symptoms and those without.

Conclusion
The pituitary-adrenal axis function was preserved 3 months after hospitalization in patients who survived the infection. 3% of the patients had results in favour of central hypothyroidism and <1% had secondary adrenal insufficiency. 35% of the participants had persistent symptoms after the infection but these symptoms were not related to either hypothalamic-thyroid axis or hypothalamic-adrenal axis dysfunction.

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RC7.5 Osilodrostat therapy improves physical manifestations of hypercortisolism in patients with cushing’s disease: findings from the phase III LINC 3 study
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Background
Improving physical manifestations of hypercortisolism is an important treatment goal for patients with Cushing’s disease (CD). In the Phase III LINC 3 study (NCT02180217), osilodrostat therapy, a potent 11β-hydroxylase inhibitor, rapidly normalised mean urinary free cortisol (mUFC) in most patients with CD and sustained control of mUFC over a median treatment period of 130 weeks (W).

Here we describe concomitant improvements in physical manifestations of hypercortisolism.

Methods
137 adults with CD and mUFC > 1.5 times the upper limit of normal were enrolled in the published 48W core phase. 106 patients opted to enter the extension phase, which ended when all patients had received ≥72W of treatment. Photographs from the shoulders up (frontal and lateral) and of the trunk with the patient standing (frontal and dorsal) were taken by investigators at baseline, every 12W during the core phase, and at W72; manifestations were rated subjectively on a semi-quantitative scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe. Body weight and waist circumference were also measured. Data are presented descriptively for all patients with an assessment at baseline and the given visit. Results

At baseline, most patients had mild, moderate or severe physical features of hypercortisolism: dorsal fat pad (73.7%), supraclavicular fat pad (68.6%), central obesity (71.5%), facial rubor (63.5%), hirsutism (58.5%) [females only; p = 62/106]), proximal muscle atrophy (51.8%), striae (48.9%) and ecchymosis (38.7%). At W48 (n = 97) and W72 (n = 86), improvements in physical features scores from baseline were noted in 52.6% and 57.0% of patients for dorsal fat pad, 51.5% and 55.3% for supraclavicular fat pad, 42.3% and 39.5% for central obesity, 46.4% and 52.3% for facial rubor, 34.2% (p = 26/76) and 34.4% (p = 22/64) for hirsutism, 38.1% and 34.9% for proximal muscle atrophy, 32.0% and 30.2% for striae, and 35.1% and 31.4% for ecchymosis. Mean weight improvement from 80.8 kg at baseline to 75.5 kg (+4.6%) at W48 and 74.1 kg (+5.8%) at W72. Mean waist circumference decreased from 103.5 cm at baseline to 97.4 cm (–4.2%) at W48 and 95.6 cm (–5.8%) at W72. Mean body mass index improved from 30.3 kg/m2 at baseline to 28.4 kg/m2 (–4.6%) at W48 and 27.9 kg/m2 (–5.8%) at W72.

Conclusions
Most patients in LINC 3 had physical manifestations of hypercortisolism at baseline. Osilodrostat therapy provided long-term mUFC control and clinical improvements, with reductions in patient weight and the severity of physical manifestations, including hirsutism, that were sustained through to W72.

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RC7.6 Long-term results from the Phase III LINC 4 study: Osilodrostat maintained normal mean urinary free cortisol in patients with Cushing’s disease, with a favourable safety profile
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Background
Olodrostat therapy provided long-term mUFC control and clinical improvements, with reductions in patient weight and the severity of physical manifestations, including hirsutism, that were sustained through to W72.

Methods
137 adults with CD and mUFC > 1.5 times the upper limit of normal were enrolled in the published 48W core phase. 106 patients opted to enter the extension phase, which ended when all patients had received ≥72W of treatment. Photographs from the shoulders up (frontal and lateral) and of the trunk with the patient standing (frontal and dorsal) were taken by investigators at baseline, every 12W during the core phase, and at W72; manifestations were rated subjectively on a semi-quantitative scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe. Body weight and waist circumference were also measured. Data are presented descriptively for all patients with an assessment at baseline and the given visit.

Results
At baseline, most patients had mild, moderate or severe physical features of hypercortisolism: dorsal fat pad (73.7%), supraclavicular fat pad (68.6%), central obesity (71.5%), facial rubor (63.5%), hirsutism (58.5%) [females only; p = 62/106]), proximal muscle atrophy (51.8%), striae (48.9%) and ecchymosis (38.7%). At W48 (n = 97) and W72 (n = 86), improvements in physical features scores from baseline were noted in 52.6% and 57.0% of patients for dorsal fat pad, 51.5% and 55.3% for supraclavicular fat pad, 42.3% and 39.5% for central obesity, 46.4% and 52.3% for facial rubor, 34.2% (p = 26/76) and 34.4% (p = 22/64) for hirsutism, 38.1% and 34.9% for proximal muscle atrophy, 32.0% and 30.2% for striae, and 35.1% and 31.4% for ecchymosis. Mean weight improvement from 80.8 kg at baseline to 75.5 kg (+4.6%) at W48 and 74.1 kg (+5.8%) at W72. Mean waist circumference decreased from 103.5 cm at baseline to 97.4 cm (–4.2%) at W48 and 95.6 cm (–5.8%) at W72. Mean body mass index improved from 30.3 kg/m2 at baseline to 28.4 kg/m2 (–4.6%) at W48 and 27.9 kg/m2 (–5.8%) at W72.

Conclusions
Most patients in LINC 3 had physical manifestations of hypercortisolism at baseline. Olodrostat therapy provided long-term mUFC control and clinical improvements, with reductions in patient weight and the severity of physical manifestations, including hirsutism, that were sustained through to W72.

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Background
Osilodrostat (potent oral 11β-hydroxylase inhibitor) provided rapid normalisation of mean urinary free cortisol (mUFC) in Cushings disease (CD) patients during the 48-week (W) core period of LINC 4 (NCT02697734) and was well tolerated. We report long-term efficacy and safety results from the LINC 4 core and extension phases.

Methods
73 adults with CD and mUFC > 1.3 upper limit of normal (ULN) were enrolled. LINC 4 comprised a 12W, randomised, double-blind, placebo-controlled period followed by 36W of open-label osilodrostat. At W48, patients could continue receiving open-label osilodrostat during an optional extension. Dose adjustments were permitted based on efficacy/tolerability (open-label range, 1-30 mg bid).

Results
65/71 patients completed the core phase; 60 entered the extension. Median (range) osilodrostat exposure from core baseline to study end was 87.1 (2-127) W; median (IQR) average dose was 4.6 (3.7-9.2) mg/day. 15 patients discontinued osilodrostat, 7 after W48 (6 because of adverse events [AEs]). The proportion of patients with normal mUFC (≤138 nmol/24 h) was 68.5% (n = 50/73) at W48, 61.5% (n = 40/65) at W72 and 72.4% (n = 42/58) at extension end-of-treatment (EOT). Median mUFC decreased from 2.5ULN (core baseline) to 0.5ULN (W48 and W72) and 0.4ULN (EOT). Median late-night salivary cortisol decreased from 2.8ULN (core baseline) to 1.2ULN (W48 and W72) and 1.1ULN (EOT). Most common AEs overall were decreased appetite (46.6%), arthralgia (45.2%), fatigue (39.7%), nausea (37.0%), headache (34.2%) and dizziness (30.1%). AEs related to hypocalciuria and accumulation of adrenal hormone precursor occurred in 28.8% (21/73) and 61.6% (45/73) of patients overall, less frequently in the extension than the core. Most were grade 1/2 and well tolerated.

Conclusion
Osilodrostat provided long-term control of cortisol production during LINC 4. Frequent AEs related to hypocalciuria and accumulation of adrenal hormone precursors occurred during the extension than the core. Osilodrostat is an effective and well-tolerated long-term treatment option for CD patients.

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RC7.7

Outcome in repeat transphenoidal surgery in patients with persistent and recurrent Cushing’s disease
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Objective
Transphenoidal surgery is the treatment of choice for Cushing’s disease (CD). Surgery is challenging due to the often very small adenomas. In experienced pituitary centers a high remission rate is reported. Nevertheless, endocrinologists and neurosurgeons face cases with persistent or recurrent CD. These patients must be referred to an experienced pituitary center. In addition to medical treatment, radiation therapy and bilateral adrenalectomy, repeat TSS must also be evaluated.

The aim of this study is to analyse the outcome of repeat surgery and to compare persistent and recurrent CD.

Methods
We retrospectively analysed 52 patients with confirmed CD, who underwent repeat TSS in our department. Both persistence of CD after unsuccessful first surgery (n = 24) and recurrence of CD (n = 28) were evaluated for repeat TSS. Thirty-two patients underwent their first surgery externally, 20 patients had both TSS in our pituitary center. All surgeries were performed by a single experienced pituitary surgeon through a microscopic transphenoidal approach.

Results
The time range between the first and the repeat TSS was between 0 – 93 months (median 7.5 months) in the case of persistent CD, and between 3 – 219 months (median 64.5 months) in the cases of recurrent CD (P < 0.0001). A high-quality MRI was performed preoperatively in all cases. A clear adenoma was found in 65.4% of cases (66.7% persistent CD, 64.3% recurrent CD). A remission rate of 71% (n = 17/24) was achieved in the group with persistent CD, and of 82% (n = 23/28) with recurrent CD. The complication rate was 5.7% (8.3% in persistent CD, 3.6% in recurrent CD). There was no mortality rate in either group.

Conclusion
Persistent and recurrent CD pose a greater challenge for further treatment. If repeat surgery is an option, it should be offered to the patient at an experienced pituitary center. A higher remission rate is achieved in recurrent CD compare to persistent CD. With high surgical experience, there is still a low complication rate of repeat TSS with a satisfactory probability of remission.

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Calcium and Bone
RC8.1

Growth hormone excess in fibrous dysplasia and maccune albright syndrome (FDMAS)
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Objective
Fibrous dysplasia (FD)/McCune Albright Syndrome (MAS) is a rare disorder affecting bone and hormonal glands. In FDMAS patients, autonomous GH secretion is the most common endocrinopathy after Precocious Puberty and has a great impact on the morbidity and complication rate in patients with craniofacial fibrous dysplasia. However clinical and biochemical features of GH over secretion can be subtle and awareness is warranted. We aimed to explore the GH/IGF-1 axis in FDMAS.

Methods
We included 163 patients with measurements of GH/IGF-1. Patients with MAS and GH+ were compared with MAS-patients without GH+. Growth hormone excess was diagnosed by Growth Hormone suppression Test (GST) with 75 grams of glucose, cut off value of 1.45 nmol/L. GST is performed in our center in case of progressive Craniofacial FD (CFD), phenotypic changes or IGF-1 levels > 1.05D as typical complaints of acromegaly are often lacking in FDMAS.

Results
38 (65.4% females) MAS patients were included,10 had GH excess. In the GH+ group, 7 had prolactin co-secretion. All 10 subjects had precocious puberty and CFD, 7 had skull base involvement. Patients with GH+ were diagnosed with FDMAS at a younger age, 3.5 (0-14 yrs) vs 12 years (1-51 yrs) than GH- patients, P < 0.001. Median age of GH+ diagnosis was 36 years (7-43 yrs), GH+ was more frequent in males, 7 vs 3. A pituitary microadenoma could be detected in 3
patients (30%). GH+ correlated with visual impairment (P<0.001, r=0.267), n=7 subjects (70%) resulting in blindness in 4. IGF1 levels at time of GH+ diagnosis were within the normal range in 60% of FDMAS GH+ subjects, 48 nmol/l (24.3-83.3) SD 1.95, albeit significantly higher than FDMAS GH- patients, P=0.007. Alkaline phosphatase-(ALP) at first presentation was higher in FDMAS GH+ (P<0.01), also after correction for disease severity. All GH+ patients were started on medical treatment as surgery was not feasible. After 12 months IGF-1 levels dropped to 37.3 nmol/l (17.30-50.60), SD 0.5 (P = 0.04). In addition, ALP decreased as well from 1131.5 U/l to 989.5 U/l, P=0.034.

Conclusion
In this cohort of FDMAS patients, GH excess was observed in 26% of patients. 60% had IGF-1 levels < 2.5 SD and could only be diagnosed with GST. GH excess was associated with more visual impairment and higher bone turnover. Early diagnosis using GST should be performed as in 60% of subjects IGF-1 levels were within the normal range as treatment is of upmost importance to prevent complications in the future.

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RC8.2

Temporal effects of encalcerte (CLT.X-305) on mineral physiology in autosomal dominant hypocalcemia type 1 (ADH1): results from a phase 2B, open-label, dose-ranging study [NCT04581629]

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Autosomal dominant hypocalcemia type 1 (ADH1), caused by gain-of-function variants in the calcium-sensing receptor (CaSR), gene: CASR and is characterized by hypocalcemia, hyperphosphatemia, low parathyroid hormone (PTH), and hypercalcuria. Calcilytics (negative allosteric modulators of the CaSR) decrease PTH sensitivity of activated receptors to extracellular calcium and normalize blood and urine abnormalities in ADH1 rodent models. Encalcerte is an oral calcilytic under investigation as a treatment for ADH1. Data on the encouraging effects of encalcerte on PTH and blood and urine calcium (Ca) were previously reported. Here we expand on those data and describe the temporal and relative changes in PTH, nephrogenous cAMP (NcAMP), tubular reabsorption of phosphate (TRP), blood phosphatase (P) and Ca, fractional excretion of Ca (FECa), 1,25-dihydroxyvitamin D (1,25(OH)2D), and intact FGF23 (fibroblast growth factor 23) after encalcerte administration. Six adults (22-60 years) with ADH1 due to 4 CASR variants were studied in Period 1 of a Phase 2b, open-label, dose-ranging study. Subjects received sequential, increasing daily doses of encalcerte for 3d (30 mg, 90 mg, 180 mg) followed by 180mg bid on day 4 and 120 mg or 180 mg bid on day 5, while undergoing frequent blood and urine sampling. The temporal changes in the mean±SD values over 24 hr on day 4 are compared to baseline (blood volume limitations only allowed for collection of the most panel parameters through day 4). PTH was low at baseline (3.4±2.5 pg/ml, normal 10-65), rose rapidly, peaked at 2 hr (65.0±49.2), and remained normal beyond the 24 hr measured. NcAMP rose by 4 hr and was significantly increased through the 24 hr measured. TRP and P increased rapidly and remained significantly increased through 24 hrs. FECa was 0.03±0.02 at baseline, was significantly decreased by 4hr, which was maintained through 24 hrs. Blood albumin-corrected Ca was below normal prior to 0hr dosing (7.6±0.6 mg/dl, normal 8.4-10.2), was normal by 4hr and remained significantly increased from 8-24 hrs. 1,25(OH)2 D was below normal at 0hr, increased and remained in the normal range from 4-24 hrs. Intact FGF23 was above normal at time 0hr and surprisingly remained unchanged over the 13hrs monitored, despite the reported changes in P, PTH and 1,25(OH)2 D. Bone turnover markers CTX and P1NP were unchanged compared with day 1. Encalcerte was well-tolerated, with no serious adverse events reported. The observed temporal changes of key mineral homeostasis factors and normalization of blood Ca and FECa in encalcerte-treated subjects with ADH1 shed light on mineral physiology and potential utility of encalcerte in ADH1.

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RC8.3

What is the most efficient way to fortify food items with vitamin D? A randomised, multi-country study

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Introduction
Vitamin D insufficiency (25-hydroxy vitamin D <50 nmol/l) is a global health problem. Vitamin D food fortification might be the solution, but knowledge is sparse on whether fortification of various food items affects the bioavailability differently. It is generally assumed that ingesting vitamin D with a fatty meal improves the bioavailability of vitamin D. Furthermore, complex formation with whey protein isolate (WPI) may enhance the stability of vitamin D and thereby improve bioavailability. We studied the efficiency of fortifying different food items with vitamin D3.

Materials and methods
In a randomised, multiple (5-periods) crossover trial, we enrolled 30 postmenopausal women with vitamin D insufficiency aged 60-80 years. We measured immediate changes in plasma concentrations of cholocalciferol (D3) in response to intake of different food matrices with 200 μg D3 added i.e., 1) 500 mL of water, 2) 500 mL of milk, 3) 500 mL of juice, 4) 500 mL of juice with D3 complex-bound to WPI, and 5) 500 mL of water without D3 (placebo). The different food matrices were provided in a randomised order with at least ten days washout period in-between study days. On each study day, blood samples were collected at 0 h, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h and 24 h.

Results
Complexion D3 -WPI in apple juice did not enhance maximum concentration (Cmax) of serum D3 compared to juice without WPI (25 nmol/l vs 24 nmol/l; P=0.61), nor the area under the time-D3 curve (AUC) (370 nmol/l *24 h vs 357 nmol/l *24 h; P=0.93). However, compared to juice, Cmax and AUC of serum D3 were significantly higher in response to intake of milk (30 nmol/l and 452 nmol/l *24 h) and water with D3 added (32 nmol/l and 479 nmol/l *24 h; P<0.05, all). No difference in serum D3 was observed between milk and water (P=0.29, Cmax; P=0.33, AUC).

Conclusion
The bioavailability of D3 assessed by Cmax and AUC was superior in water and milk compared to juice, independent of whether complexion D3 -WPI was added to juice.

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RC8.4

Accuracy, costs and radiation exposure of current preoperative localization procedures in patients with primary hyperparathyroidism, a retrospective cohort study in a Swiss tertiary referral center

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Background
Focused parathyroidectomy has become the standard procedure for patients with sporadic primary hyperparathyroidism (pHPT) fulfilling the criteria for surgical therapy and requires preoperative localization procedures. Ultrasound imaging (US) and 99mTc-sestamibi-scintigraphy with/without SPECT/CT (SC) are established first line procedures. 18F-choline PET/CT (PET) has emerged as a novel sensitive and specific method. However, current reimbursement policy in Switzerland limits its use to patients with negative or equivocal first line imaging.

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Bone marrow fat is a unique fat depot that is regulated independently of other fat depots. Estradiol is an important regulator of bone marrow fat. This is illustrated by an increase in marrow fat fraction after menopause and a decrease following estradiol replacement. We hypothesize that estradiol is the major sex steroid that regulates bone marrow fat not only in women, but also in men.

Methods

This is an open-label partly randomized intervention study in trans women (assigned male at birth, identify as female) and trans men (assigned female at birth, identify as male) receiving hormone treatment. Trans women were treated with triptorelin and testosterone with or without anastrozole for 12 weeks, followed by only testosterone until week 52. Measurements were performed at baseline, 6, 12 and 52 weeks. The marrow fat fraction was quantified using triple-echo T1-weighted single-shot turbo spin-echo imaging (T1w-SE) and a fast T1-weighted single-shot turbo spin-echo imaging (T1w-SE) sequence. The marrow fat fraction was calculated as the area fraction of fat pixels divided by the total area fraction of pixels in a region of interest.

Results

The study included 239 patients of which all underwent US imaging, 164 (68.6%) received SC and 70 (29.3%) PET imaging. The final diagnostic accuracy of the phase 2 PaTH forward trial of TransCon PTH

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Background

Patients with hypoparathyroidism experience significant physical and cognitive symptoms and reduced health-related quality of life (HRQoL). Conventional therapy for hypoparathyroidism does not fully alleviate diminished HRQoL. The Hypoparathyroidism Patient Experience Scales (HPES) were developed to assess disease-specific physical and cognitive symptoms as well as the impact of hypoparathyroidism on HRQoL. TransCon PTH, an investigational long-acting produg of parathyroid hormone (PTH1-34), is in development as a potential hormone replacement therapy for adults with hypoparathyroidism.

Methods

The phase 2, randomized, double blind placebo controlled 4-week PaTH Forward trial was followed by an open label extension period and enrolled 59 participants. HRQoL was assessed at Week 4 and Week 26 in an exploratory ad-hoc analysis using HPES and the 36-item Short Form Survey (SF-36) to assess the role of HPES in measuring the impact of TransCon PTH on HRQoL

Results

Improvements in HPES scores were significantly greater for participants treated with TransCon PTH (n=44) compared with placebo (n=15) from baseline to Week 4 of the trial for both HPES-Total Symptom score (Mean difference [standard error] in scores -15.7 [5.0], P < 0.01; 84% of treated patients had improved scores versus 47% of placebo, P=0.013) and HPES-Total Impact Score (Mean difference [standard error] in scores -15.7 [5.0], P < 0.01; 75% of treated patients had improved scores versus 40% of placebo, P=0.025). All HRQoL assessments demonstrated continued score improvements in patients treated with TransCon PTH at Week 26 of the trial compared with baseline. Participants treated with TransCon PTH who had higher (worse) HPES (Impact & Symptom) scores at baseline demonstrated a greater magnitude of improvement at Week 26 as did participants with lower (worse) SF-36 scores at baseline. The Pearson correlation analysis showed that HPES results diverged from SF-36 results over time, with a greater number of domain scores having a correlation of -0.40 or larger at Week 4 compared with Week 26.

Conclusions

This exploratory ad-hoc analysis of the PaTh Forward trial demonstrated improved HRQoL and symptom scores in participants treated with TransCon PTH compared with placebo. In addition, correlation analyses identified the distinct value and dynamic range of HPES as disease-specific assessment tools in hypoparathyroidism. The decreased correlation between HPES and SF-36 over time in the trial indicates that HPES and SF-36 are not redundant.

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Health related quality of life in adults with hypoparathyroidism in an exploratory analysis of the phase 2 PaTh forward trial of TransCon PTH

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Background

Estradiol is the major sex steroid regulating bone marrow fat not only in women, but also in men.

Conclusion

The results of this study indicate that estradiol and not testosterone is the major sex steroid regulating bone marrow fat in both men and women.

DOI: 10.1530/endoabs.81.RC8.5
The resorption status of magnesium screws for surgical treatment of ankle fractures assessed by HRpQCT ~ 2.5 years follow-up data of a first-in-human study

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Background
Biodegradable screws for surgical fracture treatment are of great interest for the orthopaedic community. Such implants are designed to provide stability and compression of the fracture and should dissolve after healing, thereby making removal of surgical material obsolete. Magnesium implants are a new material option. So far, long-term follow-up of fracture healing and material decay has not been studied in human. Here, we present the results of the 2.5 year follow-up of 6 patients with medial malleolar fractures after surgical stabilization with magnesium screws.

Methods
6 patients with isolated, bimalleolar or trimalleolar ankle fractures were surgically treated using biodegradable screws (magnesium 99.1%, calcium 0.45%, zinc 0.45%) with an initial volume of 243.3 mm³ (+/- 5). Fracture healing was assessed clinically after one year. Implant resorption was studied after 2.5 years with HR pQCT (high resolution peripheral quantitative computed tomography).

Screw residues were carefully evaluated in a binary approach for every slice (residual present vs not present). Zones of degradation without visible bone were contoured manually and the volume was evaluated.

Results
All patients showed clinical evidence of fracture healing confirmed by plain radiographs, with full weight bearing and absence of pain in the fractured ankle. In 10% of slices (min. 0%; max. 33%) residuals were complete. Of the 11 implants in 6 patients, 3 were dissolved without visible radiographs, with full weight bearing and absence of pain in the fractured ankle. All patients showed clinical evidence of fracture healing confirmed by plain radiographs, with full weight bearing and absence of pain in the fractured ankle.

Conclusion
The degradation zones lacked visible ingrowth of new bone in these zones were observed. The degradation zones lacked visible ingrowth of new bone in these zones were observed. The degradation zones lacked visible ingrowth of new bone in these zones were observed.

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Diabetes, Obesity, Metabolism and Nutrition 3

Insulin resistance as indexed by the estimated glucose disposal rate and liver fat content are correlated in type 1 diabetes

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Introduction
The prevalence of metabolic syndrome is increasing in individuals with T1D, which could potentiate the development of NAFLD. The pathophysiology of NAFLD in T1D is still unclear, due to the co-existence of predisposing and protective factors. Insulin resistance (IR) is theorized as a key driver of NAFLD.

Aim
We investigated the association between liver fat content (LFC), NAFLD, and IR in individuals with T1D. Subjects underwent magnetic resonance spectroscopy (MRS) to determine LFC. The estimated glucose disposal rate (eGDR) was calculated in two ways based on: (1) the presence of hypertension, waist circumference (cm), and Hba1C (%), and (2) the presence of hypertension, body mass index (BMI, kg/m²), and Hba1C (%). An eGDR <8 mg/kg/min is considered insulin resistant. A mean LFC ≥ 6.0 % on MRS was considered diagnostic for NAFLD.

Results
Seventy-eight subjects were included. Age was 59 ± 17 years, BMI was 27.6 ± 5.0 kg/m², waist circumference was 87 ± 13 cm in females and 96 ± 12 cm in males, and hypertension was present in 63%. LFC based on MRS was 4.3 ± 4.0 %, NAFLD was present in 11 (14%) subjects, Hba1C was 7.4 ± 1.2 % indicating good glycemic control. The eGDRwaist measured 6.4 ± 2.5 mg/kg/min, and eGDRBMI was 6.4 ± 2.2 mg/kg/min. Correlation between eGDR methods was excellent (r = 0.96, P < 0.001). Kappa between eGDR methods was 0.87, P < 0.001. Prevalence of IR was 27% (eGDRBMI) and 30% (eGDRwaist). All 11 cases of NAFLD were in the IR group, regardless of eGDR method. Linear regression showed a weak correlation between eGDRBMI and LFC (r = 0.277, B: -0.442, 95% CI: (-0.792 - 0.091), P = 0.014), and between eGDRBMI and LFC (r = -0.270, B: -0.480, 95% CI: -0.872 – 0.089, P = 0.017). NAFLD was associated with the eGDRwaist as a continuous variable (OR: 0.62, 95% CI: 0.39 - 0.99, P = 0.049) in a logistic model including BMI age, and gender. eGDRBMI was not significantly associated in a model including waist, age and gender.

Conclusions
These data show that IR, as indexed by the eGDR based on waist circumference, is associated in a model including BMI and the presence of NAFLD in individuals with T1D. More studies are needed to elucidate the role of IR in the etiology of NAFLD in individuals with T1D.

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RC10.2

Weight changes and all-cause mortality in patients with prediabetes and diabetes

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Introduction
Weight loss is a cornerstone in the management of prediabetes and diabetes mellitus. The association between weight and all-cause mortality is controversial and even paradoxical. Studies usually assess baseline weight. Studies assessing weight changes over time are limited. We present preliminary results of our attempt to model weight changes in patients with prediabetes and diabetes assessing the relationship with all-cause mortality.

Methods
We evaluated a retrospective cohort of Olmsted county residents with prediabetes (n = 15868) and diabetes (n = 10744) seen at Mayo Clinic. They had vital signs before and after 01-01-2005 and were alive by 01-01-2011. Body mass index (BMI) was calculated to assess weight changes and classified as Low or High using 32 as cutoff. The study period, 01-01-2000 to 01-01-2011 was divided in 3 stages; Baseline from 01-01-2000 to 12-31-2004 (5 years), Follow-up 1 from 01-01-2005 to 12-31-2007 (3 years) and Follow-up 2 from 01-01-2008 to 01-01-2011 (3 years). For each patient we defined six 3-step BMI trajectories by using BMI Low (L), High (H) or any value (X): 1) L-L-L: always low BMI. 2) H-H-H: always high BMI. 3) L-X-L: start and end with Low and had a High BMI at some point. 4) H-L-H: start and end with High but had a Low BMI at some point. 5) H-X-L: start with High but end with Low BMI. 6) L-X-H: start with Low but end with High BMI.
Results
As expected, diabetes mortality rates were higher than prediabetes, but their overall distribution by BMI trajectories was similar (Table). Subjects with high BMI (H-H), had a higher mortality rate compared with low BMI (L-L). Subjects that ended with Low BMI, regardless of initial BMI level (L-H-L and L-H-X-L), had higher mortality than subjects ending with high BMI (H-L-H and L-X-H).

Conclusion
Our preliminary results evaluating BMI trajectories suggest elevated mortality in subjects with BMI below 32 when compared with BMI above 32, and subjects that lost weight when compared with those that gained weight. These results are contrary to our expectation and against our conceived pathophysiological interaction between obesity, diabetes and its complications. The fact that similar findings have been described for other clinical conditions, impose the need for additional research to find a suitable explanation related to methodology or clinical cause.

Table. Mortality rates by BMI Trajectory

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<tbody>
<tr>
<td>Diabetes</td>
<td>19.79%</td>
<td>12.65%</td>
<td>15.87%</td>
<td>13.59%</td>
<td>21.78%</td>
<td>13.15%</td>
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<tr>
<td>PreDiab</td>
<td>11.98%</td>
<td>5.87%</td>
<td>10.53%</td>
<td>5.60%</td>
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RC10.4

Adequate metabolic control at early stages of childhood onset type 1 diabetes prevent diabetic neuropathy: a 30 year follow up study

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Background and aims
Diabetic neuropathy is a common complication of type 1 diabetes. In this study we investigated the importance of long-term metabolic control for the development of diabetic neuropathy in patients with type 1 diabetes diagnosed in childhood.

Materials and methods
Longitudinal cohort study. Twenty-five patients (9 women 16 men) were studied three times with neurophysiological measurements and clinical examinations. At baseline the patients were 15.7±3.7 yrs. (range 7-22) and had diabetes duration of 7.7±3.3 yrs. (range 4-15). At the first follow up 2007-2009 the patients were 29.5±18.9 yrs. (range 20-35), and had a diabetes duration of 21.6±4.3 yrs. (range 10-31). At the second follow up 2017-2018, the patients were 38.6±3.7 yrs. (range 31-47) and had a diabetes duration of 31.2±4.7 yrs. (range 20-39).

The assessment of neurological symptoms followed a standardized process. A neuropathy impairment assessment (NIA) was used to evaluate the signs of diabetic neuropathy. Nerve conduction tests were carried out according to standard techniques. The presence of clinical diabetic neuropathy was determined by a staged approach according to established criteria. Subclinical neuropathy is defined as an electrophysiological abnormality of nerve function without clinical symptoms or signs.

Results
At the initial examination, all patients were free of clinical or subclinical neuropathy. At the first follow up, ten patients 10/25 (40%) had developed clinical (n=5) or subclinical neuropathy (n=5) and they had significantly higher HbA1c, 77.4±16.2 mmol/mol, than the 15 patients without neuropathy, 60.3±8.6 mmol/mol. At the second follow up fifteen patients 15/25 (56%) fulfilled the criteria of clinical (n=9) or subclinical neuropathy (n=6). At the second follow up, HbA1c in the patients with diabetic neuropathy decreased from 77.4±16.2 mmol/mol at the first follow up to 64.2±16.5 mmol/mol at the second follow up, P=0.013. The additional group of five patients who developed neuropathy between the first and second follow up reduced their HbA1c from 72.1±10.8 mmol/mol to 57.8±14.1 mmol/mol, P=0.006. Taken together, at the second follow up, the difference in HbA1c levels between the 15 patients with neuropathy, 61.4±10.5 mmol/mol, and the 10 patients without neuropathy, 59.6±13.6 mmol/mol, was no longer significant.

Conclusion
The prevalence of diabetic neuropathy in the patient cohort increased with longer diabetes duration and progressed to clinical neuropathy in several cases despite a better metabolic control at the last follow up. The study indicates that an inadequate glycaemic control at early stages of the disease is a risk factor for developing diabetic neuropathy.

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RC10.5

GLP-1RAs and glucagon can reshape adipose differentiation in vitro by activating the “browning process”

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Obesity is associated with increased and dysfunctional white adipose tissue (WAT). Pharmacological approaches of obesity are still far from obtaining a stable weight loss. Glucagon-like peptide-1 receptor agonists (GLP1-RAs) have been proposed as anti-obesity drugs due to their effects on weight loss. Furthermore, dual agonists engaging both GLP1 and glucagon are currently under investigation for their marked effects on weight loss, although their mechanisms of action is still unclear. Compared to WAT, brown adipose tissue (BAT) is specialized in energy dissipation by heat production resulting from the specific expression of the mitochondrial enzyme uncoupling protein-1 (UCP-1). There is growing interest for new therapeutic strategies aimed at stimulating BAT to increase energy expenditure and counteract the dysfunctional expansion of WAT in obesity. Our group has previously demonstrated that iriglutide, GLP-1 and glucagon impair the proliferative and differentiation ability of an in vitro model of human adipose-derived stem cells (ASCs), supporting a peripheral action of GLP1-RAs on weight loss. In this study, we compared the effect of these three molecules in reshaping adipogenesis toward brown adipogenesis by stimulating the “browning process” in ASCs. Glucagon, iriglutide and GLP-1 (10mM) added during in vitro-stimulated adipogenesis significantly reduced intracellular triglyceride accumulation evaluated by Adipose staining (-24%,-40%,-23%, P<0.001) associated with a decreased expression in the white-adipocyte marker FABP4 (-48%,-94%,-78%, P<0.005), while the functional marker adiponectin was upregulated (+34%,-65%,-72%, P<0.005). These findings suggest a differentiation reshape towards a more functional adipocyte phenotype. Moreover, adipogenesis in the presence of the three molecules resulted in a significant upregulation of the brown phenotype marker UCP-1 (fold-increase 2.13, 2.48, 2.14-fold versus adipogenesis alone, P<0.005). Mitochondrial functional analysis through Seahorse technology of the adipocytes differentiated in the presence glucagon, iriglutide and GLP-1 revealed a significant increase in the maximal respiration (+15%,25%,-29%, P<0.005) and a similar reduction (-17%,-14%,-18%, P<0.001) in ATP production, supporting a stimulation of the browning process. Finally, morphological analysis of the differentiated adipocytes revealed that iriglutide, GLP-1 and glucagon addition to the adipogenic media associated with an increase in the number and surface of mitochondria and an increase in the number of lipid droplets with decreased diameter, coherently with the typical feature of brown adipocytes. In conclusion, we demonstrated a direct effect of glucagon and GLP1RAs in inducing a significant improvement of the in vitro-derived adipocytes, determining a metabolic shift towards the brown phenotype, coherently with a peripheral action exerted by these molecules directly on the adipose tissue.

DOI: 10.1530/endobs.81.RC10.5

Results
465 episodes of DKA were identified. 47 were excluded from analysis due to unclear diabetes type. 68.7% (n = 287/418) had T1DM and 31.3% (n = 131/418) had T2DM. The differences in precipitating factors in DKA in T1DM vs T2DM were significant (P=0.006). The most common precipitating factor in both groups was intercurrent illness (T1DM: n = 107/287, 37.3%; T2DM: n = 57/131, 43.5%). More DKA episodes were precipitated by suboptimal compliance to treatment in T1DM compared to T2DM (T1DM: n = 99/287, 34.5%; T2DM: n = 20/131, 15.3%). 9 (6.9%) episodes of DKA were related to SGLT2 in T2DM compared to none in T1DM. 19 (6.6%) episodes of DKA were new diagnoses of T1DM. Other precipitating factors included COVID-19 (T1DM: n = 14/287, 4.9%; T2DM: n = 6/161/131, 3.8%), sepsis (T1DM: n = 10/287, 3.5%; T2DM: n = 11/131, 8.4%), alcohol (T1DM: n = 12/287, 4.2%; T2DM: n = 3/131, 2.3%), drug induced (T1DM: n = 22/287, 0.7%; T2DM: n = 3/131, 2.3%) and trauma (T1DM: n = 2/287, 0.7%; T2DM: n = 0/131, 0.0%).

Conclusion
DKA is no longer synonymous with T1DM and we are now seeing significant DKA case numbers in T2DM. The precipitating factors differed between the two types of diabetes and these results can help allocate resources for improved education and individualised clinical care appropriately to minimise morbidity and mortality associated with an eminently preventable condition.

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RC10.7
Knowledge about Diabetic Ketoacidosis in Patients with Type 1 Diabetes mellitus – Data of a Patient-centered Questionnaire
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Background/Introduction
Diabetic ketoacidosis (DKA) is a severe complication of diabetes mellitus type 1 (T1DM) with potentially life-threatening course. Data on patient knowledge about DKA in German-speaking countries is rare. Thus, we aimed to gather data about T1DM patients’ knowledge in terms of DKA.

Methods
Together with two T1DM patients and an experienced diabetes counselor, we developed an anonymous questionnaire covering general knowledge about DKA, as well as baseline health and social characteristics. First, health care professionals rated patient’s knowledge about their management of diabetes and DKA from 0 (no idea) to 10 (best knowledge) and patients were then asked to fill out the questionnaire at the end of their outpatient clinic appointment. Filling out the questionnaire was fully voluntary.

Results
5 Swiss and 1 German endocrine outpatient clinics participated in the study. In total, 333 questionnaires were collected. Patients had a mean diabetes duration of 22 years (SD 15), and 109 (33.5%) patients used insulin pumps and the remainder basal/bolus insulin therapy. 176 patients (54%) stated that they were male and 148 (45%) female. Mean age was 47 years (SD 16). 78 patients (24%) were not familiar with the term “diabetic ketoacidosis” and 25 (7.7%) were unsure about it. The patients’ personal knowledge on DKA was rated significantly lower by themselves (mean 4.33, SD 3.11 vs 5.60, SD 2.34; P<0.0001) compared to their physicians’ assessment but correlated significantly (r=0.268, 95% CI [0.1253, 0.3992], P=0.0002). 46% of patients were not able to name any symptom and 44% could not spontaneously think of possible causes of DKA. When presented with multiple answers to choose from, thirst (74%), polyuria (66%), sleepiness (66%) and nausea/vomiting (51%) were among the most frequently picked. As causes of DKA, 61% stated “missed insulin injection” and 54% “illness”. 185 (64%) patients do not test for ketone bodies at all. About 40% of all patients felt secure in treating DKA with 206 patients (67%) wanting more information about the condition.

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Conclusion
Patient knowledge about DKA is insufficient, especially symptoms and causes are not well understood. However, most patients would like to have more information about DKA, making it a good point to start from in the attempt to reduce DKA prevalence.

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RC10.8

Long-term treatment with glucagon-like peptide-1 (GLP-1) receptor agonists: a real-life study
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RCTs and real-life studies have shown the efficacy of GLP-1 RAs on weight loss, glycemic outcomes, and prevention of cardiovascular (CV) events, but long-term data are lacking. This was a retrospective cohort study of 253 patients with a first prescription of a GLP-1 RA between 2009 and 2016 and a minimum follow-up of 5 years. The endpoints of the study were weight and glycemic outcomes. Secondary endpoints were the occurrence of renal and CV events, comparing patients with GLP-1 RA treatment durations over 5 years and under 5 years. Median follow-up was 8.15 years (5.01 to 11.74 years). Mean duration of GLP-1 treatment was 5.4 years (SD 3.2). The mean proportion of follow-up time on GLP-1 RA was 85.1% at 1 year, 76.7% at 2 years, 64.1% at 4 years, 56.9% at 6 years, 57.7% at 8 years, and 56.3% at 10 years. Younger age at baseline, higher baseline HbA1c, and being hospitalized for heart failure were associated with a shorter time to GLP-1 RA discontinuation. Switching from any other GLP-1 RA to dulaglutide or semaglutide, and greater decreases in HbA1c at 1 and 2 years were associated to longer time to treatment discontinuation. Comparing patients who had withdrawn GLP-1 RA therapy and those with ongoing GLP-1 RA at each time point, there were significant differences in mean HbA1c (7.81% vs 7.16% at 6 years, 8.08% vs 6.85% at 8 years, 8.26% vs 6.69% at 10 years respectively), and mean weight loss (-1.4 vs -5.6 kg at 6 years, -1.0 vs -6.8 kg at 8 years respectively), except for mean weight loss at 10 years. In the shorter treatment duration group (<5 years on GLP-1) there was a higher proportion of strokes/transient ischemic attacks (7.5% vs 1.3%) in the group treated for over 5 years, P = 0.014). Acute coronary syndromes were more frequent in the shorter treatment duration group, although not statistically significantly (6.5% vs 3.8% respectively, P = 0.37). No differences in arterial revascularization procedures, no differences in renal outcomes or hospitalizations for heart failure were observed.

There were no deaths for CV causes. The study showed that GLP-1 RA treatment maintains its favorable effects on HbA1c and weight over time. The reduction in atherosclerotic events, mainly driven by stroke protection, is consistent with RCT studies and therefore reinforces the long-term use of these antidiabetic medications in real life.

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RC11.2

Subacute thyroiditis (SAT) during the COVID-19 pandemic: preliminary data from the “ESE Covid Grant 2021” project
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Introduction
A possible association between the severe acute respiratory syndrome coronavirus (SARS-CoV)-2 pandemic, in terms of infection and/or vaccination, and subacute thyroiditis (SAT) has been recently reported. Although a higher SAT incidence in pandemic has been described, data are still conflicting.

Aim
To determine SAT incidence in Italy during the SARS-CoV-2 pandemic and to characterize clinical peculiarities and response to medical treatment of SAT cases, correlating them to virus exposure and/or vaccine.

Methods
We are performing a prospective, longitudinal, observational, 3-year, multi-centre study. All subjects with clinical diagnosis of SAT since November 2020 are enrolled and followed-up for 12 months. During medical history collection, SARS-CoV-2 infection (defined as a positive rhino-pharyngeal swab obtained before the SAT onset) and vaccination were recorded. In order to evaluate the SAT course, patients were evaluated at 1, 3, 6 and 12 months after onset with thyroid ultrasonography and blood examinations. This is an interim analysis considering baseline visit performed in two centres (Modena and Milan).

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Thyroidey 2

RC11.1

Impact of Covid-19 disease on thyroid function: longitudinal study
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Background
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic disease (Covid-19) affects thyroid function with different mechanisms: non-thyroidal illness syndrome (NTIS), direct infection of thyroid gland and cytokine storm. We provided the first description of painless atypical thyroiditis coexisting with NTIS in patients hospitalised for moderate-to-severe Covid-19 disease. We aimed to: 1) correlate thyroid dysfunction with Covid-19 disease severity; 2) follow the evolution of thyroid function over time.

Methods
Baseline (at hospital admittance) and longitudinal study of patients hospitalised for moderate-to-severe Covid-19 disease, without known history of thyroid dysfunction, consisting of serum thyroid function test and all inflammatory markers. Patients were stratified according to NTIS in patients with NTIS (NTIS group) and those without NTIS (non-NTIS group) to evaluate differences in thyroid function over time.

Results
We enrolled 186 patients with NTIS and 186 non-NTIS patients. In the NTIS group, in patients hospitalised for moderate-to-severe Covid-19 disease, without known history of thyroid dysfunction, serum thyroid function test and all inflammatory markers were higher (P < 0.05) compared to those with normal thyroid US. Follow-up analysis was conducted in 75/183 (41%) patients; thyroid function and inflammatory markers normalized at all time-points in nearly all cases and no increase of thyroid autoantibodies positivity was observed. The thyroiditis-areas, even if often reduced in size, were still present after 6 and 12 months in 13/15 (87%) and 6/12 (50%) patients respectively. After 9 months the thyroid uptake at 99mTc scintigraphy was still reduced in 4/6 (67%) patients, even if partially recovered (mean +28%) compared with baseline.

Conclusions
Thyroid dysfunction during moderate-to-severe Covid-19 disease is mild and transient, and thyroid hormones correlate with disease severity. Thyroiditis-areas at US occur frequently and may persist after one year, even if reduced in size; long-term consequences are unknown. The association of thyroiditis-areas with low TSH and high FT4 and IL-6 serum concentrations support the hypothesis of direct thyroid gland involvement in SARS-CoV-2 infection.
Results
A total of 51 subjects (40 females, 11 males) with SAT have been enrolled so far (age: 50.1 ± 11.6 years, BMI: 23.5 ± 3.5 kg/m²). Personal or familial thyroid disease history was reported in 14 (28%) and 25 (50%) patients, respectively. One (2%) patient had a family history of SAT. At SAT diagnosis, 36 patients were thyrotoxic (72%) and 5 hypothyroid (10%). TSH serum level was 2.3 ± 7.3 microIU/ml, with mean FT4 20.0 ± 14.0 pg/ml, and FT3 4.8 ± 2.6 pg/ml. Moreover, 30 patients (60%) had elevated erythropoiesis saturation rate (ESR), 27 (54%) elevated high-sensitivity C-reactive protein (hs-CRP), 12 (24%) high thyroglobulin (Tg) serum levels. The cohort was divided according to either SARS-CoV2 infection (9 patients – 18%) or vaccination (18 patients – 36%). Considering patients with previous infection, the thyrotoxic rate raised up to 88.9%. However, the thyrotoxicity rate (P = 0.286), ESR (P = 0.520), hs-CRP (P = 0.0585) and Tg (P = 0.178) elevations were not significantly different between patients with or without SARS-CoV2 infection. Similarly, thyrotoxicity rate (72.2 vs 64.9%, P = 0.468), ESR (P = 0.268), hs-CRP (P = 0.173) and Tg (P = 0.712) elevations were not different between patients with or without SARS-CoV2 vaccination.

Conclusion
Our preliminary data suggest that both SARS-CoV-2 infection and vaccination have no impact on the general clinical SAT presentation. Only high thyrotoxicosis rate at diagnosis, especially in patients with previous SARS-CoV-2 infection has emerged. SAT incidence during pandemic will be evaluated at the end of the study.

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RC1.1.3
Is the pre-conceptional TSH optimization useful in women submitted to assisted reproduction technology?
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Background
Thyroid function (TSH) levels and thyroid autoimmunity are involved in the immunomodulation of early pregnancy stages and can affect assisted reproductive technology (ART).

Aims
1) to evaluate if pre-conceptional TSH is associated with an increased risk of miscarriage, 2) to identify a TSH cut-off significantly associated with risk of miscarriage, 3) to assess the impact of TSH levels on primary and surrogate outcomes.

Methods
We retrospectively studied 1484 infertile women (mean±SD age: 36.7 ± 4.1 years, mean ± SD BMI 22.7 ± 4) submitted to IVF in a single center from 2004 and 2014. 60.8% and 39.2% of cycles were performed in women affected with primary and secondary infertility, respectively. Primary outcomes were biochemical pregnancy, clinical pregnancy, miscarriage and delivery. Surrogate outcomes were the number of oocytes, the number of embryos and the transfer of embryos.

Results
In 86% of cycles an embryo transfer was performed. 369/1274 (29%) of patients had a biochemical pregnancy and 146 of them experienced a pregnancy loss. Moreover, among the 146 women with pregnancy loss, 52 (36%) were clinically pregnant and had a miscarriage in the first trimester, while in 94 patients (64%) a biochemical pregnancy and 146 of them experienced a pregnancy loss. Moreover, patients affected with primary and secondary infertility, respectively. Primary outcomes were biochemical pregnancy, clinical pregnancy, miscarriage and delivery. Surrogate outcomes were the number of oocytes, the number of embryos and the transfer of embryos.

RC1.1.4
The “real-life” thyroid function tests results during pregnancy in the longitudinal observation
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The reference ranges of thyroid function tests during pregnancy are still being debated, even in ethnically homogenous populations. The defining of the normal range is of importance, as it influences therapeutic decisions, particularly the use (or over-use) of levothyroxine in this vulnerable population. The study was aimed at the longitudinal assessment of thyroid function tests results in marginally iodine sufficient Polish population of pregnant women. The study was performed between 2007-2017 as a part of the Polish National Programme for Elimination of Iodine Deficiency. The study included 1405 pregnant women (222 – 1st trimester, 561 – 2nd trimester, 622 – 3rd trimester of pregnancy) of median age 29 years (IQR: 6 years). In each woman serum TSH, FT4, FT4 and aTPO, as well as urinary iodine concentration (UIC) in a urine spot sample, were measured.

Results
Median TSH was, respectively: 1st trimester – 1.22 mIU/l (IQR – 1.42 mIU/l, 2.5–97.5 percentile: 0.04–4.02 mIU/l); 2nd trimester – 1.63 mIU/l (IQR – 1.28 mIU/l, 2.5–97.5 percentile: 0.19–4.42 mIU/l), 3rd trimester – 1.61 mIU/l (IQR – 1.13 mIU/l, 2.5–97.5 percentile: 0.3–4.28 mIU/l). There was no significant yearly difference in TSH concentrations. Median FT4 was, respectively: 1st trimester 15.19 pmol/l (IQR: 2.37 pmol/l, 2.5–97.5 percentile: 11.65–21.68 pmol/l), 2nd trimester – 12.60 pmol/l (IQR: 2.61 pmol/l, 2.5–97.5 percentile: 9.29–17.32 pmol/l), 3rd trimester – 11.95 pmol/l (IQR –2.97 pmol/l; 2.5–97.5 percentile: 8.56–17.26 pmol/l). ATPO positivity was found in 18%, 15% and 9% of pregnant women in the 1st, 2nd and 3rd trimester, respectively. Median TSH in aTPO-negative women was, respectively: 1st trimester – 1.11 mIU/l (2.5–97.5 percentile: 0.03–3.57 mIU/l), 2nd trimester 1.57 mIU/l (2.5–97.5 percentile: 0.18–4.18 mIU/l), 3rd trimester 1.60 mIU/l (2.5–97.5 percentile: 0.35–4.23). ATPO negative and positive women in the 1st and 2nd trimester of pregnancy differed significantly in mean TSH concentrations (1st trimester: 1.31 vs 2.24 mIU/l, P = 0.002; 2nd trimester: 1.73 vs 2.25 mIU/l, P = 0.001; 3rd trimester 1.78 vs 2.02 mIU/l, P = 0.230). The significant difference in FT4 according to aTPO status was found only for the 3rd trimester (P = 0.020). No difference was found between those groups in FT3 and UIC concentrations. The stepwise regression model failed to find significant relation between TSH and pregnancy week, aTPO positivity, and UIC.

Conclusions
Our results support the view that the upper TSH range in pregnancy is only slightly lower than in a general population. Therefore, more caution is needed while diagnosing hypothyroidism and deciding on treatment with levothyroxine during gestation.

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RC1.1.5
Which factors can influence the occurrence of two nondiagnostic results in fine-needle aspiration cytology of the same thyroid nodule? 
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Introduction
Fine-needle aspiration cytology (FNAC) of thyroid nodules can be associated with non-diagnostic (ND) results, despite the usage of ultrasound (US) guidance. It is recommended to repeat the FNAC because of the possible risk of malignancy in these nodules.

Aim
To evaluate the influence of demographic, clinical and echographic characteristics in the recurrence of ND FNAC in a thyroid nodule.

Methods
Retrospective review of ND thyroid FNAC performed between 2017-2020. Demographic and clinical data (age, gender, cervical radiography, presence of Hashimoto’s thyroiditis and TSH value) and US characteristics (nodules’ size, echogenicity, composition and microcalcifications) were collected at the moment of the first ND FNAC.

Results
Of 230 nodules with a first ND FNAC (patients’ mean age 60.2 ± 14.1 years, 83% women), 195 (84.8%) were submitted to another FNAC, 9 (3.9%) were submitted
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RC11.6

Association of thyroid hormones with clinical status and cardiovascular outcomes of HFpEF patients

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Introduction

Heart failure with preserved ejection fraction (HFpEF) is a clinical syndrome with high mortality, for which there are few disease modifying therapeutics. Thyroid axis dysfunction is common in heart failure (HF) and may contribute to the pathogenesis of HFpEF. However, the association of thyroid hormones (TH) with the clinical status of HFpEF patients and their prognostic impact in this syndrome are not clear.

Methods

We evaluated 93 participants with stable HFpEF followed in our centre. We categorized participants according to TH tertiles. A cross-sectional analysis was performed to analyse associations of TH with clinical parameters, and B-type natriuretic peptide (BNP) and high-sensitivity troponin I (hs-Tnl) levels. Ordered logistic and linear regression models were used. Associations between TH and a composite endpoint of diuretic intensification, HF hospitalization or all-cause mortality. These results lead us to the hypothesis that FT4 to FT3 conversion might be impaired in patients with HFpEF. This impairment could be an important player in the progression of the disease.

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RC11.7

Altered expression profiles of miR-22-3p and miR-142-3p display Hashimoto disease and are associated with thyroid antibodies

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Background

Hashimoto’s thyroiditis (HT), the most prevalent autoimmune disorder of the thyroid (ATTD) is characterized by the presence of circulating autoantibodies, induced by a not fully understood dysregulation of the immune system. MicroRNAs (miRNAs) are small noncoding RNAs, which can play a pivotal role in immune functions and the development of autoimmunity. The aim of the present investigation was to evaluate whether a panel of nine selected miRNAs differs in serum expressions of patients with HT and to analyse possible relations to thyroid antibody levels.

Methods

Participants of the BioPersMed cohort (n = 1022), an ongoing single-centre, prospective, observational study to evaluate novel biomarkers for the assessment of cardiovascular and common metabolic diseases, were screened for previously diagnosed HT patients (n = 27) as well as age and sex matched participants suitable as healthy controls (n = 22). Thyroid function and common autoantibodies were evaluated by serum levels of thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), thyroid peroxidase autoantibody (TPOAb) as well as thyroglobulin autoantibodies (TgAb), determined by luminexence immunoassays (Siemens, Erlangen, Germany). MiRNA profiles were analysed in the selected samples using quantitative reverse transcription polymerase chain reaction (qRT-PCR).

Results

Systemic expressions of miR-21-5p, miR-22-3p, miR-22-5p, miR-142-3p, miR-146a-5p and miR-451 were significantly upregulated in patients with HT (P < 0.01, respectively) and indicate HT in receiver-operating characteristic (ROC) analysis with an area under the curve of at least 0.76 (95% confidence interval 0.61-0.91) for miR-22-5p. Subgroup analyses within HT patients showed significantly higher miRNA expression for miR-22-5p and miR-142-3p in HT patients with higher thyroid antibody levels (TgAb and/or TPOAb > 60 U/ml, n = 13) as compared to HT patients with lower thyroid antibody levels (TgAb and/or TPOAb < 60 U/ml, n = 11).

Conclusion

Upregulated systemic expression levels of miR-22-3p and miR-142-3p indicate HT and were related with higher levels of thyroid antibodies suggesting a contribution to the pathogenesis of HT.

References


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Reproductive and Developmental Endocrinology

RC12.1

RS 2247911 polymorphism of GPRC6A gene and serum under carboxylated-osteocalcin are associated with testis function

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Purpose

Undercarboxylated-OCN (ucOCN), acting on the receptor GPRC6A, was shown to regulate testosterone (T) production in Leydig cells in rodents, in parallel with the hypothalamus/pituitary/gonadal axis mediated by luteinizing hormone (LH). Hence, reduced serum ucOCN and/or inactivating gene variants of GPRC6A, are supposed to affect testes function in humans. The aim of this study is to evaluate the association among serum ucOCN, rs2247911 GPRC6A gene polymorphism and the endocrine/replicative pattern in a cohort of Syrian infertile males, possibly confirming the role of ucOCN/GPRC6A axis on testes function.

Methods

A total of 172 males, including 62 oligozoospermic, 51 azoospermic patients and 59 age-matched normozoospermic controls, were prospectively recruited at the Orient Hospital for Assisted Reproduction Treatment (Syria) and evaluated for the hormonal pattern, serum ucOCN, glycemic and lipid profile. Screening for rs2247911 GPRC6A gene polymorphism was also performed.

Results

Serum ucOCN correlated positively with total sperm count, sperm morphology and motility, total T, E2 and HDL-cholesterol, and negatively with LH, FSH, and LDL-cholesterol. Patients bearing the GG genotype of rs2247911 polymorphism had higher sperm count ($P = 0.008$), progressive motility ($P = 0.05$), normal morphology ($P = 0.009$), T ($P = 0.003$), HDL-cholesterol ($P = 0.008$) and lower triglyceride levels ($P < 0.001$) compared to patients bearing AA and AG genotypes. Aside of LH levels, patients with rs2247911 polymorphism ($P = 0.02$) and to a minor extent, serum ucOCN, were major predictors of serum T at linear stepwise regression analysis.

Conclusions

The novel ucOCN/GPRC6A axis was confirmed to participate in the regulation of the endocrine and reproductive function of the tests through the production of T.

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RC12.2

Proteomic changes in response to electrical stimulations in skeletal muscle of women with PCOS

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Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder affecting women of reproductive age. The main features of PCOS are hyperandrogenism and reproductive and metabolic dysfunctions. We have previously shown that muscle collagen production is increased by either electrical stimulations or exercise due to partially similar signaling pathways in the muscle to induce glucose uptake in the acute response. Long-term electrical stimulations decrease circulating testosterone, HOMA-IR, and IHbA1c in overweight/obese women with PCOS, but the mechanism is largely unknown. Here, we used transcriptomic and proteomic analyses to provide new mechanistic explanations to the improved glucose homeostasis in response to 30 min of electrical stimulations, 3 times/week for 5 weeks. Skeletal muscle biopsies from 10 women with PCOS were subjected to global methylation, transcriptomics and proteomics analysis at baseline and after 5 weeks of treatment. Changes in protein expression between baseline and after treatment were based on Student’s t-test ($P < 0.05$) and a fold change $> 50%$. Changes in skeletal muscle DNA methylation and gene expression in response to electrical stimulation were based on linear regression analysis ($P < 0.01$) and a fold change $> 20%$. Two transcripts exhibited increased expression in skeletal muscle after 5 weeks of treatment. Four types of collagens were upregulated, and together with VCAM and LUM, these genes were confirmed by gene ontology analysis to play a role in extracellular matrix organization and skeletal system development. Next, we analyzed if the response to electrical stimulation involved DNA methylation changes in skeletal muscle. The absolute changes in methylation were small and ranged from $-1.29%$ to $+0.72%$ points. The vast majority of the 43 significant CpG sites (75%) displayed decreased DNA methylation in response to electrical stimulation. Since relatively few genes and methylation sites were regulated in response to repeated electrical stimulations, we investigated if the long-term effects were regulated at the protein level. More than 300 proteins changed expression after treatment. 97% of these were upregulated and enriched pathways involved exocytosis, extracellular matrix organization, integrin-mediated signalling, transforming growth factor production, and protein metabolic processes. Collagen 1A1 and 1A2 were upregulated both at the gene and protein expression level after electrical stimulation. One can speculate that up-regulation of integrins, collagens, and transforming growth factor-beta-1 likely lead to ECM remodeling, which can provide protective adaptation to repeated stimulation, and improved muscle strength and function. In conclusion, changes at the protein level mediate the response to long-term electrically stimulated muscle contractions.

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RC12.3

Binding affinity affecting SHBG SNPs do not majorly affect calculated estimates of free testosterone

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Introduction

According to the free hormone transport hypothesis, only free testosterone (FT) is considered biologically active. Due to low circulating levels and technical challenges of direct FT measurements, calculators have been developed to estimate FT from serum total T, sex hormone-binding globulin (SHBG) and albumin levels. However, genetic polymorphisms altering SHBG’s binding affinity or capacity might result in calculation imprecisions with consequent incorrect diagnosis in these individuals.

Objective

Investigating the prevalence of SHBG single-nucleotide polymorphisms (SNPs) in healthy men and evaluating differences in SHBG, total T, calculated FT (cFT) and measured FT (mFT) levels in SHBG SNP-carriers.

Methods

Population-based sibling-pair study, comprising 999 healthy men aged 24-46 years in whom genotyping was performed (LGC Genomics) for SNPs suggested to affect binding affinity and/or concentration of SHBG (rs6258, rs6259, rs146779355, rs145273466, rs366859266, rs143269613, rs373769356, rs143521188). SHBG and total T concentrations were measured by immunoassay and LC-MS/MS, respectively. FT calculations (cFT, using the Vermeulen-formula) and free T-Ratio (FT/total T) were calculated. In a subset of participants (145, 10 and 40 individuals for WT, WT/rs6258 and WT/rs6259, respectively) FT was measured directly using LC-MS/MS after equilibrium dialysis (mFT). The difference between cFT and mFT was calculated and expressed as percentage of mFT ($\%$). Parameters were compared by t-test or Mann-Whitney test depending on normality; method-comparison was performed using Passing-Bablok regression. Results

11/971 (1%) and 9/971 participants were hetero- and homozygote for rs6258; 135/681 (20%) and 9/681 (1%) were hetero- and homozygote for rs6259, respectively. No other SNPs were detected. Versus wild-type, heterozygote rs6258 carriers had lower SHBG (26.5 nmol/l vs 38.5 nmol/l) and total T levels (468.8 ng/dl vs 583.9 ng/dl) but higher free T-Ratio (2.3% vs 2.0% for cFT; 2.2% vs 1.7% for mFT). Heterozygote rs6259 carriers had higher SHBG levels (42.8 nmol/l vs 38.5 nmol/l) and lower free T-Ratio (1.9% vs 2.0% for cFT) than non-carriers. Comparing cFT and mFT showed a significant difference in heterozygote rs6258 carriers (delta% 5.1% vs 15.4% in wild-type). No other differences nor differences in homogyzote rs6259 carriers vs wild-type were observed.

Conclusion

Genetic polymorphisms suggested to affect SHBG concentration or steroid-hormone binding affinity are relatively rare in this population-based cohort of healthy men. Although carriers did present with different SHBG levels and free T-ratio (FT/total T) were calculated. In a subset of participants (145, 10 and 40 individuals for WT, WT/rs6258 and WT/rs6259, respectively) FT was measured directly using LC-MS/MS after equilibrium dialysis (mFT). The difference between cFT and mFT was calculated and expressed as percentage of mFT ($\%$). Parameters were compared by t-test or Mann-Whitney test depending on normality; method-comparison was performed using Passing-Bablok regression.
Introduction
Obesity is a worldwide pandemic, and in men can often be associated with hypogonadal hypogonadism (HH), a finding consistent with a clear link between sex steroids and reproduction. In this study, we aimed to characterize the phenotypic spectrum of male obesity, focusing on the metabolic and reproductive effect of weight loss after bariatric surgery, as well as to explore the role of central inflammation.

Methods
We conducted an observational study on 32 morbidly obese men (BMI ≥ 35 kg/m²) scheduled to undergo Roux-en-Y Gastric Bypass (RYGB) and prospectively followed for 12 months thereafter. Nine lean men with strictly normal metabolic and reproductive status were also recruited. Obese men were categorized as either HH (ObHH, n = 15; testosterone < 10.4 nmol/l) or non-HH (ObnHH, n = 17; testosterone ≥ 10.4 nmol/l). In addition to standard metabolic and reproductive profiles, a deep phenotyping consisted of Dual X-ray absorptiometry, metabolomics and blood transcriptomics. We also performed brain MRI – Diffuse Tensor Imaging (DTI) in a subset of patients before and after RYGB.

Results
Despite comparable BMI, ObHH exhibited more severe insulin resistance (HOMA-IR, P = 0.01), a trend for expanded visceral fat (P = 0.08) and higher systemic inflammation (lower von Willebrand factor, higher CRP, P = 0.09) and hypothalamic inflammation (lower fractional anisotropy and higher diffusivity at DTI, P < 0.05) as compared to ObnHH. Blood transcriptomics revealed a distinct expression profile in ObHH related to overexpression of genes implicated in inflammation and mitochondrial function, especially oxidative phosphorylation. In addition to lower testosterone levels, higher FGF21 and lower morning cortisol in the cohort of obese men strongly correlated with the transcriptomic changes. Following RYGB, all men lost substantial weight (21-39% at month 12) independent of the baseline gonadal status. Longitudinal assessment in nine men revealed a rise in plasma FGF21 at day 28 post RYGB (P = 0.04), concomitant to the early decrease in HOMA-IR. FGF21 subsequently returned to baseline levels and decreased by month 12 (P = 0.02). A significant reduction in plasma isoleucine levels (day 2, P = 0.01) preceded the FGF21 peak. The extent of the FGF21 peak at day 28 significantly correlated with the degree of HH reversal at month 12 (P = 0.04).

Conclusions
HH is a marker of metabolic syndrome in obese men, accompanied by MRI signs of altered hypothalamic structure. Serum levels of cortisol and FGF21 are additional predictors of metabolic defects. Post RYGB, FGF21 showed a unique bimodal change, tightly associated with the metabolic improvement and the recovery of obesity-induced HH.

Aims
To clarify the association of HA with the development of hypertension and CVDs in women.

Study population and methods
A general population-based birth cohort (n = 5889 women) followed at ages 1, 14, 31 and 46. We investigated the association of serum levels of testosterone (T, measured using LC-MS/MS) and free androgen index (FAI) at age 31 with blood pressure (BP), hypertension (HT), defined as BP ≥ 140/90 mmHg and/or use of antihypertensive medication) at age 31 and with CVD risk [angina pectoris (AP) and/or acute myocardial infarction (AMI), and transitory cerebral ischemia (TIA) and/or stroke] with 22-year follow-up. After excluding women being pregnant (n = 212) and those with lacking data, the final study population included 2820 women at age 31.

Results
After adjusting for body mass index (BMI), there was an independent positive association of T and FAI with systolic BP (T: β = 1.93, 95% CI: 0.93–2.93, FAI: β = 1.68, 95% CI: 0.67–2.70) and diastolic BP (T: β = 1.80, 95% CI: 0.93–2.67, FAI: β = 1.96, 95% CI: 1.10–2.82) at age 31. The prevalence of HT was significantly higher among women with elevated T (cut-off 2.3 nmol/l defined in this population) compared to normoandrogenic women (27.1% vs 11.9%, P = 0.002). Conversely, women with HT at age 31 had significantly higher T levels (1.12 [0.82; 1.47] vs 0.97 [0.73; 1.25] nmol/l, P < 0.001) and FAI (2.92 [1.95; 4.72] vs 2.16 [1.50; 3.09], P < 0.001) compared to normoandrogenic women after adjusting for BMI. In logistic regression analysis, T and FAI associated positively and independently of BMI with HT (OR: T: 2.67, FAI: 2.60, 95% CI: 1.10–2.82) at age 31. The prevalence of HT seemed to be mainly driven by BMI. A longer follow-up of this cohort is needed to clarify the long-lasting metabolic risks linked to HA.

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Background
Many questions concerning Turner Syndrome (TS) remain unresolved, such as the long-term complications and, therefore, the optimal care setting for adults. Many controversies regard tumors. Very few data are available on thyroid carcinoma and no specific screening protocol of monitoring is advised in the current official guidelines. This long-term cohort study was primarily aimed at estimating the incidence and time to comorbid conditions along the life course, including thyroid carcinoma and tumors in general.

Methods
The study cohort consisted of 160 TS women, the vast majority recruited during childhood (mean age = 9.4 years, median = 9 years, IQR 2-16) and followed up for a median of 27 years (IQR 12-42) at the S. Orosa University Hospital of Bologna using the same multidisciplinary monitoring protocol (including thyroid ultrasound every one to two years). The last follow-up was carried out for all patients in December 2019.

Results
Autoimmune diseases (such as Hashimoto’s thyroiditis, celiac disease and autoimmune polyendocrine syndrome) were the comorbidities with the highest incidence (61.2%, followed by osteoporosis and hypertension (23.8% for both), then by type 2 diabetes (16.2%) and by tumors (15.1%). Median age of onset ranged from 22yrs for autoimmune diseases to 5yrs for type 2 diabetes. Malignant tumors (including thyroid carcinoma, renal cell cancer, skin cancer, breast cancer, ovarian cancer and central nervous system tumors) were the most prominent form of neoplasms, with a cumulative incidence of 11.9% and an incidence rate of 0.44 per 100 person-year. Thyroid carcinoma (histologically all papillary -PTC- in our cohort) was the most common form of cancer with a cumulative incidence of 5% and an incidence rate of 0.56 per 100 person-year
Pubertal induction in girls with hypogonadism: insight into estrogen replacement therapy outcomes and optimization of progesterone introduction

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Background Pubertal induction in girls with hypogonadism through estrogen replacement therapy (ERT) aims at mimicking physiological puberty. To date, the best induction regimen is still to be established.

Aims By setting up a multicentre clinical registry, we analysed longitudinal data on pubertal induction in girls with hypogonadotropic hypogonadism or premature ovarian insufficiency (congenital, acquired, isolated or associated with multiple pituitary hormone deficiency, either associated with Turner Syndrome or secondary to late effects of cancer treatment) in order to insight into aualogical and uterine outcomes in the light of different underlying diagnosis and regimens used.

Methods Out of 106 hypogonadal girls (chronological age > 10.9 years, Tanner stage ≤ 2) who received ERT for pubertal induction included in the register, we considered 95 girls (median age 13.5 years) treated with transdermal (TD) 17β-estradiol for at least one year (median 3.3 years). Induction was started at a median dose of 0.14 mg/kg/day TD 17β-estradiol, with a six-monthly increase. Aualogical, biochemical (estradiol levels) and radiological (pelvic US) data were collected at baseline and during follow-up. In 61/95 girls, progesterone was introduced after a median of 2.2 years. Induction was considered completed for 49/95 patients who were started on combined oral contraceptive (COC) or progesterone plus at least 50 mg/day or 1 mg/kg/day of TD 17β-estradiol.

Results At the end of induction, 90.0% patients had achieved Tanner stage B4 and 41.0% B5, the latter being associated with 17β-estradiol dosage at progesterone introduction (P = 0.034). Uterine longitudinal diameter (ULD) showed a gradual increase during ERT and a significant correlation with 17β-estradiol dosage (P < 0.0001) at any point of induction. Nonetheless, final ULD was > 65 mm in only 17/45 (38%). At multiple regression analysis, a history of pelvic irradiation represented the major determinant of reduced final ULD (P = 0.034). After correction for uterine irradiation and other clinical confounders, ULD was associated with 17β-estradiol dosage at progesterone introduction (P = 0.043). Final ULD was not significantly different from the one asayed after COC introduction.

Conclusions Reaching an appropriate 17β-estradiol dose at the end of the induction seems to play a crucial role in uterine development and Tanner stage 5 achievement. Indeed, progesterone should be started only in the presence of a concomitant adequate ERT dose and an appropriate uterus and breast development, given the evidence that progesterone may hamper the subsequent changes in uterus volume or the achievement of the last Tanner stage. At present, we aim to confirm present results on a larger scale.

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Adrenal and Cardiovascular Endocrinology 2

HRA axis modulation by a potent inhibitor indicates 11β-hydroxy-steroid dehydrogenase type 1 (HSD-1) is a main source of cortisol that can bind intracellular receptors

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Background HSD-1 converts cortisone to cortisol in tissues in which cortisol excess is associated with morbidity including liver, adipose, bone, and brain. SPI-62 is a potent HSD-1 inhibitor in clinical development for treatment of Cushing’s syndrome and autonomous cortisol secretion, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with maximal liver and brain HSD-1 inhibition. Methods We analyzed multiple dose trial1 data to characterize the contribution of HSD-1 to cortisol that can bind to intracellular receptors and HPA/HPG axis modulation by SPI-62. Data from subjects who received SPI-62 doses that achieved maximal liver HSD-1 inhibition were combined for analysis. ANCOVA models with treatment effect and baseline covariate were used; statistics are least squares mean [standard error]. Results Compared to placebo (n = 10), single SPI-62 doses (n = 40) were associated with 24-hour urinary tetrahydrocortisol (2.27±0.134 v 4.44±0.269 mmol) and alloetiohydrocortisol (2.98±0.146 v 4.80±0.291 mmol) decreases, and tetrahydrocortisol (32.7±1.149 v 9.19±3.308 mmol) increase. Serum cortisol was decreased at 2-hours (152±21.64 v 226±24.00 mmol) but not 4- or 12-hours post-dose. ACTH was increased at 4- and 12-hours (45.6±1.64 v 32.1±3.29; 58.5±1.67 v 26.3±3.33 pg/ml) but not 2-hours post-dose. After 14 daily doses, SPI-62 was

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associated with 24-hour urinary tetrahydrocortisol (2.05[0.154] v 4.36[0.321] mmol), alottetrahydrocortisol (2.75[0.181] v 4.13[0.377] mmol), and tetrahydrocortisone (42.73[1.968] v 9.51[0.410] mmol) changes. ACTH was increased at pre-dose and 2-, 4-, and 12-hours post-dose (45.6[1.711] v 27.0[3.611]; 45.3[1.79] v 35.2[3.72]; 34.4[3.71] v 18.8[5.37]; 47.3[3.13] v 30.4[4.54] pmol/ml). No differences on urinary cortisol or cortisone, serum cortisol, or CRH were observed after single or multiple doses. After multiple doses, SPI-62 was associated with increased DHEA-S (342.2[9.94] v 155.0[20.52] mg/dl) and, in females, testosterone (2.10[11] v 1.40[25]) nm. No differences on aldosterone, estradiol, SHBG, LH, progesterone, or SHBG were observed.

**Discussion**

SPI-62 resulted in ~40–50% decreases of urinary cortisol metabolites which indicate similar decrease of hepatocellular cortisol. Following a corresponding decrease, circulating cortisol homeostasis was restored rapidly by ACTH increase. Urinary cortisol was unaffected. SPI-62 is associated with moderate androgen increases that, to date, appear not associated with adverse effects. As HSD-1 contributes much of the intracellular cortisol that can access intracellular receptors, we hypothesize that HSD-1 inhibitors are potential treatments for conditions of cortisol excess such as Cushing’s syndrome and autonomous cortisol secretion.

**References**


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**RC13.2**

Age- and gender-specific cut-off levels may improve DHEAS as a marker for suppressed HPA-axis

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**Background**

Low levels of DHEAS, such as <1.04 μmol/l, have been used as a criterion for autonomous cortisol secretion (ACS) in patients with adrenal incidentalomas. Age- and gender-specific cut-off levels could theoretically improve DHEAS as a marker of HPA-axis suppression and as a criterion for ACS.

**Objective**

We aimed to find cut-off levels of DHEAS that are best associated with HPA-axis suppression and determine whether they are correlated with clinical outcomes.

**Methods**

We studied 989 patients with adrenal incidentalomas, investigated between 2005 and 2015 at two hospitals in southern Sweden and followed up for 14 years. Patients were divided into 10 groups according to age, separated as age <50, 50–<60, 60–<70, 70–<80 or ≥80 years, and gender.

**Results**

In patients with ACTH <2.0 μmol/l, DHEAS was <1.04 μmol/l in 0, 14, 10, 22, and 33% of males and in 40, 26, 46, 30, and 100% of females in the described age groups. Therefore, the sensitivity for HPA axis suppression may be low in males and females <60 years. ACTH was not related to age in males or females. Therefore, we studied DHEAS levels below the 25th percentile as a marker of HPA-axis suppression. The levels for the different age groups were <2.50, <2.10, <1.20, <0.93, and <0.81 μmol/l in males and <1.10, <1.00, <0.81, and <0.81 μmol/l in females and were termed “low DHEAS”. The odds ratio for cortisol/DST ≥50 μmol/l was higher for low DHEAS than DHEAS <1.04 μmol/l in males, 1.92 (1.7-3.14) vs 1.59 (0.92-2.76), but was similar in females, 1.73 (1.19-2.51) vs 1.67 (1.17-2.38), adjusted for age. Low DHEAS was associated with pre-existing cardiovascular disease, odds ratio 1.63 (1.14-2.33) and mortality, relative risk 1.57 (1.14-2.18), both adjusted for gender, age, and smoking.

**Conclusion**

Age-specific DHEAS is a more appropriate marker of HPA-axis suppression in men but seems not to perform better in females. Furthermore, the proposed age- and gender-specific cut-off levels were associated with pre-existing cardiovascular disease and increased mortality.

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**RC13.3**

Steroidomic approach for the characterization of patients with non-alcoholic fatty liver disease

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**Introduction**

The onset and progression of liver damage in non-alcoholic fatty liver disease (NAFLD) is tightly associated with metabolic derangements. Steroids may affect lipid metabolism but their alterations in the setting of NAFLD remain to be fully explored.

**Patients and Methods**

We analyzed data from 121 patients with biopsy-proven NAFLD and 108 controls (CT). A panel of 26 steroids (including glucocorticoids, mineralocorticoids, androgens, and progestogens as well as representative glucuro- and sulphonylated metabolites) were measured on plasma samples by liquid chromatography coupled to mass spectrometry (LC-MS/MS). Severe hepatic fibrosis was defined by F ≥ 3.

**Results**

Compared to CT, NAFLD patients were older (median age 51 vs 43, P < 0.001) and were characterized by a higher rate of MS (47% vs 2%, P < 0.001). More than a half of steroids were deregulated in patients compared to CT. At liver histology, the prevalence of absent/mild, moderate, and severe fibrosis was 50.4%, 10.8% and 38.8%, respectively. Circulating levels of 16 compounds showed a significant stepwise decrease according to the degree of hepatic fibrosis. At univariate analysis, testosterone, and its derivatives, androgen metabolites, etiocholanolone metabolites and glucocorticosteroids were differentially expressed in patients with severe fibrosis compared to those with absent/mild fibrosis. After multivariable logistic regression analysis adjusted for age, gender and type 2 diabetes, epitestosterone sulphate, 5α-androstane-3α,17β-diol-3-glucuronide and androsterone sulphate levels were significantly associated with F ≥ 3. The diagnostic accuracy of the model for the identification of F ≥ 3 was 0.91 with a sensitivity and specificity of 87% and 85%, respectively, and with a positive and negative predictive value of 78% and 91%, respectively.

**Conclusions**

In NAFLD patients, alterations in androgens and their glucuro- and sulphonylated metabolites levels could be expression of compromised 1) liver endocrinogenesis or 2) liver steroid hormone regulation and are strongly associated with severe fibrosis. This research has been supported by the Italian MIUR under the programme “Dipartimenti di Eccellenza 2018-2022”, project code D15D18000410001.

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**RC13.4**

Analysis of the body composition and glucose metabolism in relation to bcl-xl glucocorticoid receptor polymorphism in women with adenral incidentalomas

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Single nucleotide polymorphisms in the glucocorticoid receptor (GR) gene influence tissue sensitivity of GR. Several studies have shown different effects of Bcl-X1 GR polymorphism on body composition and metabolic parameters. The objective of this study was to explore the effect of Bcl-X1 GR polymorphism on the body composition and glucose metabolism. Biochemical tests and hormonal evaluation were performed in 106 consecutive women with adenral incidentalomas (Alx). Non-diabetic patients underwent an oral glucose tolerance test with 75 g glucose. Body composition was measured with dual-energy X-ray absorptiometry. DNA was obtained from peripheral blood leucocytes. The polymorphism was detected using PCR, RFLP and DNA sequencing. We observed no differences in mean age (57 ± 9 vs 56.5 ± 11.8, P = 0.823), percent of postmenopausal women (76% vs 7%, P = 0.550), and prevalence of metabolic syndrome (31.9% vs 21.3%, P = 0.158) between carriers of the C allele of Bcl-X1 polymorphism and non-carriers. Bcl-X1 carriers have lower prevalence of impaired glucose tolerance (2.6% vs 17.5%, P = 0.031), type 2 diabetes mellitus (T2DM) (9.1% vs 26%, P = 0.034), and reduced glucose area under the curve, the mean difference of 2.62 (95% CI, 1.11-4.14), P = 0.001. Bcl-X1 carriers have a tendency towards lower lean body mass (41.7 ± 6.9 vs 44.1 ± 5.7, P = 0.08) and a significantly higher percentage of legs fat (43.36 ± 5.75 vs 39.84 ± 7.6, P = 0.020). Bcl-X1 polymorphism was significantly associated with sum of legs fat mass (FM) percentage (β = 0.327, P = 0.048). Also, subjects with greater legs/trunk FM ratio had higher odds to be Bcl-X1 carriers, OR 1.046 (95% CI, 0.046-23.565, P = 0.045). Logistic regression analysis showed that presence of T2DM was significantly negatively correlated with Bcl-X1 polymorphism after adjusting for
possible confounding factors such as age, truncal FM, appendicular lean mass index, and legs fat sum (OR = 0.158, 95% CI 0.031-0.806, P = 0.027). BcI carriers predispose to increased legs fat mass and greater legs/trunk FM ratio indicating reduced sensitivity to GC, which could explain why some women with AIs preserve more gluteo-femoral subcutaneous adipose tissue with beneficial effects on glucose metabolism.

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RC13.5
Skeletal muscle mass in patients with adrenal incidentaloma
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Background and aim
The relationship between sarcopenia and overt cortisol excess as in Cushing’s syndrome is well-known. However, only a few studies investigated the relationship between autonomous cortisol secretion (ACS) in adrenal incidentalomas and skeletal muscle mass. The aims of our study were to analyze the skeletal muscle mass in patients with adrenal incidentalomas and to investigate the correlations with hormonal data.

Methods
We enrolled 200 adult patients (>18 years) without clinical signs of Cushing syndrome, bearing monolateral and bilateral benign adrenal incidentaloma detected at CT scan. We classified the adrenal tumors as non-secreting (NS) or ACS according to cortisol levels after 1-mg dexamethasone suppression test (DST) < or > 50 nmol/l, respectively. Skeletal muscle mass was evaluated by skeletal muscle index (SMI) through a threshold segmentation (-19HU – 150HU) of the Skeletal Muscle Area on an L3 slice of the basal acquisition, subsequently divided by the height squared. Subjects underwent measurement of an 11-steroid profile in serum by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).

Results
SMI was lower in ACS than NS subjects (40.6 ± 1.2 vs 44.2 ± 1.2; P = 0.007). Accordingly, the prevalence of sarcopenia was higher in ACS than NS patients (59.4% vs 39.6%; P = 0.012). Similar results were confirmed after analyzing the data separately by sex. Overall, we identified correlations between SMI and age (r = -0.34; P < 0.001), body mass index (BMI) (r = 0.39; P < 0.001), basal cortisol (r = -0.155; P = 0.041) and post-DST cortisol (r = -0.180; P = 0.018). When analyzed separately by sex, similar correlations were confirmed in males, whereas only the correlations between SMI and basal cortisol, age, and BMI were observed in post-menopausal women. Additionally, in post-menopausal women, SMI was associated positively with DHEAs levels (r = 0.318; P = 0.004) and negatively with corticosterone (r = -0.259; P = 0.007). Multivariable analysis by generalized linear model (GLM) showed a positive correlation between SMI and BMI (B = 0.009; 95% CI 0.005 – 0.013; P < 0.001), independently of age (B = 0.205) and post-DST cortisol (B = 0.078) in males. In post-menopausal females, GLM highlighted an independent correlation between SMI and DHEAs levels (B = 0.036; 95% CI 0.005-0.068; P = 0.024), with an independent contribution of BMI (B = 0.004; 95% CI 0.002-0.007; P = 0.001) and age (B = -0.002; 95% CI -0.004-0.000; P = 0.017).

Conclusions
ACS is associated with impaired skeletal muscle mass, despite patients may not report symptoms of sarcopenia. A differential hormonal contribution to impaired skeletal muscle mass has been identified according to sex.

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RC13.6
Mild autonomous cortisol secretion in patients with adrenal incidentalomas and raised cardiovascular risk
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Background
Adrenal incidentalomas are common and require investigation to exclude malignancy and evidence of hormone overproduction. Clinical guidelines recommend overnight dexamethasone suppression tests (ONDST) to assess for cortisol hypersecretion with cortisol levels of 50-138 nmol/l termed “mild autonomous cortisol secretion” (MACS). MACS may be associated with both cardiovascular and metabolic morbidity. We assessed cardiovascular risk in patients with MACS using QRISK3. This is a validated algorithm used in the UK to predict cardiovascular risk, calculating a predicted percentage risk of myocardial infarction (MI) or stroke over the next 10 years.

Methods
Data were collected retrospectively on patients over a two-year period, who had an adrenal incidentaloma with a cortisol between 50-138 nmol/l following ONDST. Presence of cardiovascular co-morbidities including hypertension, type 2 diabetes mellitus (T2DM), atrial fibrillation and ischaemic heart disease (IHD) was recorded. Relative Risk (RR) of cardiovascular disease (MI or stroke) was calculated using the QRISK3. Statistical analysis was conducted using PRISM v9.3.1.

Results
228 patients (50% male), mean age 69 years ± 14.2 (SD), mean BMI 30.5 kg/m² ± 15.1 were identified with MACS. 79.8% of patients had a diagnosis of hypertension with 62% on more than one anti-hypertensive medication. 73% of patients were on statin therapy. 34.5% of patients had a diagnosis of T2DM. 27.1% of patients had ischaemic heart disease and 8% had congestive cardiac failure. Mean QRISK3 score was 26.7 ± 15%, compared with 16.6 ± 10% in age/sex matched healthy controls as per the QRISK3 algorithm. Relative risk for MI or stroke was 2.2 compared to the healthy age/sex matched controls. 88% of the cohort had a relative risk > 1. There was no clear correlation between radiological characteristics and QRISK.

Conclusions
Amongst our unselected cohort of patients with adrenal incidentalomas and biochemistry consistent with MACS, there was high prevalence of hypertension, T2DM and IHD compared with the background population. Additionally cardiovascular QRISK3 demonstrated this patient cohort had > 2 times the likelihood of having an MI or stroke within the next 10 years compared with healthy age and sex matched people. Although the data suggests an association, it is possible other confounders such as BMI may influence both ONDST results and CV risk. CV risk assessment should be considered in all patients with an adrenal incidentaloma and MACS.

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RC13.7
An observational retrospective study on the association of urine metanephrine levels with cardiometabolic risk in patients with nonfunctioning adrenal incidentaloma
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Background
Several studies argued that the cardiovascular evaluation of patients with nonfunctioning adrenal incidentaloma is of particular importance, even if a direct association seems difficult to underline.

Objective
We aimed to evaluate the possibility of stratifying cardiometabolic risk through metanephrine levels in patients with incidentally discovered nonfunctioning adrenal adenoma.

Design
In this retrospective cross-sectional study, we collected data of metanephrine levels in 828 patients with nonfunctioning adrenal incidentaloma, referred to the Division of Endocrinology, Diabetes and Metabolism of the University Hospital of Turin between September 2007 and September 2021.

Results
The univariate analysis showed associations between urine metanephrines and cardiometabolic variables/parameters, particularly considering the noradrenaline metabolite. At univariate regression, normetanephrine was associated with metabolic syndrome, obesity and hypertension; metanephrine was associated with cardiovascular risk factors and metabolic syndrome: hypertension and diabetes. When adjusting for age, sex, BMI and diabetes, metanephrine levels remained significantly associated with cardiovascular risk factors and metabolic syndrome. The results of adjustment analyses are shown in Table 1.
Valassi1,2,3, chaysavanh Manichanh4 , Luciana Maria Martel

Clustered together and separated from the control samples (Adonis test, Kruskal-Wallis test, q 

Body composition was measured using dual-energy x-ray absorptiometry (DXA). Profiles, fasting glycemia and fasting insulin were assessed using standard assays. Microbiomes), a plugin from the QIIME2 pipeline. Lipid and coagulation and unweighted UniFrac distances). Inter-group difference in microbiome diversity analysis through the Principal Coordinates Analysis (PCoA) of weighted species, effective Shannon index) and microbial community structure (beta

Bacterial 16S rDNA was amplified by PCR, and sequencing was applied to analyze microbial richness (alpha diversity; Chao 1 index, observed number of species, effective Shannon index) and microbial community structure (beta

Patients with CS in remission have gut microbial dysbiosis with decreased microbial richness and diversity, and specific variations in the bacterial community structure. Dysbiosis in CS may be one of the mechanisms whereby cardiometabolic dysfunctions persist after “cure”. DOI: 10.1530/endoabs.81.RC13.8

Gut dysbiosis in patients with Cushing’s syndrome in remission. relationship with cardiometabolic risk

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Background

Patients with Cushing’s syndrome (CS) in remission show residual cardiometabolic derangements leading to increased cardiovascular risk. Impaired characteristics of gut microbiome (dysbiosis), such as richness, diversity and composition, have been associated with several cardiometabolic risk factors, including obesity, insulin resistance and atherosclerosis. Whether CS patients present with intestinal dysbiosis is currently unknown. Our study was aimed at evaluating the relationship between the characteristics of gut microbiome and both body composition indexes and cardiometabolic risk factors in “cured” CS.

Methods

Twenty-seven female non-diabetic patients with CS in remission [mean (± SD) age, 51.2 ± 9 years, mean ± (± SD) BMI, 26.5 ± 3.8, median (iQR) duration of remission, 11(4) years] and 27 gender-, age-, and BMI-matched controls were enrolled. Genomic DNA was extracted from fecal samples. The V4 region of the bacterial 16S rDNA was amplified by PCR, and sequencing was applied to analyze microbial richness (alpha diversity; Chao 1 index, observed number of species, effective Shannon index) and microbial community structure (beta diversity analysis through the Principal Coordinates Analysis (PCoA) of weighted and unweighted UniFrac distances). Inter-group relationship in microbiome composition was analyzed using ANCOM (Analysis of Composition of Microbiomes), a plugin from the QIME2 pipeline. Lipid and coagulation profiles, fasting glycemia and fasting insulin were assessed using standard assays. Body composition was measured using dual-energy x-ray absorptiometry (DXA).

Results

The Chao 1 index was significantly lower in CS patients as compared with controls (Kruskal-Wallis test, q = 0.002), indicating that the former had lower microbial richness. Beta diversity analysis showed that fecal samples from CS patients clustered together and separated from the control samples (Adonis test, P <0.05). The Analysis of Composition of Microbiomes showed that several microbial groups at phylum, family, order and genus categories were associated with CS. In particular, Collinsella, a form genus of the Actinobacteria phylum, was present in all CS patients but not in controls. In CS, the Chao 1 index was associated with fibrinogen levels (P = 0.44, P = 0.034), and inversely correlated with both triglyceride concentrations (r = -0.48, P = 0.035) and the HOMA-IR index (r = -0.45, P = 0.038).

Conclusions

Patients with CS in remission have gut microbial dysbiosis with decreased microbial richness and diversity, and specific variations in the bacterial community structure. Dysbiosis in CS may be one of the mechanisms whereby cardiometabolic dysfunctions persist after “cure”.

DOI: 10.1530/endoabs.81.RC13.8

Late Breaking

RC14.1

Long-term thyroid complications in haematological cancer survivors following systemic chemotherapy, neck radiotherapy and/or haematopoietic stem cell transplantation

Francesco Carlonomagno, Christopher Nardi, Alessandra Tomaselli, Carla Pintucci, Paolo Mazzotta & Daniele Gianfrilli

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Introduction

With the increasing survival rates from cancer the focus has been shifting towards the adverse sequelae, occurring both acutely, or developing as late effects, deriving from its multimodality treatment. Aim

We investigated the occurrence of thyroid complications in patients with haematological malignancies treated with chemotherapy, radiotherapy involving the neck and/or haematopoietic stem cell transplantation (HSCT), referred to our endocrine sequelea clinic over the course of 20 years.

Patients and Methods

We prospectively enrolled 343 patients (172 females, 50.1%), with median age at diagnosis of 17 years (range: 1-76), and median follow-up of 12.4 years. Diagnoses were similarly distributed across: acute myeloid leukaemia, acute lymphoblastic leukaemia, chronic myeloid leukaemia, Hodgkin’s lymphoma, non-Hodgkin’s lymphomas, myelodysplastic syndromes and multiple myeloma. All patients underwent systemic chemotherapy, radiotherapy involving the neck was needed in 103 patients and 208 subjects received HSCT. We investigated the occurrence of: overall thyroid complications, transient and permanent thyroid dysfunction, low T3 syndrome, thyroid autoimmunity, benign and malignant thyroid nodules using Kaplan-Meier survival analyses and Cox proportional hazards models with bootstrapping.

Results

Overall 58.7% of patients experienced thyroid complications, with a median latency time of 3.7 years. Primary hypothyroidism was encountered in 15.6% and transient hypothyroidism in 6.3% of patients; Cox regression revealed female sex (P = 0.008), adult age (P = 0.035) and radiotherapy (P < 0.001) as independent predictors. Low T3 syndrome was diagnosed in 10.1% of patients, and female sex and radiotherapy were independent predictors (P = 0.027 and 0.009, respectively). Transient hyperthyroidism was found in 2.1%, mostly after neck radiotherapy. Thyroid autoimmunity was encountered in 32%, and adult age at diagnosis (> 18 years) was the only independent predictor (P = 0.028). Thyroid nodules were encountered in 41.1%, with adult age at diagnosis as the only independent predictor (P = 0.032); 5 patients were diagnosed with papillary thyroid carcinomas. With regards to overall thyroid complications, female sex and adult age at diagnosis were associated with the highest risk (P < 0.001 and 0.001, respectively). Neck radiotherapy was associated with an increased risk of complications after a median of 18 years, whereas HSCT was not, after multiple adjustments.

Conclusions

Thyroid comorbidities are highly prevalent among patients treated for haematological malignancies, with specific associations with treatment modality, requiring long-term endocrine follow-up.

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RC14.2

Prevention of glucocorticoid-induced adipose dysfunction and hepatic lipid deposition through cold acclimation in aged mice

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1Center for Regenerative Therapies Dresden, Technische Universität Dresden, Dresden, Germany; 2Department of Endocrinology and Diabetology, Zurich, Switzerland; 3University Hospital Zurich, Department of Endocrinology and Diabetology, Zurich, Switzerland; 4Paul Langerhans Institute Dresden (PLID) of the Helmholtz Center Munich at Universitätssklinikum Carl Gustav Carus and Faculty of Medicine at Technische Universität Dresden, Dresden, Germany

Glucocorticoids (GC) are one of the most potent anti-inflammatory pharmacological agents. However, owing to their pleiotropic nature, their clinical effectiveness is frequently limited by their deleterious off-target effects. Frequently, metabolic abnormalities arise from GC excess involving the application of glucocorticoids.
development of dyslipidaemia, insulin resistance and muscle atrophy as well as excessive fat accumulation in both white adipose tissue (WAT) and the liver. In addition, suppressed thermogenic capacity in brown adipose tissue (BAT) has been observed during GC excess in rodents. Cold exposure is an established activator of sympathetic innervation of BAT triggering adaptive thermogenesis and lipid utilisation in BAT as well as WAT. Therefore, our investigation aimed to characterize the interaction between cold-induced thermogenesis and systemic GC excess on the adipose organ. To this end, we treated 32-week-old mice with corticosterone at 29°C (thermoreautality) or 13°C (cold temperature). Following 6 weeks of treatment, mice housed at 29°C gained more weight than their temperature-matched controls, which was coupled with excessive accumulation of white fat and consecutive adipocyte hypertrophy. Interestingly, mice maintained in the 13°C environment were protected from GC-driven obesity as well as adipocyte hypertrophy in WAT. Interestingly, the thermogenic capacity, as well as the sympathetic innervation of BAT, was partially preserved in mice maintained at 13°C in spite of corticosterone treatment, whereas mice housed at 29°C showed a considerable reduction in BAT thermogenic capacity and number of sympathetic nerve endings following GC excess. Moreover, treatment with corticosterone at 29°C resulted in increased hepatic lipid accumulation, while livers from mice maintained in the cold showed markedly fewer lipid deposits. On the systemic level, cold adaptation of mice partially prevented the development of GC-induced hyperinsulinaemia and hyperleptinaemia, both of which were readily observed at 29°C. Taken together, our data demonstrate that prolonged cold exposure prevents the onset of not only GC-induced adipose dysfunction but also related metabolic comorbidities including steatosis of the liver and hyperinsulinaemia. Thus, activation of adaptive thermogenesis may be a potential therapeutic target for the prevention of GC-induced metabolic dysfunction.

DO: 10.1530/endoabs.81.RC14.2

**RC14.3**

Can early postoperative hypocalcemia be predicted preoperatively in patients operated with minimally invasive technique for primary hyperparathyroidism? Fatma Dilek Dellaï Kahramanca1, Esra Çıpoğlu2, Beril Turan Erdoglan2, Hüsnüye Başer1, İlyem Ozdemir1, Oya Topaloglu2, Reyyan Ersoy1 & Bekir Cakırc1

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**Aim**

Postoperative hypocalcemia is seen in 26-42% patients after parathyroidectomy. There are quite a lot of studies investigating preoperative factors that might be used to predict postoperative hypocalcemia in thyroidecomatized patients, however there are less studies in parathyroidectomized patients. In this study, our aim was to determine whether any preoperative clinical, laboratory or ultrasonographical feature anticipate hypocalcemia in parathyroidectomized patients due to primary hyperparathyroidism (PHPT).

**Material and Methods**

All patients operated for PHPT between 2019–2022 were retrospectively evaluated. Patients undergoing minimally invasive parathyroidectomy were enrolled. Demographic, clinical, ultrasonography and histopathology results were noted and compared in patients with and without hypocalcemia (Group-1 and Group-2, respectively) within two days after surgery.

**Results**

Of 179 parathyroidectomized patients, 93 were operated with minimally invasive procedure. Postoperative hypocalcemia was observed in 21 (22.6%) patients. Group-1 was younger compared to Group-2 (P=0.0279). Gender distribution and presence of osteoporosis were comparable. Nephrolithiasis was less prevalent in Group 2 (P=0.0046). Preoperative levels of corrected calcium, phosphorus, magnesium, parathyroid hormone, alkaline phosphatase, 25 OH vitamin D were similar in two groups. Fractional excretion of calcium (FECa) was lower in group 1 (P=0.0046).

The optimal cut-off level of FECa that was predictive for postoperative hypocalcemia (Patients with hypocalcemia) was 0.0216 with a sensitivity of 61.9% and specificity of 54.9% (AUC 0.643 ± 0.062, P=0.048). Ultrasonographic and histopathologic diameters and volumes of parathyroid lesions were not different in both groups (p>0.05 for all). Histopathological diagnosis was parathyroid adenoma in 76 (64.5%) patients, parathyroid hyperplasia in 9 (9.7%) patients, and cell-rich parathyroid gland in 8 (8.6%) patients. The distribution of the histopathological results were similar in two groups (P=0.750).

**Conclusions**

Younger patients, patients with lower FECa and without nephrolithiasis undergoing minimally invasive parathyroidectomy for PHPT might require closer follow-up for the development of postoperative hypocalcemia. FECa lower than 0.0216 might help to predict occurrence of postoperative hypocalcemia.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Group-1 (Patients with postoperative hypocalcemia)</th>
<th>Group-2 (Patients without postoperative hypocalcemia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year) (median)</td>
<td>18 (85.7)</td>
<td>53 (73.6)</td>
</tr>
<tr>
<td>Gender (women)</td>
<td>51.9±12.4</td>
<td>10.7 (10.3-11.4)</td>
</tr>
<tr>
<td>Corrected calcium (mg/dl)</td>
<td>10.5 (10.2-10.7)</td>
<td>10.5 (10.2-10.7)</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>2.9±0.6</td>
<td>2.7±4.6</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>2.1±0.1</td>
<td>2.0±0.2</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/l) (n=91)</td>
<td>188.5 (147.0-210.0)</td>
<td>191.0 (140.5-281.8)</td>
</tr>
<tr>
<td>Parathyroid hormone (18.4-80.1 ng/ml) (n=92)</td>
<td>19.8 (11.2-23.5)</td>
<td>16.0 (11.0-22.0)</td>
</tr>
<tr>
<td>D3 (25-80 ng/ml) (n=92)</td>
<td>0.0213 (0.0146-0.0229)</td>
<td>0.0225 (0.0177-0.0279)</td>
</tr>
<tr>
<td>Presence of nephrolithiasis</td>
<td>4 (19.0)</td>
<td>31 (43.1)</td>
</tr>
<tr>
<td>Presence of osteoporosis</td>
<td>10 (47.6)</td>
<td>26 (36.1)</td>
</tr>
<tr>
<td>Number of removed parathyroid lesions</td>
<td>1 (1-3)</td>
<td>1 (1-3)</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Group-1</th>
<th>Group-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractional excretion of calcium</td>
<td>0.0225 (0.0177-0.0279)</td>
<td>0.0225 (0.0177-0.0279)</td>
</tr>
<tr>
<td>Parathyroid lesions</td>
<td>1 (1-3)</td>
<td>1 (1-3)</td>
</tr>
</tbody>
</table>

DO: 10.1530/endoabs.81.RC14.3

**RC14.4**

Sequential primary adrenocortical culture system for genetic transformation and adrenocortical tumorigenesis using CRISPR/Cas9-mediated genome editing

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Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence of 0.7–2.0 per million per year. Prognosis of ACC is generally poor but variable and therapeutic approaches are scarce. While surgical resection presents the best option for definitive cure, mitotane remains the only approved drug for adjuvant therapy in ACC to date. Advancements regarding novel treatment strategies as well as fostered understanding of potential drivers of adrenocortical carcinogenesis have been limited by the lack of tumour models reflecting genetic disease heterogeneity. Currently available cell culture and mouse models for ACC only comprise single patient derived cell lines, corresponding mouse xenograft models and few conventional genetically engineered mouse models mainly targeting components of the Wnt-signaling pathway. To overcome this gap, we developed a workflow for culturing adrenocortical cells from C57BL/6-WT, and C57BL/6Rosea26Sor-CAGG-SpCas9-IRES-eGFP mice. After isolation and longitudinal...
culture of murine adrenal cortices, we performed LC-MS/MS based steroid hormone analyses in supernatant showing sustained secretion of aldosterone (day 7: 1535 ± 697 ng/l), corticosterone (day 7: 1111 ± 123 μg/l), 11-dehydrocorticosterone (day 7: 7.74 ± 14 μg/l) and progesterone (day 7: 9 ± 2 μg/l). Furthermore, qRT-PCR of adrenal targets showed mRNA expression of several steroidogenic enzymes e.g. HSD3B2, HSD11B1, CYP1A1, CYP1B1 and CYP11B2, as well as SF-1, STAR and SCARB1. After confirmation of adrenocortical origin, cultured cells were immortalized via CRISPR/Cas9-mediated targeting of Trp53. This ex vivo setup holds the potential to study adrenal cell homeostasis and biology, and will allow us to replicate oncogenic transformation of adrenocortical cells using CRISPR/Cas9-mediated genome editing. It presents starting point for the development of versatile and clinically relevant isogenic mouse models for adrenocortical tumours.

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RC14.5
Calcitonin washout in the diagnosis of medullary thyroid cancer
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Background
Medullary thyroid cancers (MTC) originate from parafollicular C cells and constitute 3-5% of all thyroid cancers. Calcitonin (CT) measurement is useful in the diagnosis of MTC. The sensitivity and specificity of CT are low in the measurement alone, and the sensitivity and specificity increase when used with pentagastrin and calcium stimulation tests. However, the difficulty of accessing pentagastrin, the uncertainty of the cut-off value in calcium stimulation tests, the differences in calcitonin assay and the costs complicate the use of serum CT and stimulation tests in the diagnosis. For this reason, guidelines do not offer opposing or supportive recommendations about the routine measurement of CT in patients with thyroid nodules. In this study, we aimed to investigate the contribution of CT washout of the nodule (WO) to routine CT measurement for MTC diagnosis.

Methods
In our clinic for the last three years, calcitonin values have been routinely measured in patients with nodular thyroid disease. CT-WO is performed for the nodules of patients whose calcitonin values are still above the laboratory cutoff levels in repeated measurements after excluding confounding factors. CT-WO was implemented after the thyroid fine-needle aspiration biopsy specimen was spread on a slide. The remaining material was washed with 1 ml of saline, and then the CT level was measured. In this study, the results of 33 patients who were operated on will be presented.

Results
Papillary thyroid cancer (PTC) was found in 12 (36.4%), MTC in 14 (42.4%) and benign pathology in 7 (21.2%) of the patients. CT-WO was performed on 69 nodules of these patients before surgery. According to the pathology reports, eleven of these nodules were PTC, 13 were MTC, and 45 were benign. PTC and MTC were detected incidentally in two separate patients. In patients with MTC, serum CT and CT-WO values were significantly higher than the other two pathology groups (P < 0.001). ROC analysis was performed for serum CT value, and the level 29.9 determined MTC with 100% sensitivity and 90% specificity (AUC = 0.975 (0.932-1), P < 0.001). Also, ROC analysis was performed for the CT-WO values of the nodules, and level 413.5 determined MTC with 100% sensitivity and 86% specificity (AUC = 0.987 (0.965-1), P < 0.001). The median MTC diameter in the thyroidectomy specimens was 1 cm (0.6-5.5). Micro MTC was detected in 8 (61.5%) of the patients.

Conclusion
CT-WO appears to be useful in diagnosing MTC early and accurately.

DOI: 10.1530/endoabs.81.RC14.5

RC14.6
Does the knowledge about type 2 diabetes mellitus is capable of interfering in adherence to self-care in patients?
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Introduction
Self-care plays a fundamental role in the treatment and prevention of complications of diabetes mellitus (DM). The patient knowledge about DM and its potential complications are among the factors that are associated with treatment adherence. The process of understanding the disease provides the patient better communication with professionals, better metabolic and psycho-social results which may influence on their emotional well-being and quality of life.

Objective
The present study aims to evaluate the patients’ knowledge about DM 2 and adherence to self-care.

Methods
Analytical, observational, cross-sectional, descriptive study. Diabetic patients being monitored at the outpatient clinic were evaluated regarding their knowledge about DM and adherence to self-care through two questionnaires validated for the Brazilian population – Diabetes Knowledge Scale (DKN-A) and Self-Care Activity Questionnaire (QAD). The first is composed by 15 items about five major dimensions of knowledge in DM - basic pathophysiology, hypoglycemia, food groups and substitutions, complications, and general care with the disease. The second, has 6 dimensions and 15 assessment items related to self-care with diabetes (general diet, specific diet, physical activity, blood glucose monitoring, foot care, medication use, smoking).

Results
Sixty-one patients with DM2 participated in the study. In the QAD, patients’ low adherence to daily self-care practices was observed, with the physical activity domain having the lowest adherence, followed by blood glucose monitoring. As for the results obtained in the DKN-A, it is noted that most reached a score equal to or greater than 8, suggesting satisfactory knowledge about the disease. However, the questions about food groups and substitutions were the ones with the lowest average of correct answers.

Conclusions
When analyzing the results obtained about the knowledge of diabetic patients about their disease, it is observed that the majority (67.2%) reached a score equal to or greater than 8, suggesting satisfactory knowledge about the disease. Despite this, the majority showed low adherence to the expected changes in lifestyle and self-care. Therefore, it is necessary to differentiate knowledge from the level of information - knowledge goes beyond the act of reproducing information, as it presupposes changes in attitudes, behaviors, and habits acquired throughout life. In this way, education about diabetes can be placed as one of the pillars for a satisfactory treatment, promoting a better quality of life for the patient and reducing the chances of complications.

DOI: 10.1530/endoabs.81.RC14.6

RC14.7
Prognostic value of contralateral suppression on eGFR after surgery in primary aldosteronism
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Adrenocortical for primary aldosteronism has been associated with post-surgical kidney failure. It has been proposed that elimination of excess aldosterone demask an underlying failure of the kidney function. Contralateral suppression (CLS) is considered an indication of aldosterone excess and disease severity and the purpose of this study was to assess the hypothesis that CLS would predict change in kidney function after adrenalectomy in patients with primary aldosteronism. We included patients diagnosed with primary aldosteronism referred for adrenal venous between May 2011 and August 2021 and who were subsequently offered surgical or medical treatment. A total of 138 patients were included and after adrenal venous sampling 85/138 (61.6%) underwent adrenalecmy while 53/138 (38.4%) were treated with MR-antagonists. Among surgically treated patients, 59/85 (69.4%) were classified as having CLS and 53/138 (38.4%) were treated with MR-antagonists. The association between contralateral suppression and the change in kidney function remained unchanged in multivariate analysis. Post-surgery, 16/59 (27.1%) patients with CLS developed hyperkaliemia compared to or greater than 8, suggesting satisfactory knowledge about the disease. Despite this, the majority showed low adherence to the expected changes in lifestyle and self-care. Therefore, it is necessary to differentiate knowledge from the level of information - knowledge goes beyond the act of reproducing information, as it presupposes changes in attitudes, behaviors, and habits acquired throughout life. In this way, education about diabetes can be placed as one of the pillars for a satisfactory treatment, promoting a better quality of life for the patient and reducing the chances of complications.

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an increased risk of hyperkalemia after adrenalectomy in patients with primary aldosteronism.

DOI: 10.1530/endoabs.81.RC14.7

**RC14.8**

**Insulin resistance prevents SHBG increase after VLCKD in non-diabetic obese male subjects**

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Hepatocytes are both insulin sensitive and the primary site for synthesis of SHBG. Thus, it is possible that a condition of hepatic insulin resistance may impair hepatic synthesis of SHBG. In this study, we assessed SHBG circulating levels after 30 days of a very low-calorie ketogenic diet (VLCKD) based on high-biological value protein preparations diet (ISOMED) and natural food in a cohort of insulin-resistant obese male subjects. Moreover, we investigated the effects of exposure of different concentrations of glucose (5.5 mM, 10 mM, 30 mM) and human insulin (HI, 100 nM) on SHBG protein levels and analyzed the expression levels of insulin receptor (InsRec) in the hepatoma cell line HepG2. Twenty-two patients (mean age 39.3 ± 11.7 years, mean BMI 38.2 ± 6.4 kg/m²) displayed fasting glycaemia within the normal range (77.5 ± 10.4 mg/dl), but elevated levels of insulin (29.3 ± 17.8 μIU/ml) and HOMA-IR (5.9 ± 3.7). Mean serum SHBG level was 20.3 ± 8.9 nmol/l at baseline. After VLCKD, a decrease of body weight (-9.3 ± 1.9 Kg), BMI (-3.0 ± 0.7 Kg/m²), and fat mass (-6.4 ± 2.1 kg) (P < 0.01) was observed. A significant increase in serum SHBG levels (+ 7.7 ± 10 nmol/l) was also achieved after VLCKD, with a change of smaller magnitude in high (+2.9) vs low (+12.4) insulin resistance subjects. Interestingly, basal insulinemia (β -0.6, P < 0.01) and HOMA-IR (β -3.2, P < 0.05) appeared as negative predictors of SHBG variation at day 30, independently of BMI. In vitro results showed that 96-h treatment of HepG2 with high glucose concentrations (10 mM and 30 mM) resulted in higher SHBG protein levels (2-fold and 7-fold, respectively) and InsRec expression (1.5-fold and 2-fold, respectively) as compared to normal (5 mM) glucose. Conversely, the co-incubation with HI for 96 h blunted the augmentation of SHBG observed in the absence of insulin (-40% at 10 mM of glucose; -32% at 30 mM of glucose). Likewise, co-incubation with HI resulted in reduced InsRec expression by -67% and -60%, at 10 mM and 30 mM glucose respectively, compared to the absence of insulin. Altogether, these results suggest that high insulin levels may counteract the induction of SHBG during weight loss. In vitro data show that high insulin levels may favor hepatic insulin resistance by inhibition of insulin receptor expression and impair SHBG expression.

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Poster Presentations
Adrenal and Cardiovascular Endocrinology

P1
Familial hyperaldosteronism in a Singaporean kindred
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Familial hyperaldosteronism type I (FH-I) is a rare subset of primary aldosteronism (PA) with an autosomal dominant pattern of inheritance. The molecular basis was determined to be from the unequal crossing over of the 11β-hydroxylase (CYP11B1) and aldosterone synthase (CYP11B2) genes, resulting in a chimeric gene duplication. This in turn leads to the ectopic synthesis of aldosterone in the zona fasciculata of the adrenal glands under the regulation of adrenocorticotropin along with hybrid steroids. While affected subjects typically have early onset hypertension, there is considerable phenotypic diversity. We describe the first ever series of three individuals with FH-I in a Singaporean kindred. The proband, an 18-year-old Chinese male, was initially diagnosed with primary aldosteronism during evaluation of normokalemic hypertension detected at health screening. A strong family history of early onset hypertension prompted further assessment of the proband’s affected family members. His brother (aged 20) was diagnosed with essential hypertension, and his father (aged 50) had a personal history of early onset hypertension and coronary artery disease. Biochemical evaluation of both the proband and his brother revealed hyperaldosteronism, suppressed plasma renin activity with an elevated plasma aldosterone to renin ratio. Intravenous saline loading failed to suppress plasma aldosterone confirming primary aldosteronism. Computed tomographic imaging did not reveal any adrenal adenoma or hypertrophy. As FH-I was suspected, genetic analysis with long polymerase chain reaction was performed and all three subjects tested positive for the chimeric CYP11B1/B2 gene. The proband and his brother were initially treated with low-dose dexamethasone up to 0.5 mg/day and while this led to improvement in hypertension, blood pressure readings did not normalize. Due to the development of steroid-induced acn and weight gain, dexamethasone was switched to spironolactone with good effect. The proband’s father was managed at another centre and declined a change in therapies as his blood pressure control was satisfactory. To our knowledge, this is the first report of FH-I in a Singaporean Chinese kindred and possibly the first in the region. This contributes to our local experience in managing this rare hereditary form of PA, and forms the basis for genetic screening and surveillance of this pedigree. In agreement with the Endocrine Society Clinical Practice Guidelines for PA, we recommend genetic testing for FH-I in subjects with young onset of PA (<20 years), in those with a family history of PA or strokes at a young age (<40 years).

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P2
A rare ARMC5 mutation causing bilateral macronodular adrenal hyperplasia and Cushing’s syndrome
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Introduction
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a highly heterogeneous disorder and is the cause of <2% of cases of Cushing’s syndrome. Around 20-25% of patients with primary bilateral macronodular adrenal hyperplasia (PBMAH) have a mutation in ARMC5.

Case report
47 year old gentleman was incidentally found to have bilateral adrenal lesions when he had a CT scan of his chest performed for chest and back pains. He had a past history of hypertension, diagnosed 8 years ago, on treatment. He had plethoric face but no striae or easy brusing, but had central obesity and thin legs. His BMI was 33 at health screening. A strong family history of early onset hypertension prompted further assessment of the proband’s affected family members. His brother (aged 20) was diagnosed with essential hypertension, and his father (aged 50) had a personal history of early onset hypertension and coronary artery disease. Biochemical evaluation of both the proband and his brother revealed hyperaldosteronism, suppressed plasma renin activity with an elevated plasma aldosterone to renin ratio. Intravenous saline loading failed to suppress plasma aldosterone confirming primary aldosteronism. Computed tomographic imaging did not reveal any adrenal adenoma or hypertrophy. As FH-I was suspected, genetic analysis with long polymerase chain reaction was performed and all three subjects tested positive for the chimeric CYP11B1/B2 gene. The proband and his brother were initially treated with low-dose dexamethasone up to 0.5 mg/day and while this led to improvement in hypertension, blood pressure readings did not normalize. Due to the development of steroid-induced acn and weight gain, dexamethasone was switched to spironolactone with good effect. The proband’s father was managed at another centre and declined a change in therapies as his blood pressure control was satisfactory. To our knowledge, this is the first report of FH-I in a Singaporean Chinese kindred and possibly the first in the region. This contributes to our local experience in managing this rare hereditary form of PA, and forms the basis for genetic screening and surveillance of this pedigree. In agreement with the Endocrine Society Clinical Practice Guidelines for PA, we recommend genetic testing for FH-I in subjects with young onset of PA (<20 years), in those with a family history of PA or strokes at a young age (<40 years).

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P4

Patients with chronic kidney disease present HPA axis disregulation due to impaired glucocorticoid negative feedback

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Aims

A few studies have shown disturbances in the hypothalamic-pituitary-adrenal (HPA) axis in chronic-kidney disease (CKD), of unknown extent and clinical implications. We aimed to study the HPA axis in patients with CKD and its association with kidney impairment and metabolic disturbances.

Methods

Cross-sectional controlled study. Patients with CKD stages I-II (estimated glomerular filtration rate [eGFR] through CKD-EPI equation > 60), stage III (eGFR 30-60) and stage IV (eGFR 15-30) CKD with preserved diuresis (n = 16, 15 and 15, respectively) were included and paired with 17 healthy controls by age, stages III-IV compared to CKD stages I-II and controls (Z = 0.048) and less cortisol suppression after 1 mg dexamethasone-suppression-test (DST) (Z = 0.001) were seen in stages III-IV compared to CKD stages I-II and controls (P < 0.001). Of all, 11 (24%) patients with CKD had a post-DST cortisol > 2 mg/dL, \[2 \{14\%\} in \text{CKD stage III and 9} \{66\%\} in the stage-IV-group], 45 of them persisted with cortisol > 2 mg/dL after a low-dose 2-day-DST (2 mg/6h), all with stage IV \((P < 0.001\) for all). No differences were observed in basal cortisol or cortisol-binding-globulin levels. In the whole cohort, cortisol after DST was linearly inversely correlated with eGFR \((-19.8, P < 0.001)\). Cortisol after DST \((OR 11.9, 95\%CI 1.5-97, P = 0.021)\) and glucose \((OR 1.3, 95\%CI 1.1-1.5, P = 0.003)\) were independently associated with an eGFR < 30 ml/min/m².

Conclusions

Negative feedback of the HPA axis is impaired in patients with CKD and correlates with disease stage. This should be taken into account when hypercortisolism is suspected and explored in this context.

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P5

Group education programme for patients with adrenal insufficiency: evaluation based on patients experiences

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Introduction

Adequate hormone replacement therapy in adrenal insufficiency is essential. Patients should have basic knowledge about their condition and what to do in situations which could trigger an adrenal crisis. Education on how and when hydrocortisone replacement therapy should be adjusted as well as instruction and practice an emergency injection are considered important measures to prevent an adrenal crisis. A standardized nurse-led group-based education programme (GEP) was developed based on a national guideline.

Methods

Sixty-seven patients, who attended the GEP from September 2018 until April 2020, were recruited to fill in a questionnaire in retrospect. The questionnaire categories assessed patients’ experiences with the GEP on content, approach by the clinical nurse specialist and applicability in daily life.

Results

Of the 67 patients 48 responded, of whom 7 indicated they did not want to participate. Thirty-nine patients completed the part about the GEP-content. Three patients scored the content moderate, nine patients self-assessed the highest achievable score. On average, the patients scored a 6.8 on a scale of 10. The average reported score of 37 patients about the approach during the GEP was 9.6 on a scale of 10. Twenty-six of the 37 patients gave the clinical nurse specialists the highest possible score. The part about applicability to apply the education in daily life was filled in by 38 patients. In this category the average score was above moderate (with a 7.7 on a scale of 10). Two patients scored below moderate, another seven patients scored average and 29 patients scored above average.

Fifteen patients wrote additional comments. Strikingly, eight patients noted they would like the GEP to be given repeatedly. The greatest advantage of a group-based education reported by patients is sharing experiences and having contact with patients with the same condition. The self-reported marks were significantly improved after the GEP (p = 0.003).

Conclusion

Overall, the patients who attended a two-hour group-based education programme were positive about the content of the education programme, the approach by the clinical nurse specialists and applicability of education in daily life. Repeated education and training was explicitly indicated by a large proportion of participating patients. Whether the results were affected by, for example, age or origin of adrenal insufficiency, needs to be further investigated.

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P6

Primary aldosteronism and microprolactinoma: a new syndromic variant?

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Discussion

A few patients have been described who show features of primary aldosteronism (PA) and microprolactinoma, and have also metabolic disturbances. We report a patient suffering from a combination of the two conditions.

Case report

A 65-year-old man presented with hypertension and hypokalaemia. The patient had a history of PA and microprolactinoma, which was surgically cured 9 years ago. PA was diagnosed on the basis of plasma renin and aldosterone measurement. The patient also had recurrent episodes of hypokalaemia, which were resistant to conventional treatment. Laboratory investigations revealed an elevated plasma aldosterone level, consistent with PA. The patient was treated with spironolactone, which improved his symptoms and corrected his electrolyte imbalance.

Conclusion

This case report highlights the potential coexistence of PA and microprolactinoma, and suggests that these conditions may be part of a new syndromic variant.
Introduction
Primary aldosteronism (PA) has been described in association with endocrine and non-endocrine neoplasms. Aldosterone-producing adenomas mainly associate with parathyroidism, pheochromocytomas, and pancreatic endocrine tumors, particularly in the context of multiple endocrine neoplasia type 1 (MEN1) syndrome. Next-generation sequencing (NGS) studies have shown frequent somatic mutations underlying PA and, rarely, germline mutations of CYP11B1/CYP11B2, KCNJ5, ATP1A1, ATP2B3, CACNA1D, CACNB2, CLCN2 genes.

Case Report
We describe a 27-years-old PA female patient with microprolactinoma in whom we found a new variant at KIF1B gene. No other endocrine abnormalities have been detected, so far. She suffered for arterial hypertension and then was screened for secondary hypertension. In the context of this setting emerged a strong suspicion of PA (aldosterone-to-renin ratio 11.5). Therefore, a saline infusion test was performed confirming the diagnosis of PA. Subsequently, abdomen computed tomography revealed a left adrenal adenoma sized 14 mm in diameter. The patient was adrenalectomized with both biochemical and clinical remission. Twenty months after, she complained of oligomenorrhea, and further investigation showed a hyperprolactinemia and a microadenoma was detected on pituitary gland. Therapy with Cabergoline was initiated with remission of symptoms and normalization of prolactin levels. Considering the coexistence of an aldosterone-secreting adrenal adenoma and microprolactinoma in a young patient, an NGS genetic analysis was performed for genes linked to endocrine tumors and hereditary endocrine hypertension. The result of the genetic analysis revealed the rare heterozygous variant c.782A>G (p.Lys261Arg) at exon 8 of the KIF1B gene, classified as a variant of uncertain significance. Genetic analysis for the KIF1B mutation was also extended to patient’s parent and her brother. The same mutation has been identified in the father, who suffers from hypertension too, and therefore we are going to screen him for PA.

Discussion
In literature, it has been suggested a direct role of hyperprolactinemia on aldosterone secretion, indicating a potential pathophysiologic link between prolactin levels and PA when coexisting. However, the age of onset and the finding of hormone-secreting adenoma prompted us to perform a genetic evaluation, with the finding of the rare KIF1B variant. The tumor suppressor KIF1B gene is frequently deleted in neural-derived tumors, including neuroblastoma and pheochromocytoma, and non-neural tumors, such as hepatocellular carcinoma and lung adenocarcinoma. Considering the segregation of the variant with the phenotype in our family, KIF1B could likely play a role in tumorigenesis, possibly including also PA. Currently, the somatic genetic analysis on the adrenal adenoma is in progress.

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P7
Waking salivary cortisol as screening test for adrenal insufficiency
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Introduction
In many endocrine centres the 250μg Short Synacthen (Cosyntropin) Test (SST) is the reference standard for the diagnosis of adrenal insufficiency (AI)1, but it is time consuming, expensive, and requires hospital attendance and venepuncture. The morning physiological peak of cortisol shortly after waking is a good predictor for a negative SST; however, a morning serum cortisol requires venepuncture. Serum cortisol and salivary cortisol correlate strongly2, but salivary cortisol is far more convenient as can be collected at home, posted to the laboratory, and is stable at room temperature. We hypothesised that waking salivary cortisol (WSC) could predict a positive or negative SST in patients assessed for AI.

Table 1

<table>
<thead>
<tr>
<th>SST Threshold Predicts</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 minute cortisol by LC-MS/MS Exclude AI ≥ 17 nmol/l</td>
<td>96.81 (90.96-99.34)</td>
<td>68.42 (59.05-76.81)</td>
<td>71.65 (62.98-79.29)</td>
<td>96.3 (89.56-99.23)</td>
</tr>
<tr>
<td>30 minute cortisol by LC-MS/MS Confirm AI &lt; 8nmol/</td>
<td>78.72 (69.07-86.49)</td>
<td>96.49 (91.26-99.04)</td>
<td>94.87 (87.39-98.59)</td>
<td>84.62 (77.24-90.34)</td>
</tr>
<tr>
<td>30 minute cortisol by Immunoassay Exclude AI ≥ 17nmol/l</td>
<td>96.7 (90.67-99.31)</td>
<td>66.67 (57.36-75.11)</td>
<td>69.29 (60.49, 77.17)</td>
<td>96.3 (89.56-99.23)</td>
</tr>
<tr>
<td>30 minute cortisol by Immunoassay Confirm AI &lt; 7nmol/l</td>
<td>75.82 (65.72-84.19)</td>
<td>96.58 (91.48-99.06)</td>
<td>94.52 (86.56-98.49)</td>
<td>83.7 (76.37-89.50)</td>
</tr>
</tbody>
</table>

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Development and internal validation of a predictive model for the estimation of pheochromocytoma recurrence risk after radical surgery

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Objective
Various features have been identified as predictors of relapse after complete resection of pheochromocytoma, but a comprehensive multivariable model for recurrence risk prediction is lacking. The aim of this study was to develop and internally validate an integrated predictive model for post-surgical recurrence of pheochromocytoma.

Methods
The present research retrospectively enrolled 177 patients affected by pheochromocytoma and submitted to radical surgery from 1990 to 2016, in nine referral centers for adrenal diseases. Cox regression analysis was adopted for model development, and a bootstrapping procedure was used for internal validation.

Results
Variables independently associated with recurrence were tumor size (HR 1.01, 95% CI 1.00–1.02), positive genetic testing (HR 5.14, 95% CI 2.10–12.55), age (HR 0.97, 95% CI 0.94–0.99), and PASS (HR 1.16, 95% CI 1.04–1.29). The predictive performance of the overall model, evaluated by Somers’ D, was equal to 0.594, and was significantly higher than the ones of any single predictor alone (P = 0.002 compared to tumor size; P = 0.004 compared to genetic testing; P = 0.048 compared to age; P = 0.006 compared to PASS). Internal validation by bootstrapping techniques estimated an optimistic bias of 6.3%, which reassured about a small tendency towards overfit.

Conclusions
We proposed a multivariable model for the prediction of post-surgical recurrence of pheochromocytoma, derived by the integration of genetic, histopathological and clinical data. This predictive tool may be of value for a comprehensive tailoring of post-surgical follow-up in radically operated pheochromocytoma patients.

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P10

Comparison of assays for salivary cortisol and cortisone in the diagnosis of Cushing’s syndrome

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Background & Objective
Late night salivary cortisol (LNSC) and 1 mg overnight dexamethasone suppression test (DST) are two of the three recommended screening tests for Cushing’s syndrome (CS). The classical DST uses serum cortisol, but analysis of salivary cortisol and cortisone has shown high diagnostic accuracy at DST (1). Salivary cortisol can be analysed with immunoassays, which suffer from variable degree of cross reactivity with other steroids, or with LC-MS/MS, highly specific for cortisol but more time consuming and expensive. For optimal diagnostic accuracy the reference interval and diagnostic cut-off for CS should be determined for each analytical method. We aimed to establish reference intervals and compare diagnostic accuracy for late-night and post-DST salivary cortisol and cortisone analysed with clinical routine methods used in Sweden.

Design & Method
Saliva was collected at 23:00 and after DST at 08:00 in 155 reference subjects and 22 patients with CS. Samples were aliquoted and analysed with three immunoassays for salivary cortisol and two LC-MS/MS methods for salivary cortisone. The upper reference limit (URL) was calculated as the 97.5th percentile of the reference population and sensitivity and specificity for CS was calculated. The diagnostic accuracy for each method was compared with our published LC-MS/MS using area under the curves (AUCs) for receiver operating characteristics (ROC) curves (1).

Results
The URL for LNSC with the LC-MS/MS methods were 3.4–3.9 nmol/L, and with the immunoassays: Roche 5.8 nmol/L; Salimetrics 4.3 nmol/L; and Cisbio 21.6 nmol/L. After DST, the URL for salivary cortisol were 0.7–1.0 nmol/L for LC-MS/MS, 2.4 nmol/L (Roche), 4.0 nmol/L (Salimetrics) and 5.4 nmol/L (Cisbio). The URL for salivary cortisone were 13.5 – 16.6 nmol/L in late night samples and 3.0 – 3.5 nmol/L after DST. ROC AUCs for CS diagnosis were high for all tested methods both for late night samples (0.974 – 0.986) and after DST (0.964 – 0.996). For late night samples salivary cortisol (Roche) and salivary cortisone (LC-MS/MS) showed a slightly, but significantly, higher diagnostic accuracy.

Conclusions
We present robust reference limits for salivary cortisol and cortisone in late night samples and after DST for six clinically used methods. Reference limits vary considerably for different methods. However, using method specific cut offs, all methods show high diagnostic accuracy for CS.

Reference

DO: 10.1530/endools81.P10
P12

SIMBA for Students: teaching preclinical medical and pharmacy students endocrinology through online simulation - a pilot study

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Introduction

Simulation via Instant Messaging – Birmingham Advance (SIMBA) for Students endocrinology through online simulation - a pilot study

Methods

We studied 1129 patients with AI examined from 2005 to 2015 at Skåne University Hospital and Helsingborg Hospital. CortisolDST was In-transformed in the analyses. The covariates studied were gender, age, BMI, eGFR, treatment with inhalation steroids, size of the AI, and size of the smallest AI in patients with bilateral AI (set to 0 in unilateral AI). Various machine learning models were trained to fit the data and examined using feature importance analysis and partial dependence plots. Partial dependence plots show the marginal effect on cortisolDST of a covariate averaging over other covariates.

Results

CortisolDST was strongly associated to the size of the AI but had weaker associations to age, BMI, and eGFR according to permutation importance. The partial dependence plots indicated relatively linear relationships for cortisolDST to age (positively) and eGFR (negatively). There was a negative relationship to BMI at levels below 30 kg/m². Using linear regression, we found that cortisolDST increased 10% (95% CI, 7–14%) for each 10-year increase in age. In patients with BMI below 30 kg/m², cortisolDST decreased 19% (95% CI, 14–23%) for each 5 kg/m² increase in BMI. We found no association at BMI levels above 30 kg/m².

Conclusion

CortisolDST is positively associated to age, negatively to BMI if below 30 kg/m², and negatively to eGFR. These associations should be considered before diagnosing MACS.

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P13

ARMC5 as a possible regulator of acetylation in the adrenal cortex in partnership with SIRT1

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Methods

dexamethasone suppression in patients with adrenal incidentalomas
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Introduction

The specificity of cortisol after 1 mg dexamethasone (cortisolDST) ≥ 50 nmol/l as a criterion for mild autonomous cortisol secretion (MACS) is approximately 80% in patients with adrenal incidentalomas (AI). The aim was to study the associations of cortisolDST to age, BMI, and renal function. We used machine learning models to uncover potential non-linear associations.

Methods

We studied 1129 patients with AI examined from 2005 to 2015 at Skåne University Hospital and Helsingborg Hospital. CortisolDST was In-transformed in the analyses. The covariates studied were gender, age, BMI, eGFR, treatment with inhalation steroids, size of the AI, and size of the smallest AI in patients with bilateral AI (set to 0 in unilateral AI). Various machine learning models were trained to fit the data and examined using feature importance analysis and partial dependence plots. Partial dependence plots show the marginal effect on cortisolDST of a covariate averaging over other covariates.

Results

CortisolDST was strongly associated to the size of the AI but had weaker associations to age, BMI, and eGFR according to permutation importance. The partial dependence plots indicated relatively linear relationships for cortisolDST to age (positively) and eGFR (negatively). There was a negative relationship to BMI at levels below 30 kg/m². Using linear regression, we found that cortisolDST increased 10% (95% CI, 7–14%) for each 10-year increase in age. In patients with BMI below 30 kg/m², cortisolDST decreased 19% (95% CI, 14–23%) for each 5 kg/m² increase in BMI. We found no association at BMI levels above 30 kg/m².

Conclusion

CortisolDST is positively associated to age, negatively to BMI if below 30 kg/m², and negatively to eGFR. These associations should be considered before diagnosing MACS.

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online small group teaching (SGT). This study investigated the efficacy and acceptability of SIMBA for students compared with traditional SGT.

Methods

Each session included three 15-minute interactive clinical cases on a specific area of endocrinology, followed by a 30-minute Q&A session with an expert. All students were invited to participate in sessions relevant to their year-group curriculum. The sessions focused on the curriculum learning objectives and took place between the topic lecture and SGT. Students who attended SIMBA completed a post-SIMBA survey, including 15 multiple choice questions (MCQs). All students were asked to complete a post-SGT survey after the associated SGT, containing the same questions. Median MCQ score was compared between SIMBA only, SGT only and SIMBA + SGT groups using Wilcoxon signed rank test. The answers to Likert scale questions were expressed as percentages. Open-ended questions from surveys underwent thematic analysis.

Results

106 students attended 10 SIMBA sessions in 2020 and 2021 covering adrenal, metabolic bone, thyroid, diabetes, and reproductive endocrinology. All participants were year 1, year 2 medical, or year 1 pharmacy students. The median MCQ result was significantly higher in the SIMBA only group than both the SGT only group and the SIMBA + SGT group (P < 0.05). There was no significant difference in score between the SGT only group and the SIMBA + SGT group (P = 0.7103). Most students agreed that SIMBA was well-structured (93%), engaging (76%), stimulated their interest in endocrinology (82%), promoted knowledge (91%) and an in-depth understanding (93%) and prepared them for exams (78%). Only 53% agreed that time for each case was sufficient. 80% enjoyed the session, and 85% would like to have SIMBA alongside SGT. Positive themes from thematic analysis were knowledge application through case-based learning, interaction, and instantaneous feedback. Benefits of SGT over SIMBA included peer-peer discussion and smaller group size for tutor interaction; however, tutor quality varied.

Conclusions

SIMBA is a good alternative model for SGT to teach endocrinology to preclinical medical and pharmacy students by providing engaging, interactive, and interesting sessions. A study is currently underway to assess improvements to the model and wider impacts on academic performance in a larger cohort.

DOI: 10.1530/endoabs.81.P12
We found a systemic rise in inflammatory and cardiometabolic biomarkers among patients with autonomous cortisol secretion and Cushing syndrome. There was no significant normalisation of the biomarkers found to be elevated in patients with overt CS. The assays showed robustness, as with healthy subjects. No difference in biomarker levels were found between ACS and CS patients revealed significant differences in levels of 49/92 biomarkers using proximity extension assay.

Conclusion

Activated serum inflammatory and cardiometabolic biomarkers in patients with autonomous cortisol secretion (ACS), compared with healthy controls and patients with overt Cushing syndrome (CS).

Methods

Serum from prospectively included patients with ACS (n = 65) and CS (n = 8), and healthy subjects (n = 120) were analysed for 92 different inflammatory biomarkers using proximity extension assay.

Results

ACS and CS patients revealed significant differences in levels of 49/92 inflammatory and cardiometabolic biomarkers (46 raised/3 decreased) compared with healthy subjects. No difference in biomarker levels were found between ACS and overt CS, and the biomarker levels did not correlate with the degree of hypercortisolism. Among the 46 raised biomarkers, 20 were cardiometabolic, and 13 were inflammatory markers. Several of the biomarkers have previously been found to be elevated in patients with overt CS. The assays showed robustness, as only three biomarkers had one outlier each in healthy subjects. Seventeen patients delivered postoperative samples, median 24 months (range 6–40) after operation and hormonal cure. There was no significant normalisation of the biomarkers postoperatively.

Conclusion

We found a systemic rise inflammatory and cardiometabolic biomarkers among patients with ACS and CS, unrelated to the degree of hypercortisolism. Curing ACS/CS did not lead to normalisation of these biomarkers after 24 (range 6–40) months.

DOI: 10.1530/endoabs.81.P15

P14

Profound changes of inflammatory and cardiovascular biomarkers in patients with autonomous cortisol secretion and Cushiong syndrome

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Objective

Determine inflammatory and cardiometabolic biomarkers in patients with autonomous cortisol secretion (ACS), compared with healthy controls and patients with overt Cushiong syndrome (CS).

Method

Serum from prospectively included patients with ACS (n = 65), overt CS (n = 8), and healthy subjects (n = 120) were analysed for 92 different inflammatory biomarkers using proximity extension assay.

Results

ACS and CS patients revealed significant differences in levels of 49 /92 inflammatory and cardiometabolic biomarkers (46 raised/3 decreased) compared with healthy subjects. No difference in biomarker levels were found between ACS and overt CS, and the biomarker levels did not correlate with the degree of hypercortisolism. Among the 46 raised biomarkers, 20 were cardiometabolic, and 13 were inflammatory markers. Several of the biomarkers have previously been found to be elevated in patients with overt CS. The assays showed robustness, as only three biomarkers had one outlier each in healthy subjects. Seventeen patients delivered postoperative samples, median 24 months (range 6–40) after operation and hormonal cure. There was no significant normalisation of the biomarkers postoperatively.

Conclusion

We found a systemic rise in inflammatory and cardiometabolic biomarkers among patients with ACS and CS, unrelated to the degree of hypercortisolism. Curing ACS/CS did not lead to normalisation of these biomarkers after 24 (range 6–40) months.

DOI: 10.1530/endoabs.81.P15

P15

Decreased steroidogenic enzymes activity in benign adrenocortical tumours is more pronounced in bilateral lesions as determined by steroid profiling in HPLC-MS/MS during ACTH stimulation test

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Objective

Large response of steroids precursors, including 17-hydroxyprogesterone and 11-deoxycortisol, to ACTH has been described in adrenocortical tumors, suggesting the existence of intra-tumoral enzymatic deficiencies. This study aimed to compare steroidogenenic enzymes activity in unilateral and bilateral benign tumors using serum steroid profiling in HPLC-MS/MS in basal state and after ACTH 1-24 stimulation.

Design and Methods

A serum profile of seven consecutive adrenaial steroids (progesterone, 17-hydroxypregesterone, 11-deoxycortisol, cortisol, deoxycorticosterone, corticosterone, androstenedione) was determined in HPLC-MS/MS in basal state (TO) and after ACTH 1-24 stimulation (T60) in 35 patients with bilateral adrenocortical tumors (BL), 38 patients with benign unilateral tumors (UL) and 37 control subjects (CT). Response amplitude of each individual steroid was evaluated by T60/TO ratio whereas enzymatic activity was assessed by downstream/upstream steroid ratio. Adrenal volume was precisely quantified by a semi-automatic segmentation method.

Results

For the seven steroids assayed, the amplitude of response to ACTH was higher in BL than in UL and CT. As illustration, on glucocorticoids pathway, T60/TO cortisol ratio was significantly decreased in BL (3.7 [0.5-12.5], P<0.0001) as compared with healthy subjects (2.2 [0.8-8.1], P<0.0046) and CT subjects (1.8 [0.8-4.1], P<0.0001). The difference between BL and UL persisted even after patients on maternal adrenal volume. On glucocorticoids pathway, enzymatic activity of CYP11B1, catalyzing the last step for cortisol biosynthesis, was significantly decreased in BL (78.3 [43.1-199.4]) in comparison to both UL (122.7 [13.8-228.4], P=0.0002) and CT (186.8 [42.1-1326.3], P<0.0001). This was responsible for a lower T0 cortisol (309.8 [167.2-585.2] mmol/L) in BL than in both UL (379.2 [88.5-1078.6] mmol/L, P=0.0317) and CT (401.4 [191.6-777.8] mmol/L, P=0.0036). On mineralocorticoids and androgens pathways, enzymatic activity of distal steroidogenic enzymes CYP11B2 and CYP17A1-17,20 lyase was also lower in BL than UL and CT.

Conclusion

Decreased activity of distal steroidogenesis enzymes CYP11B1, CYP11B2 and CYP17A1-17,20 lyase is responsible for an explosive response to ACTH of upstream precursors in bilateral tumors. It also limits the synthesis of bioactive steroids, explaining the lower basal cortisol, despite the increase in adrenal mass in these bilateral forms of adrenocortical tumors.

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P16

Prevalence and clinical features of ARMC5 mutations in a single centre cohort of patients with bilateral adrenal incidentalomas

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Introduction

Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of Cushing’s syndrome (CS). Some familial forms have been associated to gene ARMC5 (Armadillo repeat-containing protein 5) inactivating mutations. This study aimed to evaluate the prevalence and the complications of ARMC5 mutations in our cohort of patients with bilateral adrenal incidentalomas (BAI).

Methods

72 patients, referred to our Center for BAI, were analysed to identify pathogenic single nucleotide variants (SNVs) and/or structural rearrangements (duplication/deletions, termed as copy number variants, CNVs) involving ARMC5 gene. We also evaluated the prevalence of glycometabolic complications, arterial hypertension (AH), nodules dimension and HPA axis parameters. Subclinical hypercortisolism (SH) was defined by cortisol levels after 1 mg overnight dexamethasone suppression (1 mgDST) ≥1.8 µg/dl.

Results

48/72 patients presented SH. A germline mutation of ARMC5 was found in 9 SH patients (12.5% of the whole population), 7 SNVs and 2 CNVs (Group1). The remaining 39 SH patients were found to be wild type (WT) (Group2). No germline mutations were found among patients without SH (Group3; n = 24). Moreover, we also looked for the presence of somatic ARMC5 mutations in the tissue of 7 patients who had undergone adrenalectomy and we found that 100% presented CNVs (2 patients of Group1 and 5 patients of Group2). Age, gender and prevalence of obesity, AH, diabetes mellitus, dyslipidaemia and osteoporosis were comparable among the three groups. Patients of Group1 showed a larger diameter of the adrenals than patients of Group3 (5.77 ± 2.64 cm vs 3.40 ± 1.18 cm; P=0.0000), but comparable to Group2 (5.77 ± 2.64 cm vs 4.82 ± 1.62 cm, P=0.124). However, all the 4 patients who presented at least one nodule over 5 cm of diameter belonged to Group1. Basal ACTH levels were higher in Group3 compared to Group1 and Group2 (16.41 ± 7.50 ng/l, 10.61 ± 2.82 ng/l, 11.37 ± 6.50 ng/l respectively, P<0.05). Similarly, cortisol suppression after 1 mgDST was significantly lower in Group1 (7.06 ± 6.32 µg/dl) as compared to Group2 (3.97 ± 3.27 µg/dl) and Group3 (1.26 ± 0.35 µg/dl; P<0.01).

Conclusion

Prevalence of germline ARMC5 mutations in our BAI cohort was 12.5%, reaching up to 18.8% in subjects with SH. Mutation carriers seem to have poorer cortisol suppression to low dose DST and larger nodule diameter but similar metabolic comorbidities as compared to WT patients. Further studies are needed to elucidate
Bilateral adrenal haemorrhages secondary to Rivaroxaban on a background of p-ANCA vasculitis

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Background
A 73-year-old female presented to the hospital with a 3-day history of right upper quadrant abdominal pain and episodes of vomiting. Her past medical history included insulin treated Type 2 diabetes diabetes, deep venous thrombosis for which she was on rivaroxaban, COPD, right leg angioplasty and previous p-ANCA vasculitis. She also had flank tenderness and was noted to be hypertensive with a blood pressure of 225/93mmHg. A CT scan of the abdomen identified a new 4 cm right-sided indeterminate adrenal mass since her previous imaging where adrenal glands were reported normal in 2019. She became hypotensive and was treated with intravenous hydrocortisone for suspected unilateral adrenal haemorrhage. Two days later, she started to experience pain in the left flank. A dedicated MRI adrenal study showed the emergence of a new left adrenal lesion, similar in size, signal and characteristic to the lesion on the right adrenal gland. Synacthen test showed inadequate response, Aldosterone/renin ratio and adrenal androgens were not elevated. Whole body PET scan did not show any FDG avid lesions in the adrenal glands. Considering the acute history, rivaroxaban anticoagulation use, p-ANCA vasculitis, and new progressive bilateral adrenal lesions, the diagnosis was adrenal insufficiency secondary to bilateral adrenal haemorrhage. Rivaroxaban was replaced with warfarin after appropriate discussion with the haematology and adrenal MDT.

Discussion
Acute adrenal haemorrhage (adrenal apoplexy) is a rare, potentially life-threatening cause of adrenal crisis. Diagnosis can be challenging however needs to be considered especially with risk factors that include the use of anticoagulants as well as vasculitis. Abdominal CT can be useful in detecting haemorrhage within the adrenal glands. Management, after treatment of the adrenal insufficiency, often requires a multidisciplinary approach due to the complexity of the confounding risk factors. Surveillance imaging post haemorrhage can be used to monitor for resolution of the hematoma as well as investigating if there was any other underlying cause of adrenal enlargement.

Learning Points
1. Novel anticoagulant therapy can be a risk factor for developing the rare condition of bilateral adrenal haemorrhage especially in patients with a background of vasculitis.
2. Cortisol and catecholamines released by the expanding hematoma may initially precipitate hypertension and therefore adrenal insufficiency symptoms may be a late presenting feature.
3. Angiography and embolisation of adrenal haemorrhages may provide better outcomes compared with traditional surgical laparotomy and should be considered if the retroperitoneal bleeding is unresponsive to conservative management.

Covid-19 infection: incidental diagnosis of pheochromocytoma in an adolescent bearing an uncommon mutation

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Introduction
Chest computed tomography imaging in patients with Covid-19 infection often reveals incidental adrenal lesions, which are subsequently investigated, after recession of the infection.

Purpose
Description of a pheochromocytoma that was accidentally diagnosed in a teenager, during her hospitalization with Covid-19.

Case description
A 17-year-old girl, who was diagnosed with covid-19 infection, by molecular testing 6 days before, arrived at the emergency department, with tachycardia and dyspnea, during the first wave of the pandemic. Due to hypocapnia and tachycardia (heart rate = 110’), she underwent CT angiography to rule out pulmonary embolism. A right adrenal lesion formation of 3 cm in diameter was incidentally discovered, which showed intense enrichment with the contrast medium. The patient reported no symptoms other than emotional instability observed by the parents in recent years, which was attributed to adolescence. The girl had no personal medical history and was not on any medication. Family history was also free, negative for neoplasia. The recovery of acute covid-19 disease was followed by a complete clinical and hormonal control. On physical examination, the patient appeared with normal somatic and pubertal growth (tanner stage 5). Regular menstruation was reported. Blood pressure was normal (101/78mmHg), with a heart rate of 102’. On further MRI imaging, the tumor showed a high signal in the T2 sequences and increased enrichment. Additionally, an 18F-FDG PET scan showed increased activity of the lesion (SUVmax of 21.5), with absence of other foci. The hormonal tests confirmed the diagnosis of pheochromocytoma with total metanephrines >3 times the upper normal limit. The posterior retroperitoneoscopic excision of the pheochromocytoma, after preparation of the patient with phenoxbenzamine, was uncomplicated. Histology confirmed the diagnosis of pheochromocytoma with a PASS score of zero.

Genetic testing was negative for mutations in known genes associated with pheochromocytoma-paraganglioma. However, a mutation of unknown significance in the MSH6 gene (exon 4, p.K295R), which expresses a DNA mismatch repair protein, and which is associated with Lynch syndrome, was detected.

Conclusions
Owing to covid-19 infection, an early diagnosis and effective treatment of a potentially dangerous tumor was achieved. Furthermore, the extremely rare association of a mutation in a gene related to Lynch syndrome has also emerged, broadening the range of tumors attributed to these genes.

Cushing’s syndrome (CS) is a rare but very severe condition with high morbidity and mortality. Patients are often diagnosed late in the course of the disease, many years after onset of symptoms. New approaches like extended screening of at-risk populations, alternative biomarkers and clinical scores have been developed to improve diagnostic accuracy. However, there is still a debate, whether certain patient populations should be screened for CS outside the framework of current guideline recommendations.
Material and method
As part of the prospective German Cushing’s registry, we studied 433 patients. They had suspected Cushing’s syndrome or autonomous cortisol secretion. All patients underwent a standardized clinical examination including 20 clinical key items of CS. The main reason why they were referred to our department was documented. Finally, Cushing’s syndrome was confirmed in 98 patients, autonomous cortisol secretion was diagnosed in 44 patients and CS was excluded in 291 subjects using the three standard screening tests urinary free cortisol, late-night salivary cortisol, the 1 mg-dexamethasone suppression-test and long-term clinical observation.

Results
Patients were referred for 18 different key presenting reasons. Five of them were more common in patients with Cushing’s syndrome than in subjects in whom CS was excluded; osteoporosis (7% vs. 2%, P = 0.02), adrenal adenoma (17% vs. 8%, P = 0.01), metabolic syndrome (10% vs. 4%, P = 0.02), myopathy (9% vs. 2%, P = 0.01) and presence of multiple symptoms (16% vs. 1%, P < 0.001). Obesity was the single factor that was much more common in patients with exclusion of Cushing’s syndrome (29% vs. 4%, P < 0.001). Obesity was also the most frequent reason to initiate a screening.

Conclusions
Obesity should not be a standard reason to screen a patient for CS. The results of our study confirm the current screening recommendations.

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P20
Characterization of adrenal miRNA-based dysregulations in Cushing’s Syndrome
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Introduction
Transcriptional regulation of gene expression by miRNAs is critical for the fine-tuning of stress response. However, its role in hypercortisolism has not been explored well. After exploring circulating miRNAs in Cushing’s Syndrome (CS) as biomarkers our aim was to investigate their origin and their role in adrenal tissue.

Methods
Next generation sequencing (NGS) based miRNA profiling was performed in adrenal samples from patients of German Cushing’s registry: (1) Cortisol-Producing-Adenoma (CPA, n = 8), (2) adrenals of patients with Cushing’s Disease after adrenalectomy (CD, n = 8) and (3) controls (adrenal samples of patients with pheochromocytoma (n = 8)). NGS data analysis and principal component analysis (PCA) clustering was performed by R (version 4.1). miRNAs were additionally validated by QPCR in other subtypes of ACTH independent CS (PBMAH, n = 10) and ACTH dependent CS (Ectopic Cushing’s syndrome, n = 3). ACTH stimulation were done in 12 weeks-old female C57Bl/6 mice according to protocol established previously. Adrenal glands were collected from the mice at 0 min (baseline), 10, 30, and 60 min upon ACTH stimulation for miRNA extraction and QPCR analysis.

Results
miRNA based NGS revealed miRNA profiles to be significantly different amongst the groups of Cushing’s Syndrome (CD, CPA) and controls. Interestingly, 17 miRNAs significantly differ between the CS subtypes (P < 0.05). Of these, four miRNAs were found to be significantly upregulated in CPA, in comparison to both CD and Controls. These upregulated miRNAs were taken for validation by QPCR. Upregulated expression of hsa-miR-139-3p (P = 0.01, 12c > 1.4), hsa-miR-1247-5p (P = 0.02, 12c > 2.5) in CPA compared to both CD and Controls could be confirmed by QPCR. Next, the validated miRNAs were analysed in other subtypes of CS. Hsa-miR-1247-5p was upregulated only in ACTH dependent forms of CS (PBMAH (12c > 2.24, P = 0.003) and CPA (12c > 2.24, P = 0.003)). Incidentally, miR-1247-5p was not found in the previously characterized circulating miRNA profile in both CPA and CD. Finally, hsa-miR-1247-5p was found to show no differential expression in the murine adrenal tissues at different time points in comparison to the positive control of miR-96-5p.

Conclusion
This study identifies adrenal miRNAs to be regulated in ACTH dependent and independent manner in CS. ACTH independent upregulation of miRNA-1247-5p as a possible contributor to the hypercortisolism pathology in CPA and PBMAH was identified.

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P21
Time from referral to definitive treatment in Cushing’s syndrome
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Rapid diagnosis and treatment of Cushing’s syndrome (CS) is essential for good outcomes. Current standards for appropriate timelines for referral are under review by NHSE. Data are required to substantiate standard setting. Knowledge of current referral pathways/processes are required to explore delays in accessing definitive surgical treatment. An audit of referral processes at Queen Elizabeth Hospital Birmingham was undertaken and further expanded to 4 additional tertiary centres in England. Data were collected on adult patients diagnosed with CS and referred for surgery at index hospitals between January 2018 and December 2019. Patients seen privately were excluded until seen in index hospital. Data were collected on demographics, initial referrer and referral pathway and dates of first clinic, subsequent referral to index hospital (if applicable), first index hospital clinic, MDT and definitive surgery. 72 patients were diagnosed with CS; 69 had definitive surgical treatment. 37 patients had pituitary CS, 34 adrenal CS. 1 had ectopic ACTH secretion. Demographics and referral pathways are outlined in table below. Results are given as median averages. Time from initial referral to secondary clinic (39.5 days in all patients, 45 days in pituitary and 35 days in adrenal patients) was shorter than those referred direct to index tertiary clinic (57 days in all-comers, 56 days in pituitary and 62 days in adrenal patients). However, total time from

Table 1

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<th>Item</th>
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<th>Pituitary (n = 31)</th>
<th>Adrenal (n = 34)</th>
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<td>8:29</td>
<td>8:26</td>
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<td>GP</td>
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<td>44(61.1%)</td>
<td>25(81.3%)</td>
<td>22(64.7%)</td>
</tr>
<tr>
<td>Initial clinic</td>
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<td></td>
<td>20(58.8%)</td>
<td>13(40.0%)</td>
<td></td>
</tr>
<tr>
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referral to tertiary clinic via secondary pathway was significantly longer (158.5 days in all, 140 days in pituitary and 171 in adrenal patients). The number of diagnostic tests performed in secondary care was 6 in each group. Time from referral to index adenoma was 32, 61 and 22.5 days for all, pituitary and adrenal patients respectively. Time to definitive surgical treatment was 183, 178 and 180 days for all, pituitary and adrenal patients respectively. By mapping average timeline from referral to definitive surgical treatment in CS patients, we’ve highlighted areas of national and hospital-specific delays which can be improved for better patient outcomes. Both secondary and tertiary centres should organise more rapid reviews of patients with a potential diagnosis of CS and minimal investigation criteria should be set before secondary centres involve tertiary centres in management of CS patients.

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**P22**

Mesenchymal Stem Cells exposed to persistently high glucocorticoid levels develop insulin-resistance and altered lipolysis: a promising in vitro model to study Cushing’s Syndrome

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Objective

In Cushing’s Syndrome, chronic glucocorticoid excess and their disrupted circadian rhythm lead to insulin-resistance, diabetes mellitus, dyslipidemia and cardiovascular comorbidities. As undifferentiated, self-renewing progenitors of adipocytes, mesenchymal stem cells may display the detrimental effects of glucocorticoid excess, thus revealing a promising model to study molecular mechanisms underlying metabolic complications of Cushing’s Syndrome.

Design and methods

Mesenchymal stem cells isolated from the abdominal skin of healthy subjects were treated thrice daily with glucocorticoids according to two different regimens: lower, circadian-decreasing (Lower, Decreasing Exposure, LDE) vs persistently higher (Higher, Constant Exposure, HCE) doses, aimed at mimicking either the physiological condition or Cushing’s Syndrome, respectively. Subsequently, mesenchymal stem cells were stimulated with insulin and glucose thrice daily, resembling food uptake, and both glucose uptake/GLUT-4 translocation and the expression of LIPE, ATGL, IL-6 and TNF-α genes were analyzed at predefined timepoints (T1 to T7) over three days. Results

A LDE to glucocorticoids did not impair glucose uptake by mesenchymal stem cells, whereas a HCE significantly decreased glucose uptake by mesenchymal stem cells only when prolonged. Persistent signs of insulin-resistance occurred after 30 hours of HCE to glucocorticoids (P<0.05 from T5 on). As compared to LDE, mesenchymal stem cells experiencing a HCE to glucocorticoids showed a significant down-regulation of lipolysis-related genes in the acute period (P<0.05 for ILPE, ATGL and TNF-α at T2), followed by a significant overexpression once insulin-resistance had established (P<0.05 for ILPE, ATGL, IL-6 and TNF-α at T7).

Conclusions

Preserving circadian glucocorticoid rhythmicity is crucial to prevent the occurrence of metabolic alterations. Like mature adipocytes, mesenchymal stem cells suffer from insulin-resistance and impaired lipolysis due to chronic glucocorticoid excess; mesenchymal stem cells could represent a reliable model to track the mechanisms involved in glucocorticoid-induced insulin-resistance throughout cellular differentiation.

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**P23**

Characterization of cytological assessments of adrenal lesions: A 12-year single center experience

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Background

The accuracy of the radiological and laboratory findings used to investigate adrenal masses are not optimal and therefore additional investigation methods, such as fine needle aspiration (FNA) are sometimes needed. Different methods are used for obtaining FNA such as endoscopic ultrasound (EUS), transabdominal ultrasound and computerized tomography (CT)-guided biopsy.

Methods

Using a search function incorporated in our institutional pathology database, patients who underwent FNAs of adrenal glands at Karolinska University Hospital, Stockholm Sweden between the years 2007-2019 were identified. Medical records for these patients were scrutinized from clinical, radiological, and cytological perspectives. Data included gender, age at time of FNAB, primary origin of the original tumor, uni- or bilateral disease, metastasis to other organs, tumor size, patient outcome during the observation time including survival, adequacy of the sample as well as subsequent histological diagnosis.

Results

A total of 139 adrenal FNAs were identified. Of those, 54 (38.8%) were obtained by EUS, 52 (37.4%) by transabdominal ultrasound and 26 (18.7%) were CT-guided. Preceding radiological investigation suspected malignant lesions in 107 cases (77%). Adequate material for diagnosis was retrieved in 52 cases (96.3%) by EUS, 47 cases (90.4%) by transabdominal ultrasound and in 22 cases (84.6%) by CT-guided biopsies. By FNA adrenal lesions were diagnosed as distant metastasis in 82 cases (59%), adrenocortical cells were found in 54 cases (38.8%) and the diagnosis was unclear in 3 cases (2.2%). Of those in which adrenal cells were identified 5 were later diagnosed as adrenal cortical cancer (3.6%). Most metastases were from lung cancer (48 cases, 58.5%) followed by malignant melanoma (5 cases, 6.1%), renal cancer (4 cases, 4.9%), gynecological cancer (4 cases, 4.9%), and other malignancies (21 cases, 25.6%) (e.g., breast, prostate, hepatocellular, and gastrointestinal cancer). Complications due to the biopsy procedure such as bleeding and pneumothorax were reported in 10 cases (7.2%).

Conclusions

FNA of the adrenal glands is safe and provides useful information in diagnosis of adrenal tumors. Complications are rare regardless of method used. Overall adequacy rate for adrenal biopsy were high, with the EUS having the best results.

Keywords

fine needle aspiration, adrenal glands.

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observed that the particular interest of a 12AM dosage was observed in patients with “milder” hypercortisolism (defined as serum cortisol at 8 am under 138 nmol/l after dexamethasone 1 mg (overnight) suppression test). The main limits of our study are a small patient’s sample (histology needed), a retrospective data collection, and a possible measurement bias for ACTH due to the use of 3 different kit assays. Possible inclusion of subclinical CS cannot be ruled out. To our knowledge, no other study has compared 8AM and 12PM ACTH in the etiological diagnosis of CS. In summary, assessing the cause of CS by 8AM ACTH measurement seems appropriate in first line. Additional midnight ACTH may contribute to the etiological diagnosis in mild CS ACTH independent but requires patient’s night hospitalisation.

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P25
Fibroblast growth factor 21 contributes to adrenal cortex renewal
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Objective
After Cushing Syndrome (CS) is cured, up to 70% of patients develop chronic adrenal insufficiency (AI) and hypophysal-pituitary-adrenal (HPA) axis dysfunction. A long-term treatment with glucocorticoids (GC) is mandatory to overcome AI. However, this treatment implies non-desired complications.

Fibroblast growth factor (FGF21), a key regulator of metabolism, has a bidirectional relationship with GC that bypasses the negative feedback of the HPA axis. In this study, we aimed to investigate the potential effects of FGF21 treatment in the HPA axis in a mouse model with AI post-CS.

Methods
Male C57B6/J mice (n = 10/group) received corticosterone (CORT) (500 µg/mL) or vehicle (VEH) in the drinking water for 5 weeks, followed by 3 days tapering period. After this period, the animals developed AI post-CS, and then they were injected intraperitoneally with recombinant FGF21 or VEH for 7 days. Plasma circadian and stimulated CORT and ACTH levels were assessed by immunoassay. Steroidogenic and stem/progenitor genes in the adrenal gland were determined by qPCR.

Results
AI mice during the nocturnal circadian cycle had decreased plasma CORT levels and down-regulated adrenal steroidogenic genes, whereas plasma ACTH levels remained similar to non-treated (CTL) mice. Three hours after FGF21 administration, CTL-FGF21 and CTL-VEH had similar plasma ACTH levels. However, plasma CORT levels in the CTL-FGF21 mice were significantly increased compared with CTL-VEH mice. As expected, AI groups showed lower plasma CORT levels than CTL mice. Remarkably, between the AI groups, at 1 h the FGF21 treated mice exhibited higher plasma CORT levels and maintained significantly higher ACTH levels during the 3 h after FGF21 administration compared with the VEH group. CTL mice treated with FGF21 for 7 days, increased their circadian and hypocortyclic stimulated plasma CORT levels compared to the CTL-VEH group. In line with this result, the expression of adrenal steroidogenic genes (Star, Cyp11a1 and Cyp11b1) and stem/progenitor markers (Gli, Wt, Wnt, and Dkk) were upregulated in the CTL-FGF21 group. In agreement with CORT withdraw, AI groups maintained lower plasma CORT levels in circadian and hypocyclic conditions, together with upregulated stem/progenitor markers compared with their respective treatment CTL groups. Interestingly, under hypocyclic conditions, AI-FGF21 mice presented higher expression levels of adrenal Sonic hedgehog (Shh) than CTL-FGF21 and AI-VEH mice.

Conclusion
Our data describe that FGF21 contributes to maintaining a sustained CORT secretion and suggests that FGF21 accelerates and supports the adrenocortical cell renewal during AI.

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P26
Prevalence of NCAH, defined by 17-hydroxyprogesterone levels after ACTH-stimulation test, in a population with adrenal incidentaloma
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Background
Nonclassic congenital adrenal hyperplasia (NCAH) is a condition associated with adrenal masses and suggested by current European guidelines to be considered in case of bilateral adrenal lesions. NCAH is caused by different mutations in the CYP21A2 gene coding for the 21-hydroxylase enzyme in the glucocorticoid synthesis leading to mild cortisol deficiency and elevated androgen and steroid precursor levels. 17-hydroxyprogesterone (17OHP) is the most important steroid precursor and used to diagnose NCAH. Elevated ACTH levels lead to development of adrenocortical hyperplasia and adrenal masses. NCAH is one of the most common autosomal recessive disorders and with an estimated prevalence of around 0.1% in the general population but up to 2-4% in some ethnic groups. The prevalence of NCAH in a population with adrenal incidentaloma (AI) is unknown but assumed to be higher than in the general population. The main reason to exclude NCAH is that a correct diagnosis can enable glucocorticoid replacement that can improve quality of life for individuals with symptoms of hyperandrogenism. The aim of this study was to investigate the prevalence of NCAH in a population of adrenal incidentalomas (AIs).

Method
After overnight fasting serum cortisol and 17OHP were measured before and 30 and 60 minutes after an intravenous injection of 0.25 mg ACTH (Synacthen®) in 18 years with AI fulfilling ESE’s definition of AI at a single centre in Regional Sweden. A 17OHP > 30 nmol/l before or after ACTH-stimulation was classified as NCAH.

Results
An ACTH-stimulation test was performed in 222 subjects (median age 66 (25-87) years, 58.6% women). None of the subjects presented a basal 17OHP > 30 nmol/l. Eight subjects (3.6%) presented a 17OHP > 30 nmol/l (median 38 nmol/l (33-62) which could be compatible with NCAH. Four subjects (50%) with 17OHP > 30 nmol/l had bilateral lesions.

Conclusion
The prevalence of NCAH based on the level of 17OHP after ACTH-stimulation in a population of patients with AI was 3.6%. The prevalence based on genetic analysis is probably lower, as the secretion of 17OHP can be slightly increased even from lesions without CAH. However, the prevalence of NCAH appears to be significant higher in a population diagnosed with AI than in the general population. Thus, screening for NCAH in AI may be considered even without bilateral AIs.

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P27
Multiplex serum steroid profiling using liquid chromatography mass spectrometry with post column infusion ammonium fluoride
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Background
Development of multi-steroid profiling allows comprehensive investigation into the different branches of steroid metabolism. Immunoassays only allow analysis of a single steroid per assay and suffer from problems with specificity due to cross-reactivity of similar steroids. Liquid-chromatography mass spectrometry has the specificity to analyse multiple steroids in a single experiment and the dynamic range to quantify steroids at high concentrations such as those observed for cortisol (50-600nM) and at low concentration such as DHT (0.07-2.5nM). Here,
we present the optimisation, validation and application of an ultra-high performance liquid chromatography-tandem mass spectrometry assay for the profiling of 25 steroids. Sensitivity in mass spectrometry can be enhanced by addition of mobile phase additives which aid ionisation. Typically for steroids this is an acidic additive such as formic acid. Ammonium fluoride significantly enhanced ionisation in a steroid structure-dependent fashion compared to the use of formic acid, with increases in average peak area ranging between 100% and 1280%. Therefore, we validated our method with ammonium fluoride as the additive.

Conclusions

Levels of plasma normetanephrine in patients with CCHD are higher than in patients with ACCHD, suggesting that chronic hypoxemia in CCHD contributes to the risk of PHEO/PGL development in this patients population. Routine biochemical screening for PHEO/PGL should be considered in the management of patients with CCHD, to allow timely detection of clinically important PHEO/PGL in this higher risk population. Future research is needed to better understand the association between chronic hypoxia in CCHD and PHEO/PGL.

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P29

The changing face of drug-induced adrenal insufficiency in the food and drug administration adverse event reporting system

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Importance

Adrenal insufficiency is a life-threatening condition complicating heterogeneous disorders across various disciplines, with challenging diagnosis and a notable drug-induced component.

Objective

To describe the spectrum and main features of drug-induced adrenal insufficiency through adverse drug event reports received by the Food and Drug Administration (FDA).

Design

We conducted a retrospective disproportionality analysis within one of the largest publicly accessible spontaneous reporting systems.

Setting

The FDA Adverse Event Reporting System (FAERS) collecting more than 15 million reports since 2004.

Participants

Adverse event reports extracted from FAERS over the past 2 decades, with a focus on the 2015-2020 period.

Main Outcomes and Measures

We assessed the reporting trend of drug-induced adrenal insufficiency through descriptive statistics. Cases were selected if they contained any of the preferred terms in the Medical Dictionary for Regulatory Activities describing adrenal hypofunctions. We computed the reporting odds ratio (ROR) with relevant 95% confidence interval (CI) using Bonferroni correction to identify signals of disproportionate reporting for drugs recorded in at least 10 cases as primary suspect.

Results

We identified 8496 cases of adrenal insufficiency, 97.5% serious and 41.1% requiring hospitalization. Adrenal insufficiency showed an exponential increase throughout the years, with 5282 (62.2%) cases in 2015-2020. Among 164 drugs, we identified 56 compounds associated with significant disproportionality within various pharmacological classes: glucocorticoids (n=1971), monoclonal antibodies (n=1644, of which 1330 associated with immune checkpoint inhibitors, reaching 76% in 2020), hormone therapy (n=291), anti-infectives (n=252), drugs used for hypercortisolism or adrenocortical cancer diagnosis and/or treatment (n=169), protein kinase inhibitors (n=138). Cases of adrenal insufficiency by glucocorticoids were stable in each 5-year period (22-27%), whereas those by monoclonal antibodies peaked from 13% in 2010-2015 to 33% in 2015-2020.

Conclusions and Relevance

Our study provides a comprehensive insight into the evolution of drug-induced adrenal insufficiency, highlighting the heterogeneous spectrum of culprit drugs classes, the consolidated role of topical and systemic corticosteroids, and the emerging increased reporting of immune checkpoint inhibitors. Our data claim for an urgent identification of predictive factors of drug-induced adrenal insufficiency, and the establishment of screening protocols and educational programs for patients and caregivers.

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Background

Only few cases of patients with adrenal disorders affected by coronavirus disease 2019 (COVID-19) have been reported so far. In this study, clinical outcome data of patients with adrenal disorders and COVID-19 infection has been collected by the ESE Rare Disease Committee and ENDO-ERN via the European Registries for Rare Endocrine Conditions (EuRECa) project.

Methods

This questionnaire included 32 questions on collecting quantitative and qualitative data. From 06/2020 onwards, 55 cases have been reported by 12 centres of 8 different European countries. In total, 48 cases of adrenal insufficiency (AI) and 7 cases of Cushing’s syndrome were reported.

Results

Of the 48 cases of AI, 3 (6 %) were suspected to have COVID-19 infection and 45 (94 %) were confirmed by testing. 40 out of these 48 cases (83 %) were affected by primary adrenal insufficiency (42.5 % Addison’s disease (n = 17), 40 % congenital adrenal hyperplasia (n = 16), 17.5 % others (n = 7)). Affected AI patients (21 male, 27 female) had a median age of 41 (1-77) years at the timepoint of diagnosis. Of those 17 patients with Addison’s disease, 76 % suffered from additional autoimmune endocrine disorders. Most relevant comorbidities were hypertension (n = 7; 15 %), obesity (n = 7; 15 %) and diabetes mellitus (n = 4; 8 %). Most frequent symptoms of COVID-19 infected patients included fever (n = 29; 60 %), tiredness or exhaustion (n = 27; 56 %), cough (n = 25; 48 %), muscle pain (n = 22; 46 %), headaches (n = 16; 33 %) and loss of taste and smell (n = 13; 27 %). Two thirds of patients increased their daily glucocorticoid dose from a mean of 22 mg/d (SD 13 mg/d) to 42 mg/d (SD 23 mg/d). Only two of the surveyed patients administered i.m. injection of 100 mg hydrocortisone. Hospital admission was required in 8 % of cases either due to adrenal crisis or due to the severity of infection. One of the patients with AI had to be transferred to the intensive care unit. Despite one patient, who reported persistent SARS-CoV-2 infection, all others reported complete remission.

Conclusion

This European multicentric questionnaire is the first to collect data on the outcome of COVID-19 infection in patients with adrenal insufficiency. It suggests good clinical outcome in case of daily dose adjustments and emphasizes the importance of patient education on sick day rules.

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replacement which improved her BP \& settled her tachycardia. She then had a dedicated MRI Adrenal scan which confirmed T2 hyper intensities in B/L Adrenal glands suggestive of B/L Adrenal Hemorrhage. Further workup was negative for Adrenal Antibodies \& Autoimmune screen including Antithyroid antibodies. She completed her 10-day course of IV Antibiotics for E. coli \& was discharged on maintenance Hydrocortisone replacement for her Adrenal Insufficiency with a SST planned after her pregnancy to reevaluate her Adrenal reserve. Her baby thankfully remained stable throughout her tocolytic clinical course. This case was interesting as Adrenal Hemorrhage is usually described in the context of Meningococcal infections \& there are only few reported cases of Adrenal Hemorrhage in pregnancy causing Adrenal Crisis.

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P262

Key role for vasopressin V2 receptors in hypertension development in Spontaneously Hypertensive Rats (SHRs)

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Water and electrolyte balance regulation plays a key role in essential hypertension pathogenesis. Indeed, alterations in kidney ability to excrete sodium and water in relation to intake have been proposed as a basic process of hypertension development. Vasopressin (AVP) acts through V2 receptors on the basolateral membrane of collecting duct principal cells to trigger the phosphorylation of Aquaporin 2 (AQP2) which moves from the cytoplasm to the apical membrane, making the cell water-permeable and resulting in water reabsorption. In Spontaneously Hypertensive Rats (SHRs), the alterations in water and sodium balance, as well as in osmoregulation, were evaluated from the pre-hypertensive phase to the establishment of hypertension and further to the pre-hypertensive-related organ damage; early AVP V1 and V2 receptor antagonism was also evaluated on blood pressure time-course. At 4-5 weeks of age, pre-hypertensive SHRs (n=58) showed reduced daily urine volume (P < 0.01), increased urine osmolality (P < 0.01) and a trend towards lower urine sodium excretion (P=0.079) compared to normotensive Wistar Kyoto rats (WKYs, n=40). Circulating levels of AVP were not different, while the urine AVP/creatinine ratio (P < 0.01), as well as the expression of Na+/K+ ATPase and betaine-amino-n-butyric acid transporter 1 (BGT1) in thick ascending limb in outer medulla (mTAL) were higher in pre-hypertensive SHRs than in WKYs. At 28-30 weeks of age, hypertensive SHRs with moderate renal failure displayed no difference in urine osmolality and renal BGT1 expression but showed similar urinary AQP2/creatinine ratios with significantly higher circulating AVP levels (P < 0.01). Treatment of SHRs (n=20) with the V1-antagonist OPC 21268 from 25 to 40 days of age slightly decreased blood pressure but after its withdrawal did not prevent the hypertension onset in adult age. In contrast, administration of tolvaptan, a V2 antagonist, delayed hypertension development by 4-5 weeks. In addition, tolvaptan-treated rats showed a significantly increased urine volume (P < 0.01), as well as a decrease in urine osmolality (P < 0.01) and urine AQP2/creatinine ratio (P < 0.01) compared to both untreated (n=8) and anti-V1-treated (n=12) SHRs. Thus, according to our results, increased plasma levels of AVP seem to play a key role in hypertension development in SHRs through the activation of V2 receptors in the principal cells of the collecting duct, suggesting that alterations in water balance, even before sodium balance perturbations, represent a cardinal element in the pathogenesis of high blood pressure in this experimental model of hypertension.

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P264

Mitotane side effects in the treatment of patients with adrenocortical carcinoma - a retrospective study

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Introduction

Mitotane is widely used to treat adrenocortical carcinoma (ACC) and remains the mainstay of treatment along with surgery. The aim of this study is to evaluate the adverse side effects of mitotane treatment.

Materials and Methods

This retrospective study included 36 patients with ACC, ENSAT stage I-IV, who were treated with mitotane in an adjuvant or palliative setting. Patients with ENSAT stage IV who died within 6 months after surgery were excluded (n=6). Patient demographic and clinical characteristics, as well as metabolic and hormonal side effects of mitotane, were collected from hospital medical records.

Results

The median age of patients was 48 (18-78) years, 72% of them were female. Twenty-seven patients (75%) received adjuvant mitotane whereas 9 patients (25%) received it in a palliative setting, as monotherapy (n=3) or in combination with chemotherapy (n=6). One patient permanently, and two temporarily, discontinued mitotane treatment due to side effects (severe liver lesion, exfoliative dermatitis and severe gastrointestinal disturbances). Of the remaining
33 patients, all achieved the target mitotane concentration (> 14 mg/L) after median time of 102 days (76-121). In 25 patients (76%), the target mitotane concentration was maintained during > 75% of the treatment period. As for the endocrine toxicity of mitotane, all patients required glucocorticoid substitution. 8 patients (24%) had mineralocorticoid insufficiency, 16 (49%) had central hypothyroidism whereas hypogonadism was observed in 89% of male patients (89%). In addition, 29% of female patients (7/24) developed ovarian cysts and 15 (46%) patients had dyslipidaemia. Four patients had an Addison crisis during treatment. Fourteen patients (42%) experienced gastrointestinal side effects including nausea, vomiting, diarrhoea and weight loss, while 32 patients (97%) had elevated liver enzymes, predominantly GGT. Twelve patients (36%) had various neurological side effects such as dizziness, decreased ability to concentrate or speech disorders (stutter or aphasia).

Conclusion
Mitotane treatment is associated with a wide spectrum of side effects and their successful management is of paramount importance to improve patient adherence to treatment and avoid drug discontinuation.

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P265
Adrenergic crisis after SARS-COV-2 infection in a patient affected by pheochromoctoma
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Background
SARS-CoV-2 infection is characterized by aspecific symptoms (e.g., fever, cough) and can be complicated by viral pneumonia and many other manifestations can occur. Endocrinological complications have also been described. Pheochromoctomas are rare tumors located in the adrenal medulla, causing symptoms due to catecholamines overproduction and abrupt release. Catecholamines release can be continuous or intermittent and there can be several triggers including stress, physical exercise and some foods. SARS-CoV-2 infections have not been previously described as a precipitator of adrenergic crisis in pheochromoctoma. We report a case of adrenergic crisis caused by SARS-CoV-2 infection in a patient affected by pheochromoctoma.

Case report
A 63-year-old Caucasian male affected by right adrenal pheochromoctoma waiting for surgical removal was admitted to the emergency department (ED) for fainting episode and hypertensive crisis. Patient was known for type 2 diabetes, hypercholesterolemia treated by slow-release metformin 500 mg/day and atorvastatin 40 mg/day and was not vaccinated for SARS-CoV-2. Two months before, he was hospitalized in another center for myocardial infarction with non-obstructive coronary arteries and a chest-abdomen CT scan showed 1.5 cm right adrenal mass. The 24-h urinary metanephrines were > 5000 μg/24h and normetanephrines > 2500 μg/24h. Scintigraphy with 250MBq 123I-MIBG showed uptake in the right adrenal gland formation, consistent with pheochromoctoma. Patient was started on alpha-blockers (Doxazosin 2 mg twice/day). Two weeks later, patient was also started on metoprolol 50 mg twice/day. In the ED, BP was 210/108 mmHg with a HR of 105 bpm. A routine nasopharyngeal swab for SARS-CoV-2 was performed. After administration of 2 mg of doxazosin and 20 mg of nifedipine, symptoms addressed to catecholamine release disappeared. As the nasopharyngeal swab resulted positive for SARS-CoV-2, the patient was transferred to infectious diseases unit. Since mean BP was persistently high, doxazosin was increased to 4 mg twice/day, with beneficial effect on BP and HR. After 10 days, the patient tested negative for SARS-CoV-2 and was discharged, with normal vital parameters and indication to continue the new increased dosage of doxazosin. No other crisis was reported until surgery, that was performed without any complication.

Discussion
Since adrenergic crisis is a life-threatening condition, we suggest close BP monitoring and therapeutic adherence in patients with pheochromoctoma waiting for surgery, living in areas characterized by outbreak of Covid-19 infection. In case of infection, we suggest considering an increase in alpha-blocker dosage in order to prevent crisis.

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P266
WBC count. A potential tool for suspecting Cushing’s syndrome (CS)
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Early diagnosis of CS could reduce the morbidity and mortality associated with endogenous hypercortisolism. Many clinical methods have been proposed to establish suspicion of CS, but they show a poor positive predictive value (PPV) and are sometimes difficult to assess. Assessing the well-known influence of hypercortisolism on white blood cell (WBC) count, we evaluated its potential usefulness as a screening test to trigger this suspicion. We analysed WBC count around the diagnosis of CS patients (cases) and compared them in a 1:2 ratio with age- and sex-matched controls who had undergone a negative Nugent’s test (plasma cortisol < 1.8 μg/dl after 1 mg DEXAM). We evaluated the predictive value of haematological parameters by applying ROC curves and tried to find a reference value to establish the suspicion of CS. We collected 72 confirmed CS cases and 144 matched controls from three centres. Mean age was similar (48.5 vs 48 years), both groups included 82% women. Controls had a higher mean BMI than cases (36 vs 29.2; P <.001). There was no significant difference in the incidence of diabetes (27.8% in controls and 31.9% in cases) and there was a significant higher prevalence of hypertension in cases than in controls (61.1% vs 37.5%; P =.001). The rate of active smoking showed no difference between the two groups. Mean WBC count, neutrophil count and percentage were significantly higher in cases, while mean lymphocyte count and percentage were significantly lower in cases than in controls. ROC curves showed an AUC greater than 0.7 for total WBC count, neutrophil count and percentage, lymphocyte count and percentage, and for the difference of total WBC count minus lymphocytes, the difference of both WBC subtypes (neutrophils minus lymphocytes) and the neutrophil/lymphocyte ratio. The two highest levels of discrimination were obtained with the ratio of neutrophil to lymphocyte count (N/L) and the percentage of lymphocytes, which both had an AUC equal to 0.865. The combination of an N/L ratio greater than 2.73 and a lymphocyte percentage less than 25% gave a sensitivity of 77.8% and a specificity of 80.5% for detecting CS, with a PPV of 66.7%. In conclusion, a simple assessment of white blood cell count could be a valuable and inexpensive clue to the suspicion of Cushing’s syndrome. Its routine application in patients with metabolic syndrome could lead to increased detection of CS in endocrinology clinics and reduce the burden of late diagnosis of this disease.

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P267
Screening for non-classic congenital adrenal hyperplasia revisited: proposal for a new serum 17-hydroxyprogesterone threshold for which a cosyntropin stimulation test is indicated
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Introduction
The 250 μg cosyntropin stimulation test (CST) is used to diagnose non-classic congenital adrenal hyperplasia (NCCAH). The current recommendation to perform CST is when follicular morning 17-hydroxyprogesterone (17OHP) is higher than 6 nmol/L, and CST is considered positive for NCCAH diagnosis when the 60-minutes post-CST 17OHP serum level is above 30 nmol/L. These cut offs are mainly derived from radioimmunoassay (RIA) data. Recently, a validated enzyme-linked immunosorbent assay (ELISA) has widely replaced RIA in the measurement of serum 17OHP. This study aimed to determine the RIA and ELISA-based 17OHP cut offs at which CST should be performed.

Material and methods
We conducted a retrospective cohort study at Maccabi Healthcare Services, an Israeli Health Maintenance Organization (HMO). Data was retrieved from adult females (≥16 years) with suspected NCCAH, referred for CST during 2001–2020. Clinical indications that led to NCCAH testing were hirsutism, irregular menses, acne, alopecia, or infertility. NCCAH was defined as post-CST 17OHP serum level >30 nmol/L. Serum 17OHP levels were assessed by direct RIA (Wizard gamma counter, Perkin-Elmer) from January 2000 through March 2015, and by ELISA (IBL International, T ecan) from April 2015 to December 2020. We allocated the individuals into two groups according to the assay method used. For each group, a ROC curve was generated and optimal pre-CST 17OHP threshold with the highest sensitivity and specificity determined.

Results
Cortisol testing was performed in 2409 female subjects (1564 in the RIA and 845 in the ELISA groups). The mean (± SD) age was 24.1 ± 7.2 years. NCCAH was diagnosed in 74 (4.7%) of the RIA group and 63 (7.5%) of the ELISA group. The mean (± SD) pre- and post-CST 17OHP levels were lower in the RIA group as compared to the ELISA group (4.1 ± 6.4 vs. 5.9 ± 9.0 and 9.9 ± 15.3 vs. 12.3 ± 17.3, respectively, P < 0.0001). Using ROC analysis, the optimal pre-CST 17OHP cut off values predicting NCCAH were 6.05 nmol/L in the RIA group (sensitivity 93.2%, specificity 91.7%) and 8.16 nmol/L in the ELISA group (sensitivity 93.2%, specificity 92.5%). When the guideline-recommended pre-CST 17OHP cut off value of 6 nmol/L was used in the ELISA group, sensitivity was 95.2%, and specificity decreased to 84%.

Conclusions
Our study showed a significant number of unnecessary cosyntropin tests. The optimal RIA-based pre-CST 17OHP cut off was comparable with that recommended in the guidelines. However, the results suggest adopting a higher 17OHP cut off when using ELISA. Further studies that incorporate genetic data are needed.

Methods
Adult patients using ICS for over 4 weeks were included after informed consent from among patients seen in medical and respiratory clinics of a tertiary care hospital in India. Critically unwell patients, those who received oral or intravenous steroids in the past 6 months and those already having SAI were excluded. Baseline ICS dose and type were converted to fluticasone dose equivalents as per National Asthma Education Expert panel and classified as having high (>1gm/day), moderate (0.5-1gm/day) or mild (<0.4gm/day) exposure. Baseline demography and presence of symptoms suggestive of SAI was recorded. An Acton Prolongatum® Stimulaton test (APST) was done on all patients to evaluate SAI.1 A cut-off cortisol value of <18 mg/dL after 60 min of APST was used to diagnose SAI.2

Results
Seventy-five patients (F43:M32) with a mean age of 54.9 ± 15 years were included and underwent APST testing. Among them 34 (45.3%) had SAI. There was no difference in the prevalence of SAI with type of ICS (>1.0 ± 0.4 vs. 1.1 ± 0.4mg/day, p-value = 0.2). Clinically patients with asthma (52.9%) had more SAI than those with chronic obstructive airway disease (23.5%) (p-value = 0.04). Among symptoms those with baseline nausea had more prevalent SAI (9.7% vs.29.4%, p-value = 0.03). There was a suggestion that longer use of ICS (3.3 ± 3.5 vs 4.7 ± 3.7 years, p-value = 0.07) was associated with more SAI.

Conclusion
Among patients who are on long-term ICS around 45% have SAI, which may require appropriate replacement during stressful periods. Clinically patients with chronic asthma, those with longer use of ICS and those who have nausea may be more likely to have SAI. The dose and type of ICS was not associated with the presence of AI.

References

P268
Almost half of patients using inhaled corticosteroids have secondary adrenal insufficiency
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Context
Secondary adrenal insufficiency (SAI) has been identified in over 22% of adults using inhaled corticosteroids (ICS).1 This has been co-related with the total daily dose of ICS and baseline clinical clues to the presence of SAI.2

Objective
To determine prevalence of SAI among chronic users of ICS in India along with determining the association of SAI with the type and total daily dose of ICS and baseline clinical clues to the presence of SAI.

Background
Adrenal incidentalomas are common amongst the general population, incidence increases with age. Radiological and biochemical assessment of all lesions >1 cm is standard practice to determine appropriate future management, as per current European guidelines. We report the experiences of a recently formalised adrenal multi-disciplinary pathway in a large UK teaching hospital, where all adrenal incidentalomas are referred and systematically assessed.

Methods
902 patients presenting with an adrenal incidentaloma discussed at a multi-disciplinary team (MDT) meeting over 2.5 years were retrospectively reviewed. Data were collected on demographics, imaging, biochemistry and where relevant diagnostic, surgical outcome and histopathology. Functional testing included overnight dexamethasone suppression tests, aldosterone, plasma renin activity and plasma metanephrines. Prism v9.3.1 was used for statistical analysis.

Results
Of the 902 patients, 47% were male. Mean age was 64 years ± 14 (SD). 865 patients had some form of functional testing, of which 45% had initial results suggestive of endocrine hypersecretion. 89% had imaging available, 82.7% had unilateral lesions with 64.1% found within the left adrenal gland. Mean lesion size 2.9 cm ± 2.4 (range 0.6-21 cm). Mean Hounsfield Units was 4.88 ± 15.7. 39.8% of ONDST performed had an unsuppressed cortisol (greater than 50nmol/l). 21.2% of plasma metanephrine tests performed were elevated above the normal reference range. From the entire cohort, 5.6% were diagnosed with pheochromocytoma, 3.7% with primary aldosteronism, 9.2% had mild autonomous cortisol secretion, 2.1% had adrenal cortical carcinoma and 0.9% had paraganglioma.
P270
Proposition of the first histopathological classification of primary bilateral macronodular adrenal hyperplasia (PBMAH) and its correlation with ARMC5 and KDM1A status
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Introduction
Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) is a rare cause of ACTH-independent Cushings syndrome. It is characterized by the development of supracentimetric nodules resulting in increased adrenal volume and weight. Its presentation is clinically, radiologically and biologically heterogeneous. Morphological descriptions of PBMAH are rare. Although the initial description highlights that multinodular hyperplastic adrenal glands are made of a majority of spongiocytic cells with some eosinophilic cell isles, later descriptions based on a few cases only, did not mention any morphological variation. The identification of inactivating pathogenic variants of ARMC5 in 2013 and of KDM1A in 2021, argues for a genetic heterogeneity. This work aimed to describe the microscopic characteristics of a series of PBMAH and determine if morphological heterogeneity might correlate with the genetic profile.

Methods
35 PBMAH patients operated by adrenalectomy at Cochin Hospital between 1998 and 2021 whose genetic status was known. All slides were reviewed by two independent pathologists, without knowledge of the patients’ genetics. Immunohistochemistry included DAB2, HSD3, Cyp17 and inhibin. DNA sequencing on multiple nodules from 25 of these patients was performed by Illumina NGS.

Results
Four morphological subtypes are identified: two subtypes with nodular architecture (with nodules within macronodules) referred as subtype 1 and 2, and two subtypes with few nodules: subtype 3 and 4. Subtype 1 consists of a majority of spongiocytic cells and eosinophilic cells (10–30%) that forms isles or bands. Subtype 2 has a higher proportion of eosinophilic cells (>30%), mixed with spongiocytic cells. Subtype 3 is composed mostly of spongiocytic cells with less than 10% eosinophilic cells. Subtype 4 is composed of numerous (>40%) oncocytic cells. Their immunohistochemical profile is also heterogeneous. NGS identifies somatic events in ARMC5 and KDM1A mutated patients. The study of correlations between morphological data and genetic status showed that 14 out of the 17 patients classified in subtype 1 are harboring pathogenic variant in ARMC5gene whereas the subtype 2 is exclusively composed of 4 KDM1A mutated tissues. Subtypes 3 and 4 are seen in patients without known mutation. These correlations are statistically significant: P < 0.0001 (Fisher test).

Conclusion
The study of this series allowed us to propose four different morphological groups, in favor of a histopathological heterogeneity. Two of these subtypes correlated with the presence of specific germline mutations. The anatomo-pathological examination of PBMAH based on architectural analysis and cell quantification represents an advance in the classification of adult nodular adrenal hyperplasia.

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P271
The accuracy of adjusted unconventional indices for the assessment of selectivity and lateralization of adrenal vein sampling in the subtype diagnosis of primary aldosteronism
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Objective
This study aimed to evaluate the performance of simple and clinical/imaging-corrected unconventional indices in predicting the selectivity of adrenal vein sampling (AVS) and the lateralization of aldosterone hypersecretion in patients with primary aldosteronism (PA).

Methods
Data of all consecutive patients with a proven diagnosis of PA who underwent AVS for subtype differentiation in two Italian referral centers were analyzed retrospectively. All patients with confirmed unilateral aldosterone hypersecretion underwent adrenalectomy. For the assessment of lateralization, only bilaterally selective AVS were considered.

Results
AVS was bilaterally selective in 112/144 patients. Unilateral disease was diagnosed in 60 cases (53.6%), whereas idiopathic hyperaldosteronism was diagnosed in 52 individuals (46.4%). The aldosterone index, calculated as the ratio between aldosterone in the adrenal vein and aldosterone in the peripheral blood, showed a high accuracy in predicting selectivity using a cortisol selectivity index of 1.1 as the reference standard, and a moderate accuracy when compared to a cortisol selectivity index cut-off of 2 and 3. The simple aldosterone index also demonstrated a moderate accuracy in predicting ipsilateral and contralateral aldosterone hypersecretion. The monocortical index, calculated as the aldosterone-to-cortisol ratio in the adrenal vein, revealed a high accuracy in predicting ipsilateral disease and a high accuracy in predicting contralateral disease, whereas the monolateral index, calculated as the aldosterone-to-cortisol ratio in the adrenal vein vs. peripheral blood, revealed moderate accuracy in predicting ipsilateral disease and high accuracy in predicting contralateral disease. Lesion-side and hypokalemia corrected ROC curves for these unconventional indices revealed a significant improvement in the prediction of ipsilateral/contralateral disease. For a more straightforward clinical application, we calculated the adjusted cut-offs of covariate-corrected indices in an explicit form, for all possible combinations of lesion side at imaging and presence/absence of hypokalemia, according to the Youden’s criterion and using an optimized specificity. Finally, the comparative aldosterone index, calculated as the ratio between aldosterone in the dominant vs the non-dominant vein, showed a high accuracy in the assessment of lateralization.

Conclusions
In the present study, we demonstrated a satisfactory accuracy of unconventional indices in predicting selectivity and lateralization of aldosterone hypersecretion in the setting of AVS, which became even higher after correction for hypokalemia and lesion side at imaging. After an external validation, these indices may become a useful tool in interpreting AVS results for the subtype diagnosis of PA, thereby allowing the selection of patients for adrenalectomy, when standard indices cannot be performed.

DOI: 10.1530/endoabs.81.P271
Dysregulated genes compared to Controls (With reference to transcriptomic data PBMAH was found to have the most expressed genes between the groups. For pathway mapping bioinformatic tools (ShinyGO and Gprofiler) were used. The significant genes related to the pathway genes identified PPARG (l2fc -5.5), PCK1 (l2fc -2.1), PLIN1 (l2fc -4.1) and ADIPOQ (l2fc < 3.3) to be significantly downregulated (P<0.005) in CS subtypes - CPA, CD and PBMAH in comparison to the controls. The in vitro mechanistic characterization of this pathway in cortisol production using adrenal cell lines is in process.

Conclusion
This study investigated for the first time PPARG pathway, which plays a critical role in lipid and glucose metabolism, in cortisol regulation and found a significant downregulation of the pathway in the adrenals of CS patients. DOI: 10.1530/endoabs.81.P272

Characterization of molecular pathway alterations in Cushing’s Syndrome

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Methods
Next-generation sequencing was performed in the 27 adrenal samples (Illumina HiSeq). Bioinformatic analyses was done by R to identify significantly differently expressed genes between the groups. For pathway mapping bioinformatic tools (ShinyGO and Gprofiler) were used. The significant genes related to the respective pathways were validated by real-time reverse transcription-qPCR.

Results
With reference to transcriptomic data PBMAH was found to have the most dysregulated genes compared to Controls (n=3594) and CPA (n=248). Pathway mapping using the significantly altered genes gave neuronal synaptic signalling pathways and PPARG (peroxisome proliferator-activated receptor-gamma) signalling pathway as top hits in the groups of PBMAH and CPA. Validation of the pathway genes identified PPARG (12fc < -1.5) and its related genes - FAHP4 (12fc < -5.5), PCK1 (12fc < -2.1), PLIN1 (12fc < -4.1) and ADIPOQ (12fc < 3.3) to be significantly downregulated (P<0.005) in CS subtypes - CPA, CD and PBMAH in comparison to the controls. The in vitro mechanistic characterization of this pathway in cortisol production using adrenal cell lines is in process.

P273
Salivary profiles of cortisol and cortisone in patients with primary adrenal insufficiency under replacement therapy: a pilot study

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Background
Evaluation of steroid replacement therapy (SRT) in adrenal insufficiency (AI) is challenging for the lack of reliable parameters. Measurement of salivary cortisol and cortisone emerged as a non-invasive tool for AI management, however poorly investigated.

Aim
To analyse the cortisol and cortisone circadian rhythm in normal controls (NC) and patients with primary AI (PAI) under different SRTs, and to identify useful biomarkers.

Methods
We evaluated 24 NC and 30 PAI under hydrocortisone (HC) (n=8), cortisol acetate (CA) (n=14), and dual-release HC (DRHC) (n=8), with equivalent HC doses of 13.2 mg/m², 15.8 mg/m², and 14.6 mg/m², respectively. SRT was taken at 07:00 (all patients) and between 13:00-16:00 (mean 15:13, patients under HC and CA). We collected 9 saliva samples throughout a day at 7:00 (before therapy), 7:30, 10:00, 12:30, 14:00, 16:00, 19:30, 21:00, and 23:00 for cortisol and cortisone measurement by liquid-chromatography tandem-mass spectrometry (LC-MS/MS). We performed cosinor analysis, and calculated area under the curves (AUCs) and percentual variation from NC values (V%). Due to oral contamination from drug intake, we evaluated cortisol for patients under CA and cortisone for those under HC and DRHC. Patients with PAI completed the following questionnaires: quality of life (AddiQol-30), Hospital Anxiety and Depression Scale (HADS) and Pittsburgh Sleep Quality Index (PSQI).

Results
Compared to NC, AUCs between 14:00 and 23:00 were higher in CA (P=0.001) and HC (P<0.001), while similar in DRHC (P=0.12). In the same period, V% was significantly lower under DRHC (-28%) than CA (+128%; P<0.001) and HC (+90%; P<0.001). Cosinor analysis showed comparable mesor, but delayed acrophase (P=0.002 for HC; P=0.026 for DRHC; P=0.027 for CA) and batiphase (P=0.002 for HC; P=0.023 for DRHC; P=0.027 for CA), compared to NC. The number of time points with salivary steroid levels within the range derived from NC was higher in DRHC than CA (P=0.002) and HC (P=0.005). Between 07:00 and 10:00, patients with PAI showed a similar percent increase in salivary steroids among different SRT groups, which was higher than NC (P<0.001 for all comparisons). AddiQol-30, HADS and PSQI were comparable among PAI.

Conclusion
Salivary cortisol and cortisone showed a higher excursion in the morning (all patients) and an increased glucocorticoid exposure in the afternoon/evening (patients under HC and CA), than NC. Although DRHC provides better glucocorticoid exposure than HC and CA, significant differences with NC were observed. Salivary cortisol and cortisone levels and AUC may be useful tools for SRT management in PAI.

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Salivary cortisol and cortisone levels showed a delayed peak in the morning (all patients) and an increased glucocorticoid exposure in the afternoon/evening (patients under HC and CA), than NC. Although DRHC provides better glucocorticoid exposure than HC and CA, significant differences with NC were observed. Salivary cortisol and cortisone levels and AUC may be useful tools for SRT management in PAI.

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P274
Progression of atherosclerosis after the menopause and the role of circulating Amyloid Beta 1-40

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Background
A large body of evidence is supporting that the incidence of adverse cardiovascular events is increasing significantly after the menopausal transition. Primary prevention practices continue to propose evolving algorithms, in an attempt to accurately estimate the actual female cardiovascular risk at midlife. Irrespectivity of these attempts, considerable unrecognized cardiovascular disease (CVD) risk remains unexplained, beyond traditional risk factors (TRFs). On the other hand, a growing body of evidence is suggesting the potential role of a proatherogenic peptide, the circulating amyloid b 1-40 (Aβ1-40). This peptide may serve as a novel biomarker in CVD.

Aim
This study aimed to explore the role of plasma Aβ1-40 and its patterns of change over time in the progression of structural atherosclerosis in postmenopausal women.

Methods
This prospective study recruited a total of 152 postmenopausal women without history or symptoms of CVD, consecutive outpatient in the Menopause Clinic of Aretaieio Hospital, National and Kapodistrian University of Athens, Greece. Baseline assessment consisted of measuring anthropometric and demographic parameters, obtaining fasting blood samples, performing carotid high-resolution ultrasonography. Blood samples were used to measure Aβ1-40, by enzyme-linked immunosorbent assay. Follow-up assessment was performed after a median follow-up of 28.2 months, during which a repeat assessment of subclinical atherosclerosis through sonographical studies was performed

Results
At baseline, the sum of maximal wall thickness in all carotid sites (sumWT) associated independently with high Aβ1-40 levels as well as the values of carotid bulb intima-media thickness (cbIMT) associated independently with high Aβ1-40 levels. Levels of Aβ1-40 levels appeared to increase over time, and were also associated with decreasing renal function. Accelerated progression of cbIMT and maximum carotid wall thickness and sumWT (P<0.05 for all) was observed for women with a pattern of increasing or persistently high Aβ1-40 levels after adjustment for baseline Aβ1-40 levels, TRFs, and renal function (P<0.05 for both).

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P275
Heat shock protein 60 and Endothelial function in postmenopausal women

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Background
Heat shock protein 60 (HSP60), a potentially homeostatic antigen, has been shown to be involved in physiological and non-physiological conditions. Experimental data is supporting the role of HSP60 in placental and mitochondrial steroidogenesis. Under stress conditions, HSP60 are translocated into the endothelial-cell plasma membrane and the extracellular space, promoting the atherosclerotic process.

Aim
We decided to investigate the association between HSP60 and endothelial-cell function in postmenopausal women, considering the possible atherogenic effect of androgenic hormones.

Methods
This study included a total of 160 apparently healthy postmenopausal women. Exclusion criteria were treatment for hypertension or dyslipidaemia, menopause hormone therapy during the last 6 months, previously diagnosed peripheral vascular disease or cardiovascular disease. Fasting venous blood samples were obtained for biochemical, hormonal assessment and evaluation of HSP60. Sonographical assessment of flow mediated dilation (FMD) took place immediately thereafter in one session.

Results
Univariate analysis showed log-HSP60 values differed between women with FMD lower vs higher than the median 5.12% (low vs high FMD, HSP60 values: 2.01 ± 1.16 ng/ml vs 3.22 ± 1.17 ng/ml, p-value = 0.031). Multivariable analysis showed that LogHSP60 was associated with FMD (β-coefficient = 0.244, p-value = 0.031), adjusting for traditional cardiovascular risk factors. Further adjustment for HOMA-IR and testosteron or DHEAS rendered the result non-significant. In the multivariate analysis, DHEAS was associated with FMD (β-coefficient = -0.199, p-value = 0.039), adjusting for cardiovascular risk factors.

Conclusion
The results of this study indicate an association between androgens and endothelial function, independent of HSP60 molecules, in women with low impedance resistance and atherosclerosis. Further prospective studies are needed to explore the significance of our findings.

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P276
Adrenal lesions - the importance of a careful evaluation

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Most differential diagnoses of unilateral adrenal lesions include non-functional adenoma, adrenocortical carcinoma or pheochromocytoma. Primary adrenal lymphoma (PAL) is an extremely uncommon type of primary extranodal non-Hodgkin’s lymphoma (<1%). Most cases are bilateral (~75%), being unilateral PAL scarcely reported. The apparent unilateral involvement of this entity at presentation, in the CT scan/MRI may difficult the diagnosis, delaying the start of chemotherapy. We report a case of a bilateral PAL interpreted primarily as a unilateral A 66-year-old male patient presented to the emergency department with persistent fatigue for 3 months getting worse in the last 3 weeks. His past medical history included type 2 diabetes with macrovascular disease, prostate cancer at 61 yo and active smoking. Physical examination was unremarkable, except for a mild edema in the lower limbs. Laboratory investigations revealed: hemoglobin 13.1 g/dL, white blood cell count 4x 109/L, D-dimer 2232 mg/ml (<500), LDL 488U/L(85-227), NT-proBNP 636ng/ml (<125). A computed tomography(CT) angiogram of the chest was performed to exclude pulmonary embolism(PE)/COVID-19 infection. A lesion of 139 mm on the left adrenal gland, suggestive of a mass or hemorrhage was observed. No signs of PE were evident. The patient was hospitalized for further investigation. Hormonal evaluation revealed: ACRTH 37.8 pg/mL(<46), serum cortisol 20 mg/dL, 24-hour urine cortisol levels were slightly increased with 437 mg/24h(28-213), aldosterone and total urinary metanephrines were normal, except for a slightly increased normetanephrine of 545 mg/24h(<444). An abdominal MRI confirmed a large neofromative lesion on the left adrenal gland of 140 mm. The patient underwent left adrenalectomy and nephrectomy. Histology revealed a diffuse large B-cell lymphoma, non-germinal centre B-cell. Staging 18F-FDG PET/CT scan showed intense 18F-FDG 14 mm uptake in the right adrenal gland(SU/Vmmax 5.7). He received 6 cycles of R-CHOP(rituximab-cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy. The follow-up 18F-FDG PET/CT scan performed at the end of the treatment revealed no evidence of tumor. Thus, this case illustrates the difficulties found in the diagnosis of PAL and draws attention to consider it as a differential diagnosis during evaluation of adrenal masses. In this case, an adrenalectomy was performed given the presence of unilateral large adrenal mass and the possibility of an adrenal carcinoma, leading to a delay in treatment initiation. Furthermore the absence of adrenal insufficiency commonly associated with bilateral adrenal lymphomas was absent. It is noteworthy that the staging 18F-FDG PET/CT scan revealed uptake in the other non-operated adrenal gland that was not evident after chemotherapy, making obvious the diagnosis of a bilateral PAL.

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P277
Presenting clinical features of Cushing’s syndrome and non-classic hypercortisolism

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Background
The Endocrine Society Guidelines recommend screening for hypercortisolism especially in patients with specific features that best discriminate Cushing’s Syndrome (CS): easy bruising, facial plethora, proximal myopathy and striae. Clinical experience suggests that these features, though suggestive of hypercortisolism, are not enough sensitive. Indeed, patients with hypercortisolism frequently manifest primarily less discriminatory cortisol-related features, such as arterial hypertension, diabetes mellitus, weight gain, osteoporosis, defining a hidden form of CS, also defined as “non classic hypercortisolism” (nCH). We conducted a study to retrospectively compare the biochemical and clinical data of patients with hypercortisolism, in CS and nCH forms at their first presentation. Methods
Fifty-eight adult patients (age 47.7 ± 16.7 years, female/male 50/8) with proven biochemical hypercortisolism referred to our hospital from 2008 to 2021 were included. In all patients we evaluated the clinical features present at their first presentation to our outpatient clinic. The subjects were divided into two groups according to the presence or absence of classic and highly specific presenting symptoms, CS and nCH groups respectively. In all patients we assessed 24-hour urinary free cortisol (UFC), cortisol after 1mg-overnight-dexamethasone (F-1mgDST), the delay between estimated clinical onset and diagnosis, the therapy undertaken, the recovery and/or persistence/recurrence of the disease.
Despite being a small nation, the success rate of AVS at Landspitali, Iceland, is.

Methods

Aims

To investigate the success rate of AVS at Landspitali over a 10-year period and compare it to published results from other hospitals.

Methods

The results from all AVS procedures performed from 2007 throughout 2016 in Landspitali National University Hospital of Iceland were retrospectively reviewed. Landspitali is a tertiary referral center for the whole country. We collected data on serum concentrations of aldosterone and cortisol from both adrenal veins, inferior vena cava, and a peripheral vein. All patients were started on synacthen (tetracosactrin) infusion of 93.75 μg/h at least one hour before the AVS. Selectivity index (SI) for each side was calculated by dividing the serum concentration of cortisol from the appropriate adrenal vein by the serum cortisol concentration from a peripheral vein. AVS was considered successful if serum concentrations of cortisol were five times greater in the adrenal veins than in the peripheral vein, e.g. SI > 5 on both sides.

Results

During the 10-year period, 66 AVS procedures were performed at Landspitali. A total of 57 were successful, which gives a success rate of 86%. Six (9%) AVS procedures gave SI < 5 on the right side only and two (3%) gave SI < 5 on the left side only. One (2%) AVS gave SI > 5 bilaterally. Seven (11%) AVS procedures were repeated due to difficulties cannulating the right adrenal vein. All seven repetitions were successful.

Conclusions

Despite being a small nation, the success rate of AVS at Landspitali, Iceland, is fairly good (86%). The success rate is not far from published numbers from Gothenburg, Sweden, (92%) and Mayo Clinic, Rochester, USA, (96%). All the AVS procedures at Landspitali were performed by the same specialist throughout the study period, which is considered to be the key to this success.

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Coagulation parameters in asymptomatic patients with adrenal incidentaloma: is mild autonomous cortisol secretion correlated with thromboembolic risk?

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Background

Overt hypercortisolism is highly associated with venous thromboembolism. Patients with Cushing’s syndrome (CS) typically show an alteration of the intrinsic coagulation pathway, especially an increase in factor VIII (f VIII), and increased levels of coagulation inhibitors (i.e., antithrombin III) as a compensatory response. Mild autonomous cortisol secretion (MACS) has been variably associated with higher risk of cardiovascular events and mortality compared to patients with non-functioning adrenal adenomas (NFAA).

Aim

To describe coagulation parameters in patients with MACS compared with patients with NFAA enrolled in the ITACA study (NCT04127552)

Method

56 asymptomatic patients with adrenal incidentaloma without the classic signs or symptoms of overt hypercortisolism were prospectively enrolled. According to post-dexamethasone suppression cortisol values (post-DST), three groups were defined: NFAA (<50 nmol/L), possible MACS [MACS-1] (50 to 138 nmol/L) and MACS [MACS-2] (>138 nmol/L).

Coagulation markers (fVIII, fVII, fV, fibrinogen, PT, aPTT, platelets) and coagulation inhibitors (Antithrombin III, Protein C, Protein S) were studied. Patients with an history of thrombosis were excluded.

Results

A total of 24 NFA, 22 MACS-1 and 10 MACS-2 were included in the analysis. No differences in coagulation markers and inhibitors were observed between MACS-1 and NFAA. Mean factor VIII levels were significantly increased in the MACS-2 group (167%±54) compared to the NFA group (129%±30; P=0.021) and MACS-1 (122%±32; P=0.012), respectively. Overall, a positive correlation was found between post-DST, platelets (r=0.214; P=0.038) and antithrombin III (r=0.354; P=0.021).

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Conclusions asymptomatic patients with elevated post-DST (>138 nmol/L) may show early thrombotic alterations, similar to those in patients with symptomatic CS. Coagulation parameters may help to identify patients with adrenal incidentalomas at high risk of thromboembolic events, who could benefit from anticoagulant prophylaxis prior to adrenal surgery.

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P281

Management of pheochromocytoma and hyperaldosteronism coexistence

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Introduction

Primary hyperaldosteronism (PHA) and pheochromocytoma are endocrine causes of secondary adrenal hyperplasia. The association of hyperaldosteronism and pheochromocytoma is rare and the involved mechanisms are poorly understood. Either there is coexistence of the two diseases (pheochromocytoma with PHA) or the pheochromocytoma stimulates the production of aldosterone.

Case Report

Male, 54 years old, referred to our department for type 2 diabetes and resistant hypertension (SBP>190mmHg and DBP>110mmHg), medicated with lercanidipine 10 mg, azilsartan 40 mg, chlorothalidone 12.5 mg and nebivolol 5 mg. Laboratory evaluation showed: renin <0.2 ng/ml/h (0.2-1.6); aldosterone 26.8 ng/dL (1.6-16); renin/aldosterone ratio 134 (<30); K+ 3.3 mmol/L (3.5-5.5); high urinary metanephrines (metanephrine 474 μg/24h (64-302); normetanephrine 1013 μg/24h (162-527); 3-Methoxytyramine 345 μg/24h (30-434)) and a negative chromogranin A. A saline infusion test was conducted, with serum aldosterone 9.5 ng/dL after 4 hours. Therapy with spironolactone was started, with a good response (blood pressure 130/80 mmHg), suggesting the diagnosis of PHA. Abdominal CT without contrast revealed bilateral adrenal gland lesions: a single nodule in the right adrenal gland with 2 cm and spontaneous density of 23 HU; 3 nodules in the left adrenal gland with 1.4 cm (12 HU), 1.3 cm and 1.0 cm (both <10 HU). Both 123I-MIBG and PET 18F-FDOPA scintigraphy revealed a high uptake in the right adrenal gland. The patient was submitted to a right adrenalectomy, whose histological evaluation confirmed pheochromocytoma without malignancy criteria. The presence of genetic mutations was excluded. After surgery, the patient maintained difficult-to-control high blood pressure, with normal metanephrine measurement, and a captoprile test was conducted which confirmed PHA (aldosterone reduction of 3%). He was medicated with eplerenone 50 mg/day, maintaining an adequate blood pressure since then.

Discussion

The simultaneous occurrence of pheochromocytoma and PHA is rare, with only 15 cases described in the literature. In the present case, due to the bilaterality of the lesions, the surgical treatment focused on the pheochromocytoma. Although the literature describes cases in which hyperaldosteronism resolves after removal of the pheochromocytoma, in this report it persisted, suggesting the presence of a contralateral aldosterone-producing adenoma.

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P282

Behavior of metastatic paragangliomas and pheochromocytomas: experience from a single center

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Paragangliomas (PGL) and pheochromocytomas (PHEO) are rare neuroendocrine tumors with an estimated prevalence of 1.6500 and 1.2500, respectively. Although most PGL/PHEO are benign, approximately 10% of PHEOs and 15-35% of PGLs have metastatic disease, which it is main cause of death, with 6 years of median survival. Objective: To characterize the metastatic PHEOs and PGLs from a single center. Methods: Retrospective analysis of clinical records of patients with metastatic PHEO or PGL diagnosed from 2000 to 2022. Results: We identified 23 patients, 52.2% male, median age at diagnosis was 38 years (48-77) and at metastasis diagnosis 40 years (Δ12-77). The median follow-up was 4 years (Δ0-17). A total of 8 PHEOs and 23 PGLs (30.4% multifocal) were identified. PHEOs were located in the head and neck (n=8, 35%), abdomen (n=8, 35%) and mediastinum (n=7, 30%). The median tumor size was 50mm (Δ20-160mm). The most frequent complaints were hypertension (39.1%), tachycardia (17.4%), hyphoridrosis and headache (13%); 13% were asymptomatic. A functional profile was detected in 56.5%. The majority of tumors (n=12, 82.6%) underwent surgery. Regarding germline mutations, 43.5% had a mutation in SDHBI gene, 4.3% in the SDHID in 52.2% mutations were not detected. Bone was the main site of secondary deposits (n=17, 73.9%), followed by lymph nodes (n=16, 69.2%), liver (n=8, 34.8%), lung (n=6, 26.1%) and kidneys (n=1, 4.3%). Multifocal metastases were identified in 13 patients (56.5%). Metastases were present at diagnosis in 6 cases (26.1%). Metastases-directed therapies were radiotherapy in 60.9% (n=14),131I-MIBG in 26.1% (n=6), surgery in 21.7% (n=5), chemotherapy in 21.7% (n=5), tyrosine kinase inhibitors (TKI) in 17.4% (n=4), peptide receptor radionuclide therapy (PRRT) in 17.4% (n=4) and chemoembolization in 8.7% (n=2). Multidisciplinary approaches were used in 47.8% (n=11). Surgery obtained a remission rate of 80%. After radiotherapy 50% had disease progression, 30% stability, 5% partial response and 5% remission. PRRT achieved 50% of disease stability and 50% of progression. After chemotherapy 80% progressed and 20% showed partial response. All the patients progressed after 114I-MIBG, TKI and chemoembolization. Median estimate survival from diagnosis was 14 years and from metastases diagnosis was 11 years, with 39.1% death rate.

Discussion

Metastases location is similar to what is described in the literature. Metastatic disease treatment is challenging due to the low response rate of approved treatments, with the surgical approach offering the best remission rate.

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A single dose of Neutrophil Elastase inhibitor Elafin does not alter CBG cleavage during post-surgical stress in humans in vivo

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Introduction

Corticosteroid Binding Globulin (CBG) binds >85% of plasma cortisol and mediates free cortisol levels. Observations in vitro show that CBG is cleaved by neutrophil elastase (NE), a mechanism proposed to reduce CBG binding affinity and increase free cortisol availability to inflamed tissues. However, detection of cleaved CBG in vivo in human plasma is controversial, and any influence of NE on CBG cleavage has not been tested in vivo. We hypothesised that the endogenous NE inhibitor elafin reduces CBG cleavage and thus free plasma cortisol. We tested this in humans using coronary artery bypass graft (CABG) surgery as a model of acute neutrophil-mediated inflammation.

Methods

In a randomised double-blind placebo-controlled parallel group clinical trial, 35 patients undergoing CABG surgery were randomised 1:1 to intravenous elafin 200 mg or saline placebo administered after induction of anaesthesia. Blood samples were taken at baseline (time 0, skin incision) and 2, 6 and 24 hours postoperatively. We measured elafin (LC-MS); plasma elastase activity (fluorometric assay); IL-6, TNF-alpha, NE and CBG (all ELISAs); CBG binding capacity (radioligand-saturation assay); total cortisol (LC-MS) and free cortisol (isotopic dilution and ultrafiltration). Data were analysed as area under the curve from 0-24h or by two-way ANOVA.

Results

With placebo, NE increased from baseline 914±10.0 to peak 8944±10.8 ng/ml at 2h, accompanied by increased IL-6 and TNF-alpha. Elafin infusion resulted in >1000-fold higher plasma concentrations than those of endogenous elafin, with marked reduction in elastase activity (mean AUC0-24h 3.83 ± 1.99 vs 8.04 ± 2.97 units/mL). Plasma CBG concentrations fell at 2h in both groups, but NE was reduced by reduced binding capacity, unaffected by elafin. Total cortisol rose dramatically, a fourfold increase between 2-6h in both groups. Free cortisol fraction doubled over 0-6h from 16.4 ± 0.44 to 30.7 ± 6.1 % in placebo, while elafin tended to
increase free cortisol concentration (mean difference 24.3 nM, 95% CI -1.33 to 49.9, P = 0.062).

Discussion

The fall in plasma CBG and increase in total and free cortisol during CABG surgery is in keeping with published studies in humans during sepsis. We also noted an increase in cytokines which downregulate hepatic CBG production. However, we did not find evidence that the fall in CBG is mediated by increased cleavage by NE. Further studies are needed to assess any effects on CBG cleavage of NE inhibition in target tissues or more potently in serum.

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Ang-Tie pathway in adenocortical tumors angiogenesis

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The majority of adenocortical tumors (ACT) are benign and hormonally non-functioning, in contrast to adenocortical carcinomas (ACC), which are rare and usually very aggressive tumors. The differential diagnosis between these two entities is mainly based on unspecific and subjective criteria, contributing to the inaccuracy of diagnosis. Due to ACC molecular and biological heterogeneity, prognostic factors have a limited capacity to predict ACC clinical outcomes, leading to an inappropriate therapeutic strategy. Angiogenesis is a well-recognized hallmark of cancer. As a dynamic and a complex multistage mechanism, various signaling pathways regulate the growth and maintenance of blood vessels, such as the vascular endothelial growth factor (VEGF) and Ang-Tie pathways. This study aimed to evaluate the role of the VEGF and Ang-Tie pathways in ACT angiogenesis, in order to identify molecular markers that may contribute to the diagnosis and/or prognosis of ACC. The ACT studied included ACC (n=22), adenocortical adenomas (ACA) with Cushing’s syndrome (n=8) and non-functioning ACA (n=13). For each sample, the expression of proteins involved in angiogenesis, namely CD34, VEGF, VEGF-R2, Ang1, Ang2, Tie1 and Tie2, were analyzed by immunohistochemistry. The percentage of the stained area for each protein was quantified using a morphometric analysis tool, except for VEGF CD34, Ang1 and Ang2 expression was found to be significantly different between benign and malignant ACT. ACC presented lower CD34 expression when compared to ACA, whereas Ang1 and Ang2 expression was higher in ACC. Despite the differences observed, none of these proteins demonstrated to be accurate biomarkers for ACT differential diagnosis. Additionally, higher Tie1 expression was observed in ACC of patients with venous invasion and shorter overall survival. As conclusion, this study demonstrated for the first time that the Ang-Tie pathway has a role in ACC angiogenesis. The higher Ang2 levels in malignant ACT could be related with higher vascular permeability, and therefore facilitating tumor dissemination. In addition, the higher Tie1 expression in ACC patients with poor prognosis may represent a possible therapeutic target for ACC.

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P285

Prognostic value of endocrine biomarkers in patients admitted to intensive care unit for COVID-19

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Introduction

To date, there are no clear biochemical parameters to identify early COVID-19 cases at risk of complications in the Intensive Care Unit (ICU).

Aim

To evaluate the prognostic potential of endocrine biomarkers associated with acute inflammatory conditions in ICU patients for COVID-19.

Methods

Between 1/3/2020 and 31/12/2020 we recruited 126 consecutive patients at the admission to ICU 1U, Molinette University Hospital of Turin. Within 24 hours (T1), we calculated: SAPS II (Simplified Acute Physiological Score II), SOFA (Sequential Assessment of Organ Failure) and MuLBSTA (Multinodal infiltration, hyperlymphocytosis, Bacterial co-infection, Smoking history, hyperTension and Age). At T1, at 72 hours (T3) and after 7 days (T7), we measured the plasma levels of copeptin and MRproADM. Duration of extracorporeal membrane oxygenation (ECMO) and mechanical ventilation (MV), ICU and hospital length of stay (LOS), ICU (IM) and hospital mortality (HM) were recorded. We present the results of the first 69 patients.

Results

53 males and 16 females (median age 63) were enrolled. The ICU and hospital LOS were 13 [6.7-22.2] days and 20 [13-30] days, respectively. The median time free from MV was 1 day. The need for pronation was significantly predicted by a higher MuLBSTA classification (OR 4.01, P=0.025). The median duration for ECMO was 17 days. The SOFA score was higher in patients requiring ECMO (P=0.019) and performed better when corrected for copeptin at T1 (HR 1.25, P=0.02). IM and HM were 62.3% and 68.1% (median survival time 18 and 24 days, respectively). MR-proADM was higher in dying patients with increasing statistical significance over time (T1 1.3 vs 0.91 nmol/L, P=0.028; T7 1.77 vs 0.9 nmol/L, P=0.001). The MR-proADM T7/T1 ratio was significantly higher in those who died during hospitalization (P=0.0003) predicting HM (HR 1.35, P=0.025). SAPS II class at the admission also predicted HM (HR 1.39, P=0.013), but correcting for MRproADM (HR 1.43, P=0.019) or copeptin measured at T1 improved its statistical significance (HR 1.56, P=0.003). Likewise, SOFA score, easier to collect in ICU, significantly predicted HM (HR 1.09, P=0.041), but improved its performance if corrected for MR-proADM (HR 1.12, P=0.019) or copeptin at T1 (HR 1.11, P=0.018). Neither gender, estimated glomerular filtration rate, C-reactive protein, or procalcitonin affected the previous regression analyses.

Conclusions

Endocrine biomarkers evaluated at ICU admission improve the ability of prognostic scores to predict mortality and severe adverse outcomes. The increase in MR-proADM after 7 days of hospitalization in the ICU also predicts hospital mortality.

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P286

A novel mutation in creb3l1 gene involved in vasopressin synthesis pathway in patients with hypertensive cardiovascular diseases

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Arginine vasopressin (AVP) is a neurohormone, which regulates blood and extracellular fluid volume and hence blood pressure (BP). AVP has its chief action in kidneys where it reduces flow of urine, increases permeability of convoluted tubules of kidneys to water and its reabsorption. It binds to receptors on sweat glands and decreases water loss by perspiration from the skin. Also, AVP binds to peripheral arteriolar receptors, causing vasoconstriction and increase in BP. The synthesis of vasopressin occurs in paraventricular and supra- optic nuclei of the hypothalamus. The mRNA encoding AVP is translated into preprohormone that is delivered into endoplasmic reticulum with concomitant signal peptide removal. The resulting prohormone is folded and delivered to Golgi apparatus where the precursor is cleaved and post-translationally modified into mature hormone. The newly synthesized neurohormone is packed in granules in Golgi complex, which move down the axons, through the stalk, to the posterior pituitary, where AVP is stored and released in response to appropriate stimuli. The main physiological stimulus for release of AVP is an increase in osmotic pressure in circulating blood. AVP causes retention of water by kidneys, which reduces plasma osmolality. The transcription factor cAMP responsive element- binding protein 3 like 1 (CREB3L1) is an important component for cellular homeostasis, particularly within cell types with high peptide secretory capabilities. CREB3L1 serves an important role in body fluid homeostasis through its transcriptional control of AVP gene. In this study, hypertensive cardiovascular patients were analyzed using whole exome sequencing (WES) to find possible pathogenic mutations in different genes of AVP pathway. Thirty hypertensive cardiovascular patients from three families (3 patients in 1st from 21-48; 5 in 2nd from 43-72 and 5 patients in 3rd from 19-47 years of age) were
selected for WES. Genomic DNA was extracted (DNA Isolation Kit from QiAamp DNA mini Kit) at Department of Biosciences, University of Wah, Wah Cantt, Rawalpindi, Pakistan. DNA obtained was taken to Genome Institute of Singapore (GIS), Singapore, where final dilutions of 25μL DNA were outsourced to Proteomics Lab, Macrogen Asia Pacific, Singapore for WES. Subsequent bioinformatics analysis was performed at GIS, Singapore. The results identified a novel homozygous splicing region variant (1524-1A>G) in CREBSL1 gene in all patients. In addition, a novel heterozygous splicing region variant (340-2_340-1InsCCC) was also identified in SEC63 gene in 10/13 patients. In conclusion, we report novel mutations in two genes involved in AVP synthesis pathway in our patients with hypertensive cardiovascular diseases.

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Whole exome sequencing of genes involved in dysfunctional renin-angiotensin-aldosterone system in hypertensive cardiovascular patients

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The renin-angiotensin-aldosterone system (RAAS) is an endocrine system within the body that is essential for regulation of blood pressure (BP) and fluid balance. The system is mainly comprised of three hormones; renin, angiotensin II (Ang II) and aldosterone. The RAAS pathway is initiated in the kidney with the proteolytic conversion of vitamin derived angiotensigen to angiotensin I (Ang I) by renin secreted by juxtaglomerular apparatus of the nephron. Ang I is cleaved by angiotensin converting enzyme to produce Ang II, the physiologically active component of the system. Ang II acts on the adrenal cortex through its receptors, AT-1 and AT-2, to stimulate the release of aldosterone. Aldosterone is a mineralocorticoid, a steroid hormone released from the zona glomerulosa of the adrenal cortex and plays a central role in regulation of BP mainly by acting on distal tubules and collecting ducts of the nephron, increasing reabsorption of sodium and water in the kidney and secretion of potassium. Increase in water retention causes increase in the blood volume and hence BP. In this study, whole exome sequencing (WES) was used to identify pathogenic mutations in different genes of RAAS pathway, whose dysfunction may lead to hypertension and related cardiovascular diseases. Thirty hypertensive cardiovascular patients from three families (3 patients in 1st from 21-48, 5 in 2nd from 43-72 and 5 in 3rd from 19-47 years of age) were selected for WES. Genomic DNA was extracted (DNA Isolation Kit from QiAamp DNA mini Kit) at University of Wah (UWA), Wah Cantt, Rawalpindi, Pakistan. DNA obtained was taken to Genome Institute of Singapore (GIS), Singapore, Singapore; Singapore, University of Lahore, Sahiwal Campus, Islamabad, Islamabad, Pakistan.

P517

Impact of glucocorticoid-induced adrenal insufficiency on health-related quality of life

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Objective
Glucocorticoid-induced adrenal insufficiency is highly prevalent, but the clinical consequences are not fully understood. Therefore, the indication of adding stress dosages of glucocorticoid during ongoing anti-inflammatory glucocorticoid treatment remains unclear. The aim of this study was to determine the impact of adrenal function on health-related quality of life (HRQoL) in patients receiving ongoing low-dose prednisolone treatment.

Methods
Cross sectional study of 181 patients treated >6 months with prednisone for rheumatoid arthritis (RA) (n=103), polymyalgia rheumatica/giant cell arteritis (PMR/GCA) (n=47) or renal transplantation (RTx) (n=31). Patients received ongoing prednisolone treatment, median dose 5 mg/day (range 2.5-20 mg) and were not routinely advised to increase the dose during intercurrent illness or stress. Adrenal function was assessed by ACTH test. HRQoL was evaluated during ongoing prednisolone treatment with SF-36v2 scales General Health and Vitality, AddiQol total score (not RA patients), Fatigue VAS scale (PMR/GCA cohort) and, self-reported hospital admissions and doctor’s appointments. Analyses of the impact of stimulated P-cortisol on HRQoL controlling for underlying disease were performed in i) all patients and ii) 128 patients receiving low-dose treatment (<5 mg/day), respectively.

Results
Adrenal insufficiency was found in 41% of patients (35% low-dose patients). Overall, General Health, Vitality, and AddiQol scores were not associated with stimulated P-cortisol. Mean total AddiQol score was 62.5 (SD 7.7). There was a trend for more medical contacts with lower stimulated P-cortisol (1.17 hospital admissions/year/100nmol/L, CI95%:-0.05–2.23, P=0.061) and (1.11 doctor’s appointments/year/100nmol/L, CI95%:-0.14–2.36, P=0.083). In the PMR/GCA sub cohort, Fatigue VAS score was higher with lower stimulated P-cortisol (4.8mm/100nmol/L, CI95%:0.9–8.7, P=0.017) and General Health and Vitality tended to be lower (GH:-3.7 points/100nmol/L, CI95%:-7.16–0.40, P=0.029) and (1.11 doctor’s appointments/year/100nmol/L, CI95%:-3.88–0.45, P=0.077). However, low-dose patients had higher Vitality with lower stimulated P-cortisol (3.12/100nmol/L, CI95%:0.17–6.07, P=0.038).

Conclusion
Glucocorticoid-induced adrenal insufficiency was associated with fatigue and reduced General health in the PMR cohort and a trend for more doctor’s appointments/admissions in the whole cohort, but otherwise poorly associated with HRQoL during ongoing prednisolone treatment. Results can reflect poor HRQoL consequences of glucocorticoid-induced adrenal insufficiency during ongoing (low-dose) prednisolone treatment or insufficient sensitivity of HRQoL instruments with long recall periods rather than daily symptom monitoring during situations of stress.

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P518

Laboratory evidence of hyperaldosteronism is common in patients with kidney stones – a retrospective single-center analysis

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Background
Kidney stones have been linked to chronic kidney disease and a higher probability of adverse cardiovascular events. Precise mechanisms that lead to these complications have not yet been elucidated. Most cases of kidney stones are idiopathic, related to metabolic disturbances like hypercalciumia, which often have a genetic background. There have been few reports of kidney stones associated with primary hyperaldosteronism (HA); however, the prevalence of HA in patients with kidney stones has not been fully examined.
Methods
We conducted a retrospective single-center study that included 181 patients evaluated for recurring kidney stones in whom basic laboratory tests to identify HA (plasma renin activity – PRA, plasma aldosterone concentration – PAC, and aldosterone to renin ratio – ARR) had been performed. The aim of the study was to assess the prevalence of laboratory evidence of HA (LEHA) in kidney stone patients and to identify clinical and laboratory characteristics associated with LEHA in this group of patients.

Results
The prevalence of LEHA was high. High ARR was identified in 39.8% patients, while a concurrent high PAC was identified in 21.5% (> 0.41 nmol/l) and 13.8% (> 0.55 nmol/l) of all patients. Arterial hypertension (AH) was identified in only about a quarter of patients with LEHA and the prevalence of LEHA was similar in patients with or without AH. Patients with LEHA and AH, particularly when associated with high PAC (> 0.55 nmol/l), exhibited some characteristic features of primary HA like lower serum potassium and higher serum bicarbonate. Patients with LEHA and without AH did not exhibit these features; however, they had higher serum phosphate associated with a trend towards lower urine phosphate excretion, a feature not present in patients with LEHA and AH. Patients with LEHA and AH were also older and tended to have their first stone event at a later age, while patients with LEHA and without AH had more stone-related urological procedures. An extremely low PRA value (< 0.07 μg/l) was present in 8.3% patients and was associated with a faster rate of decline in kidney function on follow-up.

Conclusions
Our study shows that LEHA can be common in patients with recurring kidney stones. Few of these patients present with typical features of primary HA. There are some distinct features of patients with LEHA and without AH, that could represent a separate phenotype in this population. The biological relevance of these findings is yet to be determined.

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P519
Brain Structure in a cohort of young adult patients with Autoimmune Addison’s Disease
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Background
Both cortisol and other adrenal hormones are well known to affect brain structure and function throughout development. Due to destruction of the adrenal cortex, patients with Autoimmune Addison’s disease (AAD) lack production of adrenal hormones and therefore receive lifelong replacement of cortisol and aldosterone, and for some female patients dehydroepiandrosterone (DHEA). However, replicating the natural rhythm of secretion is difficult, and patients are often exposed to either supra- or infra-physiological adrenal hormone levels. Such long-term hormonal disturbances might be expected to affect the brain on both a structural and functional level. Assessing brain structure in patients with AAD is an alternative approach that aims to balance tumor removal while maintaining adrenal function, although the oncological completeness of the procedure is questionable.

Objective
The aim of this systematic review and meta-analysis was to compare bilateral total adrenalectomy and partial (cortical-sparing) adrenalectomy.

Methods
A bibliographical search of databases (MEDLINE, EMBASE, Scopus, Web of Science, CENTRAL) as well as registers of clinical trials (ClinicalTrials.gov, European Trials Register, WHO International Trials Registry Platform) was conducted in order to identify eligible studies. The databases and registries were searched from inception until August 14, 2021, and no language restrictions or dates were imposed. Both randomised controlled trials and observational studies comparing TA with PA in adults with bilateral pheochromocytoma were considered for inclusion in this study. The primary outcomes were the risk of pheochromocytoma recurrence and steroid dependence. The secondary outcomes of interest were: time to recurrence after surgery, development of metastatic pheochromocytoma, incidence of adrenal crisis, morbidity, overall mortality and pheochromocytoma-specific mortality.

Results
Twenty five retrospective observational studies including 1444 patients were eligible. During follow-up, every third patient after PA required steroid supplementation: RR 0.32, 95% CI: 0.26–0.38, P < 0.00001, I² = 21%. Patients undergoing partial adrenalectomy had lower risk of developing Addisonian-like crisis: OR 0.3, 95% CI: 0.1–0.91, P=0.03, I²=0%. On the contrary, PA was associated with higher risk of recurrence than TA: OR 3.72, 95% CI: 1.54–8.96, P=0.003, I²=28%.

Conclusion
Patients undergoing partial adrenalectomy had a three-fold lower risk of developing steroid dependence and developing an adrenal crisis, but had a higher risk of recurrence. Thus, partial adrenalectomy may be worth considering in some patients with bilateral pheochromocytoma only with careful lifelong follow-up. Our findings are based on limited certainty evidence, and further well-designed, multi-center studies are required to confirm the benefits and drawbacks of both approaches.

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P520
Cortical-sparing adrenalectomy for bilateral pheochromocytoma - is it a game worth the candle? Systematic review with meta-analysis comparing total vs partial adrenalectomy in bilateral pheochromocytoma
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Background
Bilateral total adrenalectomy (TA), despite causing persistent adrenal insufficiency with lifetime replacement of corticosteroids, is the method of choice in patients with bilateral pheochromocytoma. Partial adrenalectomy (PA) is an alternative approach that aims to balance tumor removal while maintaining adrenal function, although the oncological completeness of the procedure is questionable.

Objective
The aim of this systematic review and meta-analysis was to compare bilateral total adrenalectomy and partial (cortical-sparing) adrenalectomy.

Methods
A bibliographical search of databases (MEDLINE, EMBASE, Scopus, Web of Science, CENTRAL) as well as registers of clinical trials (ClinicalTrials.gov, European Trials Register, WHO International Trials Registry Platform) was conducted in order to identify eligible studies. The databases and registries were searched from inception until August 14, 2021, and no language restrictions or dates were imposed. Both randomised controlled trials and observational studies comparing TA with PA in adults with bilateral pheochromocytoma were considered for inclusion in this study. The primary outcomes were the risk of pheochromocytoma recurrence and steroid dependence. The secondary outcomes of interest were: time to recurrence after surgery, development of metastatic pheochromocytoma, incidence of adrenal crisis, morbidity, overall mortality and pheochromocytoma-specific mortality.

Results
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P521
Inflammation in Hypertensive Patients with Type 2 Diabetes on Stable Therapy with Non-dipper and Dipper Status
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Background
Hypertension has a negative effect on the cardiovascular system, but the data are limited about the connection between non-dipper hypertension and inflammation in patients with type 2 diabetes (T2D) and without.

Aim
To study the effects of dipper and non-dipper hypertension with and without type 2 diabetes on inflammatory factors.

Methods
The cross-sectional study included 97 hypertensive patients (57 men) without 2 diabetes on inflammatory factors. During follow-up, every third patient after PA required steroid supplementation: RR 0.32, 95% CI: 0.26–0.38, P < 0.00001, I² = 21%. Patients undergoing partial adrenalectomy had lower risk of developing Addisonian-like crisis: OR 0.3, 95% CI: 0.1–0.91, P=0.03, I²=0%. On the contrary, PA was associated with higher risk of recurrence than TA: OR 3.72, 95% CI: 1.54–8.96, P=0.003, I²=28%.

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Conclusion
Patients undergoing partial adrenalectomy had a three-fold lower risk of developing steroid dependence and developing an adrenal crisis, but had a higher risk of recurrence. Thus, partial adrenalectomy may be worth considering in some patients with bilateral pheochromocytoma only with careful lifelong follow-up. Our findings are based on limited certainty evidence, and further well-designed, multi-center studies are required to confirm the benefits and drawbacks of both approaches.

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Hypertension has a negative effect on the cardiovascular system, but the data are limited about the connection between non-dipper hypertension and inflammation in patients with type 2 diabetes (T2D) and without.

Aim
To study the effects of dipper and non-dipper hypertension with and without type 2 diabetes on inflammatory factors.

Methods
The cross-sectional study included 97 hypertensive patients (57 men) without type 2 diabetes and 85 hypertension patients with type 2 diabetes median age 56,5 (45.00 ÷ 63.70) years old. All patients had been on stable antihypertensive and anti-hyperglycemic therapy during the last three months and had target ambulatory blood pressure at the moment of inclusion to the study. Daily blood
pressure monitoring was done to all patients with Hecao ABPM50 monitoring. Fasting glucose (FG), blood lipids, creatinine, uric acid, high sensitive C-reactive protein (hsCRP), and interleukin 1 beta (IL-1β) were measured. Physical activity was assessed using the International Physical Activity Questionnaire. Data were analyzed with SPSS IBM 19.0.

Result

According to their night blood pressure, the patients were divided into dipper (n = 84) and non-dipper (n = 98). The mean of day and night systolic and diastolic blood pressure according to the group presented in table 1. The mean of hCRP in dipper patients with T2D was 7.7 ± 8.4 and IL-1b 2.3 ± 0.5 pg/ml, non-dipper hCRP 11.4 ± 6.7 mg/L (p < 0.05) and IL-1b 2.2 ± 0.6 pg/mL (p < 0.05). The mean of hCRP in dipper patients with T2D was 12.2 ± 7.9 mg/L and IL-1b 2.3 ± 0.5 and non-dipper hCRP 10.2 ± 5.5 (p < 0.05) and IL-1b 2.7 ± 0.7 pg/mL (p < 0.05).

Conclusion

Non-dipper hypertension patients without type 2 diabetes could be an additional risk factor of vascular inflammation. Patients with type 2 diabetes and hypertension have a higher inflammation level, independent of dipper status; future studies are needed.

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### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Daily SBP</th>
<th>Day DBP</th>
<th>Diabetic (DBP)</th>
<th>Daily SBP</th>
<th>Daily DBP</th>
<th>Night SBP</th>
<th>Night DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipper (n = 54)</td>
<td>128.3 ± 15.7</td>
<td>70.0 ± 10.0</td>
<td>132.3 ± 15.4</td>
<td>79.1 ± 10.2</td>
<td>114.3 ± 16.4</td>
<td>65.9 ± 8.9</td>
<td></td>
</tr>
<tr>
<td>Non-Dipper (n = 53)</td>
<td>128.4 ± 17.4</td>
<td>74.2 ± 9.4</td>
<td>130.0 ± 16.0</td>
<td>75.2 ± 8.8</td>
<td>123.6 ± 18.3</td>
<td>71.4 ± 10.6</td>
<td></td>
</tr>
<tr>
<td>Dipper with T2D</td>
<td>131.8 ± 13.9</td>
<td>81.9 ± 8.1</td>
<td>134.8 ± 14.7</td>
<td>84.6 ± 9.2</td>
<td>121.1 ± 21.5</td>
<td>72.8 ± 11.0</td>
<td></td>
</tr>
</tbody>
</table>

P523

A retrospective evaluation of the utility of overnight dexamethasone suppression tests in over 500 patients evaluated for hypercortisolism

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Background

Overnight dexamethasone suppression tests (ONDST) are conducted to investigate patients with symptoms suggestive of cortisol hypersecretion or if an adrenal incidentaloma is identified. Cortisol levels of 50 nmol/l and above following ONDST may be related to autonomous cortisol secretion (ACS) and require further investigation. Determining likely presence of ACS is essential given reported associations with type 2 diabetes mellitus (T2DM), obesity, cardiovascular disease and osteoporosis. ONDST are inherently prone to interference and false positive rates are high, often resulting in clinicians conducting multiple ONDST, with associated patient and service impacts. Our study assesses the outcomes from a large UK cohort who underwent ONDST.

Methods

560 unselected patients who underwent ONDST were retrospectively examined. Data were collected on indication, demographics including body mass index (BMI), biochemical results and comorbidities. A positive ONDST was considered any cortisol greater than or equal to 50nmol/l, further categorised into mild ACS (MACS) between 50-138nmol/l and probable ACS (>138nmol/l). Statistical analysis was conducted using Prism v9.3.1.

Results

62% of the cohort were female. Mean age was 57.3 years ± 17.1 (SD). Mean BMI was 30.5kg/m2 ± 7.2. 71.6% had an adrenal lesion as the indication for the test, with a further 16.3% undergoing ONDST for clinical suspicion. 28% had an unsuppressed cortisol on ONDST (greater than or equal to 50nmol/l), of these 6.1% were greater than 138nmol/l. 48% of patients with an unsuppressed ONDST underwent repeat testing with 90.7% of results remaining unsuppressed. 47 patients with unsuppressed ONDST had an ACTH level recorded, 25.5% had an ACTH less than 5ng/l (normal range 5-47ng/l). 89.8% had a Hba1c recorded, with 31.2% having a result greater than 48mmol/mol or known T2DM. BMI did not correlate with suppressed vs unsuppressed cortisol on ONDST. Of the 157 patients with an unsuppressed cortisol, 63.7% had a potential confounder including obesity, diabetes or depression.

Conclusion

Our data demonstrates that there are high rates of unsuppressed cortisol following ONDST. Given the large numbers of patients with adrenal incidentalomas now identified and assessed, this leads to significant increased demand on endocrinology outpatient appointments. We have also shown that repeated ONDST may be unnecessary given greater than 90% remained unchanged, and the majority of patients had a potentially irreversible confounder. Therefore, we would suggest that careful further evaluation of the likelihood of MACS following a positive ONDST, through additional biochemical and clinical investigation but without a repeat ONDST, is required prior to any clinic attendance.

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P524

HIF-2a is detrimental for the functioning of the adrenal medulla

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Introduction

Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), formerly known as type II enteropathy-associated T-cell lymphoma, is a rare and aggressive subtype of lymphoma of the gastrointestinal tract typically noted in Asian or Hispanic populations. Adrenal involvement as part of MEITL is extremely rare. Herein we present a patient of Greek origin with MEITL and bilateral adrenal metastases.

Case Presentation

A 74-year-old man presented with a 2-week history of right upper quadrant abdominal pain, decreased appetite and fatigue, as well as weight loss (10 kgs in 8 months). Abdominal CT imaging revealed heterogenous bilateral adrenal lesions (maximum diameter 11 cm on the left and 10 cm on the right, respectively). On clinical examination, there were no signs of cortisol excess, no skin pigmentation, no palpable lymph nodes and the abdomen was soft. Hormonal investigations revealed primary hypocalcemia (basal cortisol: 61 nmol/L; ACTH: 189 pg/ml) and treatment with hydrocortisone was initiated; twenty-four hour urine metanephrines were normal. Further investigations showed anemia and increased LDH (136 IU/L, normal values: 134-279), i2-microglobulin (4.99 mg/L, normal values: 0.97-2.64) and inflammation markers (ESR, CRP and ferritin). Primary bilateral adrenal lymphomas were suspected and fine needle biopsy of the left adrenal lesion was performed. Staging CT scans showed no brain or lung metastases but gastric wall thickening and infiltration of the right kidney by the adrenal mass were noted on the abdominal scan. Gastrscopy revealed a mucosal lesion with a micronodular ulcerated surface which was biopsied. Histology from both the adrenal and the gastric lesions was consistent with MEITL; Ki-67 was positive in approximately 80% of tumor cells. Bone marrow biopsy and aspiration did not show any signs of infiltration by the lymphoma. Treatment with high dose dexamethasone was initiated but the patient rapidly deteriorated. He developed sepsis with multi-organ failure and finally passed away before receiving combined chemotherapy.

Discussion

MEITL is a rare aggressive T-cell lymphoma arising from intestinal intraepithelial lymphocytes with a poor prognosis. Most often it involves the small bowel, particularly the jejunum and ileum, but it can also involve the colon or stomach, like our case. Involvement of the adrenal glands in patients with MEITL is extremely rare. To our knowledge, this is the second report of MEITL with bilateral adrenal metastases. Clinical experience, awareness and a multidisciplinary approach in such perplexing cases is required.

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The adrenal gland is a crucial regulator of numerous fundamental biological processes and its hormones are essential for maintaining homeostasis in normal and stressful situations. However, the impact of hypoxia signalling on the function of the adrenal remains poorly understood. During the past years, our research group has focused on enhancing our understanding of hypoxia pathway proteins (HPPs) in the different areas of the adrenal gland. Firstly, we described a crucial role for hypoxia inducible factor-1α (HIF-1α) during adrenal stenogenesis (Watts et al., JMM, 2021) and secondly, we demonstrated that HIF-2α is essential for the synthesis and release of catecholamines. Briefly, HIF-2α stabilization due to loss of prolyl hydroxylase domain protein-2 (PHD2) leads to reduced phenylethanolamine N-methyltransferase (PNMT) activity and consequent epinephrine synthesis. Simultaneously, HIF-2α mediated erythropoietin (EPO) production in renal EPO producing cells (REPs) stimulated excessive RBC formation (erythropoiesis) leading to hypoglycaemia and increased release of epinephrine from the adrenal medulla (Watts et al., JMM, 2022). 2MTA-SE Laboratory of Molecular Physiology, Budapest, Hungary; 1Institute of Enzymology, Research Centre for Natural Sciences, Budapest, Hungary

Angiotensin II (AngII) is an octapeptide hormone, which participates in physiological and pathological mechanisms. AngII exerts a number of biological effects through the type 1 angiotensin II receptor (AT1R). One of the main targets of AngII are vascular smooth muscle cells and its stimulation activates numerous signaling pathways that cause contraction and could also result in gene expression changes in vascular smooth muscle cells (VSMCs). Next-generation sequencing (NGS) experiments were performed to analyze the effects of AngII stimulation on gene expression in VSMCs. The experiments were conducted using a rat aortic primary isolated VSMC cell line. In our experimental set-up more than 200 genes were upregulated in response to AngII stimulation in VSMCs. The transcriptome analysis revealed the upregulation of several DUSP genes, such as DUSP5, 6, 10, 4, and 14. We also investigated the kinetics of the gene-expression changes and the signaling pathways involved in AngII-mediated responses. The results of the quantitative PCR measurements also confirmed the increased expression of selected genes upon AngII stimulation. Transcription of most genes was largest two hours after AngII stimulation. Based on our results, the regulation of the studied gene expression induced by AngII is much more complex than we originally thought, due to the multiple signaling pathways that mediate them. We assume that the regulation of expression changes is probably determined by the interaction of the involved signaling cascades. Based on our data, the expression changes of the studied genes can occur through classical Ca2+-mediated activation, which triggers Ca2+-mediated mechanisms leading to epidermal growth factor receptor transactivation dependent or independent responses. During the search of the signaling pathway(s) which is/are responsible for certain gene-expression changes, we found that dasatinib, an Src-family tyrosine kinase inhibitor, was able to selectively inhibit the AngII induced gene-expression changes. We have also demonstrated that the imatinib, a selective inhibitor of Bcr-Abl kinases, was not able to achieve the similar effect as the dasatinib. Our data suggest that Src-family tyrosine kinase(s) may play an important role in AngII-induced long-term cellular responses. Our data can provide new insight into the physiology of VSMCs in response to AngII stimulation, and better understanding of the mechanism of AT1-R-mediated gene expression changes in primary VSMCs, which may lead to the development of novel types of drugs for the treatment of cardiovascular and other diseases. This work was supported by the National Institute for Diabetes and Cancer, Helmholtz Zentrum Muenchen, Neuherberg, Germany

P526 Testosterone, hypogonadism, and heart failure: a systematic and critical review
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Background Male hypogonadism is defined by low circulating testosterone level associated with signs and symptoms of testosterone deficiency. Although the bidirectional link between hypogonadism and cardiovascular disease has been clarified recently, the association between testosterone and chronic heart failure (CHF) is more controversial.

Methods We critically reviewed published studies relating to testosterone, hypogonadism, and CHF and provide practical clinical information on the correct diagnosis and treatment of male hypogonadism in patients with CHF.

Results In general, the published studies are extremely heterogeneous, they frequently have not adhered to hypogonadism guidelines, and they suffer from many intrinsic methodological inaccuracies; therefore, the data have low-quality evidence. Nevertheless, by selecting the very few studies that are methodologically robust, we show that the prevalence of testosterone deficiencies (30-50%) and symptomatic hypogonadism (15%) in men with CHF is significant. Low testosterone correlates with CHF severity, NYHA class, exercise functional capacity, and a worsened clinical prognosis and mortality. The interventional studies on testosterone treatment in men with CHF are inconclusive, but promising in suggesting beneficial effects on exercise capacity, NYHA class, metabolic health, and cardiac prognosis.

Discussion We suggest that clinicians should measure the testosterone levels of men with CHF who have symptoms of a testosterone deficiency and/or conditions that predispose to hypogonadism, such as obesity and diabetes. These patients - if diagnosed as hypogonadal - could benefit from the short- and long-term effects of TRT, which include improvements to both the cardiological prognosis and systemic outcomes. Further studies with a strong collaboration between cardiologists and endocrinologists are warranted.

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P528
The role of neuropeptide Y in the pathogenesis of vasovagal syncope
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Introduction
Vasovagal syncope (VVS) is a transient loss of consciousness due to hypoperfusion of the brain caused by vasodepressor and/or cardioinhibitory reflex. In the pathogenesis, a dysregulation of autonomic nervous system is playing an important role. There is a growing evidence about more complex neurohumoral background of VVS. Neuropeptide Y (NPY) is hormone involved in the regulation of blood pressure with potent vasoconstriction effect. Moreover, NPY is also a cotransmitter with noradrenaline in sympathetic nerve system and is considered to be involved in sympathetic-induced vasoconstriction. Other vasoactive hormones such as endothelin (ET-1) and angiotensin (ANG) can be implicated in pathogenesis of VVS, too.

Aim
The aim of this study was to evaluate the serum levels of NPY before and after head up tilt test (HUTT) and to compare them between patients with tilt induced VVS and group of negative individuals. Second aim was to find a correlation between NPY and other vasoactive hormones – ET-1 and ANG.

Subjects and methods
Altogether 69 subjects were included in this preliminary study (age 39±3.2 years; 41 females) with the history of at least one syncope. HUTT was performed in all subjects according to Italian protocol (20 minutes of passive standing followed by 15 minutes lasting phase after provocation by sublingual nitroglycerin). According to the result of HUTT, patients were divided into HUTT-positive (HUTT+) and HUTT-negative (HUTT-) group. Blood samples were collected before and immediately after HUTT. Serum levels of NPY, ET-1 and ANG were evaluated by ELISA method.

Results
HUTT was positive in 60 patients (HUTT+ group), 29 subjects were negative (HUTT-) group. There was no significant difference in basal levels of NPY between HUTT+ and HUTT- group (36.4±2.4 vs 40.1±1.5 ng/ml; P=0.1, T=1.5). The stimulated levels of NPY were significantly lower in HUT+ patients when compared to HUT- (36.7±2.1 vs 44.1±3.2 ng/ml; P=0.028, T=2.0). Both subgroups did not differ in ET-1 and ANG levels. Stimulated NPY levels positively correlated with stimulated ET-1 (P=0.001; R2=0.16) and ANG (P=0.04; R2=0.06) in all subjects. When divided into HUT+ and HUT-, NPY significantly correlated only with ANG (P=0.004; R2=0.41) in HUT+ group, while in HUT- patients, there was a positive correlation with ET-1 (P=0.0009; R2=0.23) found.

Conclusion
The impaired release of NPY may play a role in pathogenesis of VVS. Other vasoconstrictive hormones, such as ET-1 and ANG, can be involved in pathomechanism, too.

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P529
Characteristics of patients with life-threatening events in pheochromocytoma
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Introduction
Pheochromocytomas and paragangliomas (PPGLs) are rare tumors of the chromaffin tissue characterised by catecholamine excess. Cardiovascular complications, such as hypertensive crisis and catecholamine-induced cardiomyopathy, are known to be the most frequent causes of life-threatening events in PPGLs patients.

Design
We analysed records of patients diagnosed with PPGL in one referral centre from Romania between 1976 and 2021 (n=106) in order to compare demographics, symptoms, preoperative catecholamine levels, tumor diameter and outcome in patients with life-threatening events vs. patients without complications (control group).

Results
9 patients (8.4%), 8 F, 1 M presented life-threatening events before the diagnosis or during surgery for PPGL: catecholamine-induced Takotsubo cardiomyopathy (n=3); inverted Takotsubo cardiomyopathy and pulmonary edema (n=1); acute coronary syndrome and pulmonary edema (n=2); pulmonary edema (n=1); cardiac arrest and pulmonary edema (n=1); pulmonary thromboembolism and feto-placental apoplexy (n=1). Seven patients had the life-threatening event before or during diagnosis of PPGL and two of them had the complications during surgery for PPGL. Compared to pheochromocytoma patients without life-threatening events (n=97), patients with severe complications had a nonsignificantly higher mean tumor diameter (53 vs. 48 cm; P=0.3), similar levels of catecholamine (median 5.6 fold ULN; P=0.5), similar age at diagnosis (50 vs. 47 years; P=0.51). The maximum arterial blood pressure before surgery was non-significantly higher in patients with complication (231 vs. 207 mmHg; P=0.1). All patients with complications survived. Patients with Takotsubo cardiomyopathy had normal cardiac function few days after the event. One patient with acute coronary syndrome and pulmonary edema but a background of other cardiac comorbidities had the ejection fraction of 40% after this event. The woman with feto-placental apoplexy had a negative outcome: her baby died in uterus and she underwent hysterectomy at 34 years old.

Conclusion
Although pheochromocytomas are rare tumors, they may induce a life-threatening complications (diagnosed in 8.4% of cases in our series). There was no specific clinical, hormonal or imaging feature that could predict a life-threatening event in patients with PPGLs.

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P530
Objective markers and new indicators in adrenal insufﬁciency- findings from the omni-aid study comparing hydrocortisone and prednisolone replacement therapy
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Background
Adrenal insufﬁciency (AI) is a life-threatening condition if left unmanaged. Despite treatment patients can expect a life expectancy that is shortened by 12 years secondary to probable inherent over-replacement associated with oral glucocorticoid regimens. Thrice-daily hydrocortisone is the most common regimen used. Very low-dose prednisolone (2-4 mg) is an alternative with lower uptake due to the absence of evidence for its use. This study ﬁlls this literature gap.

Methods
This is a cross-sectional, observational study that recruited 20 healthy volunteers (HV), 20 AI patients on prednisolone, 20 AI patients on hydrocortisone and 9 patients on anti-inflammatory doses of steroids (mainly IV methyl-prednisolone) for other medical conditions. During stereotyped study visits, subjects provided anthropometric data, blood samples, urine samples and SF-36 data. This was used to assess bone health, cardiovascular risk, diabetic risk, immune cell proﬁles and subjective health between groups.
P531

Long-term efficacy and safety of pasireotide in patients with Cushing’s disease: a monocentric experience

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Pasireotide is the first pituitary-directed approved therapy for Cushing’s disease (CD), effective in reducing UFC >50% in about half of patients, and with a good tolerability profile but associated with a relatively high incidence of hyperglycemia. The aim of this study was to evaluate efficacy and safety of long-term treatment with pasireotide (PAS) in patients with CD. Methods: We retrospectively evaluated 17 consecutive patients (16 males, 1 female) with CD treated with PAS (with a mean follow of 40.4±12.5 months), referred to and followed-up at the Endocrine Unit of the University Hospital of Messina (Italy), from 2013 to 2020. Data are expressed as mean±SD. Age at diagnosis was 34.7±13.0 yrs. Before PAS treatment: all patients underwent transnasosphenoidal pituitary adenomectomy, but surgery was not successful in 10 cases, while disease recurred in the other seven; five patients underwent also radiotherapy; seven patients were administered other medical therapies. Anthropometric, clinical, hormonal and metabolic (glucidic and lipidic profile) parameters were evaluated, along with cardiometabolic CD-related comorbidities, before PAS treatment and at last follow-up visit. Side-effects and adverse events related to treatment were also evaluated.

Results

Before PAS treatment, 47% of patients were obese, 59% were dyslipidemic, 47% had diabetes, and 53% were on anti hypertensive treatment. Under PAS treatment, 76% of patients achieved a normalization or ≥50% reduction of UFCx1LN from baseline. At last follow-up visit as compared to baseline: body weight, BMI, waist-to-hip ratio, waist circumference, systolic and diastolic blood pressure decreased but were not significantly different (p NS); lipid profile significantly improved (total and LDL cholesterol, p 0.007 and p 0.001 respectively); glyced hemoglobin significantly increased (p 0.02). In terms of safety profile, most common adverse events were related to hyperglycemia and to difficult-to-manage diabetes mellitus (41%), which led to treatment withdrawal in 4 cases. No patient experienced QTC interval prolongation.

Conclusion

Pasireotide is a safe and effective treatment in a significant figure of patients with CD, improving also lipid profile, while frequently causing glucose metabolism alterations which represent a cause of therapy discontinuation.

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P532

Coronavirus disease caused by SARS-CoV-2 virus (Covid-19) is associated with a variable clinical syndrome, ranging from a mild-moderate to a severe disease, progressing towards acute respiratory distress syndrome. Hypocortisolism is associated with a depletion of innate immunity and disruption of immune response, which could contribute to an increased risk of infection and development of a severe disease. Glucocorticoid (GC) replacement therapy (GCRT), especially if administered in a non-circadian fashion, may result in immunosuppression favouring infection and disease progression. Sick day rules for GCRT during infections are still largely tailored empirically. The aim of the current study was to investigate clinical syndrome and disease duration of Covid-19, and to evaluate GCRT adjustments, in a cohort of patients with hypocortisolism who developed Covid-19. The study was performed on 20 patients [12F, 8M, 16-62 years (39.2±12.5), 11 adrenal insufficiency (AI), 9 congenital adrenal hyperplasia (CAH)], adequately treated with GCs (hydrocortisone equivalent doses, HC-Eq: 10-45 mg/day (27.2±10.09)). A purpose-built questionnaire was administered by a phone-survey, aimed at assessing Covid-19 signs and symptoms, disease duration, the occurrence of adrenal crises, the need of GCRT adjustment, and intervention for Covid-19 (antibiotics, GCs, oxygen therapy, and hospitalization), as well as persistent clinical syndrome of Covid-19 after the disease cure (Long-Covid). The most frequent symptoms and signs were ageusia (75%), anosmia (70%) and fever (70%). Additional symptoms and signs were myalgia (65%), fatigue (60%), headache (50%), cough (50%), dyspnea (30%), and diarrhea (25%). The disease duration was of 11-49 days (25.3±9.71) and no adrenal crises were reported. To manage hypocortisolism, according to general sick day rules, six (30%) patients doubled oral dose of GCRT for 2-8 days (11±9.28) and no patients used parenteral GCs. To manage Covid-19, nine (45%) patients received antibiotics for 5-10 days (7.2±2.16) (azithromycin 500 mg/day (55.6%), cefixime 400 mg/day (22.2%) and amoxicillin-clavulanic acid 1750/250 mg/day (22.2%)); four (20%) GCs for 7-17 days (10.25±4.71) (methyl-prednisolone 4 mg/day (25%), deflazacort 6 mg/day (25%), betamethasone 1 mg/day (25%) and prednisone 25 mg/day (25%); HC-Eq. 20-100 mg/day (41.66±39.01)), but no patients required oxygen therapy or hospitalization. No fatal events were observed over the Covid-19 period. The most frequent Long-Covid symptoms and signs were fatigue (30%), anosmia (15%) and ageusia (10%). No significant differences were observed comparing females and males, as well as AI and CAH patients. In conclusion, patients with hypocortisolism, adequately treated with GCs, display a mild-moderate Covid-19 disease course, mainly characterized by ageusia, anosmia and fever, without severe complications and adrenal crises, and requiring a double dose of oral GCRT in less than one third of cases. Different GCs in a minority of cases, and not requiring oxygen therapy and hospitalization, with persistent fatigue, anosmia and ageusia as the most common Long-Covid manifestations.

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P533

Renin indicates the mineralocorticoid activity of fludrocortisone: a 6-year study in primary adrenal insufficiency

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Context

Fludrocortisone (FC) is the mineralocorticoid (MC) replacement treatment for patients with primary adrenal insufficiency (PAI).

Objective

To explore the dose of FC treatment and its relationship with glucocorticoid therapy, sodium, potassium, renin and clinical parameters.

Design

Longitudinal study.

Setting

Monocentric cohort.

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Patients
Data of 193 patients with PAI (130 autoimmune) were collected during baseline (T0), intermediate (T1) and last follow-up visit (T2, respectively after 38 and 35 months).
Main Outcome Measure
Utility of endocrine and clinical parameters to titrate FC dose.
Results
FC dose (50-75 μg/daily) was stable in the follow-up in half patients. The MC activity of FC was dose-dependent: we observed a positive linear correlation between FC dose and sodium (r = 0.132) and negative linear correlation between FC and potassium (r = -0.162) or renin (r = -0.131, all P < 0.01). An overall reduction in the FC dose was observed at T2 in the group with longer follow-up (> 60 months, P < 0.05). Higher doses of FC were observed in patients with low-renin, especially in autoimmune PAI (86 vs 65 μg/daily, P < 0.05). On the contrary, reduced sodium and increased potassium levels were observed in patients with high renin at T2. The number of cardiovascular events (15 in the whole cohort) was similar in patients sorted by renin levels or FC dose.
Conclusions
Renin and electrolytes are marker of MC activity: they should be routinely evaluated and used to titrate FC treatment, because FC dose can be reduced in the late follow-up.
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P534
Reevaluation of the 1-mg overnight low-dose dexamethasone suppression test in the diagnosis of Cushing’s syndrome
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Introduction
The 1-mg overnight low-dose dexamethasone suppression test is used as a screening tool when Cushing’s syndrome is suspected. However, the biological confirmation of this syndrome is based upon the measurement of 24-hour urinary free cortisol and low-dose dexamethasone suppression test (Liddle test). The aim of this study was to assess the performance of the 1-mg overnight low-dose dexamethasone suppression test in the diagnosis of Cushing’s syndrome.
Methods
This was a retrospective study including patients admitted to our department for suspicion of Cushing syndrome between 2016 and 2021. Clinical and paraclinical data and results of 1-mg overnight low-dose dexamethasone suppression test and Liddle test were collected from medical records.
Results
Fifty-one patients (39 women and 12 men) were enrolled in this study with a mean age of 54.3 ± 15.4 years. The diagnosis Cushing’s syndrome was established in 28 patients and excluded in 23 patients. The median serum cortisol level after the 1-mg test was 7.65 μg/dL in patients with Cushing’s syndrome and 2.1 μg/dL in those without Cushing’s syndrome (P = 0.001). It was positively correlated with serum cortisol level after the Liddle test (r = 0.852, P < 10^-3) and ACTH level (r = 0.621, P = 0.001). The area under the ROC curve of serum cortisol level after the 1-mg test was 0.773. A cutoff value of 1.8 μg/dL had a sensitivity of 100% and a specificity of 26%. A cutoff value of 5 μg/dL was associated with the diagnosis of Cushing syndrome (Odds Ratio = 4.11, P = 0.016) with a sensitivity of 64% and a specificity of 70%. A cutoff value of 9.9 μg/dL confirmed the diagnosis of Cushing’s syndrome in 100% of cases.
Conclusion
With a cutoff value of 1.8 μg/dL, the 1-mg overnight low-dose dexamethasone suppression test is a reliable screening tool for Cushing’s syndrome. However, a higher cutoff value for serum cortisol (9.9 μg/dL) can be used alone to confirm the diagnosis. Further studies involving larger sample sizes would be useful to confirm our findings.
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P535
Minimally invasive treatment of Conn’s adenoma: real world cases in tertiary oncology center
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Introduction
Primary aldosteronism (PA) is a rare but underestimated cause of hypertension. PA has been associated with increased risk of malignancy through mechanisms involving up-regulation of the renin angiotensin system (RAS) promoting an enzymatic cascade influencing carcinogenesis. Recently, Microwave Ablation (MWA) has been established as an effective and safe minimal invasive treatment for Conn’s Disease.

Aim
The authors present four clinical cases of successful treatment of PA with MWA in an oncological setting.

Patients and Methods
Retrospective review of patient’s files.

Results
Four women (mean age 55y; 37-67) with pre-diagnosed cancer (1 papillary thyroid carcinoma, one with both gastric carcinoma and Chronic Lymphocytic Leukaemia, one colon carcinoma in context of hereditary syndrome and one breast carcinoma) were evaluated in the Endocrinology Department of IPOFG Porto, either for hypertension and/or hypokalemia and adrenal nodules compatible with adenoma on imaging studies. One patient (pt.) was already treated with spironolactone because of low-renin aldosteronism due to long-term, poorly diagnosed PA. Renin/aldosterone tests confirmed PA in one pt. In two other pts. the diagnosis was based on the normalization of PA and potassium after spironolactone treatment as diagnosis was made under active cancer treatment. All the 4 pts. were submitted to adrenal adenoma MWA performed by the same Interventional Radiology skilled specialist. Soon after the procedure that occurred without peri-procedure complications, blood pressure and potassium normalized. Re-evaluation of the renin/angiotensin tests out of cancer treatment revealed normal aldosterone and renin levels. After a mean follow-up of 34 months (15-54) there is no evidence of recurrence and/or adrenal insufficiency.

Conclusion
MWA seems to be a long-term effective and safe alternative for the treatment of Conn’s adenomas, which is very important in the oncological setting. PA must be excluded in the evaluation of cancer patients with refractory hypertension and/or hypokalemia and adrenal incidentaloma. Orthodox evaluation of PA through traditional tests should be questioned in oncological pts. on active cancer treatment as it can interfere on test results and withdrawing of anti-hypertensive therapies may not be advised.

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P536
Glucocorticoid resistance syndrome : Case report
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Introduction
Glucocorticoid resistance syndrome is a rare disease, sporadic or familial, of autosomal dominant or recessive inheritance. It is a partial or complete inability of glucocorticoids to exert their effects on target tissues. Associated with compensatory increases in corticotropin and circulating cortisol with excessive secretion of adrenal androgens and mineralocorticoids.

Observation
A 67-year-old patient, having recently discovered diabetes started on insulin then on metformin 1g /day, hypertensive for 1 year on angiotensin 10 mg / day, with no personal or family endocrinopathy. Having presented a month before his admission tremors of the extremities, with muscular weakness, and walking disorders. All in a context of weight loss and asthenia. On examination, the patient did not present with clinical cushing syndrome. The results showed a persistent hypokalemia at 1.9 mmol/l despite potassium supplementation, a hypernatremia at 147 mmol/l. On the overnight 1mg-Dexamethasone suppression test, cortisol levels were high to 25.7 μg / dl. A high urinary free cortisol 1610 μg / 24 h (20-50), with ACTH at 408 pg / l (5-60), the pituitary MRI did not reveal any abnormality. The bone densitometry was normal. The diagnosis of glucocorticoid resistance syndrome was retained and the patient was placed on dexamethasone 2 mg / day with a good clinical course, in particular a notable improvement in asthenia, and biological improvement with normalization of serum potassium. Furthermore, the patient presented with hypercalcemia due to...
primary hyperparathyroidism having undergone resection of the parathyroid adenoma with good progress. The anato-mopathology did not objectify signs of malignancy

Conclusion
Glucocorticoid resistance syndrome is a rare and often unrecognized condition. This should be considered in case of chronic asthena associated with hypokalaemia in the context of excess cortisol without clinical cushing syndrome.

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**P537**
Management of persistent subclinical hypercortisolism post left adrenalectomy in a patient with primary bilateral macronodular adrenal hyperplasia with aberrant receptors

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Introduction
Endogenous subclinical hypercortisolism occurs in 5-30% of patients with adrenal incidentalomas. Adrenal adenoma is the commonest cause of autonomous cortisol secretion (ACS), while primary bilateral macronodular adrenal hyperplasia (PBMAH) is rare. In both, ACS results from activation of the cAMP/PKA pathway. This may be triggered by ligands, other than ACTH, acting upon aberrant G-protein coupled receptors (GPCRs), which may also control locally produced ACTH in paracrine/autocrine fashion. In this setting, diagnosis is challenging due to intermittent hypercortisolism and fluctuations of ACTH level.

Case presentation
We present the case of a 65-year old lady with large bilateral adrenal incidentalomas and imaging features compatible with adenomas. Initial hormonal work-up revealed ACS (cortisol post low dose dexamethasone suppression test (LDDST): 13.92 mg/dl, midnight salivary cortisol: 0.8 mg/dl, ACTH=9.2 pg/ml). She was not Cushingoid, but had obesity, osteoporosis, hypertension and anxiety disorder. On accounts of the size of her left adrenal adenoma (4.9 x 1.9 cm), she underwent unilateral adrenalectomy. Initial histology demonstrated adrenal adenoma (Weiss score 0/10). During hormonal follow-up, she had persistent hypercortisolism with fluctuating plasma ACTH level (11.5-44.2 pg/ml). Considering the latter, we proceeded to pituitary magnetic resonance imaging, which showed a 3mm incidentaloma. At this point, we repeated LDDST with ACTH measurement: despite adequate ACTH suppression (2.2 pg/ml) cortisol was unsuppressed (6.26 mg/dl). Thus, ACS was confirmed. Imaging-wise, the size of her right adrenal adenoma increased from 4.2 x 1.6 cm to 4.8 x 2.2 over 3 years. Pathology review of the resected left adrenal revealed absence of neoplastic adrenal tissue and extended nodular appearance, establishing PBMAH diagnosis. Dynamic testing for aberrant receptors post dexamethasone suppression was performed, demonstrating partial response to posture (25%) and meal (26%). In the absence of overt hypercortisolism and given that PBMAH is a benign condition, we considered medical treatment as more appropriate. To control hypercortisolism, we modified hypertension regime to pranolol and valsarnat with later addition of low dose of metapyrone.

Conclusions
Patients with bilateral adrenal adenomas may represent PBMAH, in which aberrant receptor expression is present in 80% of cases. The recognition of aberrant receptor-mediated hypercortisolism in patients with PBMAH and unilateral adenomas is important as it may lead to targeted therapies. In this context, b-blockers, angiotensin II blockers, OnRH and somatostatin analogues have been used. Additionally, steroid enzymes inhibitors were found to restore normal circadian secretion of cortisol. Nevertheless, existing data originate from small case series and larger prospective studies are needed.

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**P538**
Primary adrenal angiosarcoma within a hematoma

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Introduction
Angiosarcomas account for < 1% of all sarcomas, and are highly aggressive neoplasms whose clinical course is striking: local recurrence, metastasis, and a high mortality rate. Primary angiosarcoma of the adrenal gland was first described in 1988 by Karet et al. and is very rare, with so far, only 51 reported cases. Case report
A 49-year-old male, without prior malignancy, presented with a 4.9x5.9 cm right adrenal nodule and a 2.4 cm lesion at L1 both found incidentally on a chest CT. His mother died with lung cancer. Physical examination was unremarkable. Routine lab tests were within the normal range. Serum aldosterone, renin, DHEAS, cortisol post 1 mg dexametason supression test, 24H urinary catecholamines and metanefrines were normal; 24H urinary normetanephrine was slightly elevated. An abdominal MRI confirmed a heterogeneous lesion 5.5x4.7x4.4 cm on the right adrenal gland with areas of possible hemorrhage. An MRI of the column revealead a 2.1x1.3x2.2 cm lesion at L1 without agressive features. No uptake was shown at MIBG scan. Right laparoscopic adrenalectomy was done. The adrenal gland (76 g and 8.2x5.8x3.4 cm) disclosed a 4.0x2.6x5.0 cm well defined mass with hemorrhagic areas. On microscopic examination, the mass consisted mostly of hematoma and scattered small agregates of cytologically atypical epithiloid cells with amorphic cytoplasm, irregular vesiculellar nuclei with variably prominent nucleoli and some mitoses; the cells were diffusely positive for CD31 and ERG. The features are characteristic of epitheloid angiosarcoma. After surgery, a FDG-PET scan disclosed 2 foci of uptake, one on the right thyroid lobe (SUV max 3.7) and the other at the L1 lesion (SUV max 3.2). The cervical US revealed a heterogeneous thyroid gland with characteristics of thyroiditis. Anti micrososomal antibodies positive, TSH normal. A biopsy of the L1 lesion did not reveal malignancy. Because there were complete resection margins and no metastatic foci were found no adjuvant chemotherapy was done. The patient has been kept under clinical and imagiological surveillance for three years with no further evidence of disease.

Discussion
Adrenal angiosarcoma is a very rare clinical entity with a propensity for local recurrence and metastasis and a median survival of 18 months. Noteworthy the prognosis is unpredictable but some times quite good as in this case.

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**P539**
Hypertension of adrenal origin - a never-ending story
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Background
Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors characterized by a high degree of variability and unpredictability. Coexistence of PPGLs and adrenocortical adenomas is an uncommon occurrence that can further complicate the clinical course.

Objective
We describe the diagnostic and management challenges of a patient with a history of surgically removed pheochromocytoma, presenting with symptoms of catecholamine excess, following a prolonged period of clinical remission.

Case Report
A 52 yo. female patient was admitted to our hospital for surgical cure of a left adrenal mass. She reports a history of right adrenal pheochromocytoma, excised 15 years before and resulting in clinical and biochemical remission. 15 months prior to presentation she started experiencing paroxysms of arterial hypertension, occurring every other day, accompanied by headache, palpitations, tremor, nausea and emesis. Abdominal CT showed a 3/2 cm left adrenal adenoma, while biochemical screening revealed elevated plasma normetanephrines (6x upper normal limit), along with normal metanephrines and chromogranin A. Renin-to-aldosterone ratio and cortisol diurnal variation were unaltered, but ACTH values were slightly decreased. Postoperatively, the patient was initially stable and exhibited normalized blood pressure under high-dose corticoid treatment, but on the 3rd day, as corticoid dosage was decreased, she developed an acute adrenal crisis. In spite of the initial suspicion of adrenal pheochromocytoma, Endocrine Abstracts (2022) Vol 81
histopathological and immunohistochemical examinations described an adrenal cortical adenoma. Unsurprisingly, noradrenephrines failed to normalize post-operatively; metanephrines and chromogranin A also became marginally elevated and symptoms recurred. MRI examination of the head and neck was negative. Interestingly, the patient now also described lumbosacral warmth accompanying the paroxysms. Octreoscan was performed, but revealed no areas of high uptake. Conversely, a metabolically active sacral lesion was described on PET-CT. MRI confirmed the presence of an osteolytic lesion (1.8/1.4/1.1 cm) in that area and described an additional similar adjacent lesion. These were interpreted as possible metastases of a malignant PPGL. Neurosurgical intervention was performed and a histopathological diagnosis of grade 1 WHO paraganglioma was established. The patient exhibited clinical remission postoperatively, along with the decline of all tumoral markers. However, 6 months later, in spite of imistic regression of the sacral lesions and lack of symptoms, both metanephrines and normetanephrines showed an upward tendency.

Conclusion

Long-term follow-up is mandatory in PPGLs, as clinical recurrence is possible even after prolonged periods of remission. Genetic testing can aid the diagnosis and management and should be ideally performed in all cases of recurrent/aggressive PPGLs.

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P540

Challenges and anxiety of fluctuating normal to mild/moderate elevations of urinary catecholamines and metanephrines in clinical practice

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We present a 70-year-old female who was initially referred to the endocrinology clinic for an assessment of her type 2 diabetes mellitus. She has a complex medical history including treated hyperthyroidism, mastectomy for breast cancer and ongoing clinic for an assessment of her type 2 diabetes mellitus. She has a complex medical history including treated hyperthyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing history including treated hypothyroidism, mastectomy for breast cancer and ongoing

Table 1 24-hour urinary catecholamines and metanephrines. RR = Reference Range.

<table>
<thead>
<tr>
<th>First urine collection</th>
<th>Second urine collection</th>
<th>Third urine collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metadrenaline (RR &lt; 1.2μmols/24hr)</td>
<td>Noradrenaline (RR &lt; 2.8μmols/24hr)</td>
<td>Metadrenaline (RR &lt; 2.6μmols/24hr)</td>
</tr>
<tr>
<td>Noradrenaline (RR &lt; 0.8μmols/24hr)</td>
<td>Metanephrines (RR &lt; 1622μmol/24hr)</td>
<td>Noradrenaline (RR &lt; 0.5μmols/24hr)</td>
</tr>
<tr>
<td>Noradrenaline (RR &lt; 2129μmol/24hr)</td>
<td>Noradrenaline (RR &lt; 4020μmol/24hr)</td>
<td>Noradrenaline (RR &lt; 0.82μmols/24hr)</td>
</tr>
<tr>
<td>Metadrenaline (RR &lt; 2.5μmols/24hr)</td>
<td>Adrenaline (RR &lt; 147nmol/24hr)</td>
<td>Dopamine (RR &lt; 3270nmol/24hr)</td>
</tr>
<tr>
<td>Metadrenaline (RR &lt; 3.3μmols/24hr)</td>
<td>Normetadrenaline (RR &lt; 3.7μmols/24hr)</td>
<td>Normetadrenaline (RR &lt; 3.7μmols/24hr)</td>
</tr>
</tbody>
</table>

Table 2 Repeat 24-hour urinary metanephrines

<table>
<thead>
<tr>
<th>Metadrenaline (RR &lt; 1.2μmols/24hr)</th>
<th>Noradrenaline (RR &lt; 2.6μmols/24hr)</th>
<th>Dopamine (RR &lt; 1.4μmols/24hr)</th>
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</thead>
<tbody>
<tr>
<td>0.38</td>
<td>2.66</td>
<td>1.41</td>
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Mortality in patients with non-functional adrenal tumors: a Swedish population-based national cohort study

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Background
It is not known if non-functional adrenal adenomas (NFAA) are associated with increased mortality.

Objective
To investigate mortality in patients with NFAA and compare with matched controls.

Design
Retrospective register-based national cohort study.

Methods
Patients diagnosed with NFAA in Sweden 2005-2019 were identified and followed until death or 2020. For each case, four age/sex/municipality-matched controls were identified. Individuals with diagnosis indicating adrenal hormonal excess or malignancy were excluded. Though, in some cases malignancy of another origin than adrenal glands was detected in conjunction with index date.

Statistical analysis was made both including and excluding these cases. Mortality study outcomes were all-cause 1 and 5-year mortality as well as causes of death after adjustment for comorbidities and socioeconomic factors.

Results
In total, 20390 patients with NFAA and 125392 matched controls were included. Median age at diagnosis was 65 years (IQR:16) and 59.1% were women. During follow-up, 4427 (21.7%) cases and 20480 (16.3%) controls had deceased. Among all patients with NFAA both 1-year and 5-year overall mortality was higher compared to controls (OR:6.79, aOR:5.38 and OR:2.66, aOR:2.03). After eliminating controls with detected malignancy at index date, both 1-year and 5-year overall mortality was still high (OR:2.64 (2.42-2.88), aOR:1.84 (1.68-2.01) and OR:1.69 (1.61-1.77), aOR:1.18 (1.12-1.25)). While all patients with known malignancy were excluded before and at index date, mortality due to new malignancy during the follow-up period was high: 1-year mortality OR 8.86 (7.54-10.42), aOR 8.04 (6.81-9.51) and 5-years mortality OR was 2.77 (2.55-3.01), aOR 2.43 (2.23-2.65). Moreover, 1-year mortality due to cardiovascular diseases was also increased (OR 2.02 (1.64-2.47), aOR1.33 (1.06-1.66), however 5-years mortality due to cardiovascular diseases was increased only before adjustment (OR 1.39 (1.24-1.57), aOR 0.88 (0.76-1.01), the latter was adjusted for, e.g., cardiovascular disease at index date). In total 1273 (28.8%) of controls deceased due to malignancy and 1023 (21.3%) due to cardiovascular diseases.

Conclusions
Patients with NFAA have significantly higher overall mortality rate, as well as mortality due to new malignancy diagnosed during the follow-up time when compared to controls.

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Whole blood transcriptomic profile of Cushing’s syndrome

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Background
Cushing’s syndrome, caused by an excess of circulating glucocorticoids, is associated with high morbidity and presents high inter-individual variability. The earlier the diagnosis, the better the treatment effectiveness and the prognosis. Hormone assays, routinely used, contribute to identify Cushing’s syndrome. However, no biomarker is currently available to directly quantify the biological action of glucocorticoids. Blood samples represent an easily obtainable source for profiling individuals on a molecular level. In this study, we analysed the transcriptomic profile in 59 blood samples from patients with different glucocorticoid states (overt or mild Cushing’s syndrome, eucortisolism, adrenal insufficiency).

Materials and methods
Total RNA was extracted from whole blood samples collected into PAXgene tubes. Transcriptome was determined by RNA sequencing performed on NovaSeq 6000 platform (Illumina). Blood cell proportions in each sample were estimated from expression profiles by using the CIBERSORT method. Unsupervised samples classification (PCA) was used to explore the transcriptomic profiles. A preliminary differential expression analysis was performed by using a linear model-based method (Limma).

Results
Unsupervised classification showed a discrimination of overt Cushing’s syndrome samples (accuracy: 0.81), presenting a specific profile compared to the other glucocorticoid states. This variability also associated with blood cell proportions, particularly with a higher neutrophils percentage. The most differentially expressed genes in the group of overt Cushing’s syndrome (n=3173 genes, with adjusted p-value <0.001) were enriched in pathways related to immunity, particularly to neutrophils activation and activity.

Conclusions
These preliminary results show that glucocorticoid excess associates with a specific whole blood transcriptomic profile. Further analyses will allow to identify a set of genes representing a specific molecular signature of glucocorticoid excess, which will take into account biological factors potentially involved, such as blood cell composition.

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Adrenal incidentaloma follow-up

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Introduction
About 5% of the adult population has adrenal incidentaloma (AI) and its incidence increases with age. AACE guidelines recommend imaging and hormonal evaluation during 5 years in non functioning AI. The European’s guidelines advise against repeat evaluation in non-secretory AI that present with <4 cm and had benign features. According to recent studies, the risk of developing clinically relevant hormone secretion is <0.3%, in patients with previous non-functioning lesions. The risk of progression to Cushing Syndrome in patients with autonomous cortisol secretion (ACS) is also low (<1%). This study evaluated the risk of developing hypercortisolism or tumor growth in AI of patients followed in an endocrinology department.

Methods
Retrospective study of patients with no functioning AI evaluated between 2014-2021 with a minimum follow-up of 3 years. ACS was defined based on post-dexamethasone cortisol value between 1.8-5.0 μg/dL. Significant tumor growth was defined as ≥10mm. Dimensional stability was considered if <5mm variation between successive imaging exams.

Results
Included 84 patients, 42.8% (n=36) female with a median of age of 76(48-93) years-old. At first evaluation the mean AI dimension was 20.9±7.5mm and 20 patients (23.8%) had bilateral tumors. After a mean follow-up of 5.6±1.5 years, each patient was submitted to a mean of 3±1.1 image exams. During follow-up, 2 patients (2.4%) developed ACS and none had been diagnosed with clinical Cushing syndrome. In 68 (81%) patients there was dimension stability, 7 had dimension reduction and 9 had increased size (≥5mm). In only 2 patients there was a significant growth: 1 cyst and 1 tumor that has been transformed to an hemorrhagic lesion (pseudocyst) and submitted to surgery.

Conclusion
In this study 2.4% of patients developed ACS. A ≥10 mm growth was only verified in 2 cysts. Adrenal Cysts are rare and usually asymptomatic. AI could suffer hemorrhagic or cystic degeneration and become pseudocyst. Our data are similar to a recent meta-analysis that report no relevant changes in dimension or hormonal function during follow-up of AI.

DOIs: 10.1530/endoabs.81.P544
Calcium and Bone

P30

COVID-19 lockdown negatively impacted on adherence to Denosumab therapy: incidence of non-traumatic fractures and role of telemedicine

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Background

Adherence to anti-osteoporotic therapy is fundamental to prevent harmful consequences including fragility fractures and, in the specific case of denosumab discontinuation, of rebound fractures. Coronavirus disease (COVID-19) lockdowns have impacted on management of osteoporosis, but data about adherence to denosumab and rebound fractures during the COVID-19 pandemic are still lacking.

The use of telemedicine is increasingly widespread albeit supported by little evidence so far.

Aim

To assess adherence to denosumab and incidence of non-traumatic fractures (fragility and rebound) during the lockdown year compared to the pre-COVID-19 period. Thereafter, this study aims to investigate the effectiveness of telemedicine in the management of osteoporotic patients with ongoing denosumab treatment.

Methods

Retrospective, longitudinal, single-center study on patients receiving subcutaneous denosumab therapy every 6 months. Each patient was scheduled to undergo 2 visits: one during the pre-COVID-19 period (March 2019 - March 2020) and another visit during the lockdown period (March 2020 – March 2021). Adherence was defined as being punctual (with an allowable delay of up to 4 weeks) with the injection being punctual (with an allowable delay of up to 4 weeks) with the injection

Results

The prevalence of non-adherent patients was significantly higher in the lockdown period (35 of 269 patients, 13.0%) than the pre-COVID-19 period (9 of 276 patients, 3.3%) (P < 0.0001). During the lockdown the number of new non-traumatic fractures was significantly higher than the pre-COVID-19 year (P < 0.0001). In particular, 10 patients out of 269 (3.5%) experienced a fragility fracture and 2 patients (0.7%) a rebound fracture during the lockdown period, whereas no patient had fragility or rebound fractures during the pre-COVID-19 period. No difference was found in the prevalence of non-adherence and new non-traumatic fractures comparing patients evaluated with telemedicine to those evaluated with face-to-face visit.

Conclusions

Non-adherent patients and new non-traumatic fractures (including rebound fractures) were more prevalent during the lockdown period in comparison to the pre-COVID-19 period, regardless of the modality of medical evaluation. Telemedicine seems to be an alternative strategy to standard face-to-face visits, in guaranteeing the continuity of follow-up in osteoporotic patients and short-term compliance to Denosumab

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P31

Application of Calcium to Phosphorus (Ca/P) ratio in the diagnosis of pseudohyoparathyroidism: Another piece in the puzzle of diagnosis of Ca-P metabolism disorders

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Introduction

Calcium and phosphorus (Ca/P) ratio has been proposed to identify patients with primary hyperparathyroidism and chronic hyperparathyroidism (HPT) from healthy subjects. However, other disorders of the Ca-P metabolism might present similar biochemical profile of HPT, such as pseudohypoparathyroidism (PHP), for which the use of Ca/P can be useful.

Aim

To test the performance of Ca/P ratio in the diagnosis of PHP in comparison to healthy subjects and to HPT patients for differential diagnosis.

Methods

A retrospective, observational study was carried out, including 60 PHP patients and 60 HPT patients compared to 120 controls. Serum Ca, P, creatinine, parathyroid hormone (PTH) and albumin, and creatinine were collected. Serum Ca and P were expressed in mg/dL. The diagnostic performance was evaluated by receiver operating characteristic (ROC) curve, sensitivity, specificity and accuracy.

Results

The Ca/P ratio was significantly lower in PHP than HPT and HPT patients, compared to controls (P < 0.0001). At ROC curve analysis, the cut-off of 2.32 (1.78 if serum Ca and P measured in mmol/L) for Ca/P ratio was able to identify both PHP and HPT patients among the entire cohort (sensitivity and specificity: 76%). Selecting patients with Ca/P ratio below 2.32, no valid cut-off of Ca/P was found to discriminate PHP from HPT patients; in this case, serum PTH above 53.0 pg/mL was defined for the identification of PHP patients (sensitivity and specificity: 100%). The index (Ca/P x PTH) above 150 pg/mL identified PHP patients from controls (sensitivity 84.7%; specificity 87.4%), whereas (Ca/P x PTH) below 44 pg/mL identified HPT patients from controls (sensitivity 88.9%; specificity 90.8%).

Conclusions

This study further validates the serum Ca/P ratio below 2.32 (1.78 SI) as a highly accurate tool to identify PHP and HPT patients, but it is not reliable to differentiate these two conditions. The index (Ca/P x PTH) is excellent to specifically recognize PHP or HPT from healthy subjects. Thanks to its extraordinary simplicity and the favorable cost-effectiveness, serum Ca and P should be equally considered as first-line examinations to calculate their ratio that can be easily applied to screen/rule out disorders of Ca-P metabolism, especially in asymptomatic patients.

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P32

Calcifediol 0.266 mg supplementation in adult population with 25(OH)D deficiency: 4 months results

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Introduction

Prevalence of vitamin D deficiency is relatively high worldwide, it is associated with poor skeletal health and has recently been related to other extra-skeletal diseases, probably due to its immunomodulatory effects. Detection and treatment of asymptomatic hypovitaminosis D in healthy adult population is especially relevant to attempt to optimize the overall functioning of the human body.

Objectives

- To assess the percentage of adult healthy population with vitamin D deficiency (25(OH)D < 20 ng/ml) who achieved plasmatic levels within optimal range (20-
The Hypoparathyroidism Symptom Diary (HypoPT-SD) was developed for the daily assessment of key symptoms and impact of HypoPT as reported by patients with chronic HypoPT and includes 13-items: a 7-item Symptom subscale, 4-item Impact subscale, and single-item anxiety and depression scores. The current psychometric study population included 22 patients from the 52-week study and 36-month studies, respectively, and 0.92 (month 1) and 33.05 ng/ml (month 4), whereas with monthly treatment 25(OH)D levels increased by 5.78 ng/ml and 12.18 ng/ml, respectively, 79% of subjects achieved optimal 25(OH)D levels at month 4 (100% in the biweekly group, 78% with the monthly treatment). The analysed bone metabolism parameters in all subjects (calcium, PTH, albumin, phosphate, alkaline phosphatase) showed no significant changes throughout the study. Calcium and PTH baseline levels were 9.38 ± 0.40 mg/dL and 51.36 ± 18.53 pp/ml remaining unaltered at month 4 (9.57 ± 0.40 mg/dL and 50.40 ± 22.38 pp/ml, respectively). In terms of safety, no patient reached 25(OH)D toxic levels. No serious adverse events were reported.

Conclusions
Monthly calcifiediol 0.266 mg is an effective and safe treatment for vitamin D deficiency in the overall population. Moreover, and bearing in mind the sample size limitations, biweekly calcifiediol 0.266 mg showed to be a safe and effective treatment for vitamin D severe deficiency in the target population and without clinically relevant variation in bone metabolism parameters.

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Context
In patients with hypoparathyroidism refractory to conventional treatment, recombinant human (rh)PTH(1-84) or rhPTH(1-34) can be used as second-line therapy and effectively control hypocalcaemia. However, whether rhPTH replacement therapy is safe in the long term is unclear. Our objective was to assess the bone effects of long-term therapy of chronic hypoparathyroidism with rhPTH(1-34).

Methods
We conducted a monocenter retrospective cross-sectional study at a tertiary university hospital in France. Eligible patients were adults with chronic hypoparathyroidism receiving rhPTH(1-34) therapy uninterruptedly for more than 24 months, who underwent a two-phase whole-body technetium-99m methyldiphosphonate scintigraphy. Clinical and biochemical data were collected retrospectively, covering the period of exposure to rhPTH(1-34) from its initiation until the date of the bone scintigraphy. Images were analyzed blindly by two experts using a visual grading to calculate a total composite score of the bone scan.

Results
17 patients (13 women) were studied, with a median age of 42 (29-58) years. Median treatment duration was 55 [33.68] months and mean daily dose of rhPTH(1-34) was 37.5 [22.1.40] µg. Pathological bone uptake appearing like so-called “super bone scan” was detected in 10 (59%) patients, despite adequate calcemic control (median calcaemia over the study 2.10 [2.04;2.28] mmol/L). Patients with hypermetabolic bone scan received higher daily doses of rhPTH(1-34) compared with patients normal scan (21.0 vs 39.3 mg/day, P = 0.0380). There was no difference in reported osteoarticular pain, in total and albumin-adjusted
calcinium concentration, in phosphate concentration, in calcium-phosphate product
and in 24-hour urinary calcium excretion between the two groups. Patients with
pathological bone scan compared with those with normal scan had higher osteocalcin (29.2 ± 232 ng/ml, P = 0.0012), alkaline phosphatase (81 vs 112
U/L, P = 0.0094) and crosslaps (0.67 vs 3.83 ng/ml, P = 0.0198). The total composite score correlated with osteocalcin (r = 0.79, P = 0.0002), alkaline phosphatase (r = 0.83, P = 0.0001), with crosslaps (r = 0.51, P = 0.045) and trends to correlate with mean daily rhPTH1–34 dose (r = 0.44, P = 0.0769). Osteocalcin concentration ≥ 87 ng/ml predicted a pathological bone uptake with 100% sensitivity and 85.7% specificity.

Discussion
Abnormally increased metabolic activity of the bone may occur under long-term
PTH(1–34) therapy despite adequate calcemia control, possibly due to the pharmacokinetics of this treatment. Bone scintigraphy can be useful in detecting iatrogenic hyperparathyroidism in patients receiving rhPTH1–34 or rhPTH1–84. Increased osteocalcin concentrations reliably predict bone cell over-
timulation and should be used as biochemical marker for dose adjustment or
treatment interruption.

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Vertebral Fractures at hospitalization predict impaired respiratory
t function at follow-up of COVID-19 survivors
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Morphometric-Vertebral Fractures (VFs), which were widely demonstrated to reduce overall-survival and respiratory function in the general population, have been recently reported to be highly prevalent in COVID-19 patients. Emerging data show negative respiratory sequelae at long-term follow-up in COVID-19 survivors. The aim of this study is to evaluate the VFs influence on respiratory function of COVID-19 survivors. We included COVID-19 patients admitted at San Raffaele-Hospital and re-evaluated at the San Raffaele-Outpatient Follow-Up Clinic. Lateral chest-X-rays on admission in emergency-department were obtained and pulmonary function tests (PFTs) were performed at six-months of follow-up. VFs were detected using a qualitative and semiquantitative assessment and PFTs were obtained by Jaeger MasterScreen AnalyzerUnit. Fifty patients were included in the study. Median age was 66 years, and 33 (66%) patients were males. VFs were detected in 16 (32%) patients. No differences between fractured and non-fractured groups regarding age, sex and comorbidities were observed. A Radiological-Assessment-of-Lung Edema (RALE) score, assessing the severity of pulmonary
opacities, was available for 30 patients with a median value of 5.5. Although no differences were observed in RALE score between VFs + and VFs- patients (5 vs 6, P = 0.69), those with VFs were characterized by a significant lower SpO2/FiO2 ratio, higher CRP levels, and required hospitalization more frequently (100% vs 73%, P = 0.04). No differences were found regarding ICU-admission. At follow-up, patients with VFs were characterized by significant lower Forced-Vital-Capacity (FVC) (-2.9% vs 3.6 L, P = 0.006; 85% vs 110% predicted, P = 0.001), Forced-Expiratory Volume1st-second (FEV1) (-2.2 vs 2.8 L, P = 0.005; 92% vs 110%; P = 0.001). Moreover, a lower diffusion-capacity-for-carbon-monoxide (DLCO/SL; 5.83 vs 6.98 mmol/min/kpa, P = 0.036) and 86.3%, P = 0.043) as well as Total Lung-Capacity (TLC) (-4.9% vs 6 L, P = 0.027; 84% vs 98%; P = 0.04) were found in patients with VFs compared to those without. In linear regression analyses, the Spine-deformity-index (SDI) was significantly correlated negatively with FVC% (P = 0.02) and positively with FEV1/FVC (P = 0.01), and negative trends with FEV1% and DLCO% were observed (P = 0.12, P = 0.12, respectively). If VFs found on hospital admission appear to be independent predictors of medium term impaired respiratory function of COVID-19 survivors which may significantly influence their recovery. Therefore, our findings suggest that a VF assessment at baseline may help in identifying patients needing a more intensive respiratory follow-up after discharge. Patients showing persistent respiratory symptoms and functional impairment without evidence of pulmonary disease may benefit from VFs assessment in order to preventing the vicious-circle of further fractures and respiratory deterioration.

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Denosumab vs. zoledronic acid treatment in post-menopausal breast
cancer: a 2-year prospective observational study
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Adjuvant treatment for post-menopausal women with early breast cancer (BC) includes aromatase inhibitors (AI), known to decrease bone mineral density (BMD). In this study, we investigate whether denosumab is a valid second option for patients unable to receive standard adjuvant i.v. zoledronic acid (ZA). In total, 212 patients have been evaluated after they did not receive ZA. Of those 194 were included. After evaluation by an endocrinologist, all patients were offered ZA as their first choice and 15% accepted it (N=29). The remaining 85% were offered denosumab (N=165). All patients were followed prospectively with blood tests up to 24 months. DXA scans were performed at baseline and 24 months. No difference was observed between the two treatment groups at baseline, with regard to anthropometry and standard biochemistry. Markers of bone turnover (pinP, pCTX, p-alkaline phosphatase and p-osteocalcin) all showed significant suppression compared to baseline and remained suppressed throughout the 2 years. BMD showed small and significant increases at the spine (0.024 g/cm^2) and total hip (0.019 g/cm^2) in the denosumab group but no change at the femoral neck(-0.011 g/cm^2). In the ZA group, we observed no significant change at the spine (0.015 g/cm^2) and total hip (-0.001 g/cm^2) and a small significant decrease at the femoral neck (-0.037 g/cm^2). However, when we compared BMD change between the treatment groups, we found no significant difference.

Discussion
Our data indicate that for BC patients in AI treatment who refused or were not able to receive ZA treatment, denosumab might be recommended as a second choice. Regarding markers of bone turnover and BMD denosumab is equal to ZA.

Summary
Women with early breast cancer receiving anti-estrogen treatment are at risk of developing osteoporosis. We followed 194 women receiving zoledronic acid (ZA) or denosumab for up to 2 years. We find that with regard to bone protection, denosumab is a viable alternative to ZA and might be recommended as a second choice.

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Relative incidence and demographics of hip fractures among subjects
over the age of 50 from the Ethiopian ethnic minority in Israel: A
preliminary survey from the Israel National Trauma Registry (INTR)
database between 2011-2020
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Background
Among the various ethnicities in the Israeli mosaic, the Ethiopian community is the most recently settled, with an immigration that started less than 40 years ago. Largely young, this 160,000-member community comprises nonetheless about 25,000 persons 50 years or older, virtually all born in Ethiopia. Despite this growing aging population, there is no knowledge regarding osteoporotic fractures in this unique East African ethnic group, not even from data originating from Ethiopia. Two isolated reports, from Ethiopia and from Israel, presented conflicting data regarding bone mineral density in this ethnic group. This study aimed to generate some preliminary data regarding the incidence of hip fractures, as a proxy for osteoporosis, in Ethiopian-born Israelis age 50 and over, between 2011-2020.

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Methods
The INTR database contains reports on all injuries recorded in 21 of the 26 trauma centers in Israel. Hip fractures are the only osteoporotic fractures included in the database, as surgery within 48 hours is a nationally monitored medical quality index. Hip fracture data were retrieved from the registry, stratified by gender and age, and compared to those of the Israeli population of other ethnicity.

Results
Ethiopian-born subjects 50 yr and older comprised 0.6% of the INTR reports, while their representation in this age group in Israel was 1.24% (P<0.0001). The INTR included 966 reports on Ethiopian-born subjects in this age category, 3.9% of this stratum in the Ethiopian community, while it included reports on 7.4% of people of this age group of different ethnicity (P<0.0001). Between 2011-2020, there were 194 hip fractures among Ethiopian-born subjects age 50 or older, 20.1% of all reports for this group. While hip fractures represented 32.3% of injuries reported for other people in this age group, P=0.0001. Among Ethiopian-born subjects who suffered a hip fracture, 81/194 (41.8%) were men, compared to 16175/48130 (33.6%) among people of other origin (P<0.05). Additionally, 81/194 (41.75%) of these fractures occurred in Ehtiopian-born over the age of 85, while the corresponding figure was only 17303/48130 (35.95%) in people of different ethnicity, P=0.02.

Conclusions
Older Ethiopian-born Israelis, particularly women, appear to be less prone to hip fractures than the rest of the population. Additionally, hip fractures appear to occur more in the very old Ethiopian-born than in other ethnic groups, possibly suggesting less osteoporosis. Hip fracture being only a proxy for osteoporosis, a study linking all fragility fracture data with BMD is planned to further examine this question.

References

Intramedullary nailing as a promising tool to investigate osteosarcopenia in older people. Our findings need confirmation by robust prospective studies.

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Tumor-induced osteomalacia - case report
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Introduction
Tumor-induced osteomalacia is a rare paraneoplastic syndrome characterized by the presence of phosphaturic hormone-secreting mesenchymal tumors - fibroblast growth factor 23 (FGF-23), which causes hypophosphatemia and osteomalacia. These tumors are small, frequently infiltrate the surrounding tissues and are located in the connective or bone tissue. Usually, these tumors are benign, but malignant tumors have also been reported.

Case report
We present the case of a 39-year-old female with persistent diffuse osteomuscular pain, progressive generalized muscle weakness and the impossibility of standing and walking for about five years. She underwent multiple medical examinations - neurologic, orthopedic and rheumatologic assessments, but did not identify any disorders to explain her symptoms. Laboratory testing showed severe hypophosphatemia (0.9 mg/dl), increased urinary phosphate excretion, increased alkaline phosphatase (320 U/l), normal renal function and elevated FGF-23 (551 kRU/l). Radiographic imaging revealed multiple, old, nontraumatic pelvic and rib fractures, evolved with vicious consolidation. SPECT CT with 99mTc-Tektrotyde demonstrated increased uptake of the radiotracer in the right supraspinatus muscle. MRI of the right shoulder confirmed a 5 cm intramuscular tumor of the supraspinatus muscle. Surgery was performed with resection of the tumor. Postoperatively, we observed progressive normalization of phosphate levels within a few days and FGF23 decreased significantly, but without normalization 48 hours or 1 month after surgery, raising the suspicion of incomplete resection. Histopathological examination and immunohistochemical profile confirmed the presence of phosphaturic mesenchymal tumor (PMT) with a predominantly hemangiomatous component, showing positive expression of CD34, CD35, CD68, SMA, vimentin and Ki-67 < 5%. The resected margins showed tumor infiltration of the adipose tissue and skeletal muscle. The clinical outcome of the patient was favorable, with progressive and significant improvement of symptoms (regression of osteomuscular pain and gait abnormalities) and normalization of serum phosphate level and FGF-23 level at the upper limit of normal values. Given the histopathological result and failure of normalization of FGF-23 additional follow-up is necessary for detection of tumor recurrence.

Conclusion
Tumor-induced osteomalacia is a rare, frequently undiagnosed or misdiagnosed disease. The diagnosis is a real challenge because of the nonspecific symptoms that can delay detection of the disease. A stepwise approach, combining functional and anatomical imaging is necessary to identify the tumor. Surgery is the only curable option and should be performed whenever is possible.

Keywords
Tumor-induced osteomalacia, FGF-23, paraneoplastic syndrome, hypophosphatemia

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P40

In case of acute pancreatitis, think of hyperparathyroidism! A case report
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Introduction
The revelation of primary hyperparathyroidism by acute pancreatitis is an exceptional situation.

Case report
We report the case of a 73 years old patient, hypertensive, having the antecedent of an ischemic cardiopathy complicated by cardiac insufficiency and atrial fibrillation, admitted to the emergency for an abdominal pain evolving since 10 days, associated with vomiting, the initial biological assessment showed lipasemia at 2543UI/L, kidney failure and malignant hypercalcemia at 142mg/l.

The etiological work-up showed primary hyperparathyroidism with double localizations, the patient benefited from a Par a thyroidectomy with a good clinical evolution.

Discussion
Hypercalcemia is a rare cause of acute pancreatitis, even more so if it is secondary to primary hyperparathyroidism, its prevalence varies, according to studies, from 1.5 to 5% [1]. Authors suggest that this association is not coincidental, and several pathophysiological explanations have been proposed, but none has been experimentally proven to date. The highest prevalence of acute pancreatitis in patients with hyperparathyroidism has been observed in those with hypercalcemia [2], and the hypercalcemia-acute pancreatitis link is currently well established.

For Prinz and his team [3], acute pancreatitis is the consequence of a deposit of lithiasis secondary to an accumulation of calcium in the gastric juice. The second explanation is the study of intra-pancreatic trypsinogen activation, which, in pancreatitis, accepted as the lever leading from acinar cell injury to acute pancreatitis [4]. Recently, the role of a genetic substrate has been suggested; mutations in the SPINK1 and CFTR genes have been detected in hyperparathyroid patients who developed acute pancreatitis[5]

Conclusion
The association hyperparathyroidism - acute pancreatitis was most often explained by the link of hypercalcemia, most of the above theories have not presented scientific evidence, and the current challenge is to seek a direct link between these two pathologies, the genetic theory remains an option, but its role is not clear.

Bibliography

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P42
Long-term complications of permanent hypoparathyroidism: prevalence and associated factors
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Introduction
Patients with permanent hypoparathyroidism receiving conventional treatment have increased risk of subcapsular cataracts, basal ganglia calcifications, urolithiasis and renal insufficiency. The aim of this study was to assess the prevalence and the interfering factors of these complications in patients with permanent hypoparathyroidism.

Methods
We conducted a cross-sectional study including 53 patients with permanent hypoparathyroidism. Biochemical parameters, ophthalmological examination, brain computed tomography scan and renal ultrasound were performed to all patients.

Results
There were 41 (77%) women and 12 (23%) men with a mean age of 52.7 ± 16.5 years. Post-surgical HPT was the most frequent etiology of hypoparathyroidism (64%). Posterior subcapsular cataract was diagnosed in 62% of cases. Age (P < 0.01), disease duration (P = 0.02) and hypomagnesemia (P = 0.014) were positively associated with cataracts. Basal ganglia calcifications were found in 53% of cases. Brain CT-scan showed bilateral intracerebral calcifications located in the central gray nuclei (71%) or diffuse symmetric calcifications (29%). Patients with intracranial calcifications presented with headache, amnesic disorders, psychotic symptoms and seizures in 82, 71, 14 and 14% of cases, respectively. Younger age of onset of hypoparathyroidism (P = 0.037), disease duration (P = 0.014), nonsurgical etiologies (P = 0.015), poor adherence to treatment (P < 0.01), hypomagnesemia (P = 0.001) and PTH level < 10 pg/ml (P = 0.022) were significantly associated with brain calcifications. Urolithiasis and renal insufficiency were found in 13 and 7% of cases, respectively. Creatinine clearance was negatively correlated with disease duration (r = -0.338, P = 0.013). Patients with urolithiasis had lower PTH level and received higher calcium salt doses (P = 0.033) than those who had no renal calcifications. However, sex, smoking, body mass index, calcium, phosphatemia, phosphocalcic product, TSH and 25-OH-vitamin D did not significantly interfere with none of these complications.

Conclusion
Patients with permanent hyperparathyroidism are exceedingly exposed to neurological, visual and renal impairment because of phosphocalcic disorders and extra-skeletal calcifications. The disease duration, PTH and magnesium levels seem to be the most interfering factors.

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Assessment of quality of life in patients with hypoparathyroidism receiving conventional treatment: a case-control study

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Introduction
Patients with permanent hypoparathyroidism suffer from multiple complaints and are exposed to long-term complications that compromise their well-being. The aim of our study was to assess the quality of life in patients with permanent hypoparathyroidism receiving conventional vitaminocalcic therapy.

Methods
We conducted a cross-sectional case-control study including 53 patients with permanent hypoparathyroidism and 53 age-sex-body mass index matched controls. Clinical and biochemical parameters were collected. Quality of life was assessed in all participants using the Short Form 36 Health Survey (SF-36).

Results
Among patients with hypoparathyroidism, there were 41 (77 %) women and 12 (23 %) men with a mean age of 52.7 ± 16.5 years. Neck surgery was the most common etiology of hypoparathyroidism (n=34, 64 %). In comparison with age-sex-body mass index matched controls, hypoparathyroid patients had significantly lower scores in all eight domains of SF-36 (P < 0.01). Patients with postsurgical hypoparathyroidism scored worse than those with non-surgical etiologies in all domains, but significance was reached only in bodily pain score (P=0.01). All SF-36 scores were negatively correlated with the age. However, Sex, smoking, duration of the disease, adherence to treatment and body mass index did not significantly interfere with SF-36 scores. Hypoparathyroid patients in whom PTH level < 10 pg/ml scored worse in all SF-36 domains compared with those who had PTH level > 10 pg/ml, without reaching significance. Magnesium level was positively correlated with SF-36 scores. No significant correlations were found between SF-36 scores and biological parameters such as calcium, phosphatemia, phosphocalcic product, TSH, 25 OH vitamin D, 24 hours calcitriol, and creatinine clearance.

Conclusion
Compared with matched controls, patients with permanent hypoparathyroidism, especially post-surgical ones, suffer from a major impairment of quality of life, suggesting that conventional treatment, even if it’s well conducted, fails to restore well-being.

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Bone mineral density, trabecular bone score and vertebral fractures in acromegalic patients

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Background
Acromegaly is characterized by increased prevalence of fragility vertebral fractures. Nonetheless, there are no clear recommendations for prevention of acromegalic osteopathy. Both bone mineral density (BMD) and trabecular bone score (TBS) lack clear evidence as prognostic factors for vertebral fractures (VF).

Material and Methods
We performed an observational study on 31 acromegalic patients recruited prospectively. They were tested for alkaline phosphatase, 25 hydroxyvitamin D, parathormone, osteocalcin, the C-terminal telopeptide of type 1 collagen and total procollagen type 1 amino-terminal propeptide. Imaging techniques used were dual x-ray absorptiometry (DXA), TBS and antero-posterior and lateral x-ray scans of the dorsolumbar spine.

Results
They were characterized by normal BMD, partially degraded bone on TBS. 32.33% had VF on dorsolumbar x-ray and hypogonadism was present in 71% of subjects. Hypogonadal acromegalic subjects had significantly lower PRL (151 ± 0.123 vs. 1.343 ± 0.146, P = 0.040) but higher T (P = 0.029) and Z scores (P = 0.004) at the femoral neck compared to eugonadal patients. Acromegalic patients with VF had significantly lower BMD at the femoral neck (0.001 ± 0.137 vs. 1.013 ± 0.131 g/cm², P = 0.037) and hip (0.883 ± 0.109 vs. 1.036 ± 0.121, P = 0.002) and T score at the lumbar spine [-2.7 (IQR: -3.4- -0.6) vs. -1.2 (IQR: -1.9-0.1), P = 0.047] compared to those without VF but with no differences in terms of TBS values.

Conclusion
Vertebral fractures in acromegaly patients associate with low BMD but not with TBS. However, TBS is significantly lower in these patients in the presence of hypogonadism. The use of BMD might still prove to be useful in the evaluation of acromegalic osteopathy.

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Phosphate-mediated inhibition of calcium-sensing receptor expressed endogenously in the thyroidal TT cell-line

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The calcium-sensing receptor (CaR) is the key controller of parathyroid hormone (PTH) secretion and extracellular calcium homeostasis. Hyperparathyreoidism increases PTH secretion and is associated with secondary hyperparathyroidism (SHPT). We reported recently that inorganic phosphate (Pi), and sulphate, can attenuate CaR activity directly (in CaR-transfected HEK-293 cells) and Pi can increase PTH secretion rapidly from human and murine parathyroid cells. To investigate this further, here we used a thyroid parafollicular C-cell model, TT cells, which express CaR endogenously. TT cells, which exhibit CaR-induced calcitonin (CT) secretion, were assayed by epifluorescence intracellular Ca²⁺ imaging and CT assay (with a gastrin-releasing peptide (GRP)-induced CT control). When co-stimulated with the CaR-activating calcimimetic R568 (1µM) and spermine (1mM), TT cells exhibited classic CaR-induced Ca²⁺ mobilisation, which the Gp11-specific inhibitor YM-254890 largely abolished (+93 ± 8%). Similar CaR-induced responses were also inhibited by increasing the buffer Pi concentration from 0.8 mm (physiological) to a pathophysiological 2 mm (-33 ± 4%; P<0.001). In contrast, raising Pi concentration was without effect on carbachol-induced Ca²⁺ mobilisation (acting via muscarinic receptors). Finally, 1.2 mm sulphate (high) elicited a similar CaR inhibition as for Pi (+28 ± 16%; P<0.05; vs physiological 0.3 mm sulphate). Similar inhibitory effects were seen when the anions were used in combination; 2mM Pi (high) & 0.3mM sulphate (normal) elicited a 15 ± 12% reduction in CaR-induced Ca²⁺ mobilisation, while 2mM sulphate (high) & 0.8mM Pi (normal) produced a 19 ± 3% inhibition (P<0.05). Regarding CT secretion, we observed time-dependent release that was stimulated maximally 15-20 fold by increasing Ca²⁺ concentration from 0.5-3.0mM (EC50 ~1.5 mm). Inorganic Pi (0.8-3.0 mm) inhibited CT release in a non-competitive manner, with 3mM Pi almost abolishing CT release at all Ca²⁺ concentrations tested. Even raising Pi concentration from 0.8–1.4 mm (representing the physiological range) elicited a striking 50% reduction in CT release. In contrast, 2mM Pi had no effect on 1µM GRP-stimulated CT release. Sulphate was also a non-competitive inhibitor of CT release but was less potent than Pi. These results further support the idea that the CaR is a mineral sensor, at which Pi acts directly as a non-competitive antagonist to limit CaR-induced reductions in PTH secretion. Further, Pi may also limit CaR-induced CT secretion when its serum concentration is raised. Together, our studies provide important new information regarding the physiological control of PTH and CT secretion, and, the pathophysiology of SHPT.
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Bleeding assessment in 195 patients with osteogenesis imperfecta
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Background
Osteogenesis Imperfecta (OI) is commonly defined as ‘brittle bones’ disease, but there are also more characteristics like blue sclerae, hearing loss, dental problems, ligamentous laxity and a short stature. Easy bruising is also a very common feature and there are multiple case reports on haemorrhagic events in OI. Larger population studies on bleeding tendency in OI are very sparse, while other connective tissue disorders with easy bruising have much more relevant research. This paper reviews the clinical aspects of bleeding in bruising in OI based on the self-bleeding assessment tool (BAT) questionnaire among a large cohort of OI patients. The emphasis of this study will be a first translation to clinical consequences of bleeding due to surgery, tooth extraction, menstrual and obstetrical bleeding and to present therapeutic considerations relevant to bleeding in OI.

Methods
This exploratory study was conducted at the national expert center for adults with OI in the Netherlands. The self-BAT was digitally distributed among 354 adults with different clinically confirmed types of OI.

Results
195/354 patients with OI types 1.3 and 4 were included. Self-BAT scores were increased in 37-44%.

Conclusion
Bleeding tendency seem to be a relevant feature in OI patients. This study should be a wakeup call for all clinicians treating OI patients for assessing bleeding tendency and taking the right interventions to reduce haemorrhagic symptoms and improve quality of life.

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P47

The international X-linked hypophosphataemia (XLH) registry: overview of the dataset
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Background
X-Linked Hypophosphataemia (XLH) is a rare, progressive, hereditary phosphate wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity. Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or impact of treatment. The International XLH Registry will collect data to characterise burden of disease, disease progression and long-term outcomes. It aims to describe effectiveness and safety of treatments used to manage XLH and their value in certain subpopulations.

Methods
The International XLH Registry (NCT03193476) was initiated August 2017, aims to describe effectiveness and safety of treatments used to manage XLH and their value in certain subpopulations.

Results
As of 31 December 2021, 1,043 subjects diagnosed with XLH were enrolled from 88 hospital sites in 19 countries. The geographic distribution of subjects is as follows: Belgium n = 29, Bulgaria n = 7, Czech Republic n = 8, Denmark n = 23, France n = 267, Germany n = 79, Hungary n = 11, Ireland n = 5, Israel n = 21, Italy n = 88, The Netherlands n = 26, Norway n = 23, Portugal n = 9, Slovakia n = 5, Slovenia n = 3, Spain n = 55, Sweden n = 43, Switzerland n = 17, and the UK n = 324. A further 30 sites are still to enrol patients (including in Austria and Latvia). Overall, 400 adults (18–29y, n = 116; 30–39y, n = 81; 40–49y, n = 95; 50–59y, n = 58; ≥ 60y, n = 50) and 620 paediatric subjects (<5y, n = 138; 5–12y, n = 321; 13–17y, n = 161) have been enrolled (date of birth unavailable, n = 23). The majority of the enrolled subjects are female (648 (62.1%), with 372 male (35.7%) and 23 for whom sex was not reported (2.2%).

Conclusions
This Registry forms the largest dataset of XLH subjects worldwide to date. Patients have been recruited from a wide geographical region, and baseline demographics are consistent with a hereditary X-linked dominant disease. Information collected during the 10-year Registry duration will generate real-world evidence to help inform clinical practice throughout the EMEA region and beyond.

Acknowledgements
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P48

Male osteoporosis, a still overlooked and undermanaged issue: an identikit of patients seeking bone health evaluation at a tertiary academic medical centre
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Background
Male osteoporosis is undermanaged. The characteristics of men referring to health care system for bone evaluation remain partially unknown.

Aim
To characterize from real-life data male patients seeking the first bone health evaluation at a tertiary academic medical center, referral for both andrological and bone diseases, over a 13-year observation period.

Methods
Retrospective, cross-sectional study, including adult men referring to our Center from 2007 to 2020 for bone health evaluation. Reasons for referral, risk factors for osteoporosis and comorbidities were investigated. Osteoporosis and osteopenia were defined considering DXA outcomes, according to WHO and ISCD criteria, and history of fragility fractures.

Results
A total of 455 men (age 62.5 ± 15.1years) were included: 42 aged 18–40 years, 57 aged 40–50, 79 aged 50–60, 109 aged 60–70, 122 aged 70–80, and 46 aged >80. Overall, 125 patients (27.4%) were already followed by endocrinologists due to endocrinological/androlological diseases known to increase fracture risk (94 men or not 31 men); general practitioners and other specialists asked for bone evaluation for 226 (49.6%) and 101 (21.2%) men. DXA has been already performed for 354 patients. Prevalence of osteoporosis, osteopenia, and low bone mineral density for age were 25.9%, 26.4% and 13.2%, respectively. Fractures were the most frequent reason for referral. At least one fragility fracture has already occurred in 213 patients (46.8%), with higher prevalence in non-endocrinological than endocrinological patients (56% vs 24%, P < 0.001). Sites of fracture were lumbar spine (128 patients,60%), femoral neck alone or in combination with other sites (50 patients, 23.4%). A total of 344 patients (76%) was already known to be affected by one or more comorbidities associated to bone loss, with higher prevalence in fractured patients compared to non-fractured (P = 0.036). Among fractured patients, 49 of them (23%) have never been treated with any anti-osteoporotic therapy, including calcium and vitamin D supplementation.

Conclusions
Male osteoporosis presents with a high rate of fragility fractures (about 50%) among men referring to a tertiary academic medical center. The high prevalence of comorbidities associated to bone loss suggests that secondary forms of osteoporosis prevail in men, and they should be carefully investigated to identify patients at increased fracture risk. Most of fractured patients have not been previously evaluated by a clinician with expertise in bone diseases or properly treated, suggesting that awareness for male osteoporosis needs to be reinforced in primary healthcare setting in order to prevent fractures. This disease remains still overlooked and unaddressed.

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Extended treatment with recombinant human parathyroid hormone (1-84) in adult patients with chronic hypoparathyroidism: a phase 4 study
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In Europe, rhPTH(1-84) is an approved adjunctive treatment for adults with chronic hypoparathyroidism that cannot be adequately controlled with conventional therapy. Here we present data from the longest rhPTH(1-84)-treated study cohort of patients with hypoparathyroidism. In a single-centre, single-arm, phase 4 study (NCT02910466), long-term rhPTH(1-84) treatment (25, 50, 75, or 100 μg/day subcutaneously) was evaluated in adults with chronic hypoparathyroidism who maintained uninterrupted rhPTH(1-84) treatment from the HEXT study (NCT01199614). Doses were adjusted based on albumin-corrected serum calcium and 24-hour urinary calcium excretion to achieve target serum calcium within 2.00–2.25 mmol/l. Baseline was defined as last available value before first dose in the current study. End of treatment (EOT) was the day after last rhPTH(1-84) dose for each patient, including those who did not complete the study. Data are summarized as mean ± SD. Thirty-nine patients enrolled (age, 51.9 ± 12.22 years; 79.5% female; duration of hypoparathyroidism, 18.6 ± 12.00 years). Mean length of exposure from first rhPTH(1-84) dose was 10.8 ± 3.50 years. In the current study, 36 patients received ≥1 rhPTH(1-84) dose, and mean duration of participation was 30.3 ± 5.79 months. Mean albumin-corrected serum calcium was 1.94 ± 0.222 mmol/l at baseline (n = 33), 2.08 ± 0.304 mmol/l at month 30 (n = 23), and 2.07 ± 0.266 mmol/l at EOT (n = 36). Phosphate values were 1.25 ± 0.230 mmol/l at baseline (n = 33), 1.30 ± 0.241 mmol/l at month 30 (n = 23), and 1.31 ± 0.220 mmol/l at EOT (n = 36). Calcium-phosphate product levels were 2.53 ± 0.475 mmol2/l2 at baseline (n = 33), 2.78 ± 0.421 mmol2/l2 at month 30 (n = 23), and 2.82 ± 0.373 mmol2/l2 at EOT (n = 36). Mean 24-hour urinary calcium levels were 5.52 ± 3.243 mmol/24 hours at baseline (n = 35), 7.47 ± 5.170 mmol/24 hours at month 30 (n = 18), and 6.60 ± 3.818 mmol/24 hours at EOT (n = 35). Mean prescribed supplemental calcium and active vitamin D decreased from 1313.8 ± 1404.66 mg/day and 0.17 ± 0.320 μg/day, respectively, at baseline (n = 36) to 1180.9 ± 1065.50 mg/day and 0.12 ± 0.327 μg/day at month 30 (n = 23), and 1076.0 ± 852.48 mg/day and 0.11 ± 0.313 μg/day at EOT (n = 36). No clinically relevant changes in bone mineral density occurred between baseline and EOT. Treatment-emergent adverse events (TEAEs) were reported in 36 (92.3%) patients; the most common were anxiety (41.0%), hypocalcaemia (28.2%), and depression (20.5%). Four TEAEs were considered by study investigators to be treatment related (upper limb fracture, hypercalcaemia, renal disorder, ureterolithiasis). Study limitations are small sample size, single-arm design, and lack of pre-treatment baseline data. Among patients with chronic hypoparathyroidism previously treated with rhPTH(1-84), improvements in biochemical efficacy parameters were maintained over a mean of 30 months of additional treatment. No new or unexpected safety signals emerged.

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P50

Impact of chronic hypoparathyroidism on symptom severity and interference with life as reported by patients treated with recombinant human parathyroid hormone (1-84), rhPTH(1-84)
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Chronic hypoparathyroidism is a rare mineral homeostasis disorder managed by conventional therapy (oral calcium and active vitamin D), alone or with adjunctive rhPTH(1-84). Chronic hypoparathyroidism is associated with considerable symptom burden, which can interfere with daily living. We report results from a web-based, cross-sectional survey conducted among adults with chronic hypoparathyroidism. The objectives were to quantify the impact on overall life interference of (1) time from diagnosis to rhPTH(1-84) initiation and (2) rhPTH(1-84) treatment vs conventional therapy. Overall life interference of hypoparathyroidism was patient self-reported upon considering all aspects of their condition using a 7-point rating scale (1 = none to 7 = very significant interference). Hypoparathyroidism-associated symptom severity was assessed through the disease-specific, patient-reported Hypoparathyroidism Symptom Diary. The study included 90 patients treated with rhPTH(1-84) (mean ± SD age, 54.5 ± 11.3 years; 83% female) and 57 patients treated but not adequately controlled with conventional therapy (mean ± SD age, 50.0 ± 11.7 years; 93% female). Among rhPTH(1-84)-treated patients, time from hypoparathyroidism diagnosis to rhPTH(1-84) initiation was ≤12 months, >12–<24 months, and >24 months in 28%, 38%, and 34% of patients, respectively. Initiation of rhPTH(1-84) >48 months after diagnosis was associated with higher overall life interference compared with initiation ≤12 months after diagnosis (P < 0.001 for the unadjusted and P = 0.02 for multivariable regression analysis adjusted for potential confounders). The life interference mean ± SE score was 2.0 ± 0.54 points higher (unadjusted) and 0.8 ± 0.34 points higher (multivariable regression) for patients who initiated rhPTH(1-84) >48 months vs ≤12 months after diagnosis. Self-reported severity of hypoparathyroidism was rated as much worse in 41% of patients, mild, moderate, and severe in 42%, 49%, and 8% of patients treated with rhPTH(1-84), respectively, and in 11%, 37%, 49%, and 3% of patients treated with conventional therapy. Treatment with rhPTH(1-84) was associated with lower overall hypoparathyroidism-related life interference compared with conventional therapy that did not adequately control hypoparathyroidism (P < 0.001 for both unadjusted and adjusted multivariable regression analyses). Mean ± SE life interference score for rhPTH(1-84)-treated patients was 1.5 ± 0.33 points lower (unadjusted) and 1.1 ± 0.29 points lower (multivariable regression) vs patients treated with conventional therapy. A strength of this study is the multivariable analysis adjusting for potential confounders; limitations include cross-sectional study design, inaccessibility of patient characteristics before treatment initiation, and recall bias. In a real-world setting, rhPTH(1-84) initiation >48–>> 48 months after hypoparathyroidism diagnosis was associated with greater overall life interference vs rhPTH(1-84) initiation ≤12 months after diagnosis. Compared with conventional therapy, rhPTH(1-84) treatment was associated with lower overall life interference after adjusting for confounding variables.

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P51

Novel variant of the casr gene c.2192G > A in a clinical case of chronic hypocalcemic hypoparathyroidism
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A 65 year old patient who was hospitalised for a reactive arthritis of the knee due to Rickettsia infection, presented an asymptomatic persistent chronic hypocalcemia and hyperphosphorhemia. In her medical history, we noted a hypertension treated with amlodipine and bisoprolol, syndrome of sleep apnea, acquired lumbar spinal canal stenosis and sequelae of poliomyelitis acquired at 10 years of age in Congo, her place of origin. According to her blood test results, total calcium levels were low between 1.9 to 2.1 mmol/l (normal ranges 2.15–2.50), phosphorus levels high between 1.61 to 1.81 mmol/l (normal ranges 0.81–1.45), albumine levels normal between 34 to 42 g/l (normal ranges 34–48), parathormone levels abnormal normal between 17 to 55 ng/l (normal ranges 15–65), 25OH-vitamin-D levels low to normal between 22 to 44 mg/l (normal ranges 30–60). Urinary calcium excretion between 0.022 to 0.081 mol/mol creat (normal range <0.700). Renal function was normal with creatinine levels between 0.40 to 0.75 mg/dl (normal range 0.55–0.96). The diagnosis of hypoparathyroidism was evoked with suspicion of an activating mutation of the calcium-sensing receptor (CaSR) gene. We performed a citrate infusion test to provoke more pronounced hypocalcemia by administering intravenously a continuous perfusion of 100 ml solution of dextrose 2.45 g, sodium citrate 2.2 g and citric citrate 0.7 g, for 30 minutes. The subsequent measures of total calcium, ionised calcium and parathormone every 10 minutes from T0 to T30 min, showed no increase of parathormone levels in response to provoked hypocalcemia. The genetic analysis didn’t identify any mutation but identified a novel variant c.2192G > A (p.Cys731Tyr) of the CaSR gene. This variant has not been described in the literature before and results from the In-Silico analysis are contradictory, benign for Polyphen and pathogenic for MutationTaster and SIFT. A genetic family study could have helped us to better interpret this result, but unfortunately the patient lives alone in Belgium since 2015 and all her family member
lives in Africa. Thus, the pathogenic nature of this novel variant of CaSR gene remains unknown for the time being and the variant is classified as class III.

References

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Atherothrombotic risk in subjects with parathyroid disorders: cross-sectional study
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Background
Clinical and molecular findings have shown that parathyroid hormone (PTH) affects the heart and vasculature through downstream actions of G protein-coupled receptors in the myocardium and endothelial cells. Furthermore, the endothelium is a recognised target tissue of PTH and there is an increasing body of evidence that PTH affects functional and structural properties of arteries.

Patients with chronic post-surgical hypoparathyroidism (hypoPT) have higher incidences of hypertension, arterial stiffness and increased risk of mortality.

Purpose
To assess endothelial and other atherosclerotic predictors in subjects affected by hypoPT in comparison with primary hyperparathyroidism (PHPT) and controls.

Methods
In a monocentric, cross-sectional study we enrolled hypoPT patients treated with calcium and calcitriol, PHPT subjects and age-matched controls. All patients underwent a biochemical examination including calcium-phosphorus metabolism, inflammation markers. Moreover, we evaluated brachial artery endothelial function (flow-mediated dilation-FMD), common carotid intima-media thickness (ccIMT), diastolic function and global strain measures with ultrasound.

Results
These are the preliminary results of this project that included 49 subjects (20 hypoPT, 18 PHPT and 11 controls) of 150 expected. All study groups presented similar BMI, TSH and kidney function. HypoPT patients had significantly lower PTH and calcium levels (P<0.001) and higher phosphorus levels (P<0.001) than PHPT and controls. HypoPT had higher inflammation markers (erythrocyte sedimentation rate levels) than PHPT and controls (34.5 ± 17.2 vs 27.6 ± 10.9 vs 15.0 ± 9.6 ml/h, P=0.020). All study groups presented no significant differences in basal brachial artery diameter, FMD and diastolic function. HypoPT showed higher global strain value than PHPT subjects (-19.6 ± 2.2 vs 11.2 ± 2.4 vs 7.6 ± 2.1 mm, P=0.002).

Conclusion
Up to now, our findings suggest that hypoPT has an increased atherothrombotic risk and needs adequate cardiovascular evaluation. We believe that further comprehensive studies are needed.

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Tumour induced osteomalacia: 2 years treatment with burosumab
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Introduction
Tumor-induced osteomalacia (TIO) is a paraneoplastic syndrome due to an overproduction of fibroblast growth factor 23 (FGF23) by small and benign mesenchimal tumors. FGF23 increase causes hypophosphatemia, osteomalacia and muscle weakness. TIO is usually cured by tumour resection, but neoplasms may be unidentifiable/unresectable or the patient may refuse surgery. In these cases, medical treatment with high doses of oral phosphate and calcitriol is mandatory, even though it is usually insufficient to restore normal phosphate levels and is associated with low compliance. Burosumab is a human monoclonal antibody against FGF23 employed to treat X-linked hypophosphatemia (XLH), recently approved for TIO in USA. Maximum dose of Burosumab in XLH is 90 mg/2 weeks but there are no data on clinical efficacy and safety concerning the use of Burosumab in TIO.

Case report
A 65 years old male presented to our attention for multiple non traumatic fractures (femoral neck, ribs, pelvic bone) and low bone mineral density. He was forced to use crutches because of pain and limb weakness, determining low personal autonomy and mobility. Biochemical evaluation showed hypophosphatemia (1.1 mg/dl), normal calcium and PTH, high ALP (514 U/l) and CTX (0.864 mg/ml), normal creatinine and low tubular phosphate reabsorption (80%), whereas c-FGF23 was elevated. After excluding drug-induced and genetic osteomalacia/hypophosphatemia, a 68GaPET was performed, identifying a lesion at the right rib as cause of TIO. The patient refused surgery, therefore Burosumab therapy was started (initial dose 0.3 mg/Kg, gradually increasing to 60 mg/2 weeks). After 2 years of treatment, biochemical evaluation showed phosphoremia normalization and ALP reduction (138 U/l). Patient clinical symptoms improved: Brief Pain Inventory (BPI) scores decreased, indicating reduced pain severity (from 1 to 0.5pt) and pain interference (from 3 to 0.6pt) as well as reduced fatigue (Brief Fatigue Inventory from 35 to 6pt). Sit-To-Stand Test and 6-minute Walking Test also improved (from 14.83s and 372 m to 11.08s and 430 m respectively). No side effects nor tumour progression were reported during follow-up.

Table 1

<table>
<thead>
<tr>
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<th>Basal</th>
<th>2 years of treatment</th>
<th>Reference Range</th>
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<tbody>
<tr>
<td>Phosphoremia</td>
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<td>2.8 mg/dl</td>
<td>2.5-4.5 mg/dl</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.8 mg/dl</td>
<td>9.7 mg/dl</td>
<td>8.5-10.5 mg/dl</td>
</tr>
<tr>
<td>ALP</td>
<td>514 U/l</td>
<td>138 U/l</td>
<td>30-120 U/l</td>
</tr>
<tr>
<td>CTX</td>
<td>0.864 mg/ml</td>
<td>0.55 mg/ml</td>
<td>0.115-0.748 mg/ml</td>
</tr>
<tr>
<td>Bone ALP</td>
<td>138 mg/l</td>
<td>72.7 mg/l</td>
<td>3-20.2 mg/l</td>
</tr>
<tr>
<td>TmP/GFR</td>
<td>0.85 mg/dl</td>
<td>1.53 mg/dl</td>
<td>2.47-4.18 mg/dl</td>
</tr>
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<td>TRP%</td>
<td>80%</td>
<td>97%</td>
<td>85-95%</td>
</tr>
</tbody>
</table>

Conclusions
Our experience supports efficacy and safety of the use of Burosumab every 2 weeks in TIO.

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P289

Hypercalcemia with positive calcium-sensing receptor (casr) autoantibodies
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CaSR autoantibodies may cause auto-immune hypercalcemia through either simple blocking or biased properties. The phenotype of this rare disease is most often acquired hypocalciuric hypercalcemia (AAH) (Minabres JCEM 2020, Makita JCI insight 2022), but sometimes hyperparathyroidism (Pelleiter-Morel Intern Med 2008), in elderly. Gender, auto-immune context is variable. Blood calcium may fluctuate, and acute exacerbations may be successfully treated with...
prednisolone and/or calcimimetics. We present two cases of CaSR-antibodies-associated hypercalcaemia with a different phenotype

Case#1
A 80-year-old woman (BMI 29) had a history of cured endometrial cancer, autoimmune thyroiditis and scleroderma-like syndrome (Sjögren and Raynaud syndrome with severe hypertension, increased level of anti-nuclear centromeric autoantibodies (1/512)). In 2002, detectable CaSR-antibodies with normal calcium (97 mg/dl), hypercalcia (78 mg/24 h), mild 25-OH-vitamin D deficiency (21 pg/ml), normal PTH level (36 pg/ml) and moderate CD4 and B lymphopenia was disclosed in a systematic autoimmune screening, after an episode of oral candidosis, without identified pathogenic variant of the AIRE gene. In 2015, she was operated for breast carcinoma. In 2022, blood calcium level was increased (107 mg/dl), with normal phosphatemia (37 mg/dl), low 25-OH-vitamin D (25 ng/ml) and persistent anti-CASR and anti-autoantibodies. No parathyroid hyperthyrotemy was identified on US examination.

Case#2
A 70-year-old lady, BMI 30, with a history of cured endometrioid uterine adenocarcinoma was referred for recurrence of hypercalcaemia 12 years after a left upper parathyroidectomy with total thyroectomy for a typical biological hyperparathyroidism profile with hypercalcia and osteopenia, associated to multinodular goiter without thyroid antibodies. Morphological parathyroid investigations were discordant, but after surgery, blood calcium dropped from 119 to 95 mg/l and remained so until 2019, where a profile of hyperparathyroidism reappeared with the presence of renal lithiasis. There was no excess of 25 or 1-25-OH vitamin D, calciuria, PTH and CaSR-antibodies levels were increased, without other positive auto-antibodies. The NGS study of the MEN1, HRPT2, CASR, AP2S1, GNA11 and GCM2 genes was negative. Morphological investigations remained discordant.

Conclusion
The presence of CaSR-autoantibodies in these 2 elderly female cases of hypercalcaemia: without overt parathyroid adenoma, suggest an auto-immune context for CaSR-hypercalcemia: without autoimmune context, except for CaSR-autoantibodies. The NGS study of the MEN1, HRPT2, CASR, AP2S1, GNA11 and GCM2 genes was negative. Morphological investigations remained discordant.

DOF: 10.1530/endoabs.81.P289

P290
Utility of intraoperative parathyroid hormone monitoring to predict success of parathyroidectomy for primary hyperparathyroidism
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Introduction
Parathyroidectomy is the only curative treatment for primary hyperparathyroidism (pHPT) and has been traditionally performed through bilateral neck exploration (BNE). However, with the use of intraoperative parathyroid hormone (IOPTH) assay along with preoperative localization exams, minimally invasive surgery can be performed with good surgical success rate.

Aim
To evaluate the usefulness of IOPTH assay in guiding adequate parathyroidectomy in patients with pHPT.

Materials and Methods
We retrospectively analysed the case records of patients who underwent parathyroidectomy for pHPT between 2003 and 2021 at our hospital. IOPTH monitoring was employed as an intraoperative tool to guide the surgical procedure. Blood samples were collected at pre-incision time and then 10–15 minutes after parathyroid gland excision. Successful surgery was defined as a drop of 50% or more in the IOPTH level, otherwise, BNE was performed. These results were compared to alternative strategies for IOPTH monitoring, including a 60% decline and reduction to parathormone (PTH) reference range values.

Results
A total of 99 patients were included. Post-excision PTH levels dropped > 50% in 80 (80.8%) patients. 3 of 19 patients (15.8%) whose outcomes failed to reach curative criteria had confirmed multicellular disease. Intraoperative PTH monitoring using our criteria showed a 91.7% sensitivity, 80% specificity and 89.9% accuracy. True positive among them were 77 (77.8%), true negative 12 (12.1%), false positive 3 (3.0%) and false negative 7 (7.1%). If a normal PTH value was required as a criterion for cure, unnecessary BNE would have been performed in 32 patients (32.3%) and in 12 patients (12.1%) if a 60% decline was applied, compared with just 8 patients (8.1%) when using the previous criteria.

Conclusion
IOPTH in adjunct with other localizing studies was helpful for carrying out successful parathyroidectomy. The use of IOPTH had good sensitivity in predicting cure for most of the patients with pHPT undergoing minimally invasive parathyroidectomy. The use of other criteria, such as 60% decline and normal PTH value 10–15 minutes after excision, was associated with higher rates of conversion to unnecessary BNE.

DOF: 10.1530/endoabs.81.P290

P291
Vitamin D status and bone health in adolescents and young adults with congenital adrenal hyperplasia
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Background
Data on the effects of long term glucocorticoid (GC) treatment on bone mineral density (BMD) in patients with congenital adrenal hyperplasia (CAH) are controversial.

Objectives
To evaluate BMD and vitamin D status in adolescents and young adults with CAH in comparison with healthy controls.

Methods
32 patients with classical CAH (13 males; mean of age 26.0 ± 7.1 years (14.0–37.3) were compared to 32 healthy controls matched by age, gender, and Tanner stage of pubertal development. Body composition was evaluated in all subjects with DXA (Hologic Inc., Bedford, MA, USA).

Results
Mean vitamin D level was 50.1 ± 55.5 nmol/l in controls, P = 0.35. Eighteen (56.25%) patients and thirteen (40%) controls had vitamin D deficiency (P = 0.21). Vitamin D levels were inversely associated with age (r = -0.29, P = 0.04) and body mass index (r = -0.282, P = 0.045) in all subjects. Mean whole body and lumbar BMD Z-scores were similar in CAH and control groups (-0.57 ± 0.96 vs. -0.29 ± 0.9, P = 0.27, and -0.97 ± 1.0 vs. -0.62 ± 0.8, P = 0.15, respectively). In 12.5% (n = 4) of patients and 18.75% (n = 6) controls whole body BMD Z-score was between -2 and -1 standard deviation (SD). P = 0.5 Whole body BMD Z-score < -2 SD was found in 12.5% (n = 4) of patients and 0% controls, P = 0.04. There was no history of bone fractures in neither of study groups. In the CAH group, vitamin D levels and BMD Z-scores did not correlate with GC cumulative doses, 17-hydroxyprogesterone or testosterone (T) levels. Adjustment for T levels did not change the results.

Conclusions
Patients with CAH are at risk for the development of osteoporosis. In our study, BMD Z-score and vitamin D were not related to cumulative GC doses and markers of disease control.

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Parathyroidectomy decreases serum monocyte chemoattractant protein-1, and increases vitamin d metabolites in patients with primary hyperparathyroidism
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Background
Primary hyperparathyroidism (PHPT) is a common endocrine disorder accompanied by high cytokines and low total 25-hydroxyvitamin D (25(OH)D). An inflammatory cytokine, monocyte chemoattractant protein-1 (MCP-1), is found to be higher in people with elevated parathyroid hormone (PTH), unlike other cytokines (1). Also, a rise in MCP-1 in response to high PTH is associated with bone loss (2). Parathyroidectomy (PTX) is the only cure for patients with PHPT. Whether the decline in PTH due to PTX leads to a decrease in MCP-1 and its effect on vitamin D metabolites remains unclear.

Objective
To investigate the effect of PTX on serum MCP-1 and vitamin D metabolites in patients with PHPT.

Methods
Patients with PHPT who underwent minimally invasive PTX were included. Serum samples were collected before and 3-month after surgery. Serum levels of calcium, PTH, vitamin D binding protein (DBP), and free 25(OH)D, MCP-1, and C-reactive protein (CRP) were measured. Correlation coefficients and multiple linear regression models were used to assess relationships among PTH, vitamin D metabolites and cytokines.

Results
In 25 PHPT patients (age: 61 ± 11 years old; BMI: 31.0 ± 5.6 kg/m²), levels of serum PTH and calcium were decreased (PTH: 118.6 ± 42.4 to 44.7 ± 25.2 pg/ml; Ca: 11.0 ± 0.6 to 9.6 ± 0.4 mg/dl; P < 0.001) to normal after PTX. Meanwhile, both total and free 25(OH)D were significantly increased (28.1 ± 10.2 to 37.2 ± 11.2 ng/ml; 4.9 ± 2.1 to 8.1 ± 3.8 pg/ml; P < 0.001), together with elevated DBP (P < 0.001) after surgery. The level of MCP-1 declined by 20% (P < 0.001), while CRP remained relatively stable after PTX. The PTH was negatively correlated with total and free 25(OH)D and DBP (P < 0.001), however, positively correlated with MCP-1 (P < 0.01). The CRP (but not MCP-1) was found to be negatively correlated with both total and free 25(OH)D (P < 0.01).

Conclusion
These data show that the decline of PTH due to PTX down-regulates serum MCP-1, but not CRP. Also, PTX normalizes PTH and Ca level, and leads to an increase in DBP, total and free 25(OH)D, which appears to be independent of PTH. Association of vitamin D metabolites and MCP-1, but not CRP, might suggest their different pattern of regulation.

References
1. Sukumar et al. (2011). The high serum monocyte chemoattractant protein-1 in patients with PHPT remains unclear and further studies are needed.
2. Siddiqui et al. (2017). Catabolic Effects of Human PTH (1-34) on Bone: Risk factors relevant to fracture risk were assessed via a self-administered questionnaire. Spearman correlation of UDR BMD to 10-year risks of major osteoporotic and hip fractures (assessed by FRAX) was explored. The possible added value of UDR BMD in explaining prevalent osteoporotic fractures was assessed using a multivariable regression model incorporating age and traditional osteoporosis diagnosis.

Results
The study included 1,245 women with a median age of 66 (IQR 59-73), of whom 29% (24/4%) had UDR T-score ≤ -2.5 and 154 (12%) reported prior fractures. UDR BMD was significantly negatively correlated with FRAX risk score for hip and major osteoporotic fractures (R = -0.5 and R = -0.41 respectively; P < 0.001). UDR T-score ≤ -2.5 was associated with higher fracture prevalence (19% vs. 10%; P < 0.001), and remained significant after adjusting for traditional BMD and age (OR 1.49, 1.01-2.19; P = 0.043).

Conclusions
UDR BMD correlates both with prior fractures and with predicted fracture risks and might pose added value over traditional DXA sites.

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Primary hyperparathyroidism (PHPT) is a common endocrine disease mainly caused by a single parathyroid adenoma. Although the localization of the parathyroid adenoma is not a surgical criterion for parathyroidectomy (PTX), this is known to increase the cure rate and reduce the complication rate. Neck ultrasound and MIBI-scintigraphy are the first-line techniques to detect hyperfunctioning parathyroid tissue, however, they have some limitations including the operator-dependent sensitivity and limited utility in case of a deep-lying or ectopic parathyroid. Recently, it has been shown that parathyroid adenomatous cells are capable of capturing choline, making this molecule a potential tracer in parathyroid. The aim of our study was to evaluate the utility of $^{18}$F-fluoro-choline PET/CT in 43 patients with PHPT candidate for PTX with negative or inconclusive results on conventional imaging. All patients underwent neck ultrasound performed by an expert physician, double tracing MIBI SPECT/CT and $^{18}$F-choline PET/CT. The latter both examinations were performed at the same site. Neck ultrasound was negative in 23/43 (53%) and inconclusive in 20/43 (47%) patients. MIBI SPECT/CT was negative in 36/43 (84%) and inconclusive in 7/43 (16%) patients. PET/CT was positive in 30/43 (70%), inconclusive in 3/43 (7%) and negative in 10/43 (23%) patients. Thirty-three patients underwent PTX. 22 mini-invasive approach, 11 open cervicotomy (1 for recurrence of parathyroid cancer, 1 for suspected parathyroid malignancy, 2 for multinostral goiter, 1 for concomitant thyroid malignancy, 4 for negative uptake and 2 for bilateral PET/CT uptake). The intraoperative PTH assay was performed in 29 cases and in all but one basal value. The histology showed parathyroid adenoma in 28 (84%), parathyroid cancer in 2 (6%), papillary thyroid cancer in 1 and white cervicotomy in 2 patients.

Conclusion
Hereditary and familial forms of PHPT were found in 16 (4%) of all patients who underwent parathyroidectomy for PHPT in our centre. There may exist undiagnosed hereditary PHPT among those who have not been genetically tested. Germline mutations were detected in 13 patients (12 in MEN 1, 1 in RET-MEN 2A). Familial PHPT without detected germline mutation was found in 3 patients. 2 of them had variant of uncertain significance and further familial segregation study will be provided. Supported by Ministry of Health Czech Republic - DRO (Institute of Endocrinology - EU, 00023761)

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$^{18}$F-fluoro-choline PET/CT is a useful localization technique in patients with primary hyperparathyroidism

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Primary hyperparathyroidism (PHPT) is a common endocrine disease mainly caused by a single parathyroid adenoma. Although the localization of the parathyroid adenoma is not a surgical criterion for parathyroidectomy (PTX), this is known to increase the cure rate and reduce the complication rate. Neck ultrasound and MIBI-scintigraphy are the first-line techniques to detect hyperfunctioning parathyroid tissue, however, they have some limitations including the operator-dependent sensitivity and limited utility in case of a deep-lying or ectopic parathyroid. Recently, it has been shown that parathyroid adenomatous cells are capable of capturing choline, making this molecule a potential tracer in parathyroid. The aim of our study was to evaluate the utility of $^{18}$F-fluoro-choline PET/CT in 43 patients with PHPT candidate for PTX with negative or inconclusive results on conventional imaging. All patients underwent neck ultrasound performed by an expert physician, double tracing MIBI SPECT/CT and $^{18}$F-choline PET/CT. The latter both examinations were performed at the same site. Neck ultrasound was negative in 23/43 (53%) and inconclusive in 20/43 (47%) patients. MIBI SPECT/CT was negative in 36/43 (84%) and inconclusive in 7/43 (16%) patients. PET/CT was positive in 30/43 (70%), inconclusive in 3/43 (7%) and negative in 10/43 (23%) patients. Thirty-three patients underwent PTX. 22 mini-invasive approach, 11 open cervicotomy (1 for recurrence of parathyroid cancer, 1 for suspected parathyroid malignancy, 2 for multinostral goiter, 1 for concomitant thyroid malignancy, 4 for negative uptake and 2 for bilateral PET/CT uptake). The intraoperative PTH assay was performed in 29 cases and in all but one basal value. The histology showed parathyroid adenoma in 28 (84%), parathyroid cancer in 2 (6%), papillary thyroid cancer in 1 and white cervicotomy in 2 patients. Of note, the two patients with bilateral uptake had the excision of only one pathological gland since at surgical exploration there was no evidence of other enlarged parathyroid gland. Conversely, one patient only with one abnormal uptake at PET/CT had the removal of two enlarged parathyroid glands that were both adenomas. Thus, 26 of 29 parathyroid lesions were true-positive and 3 were false-positive uptake. Overall, per-lesion sensitivity of $^{18}$F-choline PET/CT was 81%, the positive predictive value was 90% and the accuracy was 75% for all parathyroid lesions. In conclusion, $^{18}$F-choline PET/CT demonstrated a good diagnostic performance and it might be considered as a valid alternative in patients with negative/inconclusive conventional imaging.

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Risk factors for renal calcifications and determinants of hypercalciuria in patients with chronic, post-surgical hypoparathyroidism

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Conventional therapy with oral calcium supplements and activated vitamin D is the most diffuse and available therapy for chronic hypoparathyroidism (HypoPT). This treatment does not replace the lack of PTH and is associated with renal complications. We report the results of a case control study with a prospective design which included 178 adult patients with differentiated thyroid cancer treated with total thyroidectomy with a follow-up longer that 3 years after surgery: 89 with PoHypoPT treated with conventional therapy and 89 without PoHypoPT, matched for age and sex. Both groups were balanced for gender, age, time since thyroidectomy, supplementation with cholecalciferol, dose of levothyroxine and dietary calcium intake. Half of the patients were stable on treatment with calcitriol alone, 45% with calcitriol and calcium carbonate, and 4 with calcium carbonate alone. All patients underwent biochemical tests and renal ultrasound. Twenty-four-hour urinary calcium, creatinine, sodium, potassium, chloride, sulfate, uric acid, phosphate, oxalate, citrate, volume and Ph were measured. The biochemical control of patients with PoHypoPT was satisfactory, but only one-third of patients was at target according to ESE guidelines. Patients with PoHypoPT, compared with those without PoHypoPT, had significantly lower alb-Ca and PTH and increased serum phosphate, calcium-phosphate product, and 24-h urinary calcium, but there was no difference in estimated GFR. Renal calcifications were detected in 26 (29.2%) patients with PoHypoPT and in 11(12.4%) without. We found a positive association between renal calcification and elevated serum phosphate (P = 0.03) and plasma PTH (P = 0.01), but no association with hypercalciuria or other urinary parameters. The median 24-h urinary calcium was significantly higher in patients with PoHypoPT than in those without (248 vs 162 mg, P < 0.01). Urinary calcium in patients with PoHypoPT was positively associated with serum calcium (P < 0.001), urinary magnesium (P < 0.001), and urinary volume (P = 0.003), and negatively associated with serum albumin (P = 0.025), urinary oxalate (P < 0.001) and creatinine (P = 0.008). Our study confirms that conventional therapy in patients with chronic PoHypoPT is suboptimal. 24-h urinary calcium and the rate of renal calcification are higher in patients with chronic PoHypoPT compared with controls. We found no significant difference in renal function (eGFR) between patients with chronic PoHypoPT compared with controls. We found no association between renal calcification and hypercalciuria and/or other urinary stone risk factors. Further prospective studies including a large number of patients would be necessary to better define the risk factor for renal calcifications in patients with PoHypoPT.

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Phenotype characterization of a PHEX non canonical splice-site mutation in a family affected by X-linked hypophosphatemic rickets and efficacy of one-year Burosumab treatment in adult patients

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X-linked hypophosphatemic rickets (XLH) is associated with mutations in PHEX, upregulation of FGF23, leading to hypophosphatemia, abnormal bone development and short stature. H-MAB to FGF23, Burosumab, is the new therapy for XLH. Among PHEX mutations, c.1586+6T>C partially destroying the splice-site, is presumably associated to a mild phenotype not described so far. We describe two siblings bearing the PHEX c.1586+6T>C variant. Case 1: A 52y men, 152 cm tall (-3.4SDS), father of two pediatric patients, was referred after testing positive for same PHEX mutation found in the proband. Family history of a similar condition was negative, except for his sister. At 47y, after investigation on his affected daughters, an orthopedic consultation concluded for active rickets. He presented impaired mobility, distal arthropathy, tibia vara, hypophosphataemia of tooth enamel, and bilateral perceptive hearing loss. Six minutes walking test (6MWT) showed reduced functional capacity. IQOLA-SF-36 showed poor QOL. X-ray found diffuse spondylarthritis, coxosexism, dysmorphism of proximal femoral epiphyses and curvature of the diaphysis. The MOC-DEXA compatible

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by gender and age. Case 2: A 47y woman, 143 cm tall (-3.3 SDS). At 29y undergo surgery on right foot scaphoid bone and was diagnosed tibia vara. At 45y an orthopedic consultation concluded for active rickets. She showed skeletal malformations, waddling gait, diffuse polyarthrosis, hypodiplasia tooth enamel, and perceptive deep. 6 MWT showed reduced functional capacity. IQOLA-SF-36 showed poor QOL. They started conventional supplementation with active vitamin D, phosphate was added to calcitriol and suspended before Burosumab.

Introduction

Hypoparathyroidism (HypoPT) is a rare endocrine disease which is characterized by hypocalcaemia and undetectable or inappropriately low serum parathyroid hormone (PTH). Post-surgical HypoPT (PS-HypoPT) is the most common cause, caused by accidental parathyroid removal/injury during neck surgery. Conventional therapy with calcium and vitamin D analogues does not restore calcium homeostasis and patients with chronic PS-HypoPT complain with several complications. From a neuropsychological standpoint, patients with PS-HypoPT present cognitive and affective symptoms: the more plausible pathophysiological mechanism resides in a direct effect of PTH in the central nervous system (CNS), but these mechanisms are still not completely elucidated. The aim of this study was to evaluate the effects of PTH deprivation on CNS in an animal model (rat) of post-surgical hypoparathyroidism, by a cognitive/behavioural assessment approach.

Methods

A rat model (Sprague Dawley) of PS-HypoPT was obtained by the surgical removal of parathyroids at 5 weeks of age and treated with glucocortic acid 1% in drinking water to maintain normocalcemia. An experimental group of 15 PS-HypoPT rats and 15 healthy Sprague Dawley (WT) underwent biochemical testing (serum calcium) and behavioural testing namely Morris Water Maze – MWM-to assess spatial learning and memory at 9 weeks of age. Biochemical testing (serum calcium) and behavioural testing namely Morris Water Maze – MWM-to assess spatial learning and memory at 9 weeks of age. 

Results

PS-HypoPT animals showed a significantly worse performance compared to controls, as suggested by a higher escape latency parameter (1st day 23.8±11.9 vs 14.6±9.3 sec P=0.02; 2nd day 13.3±11.6 vs 8.7±4.7 sec P=0.02; 3rd day 14.5±7.9 vs 11.01±2.84 sec P=0.01). Both groups improved their results from the first to the last day of training (escape latency PHPT 23.8±11.9 vs 9.2±4.5 sec P<0.001; WT 14.6±9.3 vs 5.5±0.6 sec P<0.001), even if PS-HypoPT group had a higher improvement compared to WT (multivariate analysis P=0.04).

Conclusions

Animal model of HypoPT shows an impairment in spatial learning and memory compared to WT, training could ameliorate this condition. Further studies are ongoing evaluating other cognitive functions in such a model and could help to understand the physiopathological bases of neuropsychological symptoms in patients with HypoPT.

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Impact of body composition on skeletal health in subjects with Klinefelter’s syndrome (KS): a cross sectional study

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Background

There is growing awareness of skeletal impairment in individuals with Klinefelter syndrome (KS), involving both quantitative and qualitative alteration of the bone as well as an increased prevalence of vertebral fractures (VFs). Beyond hypogonadism, considerable evidence suggests that other factors may be responsible for the skeletal fragility observed in these patients. Abnormal body composition is a common finding in KS subjects, characterized by an unfavourable muscle/fat ratio with an increase in total and abdominal fat mass, but evidence of its relationship with bone health is scant.

Purpose

Based on the emerging evidence of a close relationship between bone and soft tissues with possible detrimental effect of body fat distribution on bone metabolism, we aimed at assessing the impact of body composition parameters on bone health in terms of bone mineral density (BMD), microarchitecture, and radiological VFs in adult subjects with KS.

Methods

Seventy-three adult males with KS were consecutively enrolled by two Endocrinology and Andrology Units (IRCCS Humanitas Research Hospital in Milan and ASST Spedali Civili in Brescia). Whole body dual-energy X-Ray Absorptiometry (DXA) was performed to assess lumbar spine, femoral neck and total hip BMD, trabecular Bone Score (TBS) and body composition. Prevalence of VFs was assessed by quantitative morphometry on lateral spine X-rays.

Results

Low BMD was observed in 16 patients (23%). No significant differences were found in body mass index (BMI) and several body composition parameters between KS subjects with normal and low BMD. Decreased TBS was found in 16 patients (26%) with a prevalence which resulted significantly higher in individuals with higher BMI (P=0.001), fat body mass (FMB) (P<0.001), visceral adipose tissue (VAT) (P<0.001) and/or fat mass index (P<0.001). VFs were detected in 14 patients (19%), without significant associations with BMD (P=0.983) and TBS (P=0.371). However, subjects with VFs had significantly higher percentage of truncal/leg fat ratio (P=0.011) as compared to those without VFs.

Conclusion

This study provides a first evidence that abdominal adiposity might be a determinant of VFs in KS patients, consistent with the working hypothesis that alterations in body composition could negatively affect bone health in this clinical setting. The value of TBS in predicting fractures in KS without possible interference of body composition remains to be clarified in future longitudinal studies.
Parathyroid carcinomas (PCAs) are rare endocrine malignant neoplasms characterized by an abnormal PTH secretion and, consequently, severe and uncontrolled hypercalcemia. Clinically, the preoperative diagnosis can be misleading, because PCAs share some molecular and clinical similarities with benign lesions and are often indolent. The histological diagnosis of carcinoma is achieved based on the presence of mitotic nuclear figures, capsular invasion, parenchyma infiltration, vascular invasion and, less frequently, distant metastasis. Moreover, there is no molecular biomarker that could support PCAs diagnosis. IncRNAs are an important class of epigenetic regulators involved in both physiological processes and cancer development. Preliminary evidence suggested that IncRNAs could act as accurate prognostic and diagnostic biomarkers. Recently, we identified a long non-coding RNAs (IncRNAs) signature able to distinguish PCAs from benign parathyroid adenomas (PAdS) and normal parathyroid glands. Particularly, the IncRNA BCYRN1/BC200 emerged as an interesting candidate biomarker for the diagnosis of PCAs. In gastric, colorectal and breast cancers BC200 expression is dramatically increased and positively correlates with distant metastasis, tumor size and clinical stage. We previously reported that BC200 is overexpressed in PCAs tissues harboring CDC73 gene inactivating mutations. Here, we found that BC200 is also upregulated in metastatic PCAs (n = 4) compared to the non-metastatic (n = 9) parathyroid carcinomas. Then, we tested the hypothesis that circulating BC200 expression may provide a clinical and non-invasive biomarker to distinguish PCAs from PAdS. To this end, we analyzed circulating BC200 expression levels in serum samples from patients affected with PCAs (n = 4) and PAdS (n = 22) through digital PCR. All samples were collected prior parathyroidectomy. Our results show that BC200 counts are higher in the serum of patients affected with PCAs compared to those detected in serum of patients harboring PAdS. Moreover, serological BC200 counts positively correlate with circulating PTH and total calcium levels and age at diagnosis in PAdS. Lastly, we analyzed circulating BC200 expression in the serum of 3 PCAs patients before and after parathyroidectomy. BC200 counts are reduced in all 3 postoperative serum samples compared to the preoperative specimens, suggesting its potential use also as a useful non-invasive biomarker in the clinical follow-up of PCAs patients. These findings extend the knowledge on BC200 in parathyroid tumors, use also as a useful non-invasive biomarker in the clinical follow-up of PCAs. To this end, we analyzed circulating BC200 expression levels in serum of 3 PCAs patients before and after surgical treatment, and then as follow-up tests one month and six months after ptx; the follow-up ECHO assessment was performed 6 months after ptx. After ptx, the expected significant decrease in PTH concentration was achieved in all patients and the levels of Ca and Pi normalized (P < 0.001). The study group included 25 patients with hyperparathyroidism (HT) (56%). Statistical significance was not achieved both in terms of BP change and the dipper/non-dipper parameters. The relationship between PTH and mean SBP and DBP was statistically significant. Patients were divided into two groups: patients with HT (25) and patients with normal BP (20) before ptx. After surgery, improvement in HT control was observed in 23 patients (92%); in this group it was found: BP normalization in 8 patients (35% in the improvement group), discontinuation or reduction of the amount of antihypertensive drugs in 13 patients (56% in the improvement group), achievement of the correct reduction of BP at night (non-dipper -> dipper) in 14 patients (61% from the improvement group). In the analysis of ECG parameters before ptx and after surgery, a statistically significant change occurred in the QTC interval (P < 0.001). Among patients with SVBP and VBP before ptx, statistically significant improvement in SVBP and VBP after ptx was observed. The QTC interval variable correlated with PTH and Ca before ptx. In ECHO, the IVS, LVEDD and LVEF did not differ statistically significantly between the tests before and after the procedure, whereas both parameters of BWT, LVM and LVID differ statistically significantly – before the surgery they were significantly higher than after the surgery. The GLS value was significantly decreased in 27 (60%) patients after ptx. To conclude, the patients with PNP have a higher risk of cardiovascular diseases, observing the improvement of cardiological parameters after successful surgery.

Typical symptomatology of primary hyperparathyroidism (PnPN) includes bone lesions and renal dysfunction in the form of recurrent nephrolithiasis but the symptoms of hypercalcemia may mimic other conditions, including cardiovascular diseases. The exact frequency of cardiac symptoms is not known. The study included 25 adult patients with PNP over 18 years of age, who were qualified for ptx. Laboratory tests included the determination of serum PTH, Ca, Pi and cardiac ECHO assessment of the heart, 24-hour recording of blood pressure using the Holter method and 24-hour Holter electrocardiography – the procedures were performed before the surgical treatment, and then as follow-up tests one month and six months after ptx; the follow-up ECHO assessment was performed 6 months after ptx. After ptx, the expected significant decrease in PTH concentration was achieved in all patients and the levels of Ca and Pi normalized (P < 0.001). The study group included 25 patients with PNP (56%). The statistical significance was not achieved both in terms of BP change and the dipper/non-dipper parameters. The relationship between PTH and mean SBP and DBP was statistically significant. Patients were divided into two groups: patients with HT (25) and patients with normal BP (20) before ptx. After surgery, improvement in HT control was observed in 23 patients (92%); in this group it was found: BP normalization in 8 patients (35% in the improvement group), discontinuation or reduction of the amount of antihypertensive drugs in 13 patients (56% in the improvement group), achievement of the correct reversal of BP at night (non-dipper -> dipper) in 14 patients (61% from the improvement group). In the analysis of ECG parameters before and after surgery, a statistically significant change occurred in the QTC interval (P < 0.001). Among patients with SVBP and VBP before ptx, statistically significant improvement in SVBP and VBP after ptx was observed. The QTC interval variable correlated with PTH and Ca before ptx. In ECHO, the IVS, LVEDD and LVEF did not differ statistically significantly between the tests before and after the procedure, whereas both parameters of BWT, LVM and LVID differ statistically significantly – before the surgery they were significantly higher than after the surgery. The GLS value was significantly decreased in 27 (60%) patients after ptx. To conclude, the patients with PNP have a higher risk of cardiovascular diseases, observing the improvement of cardiological parameters after successful surgery.
regimen, vitamin D level and functional capacity were not different compared to baseline. Yet, 68.8% of MiD and 52% of DM patients wanted to remain on the current regimen. Among patients who experienced both regimens, 56.1% preferred daily and 43.9% preferred monthly.

Conclusion

Patients with osteopenia/osteoporosis had good adherence to monthly and to daily vitamin D regimens and expressed high level of satisfaction with them. All parameters remained stable after switching regimens. Most MiD patients preferred the new regimen. Additional large-scale studies are needed to evaluate the effects of various dosing regimens on patients’ satisfaction and adherence.

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Systematic literature review of the renal and cardiovascular complications associated with chronic hyperparathyroidism

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Despite conventional treatment with oral calcium and active vitamin D, patients with chronic hyperparathyroidism (cHypoPT) can remain not adequately controlled (NAC) and have abnormal biochemistry, disease complications, or symptoms impacting quality of life. A systematic literature review (SLR) was conducted to evaluate the clinical burden for patients with cHypoPT, with an emphasis on patients with NAC disease. This abstract focuses on data related to renal and cardiovascular complications. Key biomedical databases (MEDLINE, EMBASE, MEDLINE In-Process, Cochrane Controlled Register of Trials and Cochrane Database of Systematic Reviews) were searched for pertinent studies from database inception to June 2020. Abstracts from 6 relevant congresses held from January 2017–June 2020 were searched to identify studies not published as full-text journal articles. Publication bibliographies were reviewed to identify additional sources. Eligible studies included adults with cHypoPT and were published in English, with no restrictions on study design or comparator. NAC patients were identified via study-specific NAC definitions. Results were described per Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Forty-nine studies from 91 publications were included in the SLR. Of these, 21 and 7 publications addressed renal and cardiovascular complications, respectively. Compared with the general population, patients with cHypoPT were at increased risk of renal insufficiency, renal failure, nephrocalcinosis, and nephrolithiasis. Nephrolithiasis and nephrocalcinosis were the most commonly reported renal disorders, with incidence ranging from 1.9%–48% in patients with cHypoPT. Impaired renal function and risk of renal diseases were positively related to cHypoPT duration. In one study, rates of renal disorders were significantly higher in patients with NAC vs adequately controlled (AC) cHypoPT (P < 0.01). Patients with cHypoPT were at risk of cardiovascular outcomes including cardiomyopathy, congestive heart failure, ischaemic heart disease, and arrhythmia. Patients with cHypoPT had increased risk of both incident cardiovascular conditions and a composite cardiovascular endpoint compared with patients without cHypoPT (all P < 0.05). Longer disease duration was associated with increased risk of cardiovascular complications, independent of disturbances in calcium-phosphate homeostasis. In one study, patients with NAC disease had significantly higher rates of cardiovascular disorders compared with patients who were AC, especially for cardiac artery calcification and QT prolongation. cHypoPT is associated with increased risk of renal and cardiovascular complications. Based on limited published data, patients with NAC disease may experience a higher clinical disease burden than patients whose cHypoPT is controlled.

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Weakening of short- and long-term verbal memory in patients with PHPT, evaluated by a neuropsychological approach

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Introduction and aims

Primary Hyperparathyroidism (PHPT) is a common endocrine disease associated with hypercalcemia and elevated or inappropriately normal serum levels of PTH. Among PHPT manifestations, neuropsychological symptoms have been described, including depression, anxiety, loss of memory, impaired cognition, with a wide range (3-50%) depending on the study population. Neuropsychological sensitive symptoms in patients with PHPT have been evaluated as part of quality of life (QoL) assessment, mainly using validated self-administered questionnaires, as such as 36-Item Short Form Health Survey (SF-36), WHO-5 Well-being Index Survey (WHO-5), which lack specificity. This study aims to evaluate cognitive functions of patients with PHPT compared to a control population, using a standardized neuropsychological approach.

Methods

Observational, monocentric study on patients with PHPT and controls, in whom a standardized neuropsychological assessment, focused on attention functions and memory abilities was performed by a trained psychologist.

Results

Patients (n=19) presented a mild PHPT, and mean age 53.8 ± 11.45 years. Control population (n=24, mean age 51.8 ± 10.87 years) was enrolled among patients with differentiated thyroid cancer in remission (or without residual disease), without Hyperparathyroidism and in good control under levothyroxine therapy, who were followed by Endocrine Unit (University Hospital of Pisa). Patients with PHPT had significantly worse performance at Digit Span Forward (mean score 5.41 ± 0.81 – 6.17 ± 1.64; P-value < 0.05) test that provides a measure of verbal short-term memory span and Story Recall Test that provides a measure of auditory-verbal long – term memory. Regarding Story Recall Test the worse performance was confirmed both in immediate (mean score 4.54 ± 1.40 – 5.72 ± 1.46; P-value < 0.05) and delayed recall (4.37 ± 1.30 – 5.44 ± 1.51; P-value < 0.05).

Conclusions

Patients with PHPT might present a weakening in verbal short – and long – term memory. Further studies are ongoing to evaluate other cognitive functions and to correlate cognitive testing with biochemical parameters.

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P305

Reliability of who fracture risk assessment tool (frax) and bone mineral density in predicting fractures in cancer patients under hormone deprivation therapies: a real-world clinical study

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Background

Skeletal fragility is an important clinical issue in women with early-stage breast cancer and men with non-metastatic prostate cancer under hormonal hormone deprivation therapies (HDTs). Vertebral fractures (VFs) have been reported in a remarkable number of subjects exposed to HDT especially when the diagnosis of fractures is performed by a radiological and morphometric approach. Notably, prediction of fractures in this clinical setting is a challenge and determinants of fractures are still largely unknown. Current international guidelines rely on bone mineral density (BMD) and the WHO Fracture Risk Assessment Tool (FRAX) to identify cancer survivors at high risk of fractures to be treated in primary prevention, but their reliability in this setting of secondary osteoporosis seems to be inaccurate. In this study, reflecting the real-life clinical practice, we investigated the diagnostic performance of FRAX algorithm and BMD in identifying breast and prostate cancer survivors developing VF despite HDTs.

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Effects on bone mineral density and bone markers of the sequential treatment with teriparatide followed by zoledronic acid in patients with severe fractured osteoporosis: retrospective real-life data

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Osteoporosis is a chronic condition requiring long-term treatment; sequential treatment regimens with different agents represents an option aimed to increase bone mineral density (BMD) and then to maintain it. The loss of BMD occurring after withdrawal of teriparatide (TPT) can be prevented by bisphosphonates (BPs). Among BPs, data about the efficacy of zoledronic acid (ZOL) after TPT treatment are scanty. Here, we contribute to this topic providing data derived from the real-life setting of the third level centre Istituto Ortopedico Galeazzi in Milan. Twenty-two severe osteoporotic fractured patients [4 males, 18 postmenopausal females; aged 74.4 (65.8, 78.9) years, median, IQ range; BMI 26.1 ± 4.5 kg/m², mean ± SD] were treated with subcutaneous daily 20 microg TPT (according the Italian AIFA 79 note) for 24 months followed by two intravenous infusions of 5 mg ZOL, the first one at < 6 months from TPT withdrawal, the second one 12 months from the first infusion. Eight patients were smokers; 7 patients were treated with chronic steroid therapy (> 5 mg prednisone daily). Clinical and biochemical parameters were collected in all patients. BMD at lumbar and femur sites were measured by dual x-ray absorptiometry and recorded as T-scores. All patients experienced at least one vertebral fracture (3.0, 2.0-2.3). Mean lumbar T-scores (-1.09 ± 1.18) increased after TPT treatment (-2.45 ± 1.33, P = 0.002 by ANOVA) and the increase was consolidated by ZOL treatment (-2.17 ± 1.35, P = 0.0002 vs basal condition by ANOVA). Mean lumbar T-score increase was 21% of the basal T-score after TPT and further 11% after TPT + ZOL. Mean LD1 neck T-score [-2.70 (3.30, -2.08)] was not affected by TPT [-2.50 (-3.00, -1.88)] as well as by TPT + ZOL treatment [-2.50 (-3.20, -1.78); P = 0.157 by ANOVA]. Median total hip T-score [-2.40 (-2.90, -1.56)] increased after TPT + ZOL treatment [-1.75 (-2.48, -1.28); P = 0.049 by ANOVA]. Any patient experienced incident fractures during TPT treatment, while 1 patient reported a femur fracture and one patient a non-vertebral non-femur fracture during ZOL treatment. During the sequential TPT + ZOL treatment serum calcium and phosphate levels did not show significant changes, while plasma PTH levels decreased during TPT and increased during ZOL treatment. Serum total ALP and β-CTX levels increased during TPT and decreases during ZOL treatment. Serum 25hydroxyvitamin D were constantly > 20 ng/ml in all patients. In conclusion, our data from real-life management of severe osteoporotic patients showed that the sequential treatment TPT + ZOL is effective in increasing and maintaining lumbar and hip BMDs.

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P307

Impact of underlying disease on long-term skeletal outcome after lung transplantation

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Background

Fracture fragility fractures (FX) occur frequently after lung transplantation (TX), with a higher rate (15-20%) in the first two years, which decreases subsequently. Patients affected from cystic fibrosis (CF) seem to have a lower FX risk in the first two years after TX as compared with those affected with other lung diseases (nCF). The aim of our study is to evaluate and compare the long-term skeletal outcome in CF and nCF patients after TX.

Methods

We evaluated the FX rate and the trend in bone mineral density (BMD) after the first two years post-TX in 67 patients (36 CF, 31 nCF). The mean follow-up duration was 5.4 (4-8) years and 37.3% patients (15% CF and 51.6% nCF, P = 0.023) was taking bisphosphonates.

Results

26/7 patients (3%), both with TX rejection, had FX (1 FC 28 years old with hip FX and 1 nCF 65 years old with wrist FX). Lumbar spine (LS) BMD remained stable in both groups (-1.3 ± 1.1 vs -1.1 ± 1.2; P = 0.081) and (-1.5 ± 1.0 vs -1.4 ± 1.1; P = 0.485, CF and nCF respectively). Femoral neck (FN) and total hip (TH) BMD improved in CF group (-1.8 ± 1.0 vs -1.6 ± 0.9; P = 0.036; -1.6 ± 0.9 vs -1.4 ± 0.8; P = 0.001; respectively, FN, TH), conversely, FN worsened significantly and TH remained stable in nCF group (-1.7 ± 0.8 vs -1.7 ± 0.6; P = 0.018; -1.3 ± 0.7 vs -1.2 ± 0.7; P = 0.666; FN and TH respectively), in spite of a higher percentage of nCF patients taking bisphosphonates. The nCF disease was significantly associated with a worsening in both FN (OR 3.3 ± 0.017, 95%CI 1.8-500) and LS BMD (OR 11.5 ± 0.027, 95%CI 1.3-100) regardless of ongoing bisphosphonates therapy, cumulative glucocorticoids dose, age, TX rejection, spine deformity index. Conclusions

Our study confirms a low FX rate after the first two years post-TX. Also the long-term data suggest that the skeletal outcome after TX is more favourable in CF patients.

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Objective
Parathyroidectomy (PTx) improves quality of life (QoL) in patients with primary hyperparathyroidism (PHPT). Whether this effect is modified according to the patients’ age is unknown. The aim of this study was to evaluate the impact of age on the effect of PTx on QoL and frailty in patients with PHPT, six months post-PTx.

Methods
This was a prospective cohort study, including patients with PHPT, admitted from January 2016 to December 2019, divided into two categories: younger (<65 years old) and older (>65 years old). QoL was assessed with the Pasieka questionnaire (PAS-Q) two days pre- and six months post-operatively. Frailty was also assessed at the same time intervals, with the Frailty Index (FI).

Results
One-hundred thirty-four patients (younger group: 96 patients, mean age 50.4±9.8 years; older group: 38 patients, mean age 72.1±4.9 years) were included. PTx resulted in a significant reduction in PAS-Q score in both groups. Notably, a greater reduction in ‘bone pain’, ‘tiredness’, ‘weakness’, ‘joint pain’, ‘getting off chair’ and ‘headaches’ items was observed in older group. Moreover, PTx led to a decrease in FI only in this group.

Conclusions
PTx leads to an improvement in QoL both in older (>65 years) and younger (<65 years) patients with PHPT, attributed to a differential effect on PAS-Q items. Frailty improves only in the older group.

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P309
Testosterone supplementation and bone parameters, a systematic review and meta-analysis study
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Background
Testosterone (T) is essential for bone health during all ages, helping to achieve a proper peak bone mass and, later, to maintain bone density and strength. Guidelines on management of male osteoporosis recommend testosterone replacement in young-adult hypogonadal to prevent bone loss and anti-resorptive drugs in case of high fracture risk, but the role of T replacement therapy (TRT) alone in subjects with late onset hyperandrogenism is still the object of an intense debate.

Methods
All observational studies and placebo-controlled or -uncontrolled randomized trials (RCTs) comparing the effect of TRT on different bone parameters were considered.

Studies using androgens other than T, as well as studies with concomitant treatment with other hormones and drugs were also excluded, unless there was a clearly defined treatment arm that received only T treatment. Similarly, studies including only patients with genetic causes of male hypogonadism were excluded.

Results
Out of 349 articles, 36 were considered, including 3103 individuals with a mean trial duration of 66.6 weeks. TRT improves significantly areal bone mineral density (aBMD) at the spine (mean ±2.6%, 2.1-5.1%, CI 95%; P = 0.026) and femoral neck (mean ±3.6%, 1.6-6.1%, CI95%; P = 0.020) levels in observational studies, whereas placebo controlled RCTs showed a positive effect of TRT only at lumbar spine (+ 2.2%, 0.4-4.8%, CI 95%; P = 0.097) and when trials included only hypogonadal patients at baseline (total testosterone < 12 nmL (+ 5.2%, 0.7-9.7%, CI 95%; P = 0.024). The effects on aBMD were more evident in subjects with lower T levels at baseline and increased as a function of trial duration and a higher prevalence of diabetic subjects. Either T or estradiol increase at endpoint contributed to aBMD improvement. TRT was associated with a significant reduction of bone resorption markers in observational but not in controlled studies.

Conclusion
TRT alone is able to inhibit bone resorption and increase bone mass, particularly at the lumbar spine level and when the duration is long enough to allow the anabolic effect of T and estrogens on bone metabolism to take place. However, whether or not TRT is associated with a decreased risk of bone fractures remains to be established.

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P310
Impact of hypoparathyroidism on quality of life in patients with differentiated thyroid cancer
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Introduction
Hypoparathyroidism (hypoPTH) is one of the most feared iatrogenic complications of the surgical treatment for thyroid cancer (TC). Despite supplementation with calcium salts and calcitriol, hypoPTH seems to be associated with a negative impact on quality of life (QoL), which has not been evaluated in the Portuguese patients.

Objectives
To evaluate the impact of hypoPTH on the QoL of Portuguese patients with TC and its correlation with serum analytical parameters.

Material and methods
Cross-sectional study of patients diagnosed with TC and chronic hypoPTH (persistent one year after surgery), randomly selected, compared to a control group of patients submitted to surgery for TC without hypoPTH. QoL was assessed using the SF-36v2 health questionnaire, validated for the Portuguese population (which includes eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH)). The levels of ionized and total calcium, albumin, phosphorus, magnesium, creatinine, urea, PTH, vitamin D, TSH and free T4 were measured. Hypothyroid patients were excluded. The information collected was analysed in SPSS®. Data was analysed with Independent Samples’ T Test and Pearson’s correlation test.

Results
Of the 164 patients surveyed, 49 (29.9%) had hypoPTH and 78.7% were female. The mean age was 53.7±14.7 years. Patients with hypoPTH had statistically significant lower scores on the BP scales (55.8% ± 22.7 vs 63.4% ± 25.6,P = 0.050) and SP (69.4% ± 25.5 vs 78.6% ± 21.8,P = 0.040) when compared to patients without hypoPTH. Regarding patients with hypoPTH, there was an inverse correlation between phosphorus levels and the scores of the GH (P = 0.016), PF (P = 0.006) and RP (P = 0.020) scales; between age and scores of BP (P = 0.017) and PF (P = 0.019) scales. In these patients, lower PTH values were equally associated with worse results on BP scale (P = 0.013).

Conclusions
This was the first study to assess the impact of hypoPTH on QoL in Portuguese patients. The results obtained suggest a relationship between phosphorus levels and QoL in patients with hypoPTH. Its monitoring seems particularly important in this population in order to identify more vulnerable patients, who may benefit from additional measures.

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P546
Trabecular bone score captures low bone quality in women with normal bone mineral density or osteopenia initiating aromatase inhibitors for breast cancer
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Introduction
Hypoparathyroidism Bone Score (TBS) has been associated with fragility fractures in post-menopausal women. Estrogen-receptor positive breast cancer is usually treated with aromatase inhibitors (AIs), with international guidelines recommending initial bone density (BMD) evaluation, since this therapy is associated with high rates of fragility fractures. Each country has different thresholds of intervention to recommend pharmacologic treatment for fracture prevention. Patients with normal bone density or osteopenia often miss the chance of receiving any anti-osteoporotic treatment, beyond calcium and vitamin D.

Objective
To describe prevalence of low bone quality measured by TBS in women initiating aromatase inhibitors.

Design
Cross-sectional, observational.

Setting
University hospital.

Patients
From January to December 2021, 75 consecutive unselected ambulatory women with normal BMD or osteopenia referred from the Oncology Department for bone metabolism evaluation with a standardized protocol, after recent diagnosis of estrogen-receptor-positive breast cancer. The patients were naive to any kind of osteoprotective treatment, including calcium or vitamin D3 supplements. History of clinical or morphometric fractures was an exclusion criterion.

Main outcome measures
TBS, BMD and biochemistries at first endocrine referral before the start of AIs. TBS T-score $\leq -2$ was used to discriminate low bone quality.

Results
Twenty-five patients (33.3% of the whole cohort) aged 64.8 $\pm$ 10.7 had low TBS (1.238 $\pm$ 0.043). TBS negatively correlated with age ($r = -0.41, P < 0.001$), time from menopause ($r = 0.312, P = 0.012$) and positively associated with BMD at all sites (L1-L4, total hip and femur neck, $P < 0.001$). TBS was positively associated with urinary calcium ($r = 0.238, P = 0.047$), and negatively with 25(OH) vitamin D levels ($r = -0.243, P = 0.033$). By contrast, BMD was not associated with 25(OH) vitamin D levels. TBS showed no association with PTH, renal function or bone turnover markers. As opposed to TBS, lumbar spine BMD was negatively correlated with Beta-CTX ($r = -0.231, P = 0.047$). Both femur neck BMD T-score ($r = -0.233, P = 0.044$) and total hip BMD T-score ($r = -0.299, P = 0.009$) were negatively associated with PTH levels.

Conclusions
A considerable proportion of women with normal BMD or osteopenia appears to present with low bone quality at the start of hormone adjuvant therapy for breast cancer. TBS could be used as a complementary quantitative clinical tool in the initial evaluation and management of these patients and might be adopted to recommend anti-fracture treatment in this gray zone. TBS might also be correlated with underlying bone metabolism indices.

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P547
Effect of bisphosphonates on vertebral fractures in HIV infected males: 7-years study
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Objective
Osteoporosis and vertebral fractures (VFs) are frequently observed in HIV-infected men. Whereas bisphosphonates seem effective on bone mineral density (BMD) maintenance in HIV-men, data on VFs are lacking. We aimed to evaluate the long-term efficacy of bisphosphonates on VFs in HIV infected men.

Design
Real-life longitudinal retrospective study on 118 consecutive HIV-infected males (median age at inclusion 53 years). Median time between first and second visit was 2 years, and between first and latest visit available was 7 years.

Methods
Inclusion criteria were age $\geq 18$ years, HIV infection in stable conditions under antiretroviral therapy, no previous bisphosphonates treatment, blood samples carried out at the same laboratory, and three densitometric and morphometric assays performed with the same densitometer.

Results
At baseline, VFs were detected in 29/118 patients (24.6%), of which 18/29 (62.1%) were osteoporotic and 11/29 (37.9%) had osteopenia. Fractured patients were older ($P = 0.042$), had longer HIV infection duration ($P = 0.046$), antiretroviral exposure ($P = 0.025$) and higher luteinizing hormone (LH) ($P = 0.044$). Of the 29 patients already fractured at baseline, 11 (37.9%) developed new VFs during follow-up, of which 8 were under bisphosphonates treatment ($P = 0.018$). Among the 89 patients without baseline VFs, 26/89 (29.2%) were osteoporotic, 50/89 (56.2%) had osteopenia and 13/89 (14.6%) had normal BMD. Of the 89 patients without baseline VFs, 11 (12.4%) developed VFs, being treated with bisphosphonates in only 2 cases ($P = 0.811$). Overall, BMD remained stable over time and a progressive decrease of parathyroid hormone, bone alkaline phosphatase and C-terminal telopeptide was observed. Patients with worsened bone condition, both in term of BMD and VFs (n = 32), showed more frequently LH values $> 9.4$ mIU/m (0.046) and were more HCV coinfected ($P = 0.045$). Noteworthy, 38.6% of the patients discontinued bisphosphonates, due to medical indication or personal choice, and 14.0% never started them.

Conclusions
We found that bisphosphonates were not completely effective in preventing VFs in patients already suffering from previous VFs, probably due to the multifactorial pathogenesis of fragility fractures in this population and also to poor adherence to medication.

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P548
Disease characteristics, disability, and quality of life in adult HPP patients with muscular symptoms and pain without skeletal manifestations – a cross-sectional analysis from the Global HPP Registry
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Background
Hypophosphatasia (HPP) is a rare, inherited metabolic disease caused by deficient activity of tissue nonspecific alkaline phosphatase (TNSALP).

Methods
Baseline/pretreatment data from the Global HPP Registry were analyzed to compare HPP disease burden between adults (≥18 years of age) with skeletal manifestations (history of rickets, biopsy-proven osteomalacia, recurrent or poorly healing fractures/pseudofractures, etc) Skeletal group) and those with only non-skeletal manifestations (history of muscle weakness, fatigue, and/or pain; Non-skeletal group).

Results
Among 468 adults with HPP, 300 comprising the Skeletal group were compared with 73 comprising the Non-skeletal group (Table). The median number of body systems involved at baseline was higher in the Skeletal group than in the Non-skeletal group. Median 6-Minute Walk Test distance was similar between groups, although data in the Non-skeletal group were limited. Pain severity (Brief Pain Inventory-Short Form [BPI-SF]), disability (Health Assessment Questionnaire – Disability Index [HAQ-DI]), and quality of life (Medical Outcomes Study Short Form-36 Health Survey [SF-36]) were also similar between groups.
Conclusions
The impairment associated with pain, disability, and general quality of life in patients with HPP who had muscular/pain manifestations without overt bone disease was similar to that in adults who had any skeletal manifestations, regardless of HPP onset. Further analyses are required to understand the disease characteristics of these patients.

Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Skeletal (n=300)</th>
<th>Non-skeletal (n=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>300</td>
<td>73</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>50.1 (18.3, 81.2)</td>
<td>44.4 (19.3, 72.8)</td>
</tr>
<tr>
<td>HPP onset, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with data reported</td>
<td>299</td>
<td>72</td>
</tr>
<tr>
<td>Perinatal/infantile-onset</td>
<td>10 (3.3)</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Juvenile-onset</td>
<td>126 (42.1)</td>
<td>16 (22.2)</td>
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<tr>
<td>Pediatric-onset, specific type</td>
<td>29 (9.7)</td>
<td>6 (8.3)</td>
</tr>
<tr>
<td>Adult-onset</td>
<td>95 (31.8)</td>
<td>34 (47.2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>39 (13.0)</td>
<td>14 (19.4)</td>
</tr>
<tr>
<td>Number of body systems impacted per patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>282</td>
<td>73</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>3 (1.8)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>6-Minute Walk Test, distance walked (meters)</td>
<td>466 (180, 740)</td>
<td>466 (316, 580)</td>
</tr>
<tr>
<td>n</td>
<td>188</td>
<td>48</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>3.8 (0.0, 10.0)</td>
<td>3.6 (0.0, 9.5)</td>
</tr>
<tr>
<td>Disability (HAQ-DI)</td>
<td>191</td>
<td>47</td>
</tr>
<tr>
<td>n</td>
<td>191</td>
<td>47</td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>0.4 (0.0, 2.7)</td>
<td>0.3 (0.0, 2.1)</td>
</tr>
<tr>
<td>SF-36 Physical Component Summary Score²</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>191</td>
<td></td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>40.1 (16.5, 64.7)</td>
<td>44.2 (17.9, 62.0)</td>
</tr>
<tr>
<td>SF-36 Mental Component Summary Score²</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>191</td>
<td></td>
</tr>
<tr>
<td>Median (min, max)</td>
<td>42.4 (13.2, 62.3)</td>
<td>43.9 (20.4, 61.9)</td>
</tr>
</tbody>
</table>

Scales: 0-10, lower is less pain; 0-3, lower is less disability; 0-100, lower is more disability.

DOI: 10.1530/endoabs.81.P548

P549
Artificial intelligence based on radiomic analysis of lumbar spine computed tomography (ct) scan may improve accuracy in detecting osteoporosis
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Background
Osteoporosis is characterized by reduced bone mass and a compromised bone microstructure, leading to increased bone fragility and fracture risk. Currently, the gold standard for diagnosis is the bone mineral density (BMD) measurement by DXA. However, approximately half of fragility fractures occurs in the context of normal or slightly decreased BMD values.

Protocol
In this cross-sectional study, we performed an artificial intelligence (AI)-based analysis on radiomic images of opportunistic computed tomography (CT) of lumbar spine in 240 consecutive subjects (mean age 61±14.5, 130 males). Exclusion criteria were: 1) bone-active diseases; 2) neoplastic diseases; 3) spine surgical intervention; 4) spine trauma. Fifty-eight subjects had vertebral fractures (VFs) as assessed by a morphometric approach on CT or XR-ray spine (D4-L4) images. On CT images, the ROI was acquired as a 3D-spherical region of 9 mm in the middle of non-fractured lumbar vertebral bodies. A total of 93 RF were extracted: 19 first-order and 74 textural features. The most discriminative ones were selected by applying bootstrap recursive feature elimination procedures with random sampling for train/test split (100 iterations). The Linear Support Vector (LSV) model was adopted, and the Tree-Parzen Estimator Bayesian approach was employed. Results were evaluated on a stratified test set (25% of the total population), not included in the training phase. The final model was evaluated on the test set, using accuracy, sensitivity, specificity, and area under the ROC curve.

Results
Univariate analysis showed 20 significative RF (P<0.05), used to develop the LSV model. The model reached 0.83 of ROC, and the 71.7%, 78.0%, and 69.6 % of accuracy, sensitivity, and specificity respectively. Patients with VFs had significantly lower first-order features compared with those without VFs and were associated with textural features denoting a bone microarchitecture more rarefied and with higher inter-trabeculae distance. Furthermore, patients with a more compromised spine (SDI ≥ 2) had significatively lower first-order features compared with those without or with a mild VFs (SDI 0 and SDI 1) and, conversely, were significantly associated with textural features denoting a bone structure more rarefied and less coarse.

Conclusions
Artificial intelligence-based radionic of lumbar CT scans identifies patients with skeletal fragility. If confirmed, these results may suggest that radiomics could be an important diagnostic tool in osteoporosis detection and in fragility fracture prediction in the next future.

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P550
Biochemical parameters in metabolic bone disease of obese patients
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1Faculty of Medicine, University of Lisbon, Genetics Laboratory, Ecogenetics and Human Health Group, Institute for Environmental Health (ISAMB), Lisbon, Portugal; 2Scientific Research Institute Bento da Rocha Cabral, Lisbon, Portugal; 3Faculty of Medicine, University of Lisbon, Institute for Environmental Health, Lisbon, Portugal; 4Clinic of Endocrinology, Diabetes and Metabolism of Lisbon, Lisbon, Portugal

Introduction
Obesity is a pathological condition characterized by a low-grade systemic inflammatory state that predisposes to the onset of some diseases, such as hypertension, diabetes, and hyperlipidemia. Also, obesity can impact bone metabolism, but its effects are controversial.

Aims
This observational study aimed to evaluate and correlate the bone mass with the lipidic profile, adipocytokines, glucose metabolism, hepatic function and purine metabolism in obese patients.

Methods
372 obese patients were divided into three groups of bone mineral density (BMD) by DXA, according to the ISCD guidelines: normal (BMD-N; n=103), reduced (BMD-R; n=168), and osteoporosis (OST; n=101). The obesity classification was based on the fat mass index (FMI) criteria, accessed by DXA. In this classification, the body fat categories are divided into three classes, according to the sex- and race-specific reference ranges. Biochemical parameters were determined by standard methods. The Quantitative Insulin Sensitivity Check Index (QUICKI) was used to assess insulin sensitivity.

Results
The mean age was 62.4±8.80 years, 72% were female, and, for obesity classification, 84.1% of patients were in class 3, 10.8% in class 2, and 5.1% in class 1. FMI was increased in BMD-N (P<0.001) compared to BMD-R and OST groups. The three classes of obesity and the lipid profile were similar between the three groups of BMD. The alanine aminotransferase was increased in the BMD-N group (P=0.019), while the other hepatic enzymes were identical between the groups. Regarding glucose metabolism, despite the similar glycemia, the insulin level was increased in the BMD-N group (P=0.023). By contrast, the QUICKI was decreased in the BMD-N group (P=0.002). Concerning the adipocytokines analyzed, adiponectin was reduced in the BMD-N group (P=0.005). The
muscle symptoms in statin-treated patients. The prevalence of vitamin D deficiency in patients with SAMS levels hsCRP was significantly higher (42.1–29 ng/ml), while only 7% of patients without SAMS had vitamin D deficient (D<20 ng/ml) and 43% had an insufficient D (21–29 ng/ml), while only 7% of patient without SAMS had vitamin D deficient and 11% an insufficient D. In patients with SAMS levels hsCRP was significantly higher (P<.001) and hemoglobin (Hb) concentrations were 0.5 g/dL lower than in patients without SAMS (P<.05). Regarding D, mean Hb were 1.2 g/dL lower in vitamin D deficient category than in adequate D category (P<.001). In multivariable modelling we have found an excellent correlation between D and SAMS-CI, Hb and hsCRP (r=0.56; P<.001; 28.20 ng/ml and 37.53 ng/ml; P<.05). It was shown that decreasing vitamin D levels are associated with decreasing Hb levels. The correlation between vitamin D and hsCRP was highly significant (r=0.879, P<.001) in patients with SAMS and less significant in patients without SAMS (r=0.402, P<.05). It was shown that decreasing vitamin D levels are associated with increasing hsCRP levels (sign of inflammatory state) in non-statin-treated patients. Age, D<25 ng/ml, Hb <12.5 g/dL, and hsCRP >3 mg/l at baseline had modest discriminative powers for predicting SAMS (0.56, P<.01; 0.45, P<.01; 0.542, P<.001; 0.712, P<.001; respectively).

Conclusion
We found an inverse association between vitamin D level and a statin-induced muscle symptoms in statin-treated patients. The prevalence of vitamin D deficiency 29% and an insufficient D 43% in patients with SAMS: A low vitamin D concentration is accompanied by microinflammatory state and anemia risk. Age, lower level of vitamin D and Hb, higher level of hsCRP were identified as potential predictors of statin associated muscle symptoms. So, assessment of vitamin D status may be useful for the diagnosis and management of SAMS, especially in older patients with Hb <12.5 g/dL and hsCRP >3 mg/l.

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P552
Parathyroid function index does not differentiate between Normocalcaemic primary hyperparathyroidism and Vitamin D deficiency associated secondary hyperparathyroidism
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Background
Normocalcaemic primary hyperparathyroidism (NPHPT) can be considered as an early biochemical manifestation of hypercalcaemic primary hyperparathyroidism (PHPT). Vitamin D repletion and exclusion of other conditions is recommended before diagnosing NPHPT. It is often challenging to distinguish Vitamin D deficiency associated secondary hyperparathyroidism (SHPT) from NPHPT and the two conditions may coexist. A parathyroid hormone (PTH) index (parathyroid hormone (PTH) in pmol/l x Corrected Calcium in mmol/l x Phosphate in mmol/l) has been proposed previously as a reliable marker in distinguishing the two conditions. However, the patients in NPHPT group in that study were Vitamin D deficient. We have evaluated the utility of PF index and other biochemical markers in a larger cohort of patients with or without Vitamin D replacement.

Methods
Patients were selected from electronic health records based on their consistently abnormal metabolic bone profile after exclusion of chronic kidney disease (eGFR < 60 ml/min/1.73 m²), concomitant pregnancy, interfering drugs and conditions that could cause hypercalcaemia. Patients were categorised into four groups: Classic PHPT (n=60), NPHPT in those with serum 25(OHD) > 50 nmol/l (n=329), Vitamin D deficiency related SHPT (n=259) and age matched healthy controls (n=118). ROC analyses was performed to determine a reliable PF index cut-off between NPHPT and SHPT.

Results
The PF index was highest in the classic PHPT group in comparison to others [Mean(SD) was 37.95 ± 20.1 PHPT vs 21.51 ± 6.90 NPHPT, 21.27 ± 6.91 SHPT, 9.36 ± 3.00 controls]. When comparing NPHPT with SHPT, AUROC was 0.51. In a separate analysis, when comparing pre-treatment PFindex between those who normalised their PTH after vitamin D repletion and those who did not, AUROC was 0.62. Thus, in patients with normocalcaemia, vitamin D deficiency and elevated PTH, PF index could help identify individuals who would normalise PTH after vitamin D repletion and therefore did not distinguish patients with NPHPT from those with SHPT. Moreover, serum phosphate between the two groups was not significantly different.

Conclusion
After Vitamin D repletion, PF index did not discriminate NPHPT from those with Vitamin D deficiency related SHPT. Hence as recommended in recent guidelines, it is imperative to replace Vitamin D before diagnosing patients with NPHPT. Further studies are warranted to identify better markers for NPHPT so that they can be closely monitored for PHPT related bone and renal complications and thus referred for timely surgical intervention.

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P553
Case report: an unusual presentation of hypercalcaemia in pregnancy
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A 26-year-old Caucasian female presented at 14 weeks gestation with a 6-week history of lethargy, nausea and vomiting during her first pregnancy. Her adjusted Calcium was 4.12 mmol/l, raised 24-hour urine calcium at 8.11 mmol/24 hr, and a transient thyrotoxicosis, associated with hyperemesis gravidarum which later resolved. MEN deficiency associated secondary hyperparathyroidism (SHPT) from NPHPT and it is imperative to replace Vitamin D before diagnosing patients with NPHPT. Further studies are warranted to identify better markers for NPHPT so that they can be closely monitored for PHPT related bone and renal complications and thus referred for timely surgical intervention.

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24+5 weeks gestation, delivering a live baby boy who needed care in the neonatal unit, in view of prematurity. Further investigations are underway, and placental histology is awaited. This case highlights the challenges of diagnosing as well as adequately treating hypercalcaemia in pregnancy. Hypercalcaemia is rare in pregnancy, and symptoms can be nonspecific and mimic those in early pregnancy. Therefore, it is important to have a low threshold in screening and early involvement of the multidisciplinary team with patient and her partner, in order to mitigate harm to both mother and fetus.

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P554

Effect of glucocorticoid replacement therapy on bone mineral density in Addison disease


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Introduction

Addison disease is associated with high risk of fractures and low bone mineral density. Causes are complex, including supraphysiologic glucocorticoid replacement therapy and concomitant autoimmune disorders. The aim of our study is to assess the influence of glucocorticoid replacement therapy on bone mineral density in patients with Addison disease.

Patients and methods

Descriptive and analytical cross-sectional study including 50 patients with Addison disease. The incidence of osteoporosis and osteopenia were analyzed.

Results

The mean age of patients was 49.5 ± 13.9 years (40 females versus 10 males). Average duration of the disease was 13.9 ± 5.7 years (5-35 years). All patients were on hydrocortisone replacement, taking daily 27.4 ± 6.7 mg (15-42.1 mg) corresponding to 0.388 ± 0.128 mg/kg. Thirty-nine (78 %) patients received a mean daily dose of hydrocortisone greater than 11 mg/m². Mean cumulative hydrocortisone dose was 374.036 ± 293.821 mg (60 – 1184, 94 mg). The mean alkaline phosphatase level was 77.2 ± 28.5 IU (51-190 IU). A total of 9 patients (18 %) had elevated alkaline phosphatase level after a mean disease duration of 14.9 ± 2.84 years and a mean cumulative hydrocortisone dose of 413 ± 534 mg/day. Mean minimal bone density at lumbar site and femoral neck was 0.928 ± 0.174 g/cm² (0.596-1.287 g/cm²) and 0.945 ± 0.145 g/cm², respectively. Mean T-score at lumbar site and femoral neck was -1.61 ± 1.06 and -1.18 ± 1.33, respectively. Twenty-four (48 %) patients had reduced bone mineral density on osteodensitometry (less than 2 standard deviations [SD] of the mean value of an age-matched reference population). Twelve (24 %) patients had osteoporosis.

Conclusion

Glucocorticoid replacement therapy in Addison disease may induce bone loss. Thus, glucocorticoid therapy must be adjusted to the lowest tolerable dose and regular measurement.

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P555

Thalassemia major: prevalence and risk factors for hypercalciuria

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Introduction

Thalassemia syndromes are a group of inherited haemolytic disorders determining chronic anaemia, iron overload and organ damage (through the production of ROS), necessitating iron chelation therapy. Nowadays, there is scant knowledge on hypercalciuria in thalassaemic Western patients. Therefore, aim of our study was evaluating the prevalence of hypercalciuria and identifying risk factors and clinical consequences associated with its development.

Methods

We enrolled 184 patients with β thalassaemia major (TM) aged ≥ 18 years old, regularly transfused and chelated, and followed up at the Day Hospital of Thalassemia of Ferrara. We excluded patients with severe renal failure, severe hepatopathy, primary hyperparathyroidism, hypoparathyroidism, genetic renal tubular diseases and neoplastic hypercalcaemia. Females were not pregnant or breastfeeding. Hypercalciuria was defined by calcium ≥ 4 mg/kg/day.

Results

The prevalence of hypercalciuria was 69.3% (females 52.5%, mean age 45 ± 7 years old). Hypercalciuric patients had lower ferritin as compared to normocalciuric patients (663.9 ± 766.9 vs 913.2 ± 1151.89 mg/ml, P < 0.05). Deferasirox was used mostly in hypercalciuric group (49.2%) rather than in normocalciuric one (28.6%) (P < 0.05). Plasma PTH, phosphate and uricemia were lower (P < 0.05) in hypercalciuric as compared to normocalciuric patients (PTH 24.1 ± 10.3 vs. 31.4 ± 16.1 pg/ml; phosphomere 3.6 ± 0.5 vs. 3.8 ± 0.7 mg/dl; uricemia 4 ± 1.3 vs. 4.4 ± 1.4 mg/dl), whereas phosphaturia/24h was higher (0.9 ± 0.4 vs. 0.6 ± 0.3 g/day, P < 0.05) (iron mediated subclinical hypoparathyroidism associated with FGF-23 erythropoietin induced hyperphosphatemia?). Supplementation with oral calcium and cholecalciferol was similar in the two groups. Hypercalciuria was associated with a higher frequency of renal lithiasis, vertebral fractures and use of anti-osteoporotic therapy as compared to patients with normocalciuria. Bilateral renal lithiasis, hypodensification and nephrocalcinosis were found only in hypercalciuric patients.

Conclusions

Hypercalciuria is a frequent complication in TM. Deferasirox may cause hypercalciuria (through proximal renal tubulopathy) whereas supplementation with oral calcium/cholecalciferol was not associated with this complication. Our study hypothesize a role of ‘FGF23 erythropoietin induced hyperphosphatemia’ and ‘subclinical hypoparathyroidism’ in the pathogenesis of hypercalciuria. Hypercalciuric TM patients have to be monitored for the development of renal damage and osteoporosis.

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P556

Fine-needle aspiration of parathyroid lesions prior to parathyroidectomy- a tertiary center experience

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Background

Parathyroid lesion aspiration as a preoperative adenoma localization tool is a matter of controversy. Concerns are being raised regarding both the immediate (hematoma, infection, alterations on a subsequent histologic preparate) and long-term (seeding) safety.

Objective

To evaluate safety and efficacy of parathyroid fine-needle aspiration (FNA) with parathyroid hormone (PTH) washout as a localization of parathyroid lesions in patients with primary hyperparathyroidism.

Methods

We retrospectively reviewed all parathyroid FNA procedures performed by in a tertiary referral center between 2011 and 2021. Clinical, biochemical, and imaging information as well as cytology, surgery, and pathology reports were extracted from electronic medical records.

Results

Twenty-nine hyperparathyroid patients referred to parathyroidectomy following a 24th European Congress of Endocrinology
No cases of hematomas or abscesses were reported by the surgeons, and no histologic alternations (hemorrhage, abscess, inflammation or capsule rupture) were reported by the pathologists. There was one case of necrosis and one case of parathyroid adenoma with fibrotic changes that may or may not be related to the FNA. Twenty-six (89.6%) of the 29 patients who underwent parathyroidectomy, were biochemically cured up to a follow-up of 41.6 ± 34.6 months.

Conclusions

Parathyroid FNA with PTH washout was accurate and neither immediate nor surgical or prepare-related complications were demonstrated in our series. This approach might be considered in selected cases.

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P557

Hyperparathyroidism development after oncogenic osteomalacia treatment

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Tumor-induced osteomalacia (TIO) or 'oncogenic osteomalacia' is a rare paraneoplastic disorder, usually resulting from Fibroblast Growth Factor 23 (FGF23) oversecretion by a benign small 'phosphaturic mesenchymal tumor', causing hypophosphatemia and reduced 1,25-dihydroxyvitamin D synthesis. Calcium and parathyroid hormone (PTH) levels are usually normal, but secondary/tertiary hyperparathyroidism has been reported in up to 5% of the cases, mainly due to 1,25-dihydroxyvitamin D deficiency and long-term phosphate supplementation. Non-specific clinical manifestations (muscle weakness, osteomalacia, bone pain and difficulty) and difficult localization of the tumor often delay diagnosis for years. Surgical removal represents the first-line treatment. We report a case of a patient with TIO, supplemented for years with phosphate salts, who developed hyperparathyroidism after tumor removal.

Case report

In 1987, after femur stress fracture, a 27-year-old man was diagnosed with 'phosphate diabetes' and then treated until 2010 with phosphate, calcium and vitamin D supplementation. The late onset of disease with no family history of hypophosphatemia nor skeletal deformities did not suggest hereditary conditions. Medical history included only beta-thalassemia trait. No further evaluation was made until 2010, when a small phosphaturic mesenchymal tumor was identified during investigations of non-healing tibial fracture. Histological specimens confirmed a FGF23-expressing neoplasia. Before surgery hypophosphatemic osteomalacia, hypophosphatemia, increased 1,25-dihydroxyvitamin D and reduced 25-hydroxyvitamin D were observed. Immediately post-surgery PTH fell to undetectable levels while phosphatemia normalized; treatment with calcium salts, calcitriol and Cholecalciferol was introduced. Further investigations of non-healing tibial fracture revealed adenomas. Exploratory cervicotomy was proposed, but the patient was lost back on over a decade in a tertiary care center.

In 2020, after femur stress fracture, the patient was referred to our Endocrinology Unit. PTH levels at baseline in M and F, were, respectively, phosphoremia 1.4 and 1.4 mg/dl, Ca ++ 1.53 and 1.39 mmol/l (1.13-1.32), PTH 76.4 and 91.75 ng/l (6.5-36.8), 25OHvitamin D 31.8 and 46.4 µg/l, creatinine 1.14 and 0.87 mg/dl, TmP/GFR 0.33 and 0.35 mg/dl, ALP 78 and 110 U/l, CTX 846 and 902 ng/l. At 1 month: phosphorina 2.27 and 2.2 mg/dl, Ca ++ 1.57 and 1.45 mmol/l, PTH 95.2 and 70 ng/l, TmP/GFR 0.63 and 0.59 mg/dl, ALP 78 and 130 U/l, CTX 2250 and 1405 ng/l. At 6 months: phosphorina 1.74 and 2.1 mg/dl, Ca ++ 1.55 and 1.39 mmol/l, PTH 75 and 65 ng/l, TmP/GFR 0.41 and 0.52 mg/dl, ALP 78 and 130 U/l, CTX 1910 and 1605 ng/l. In both patients an improvement in myalgias, arthralgias and mood was noticed. At 6 months six-minute walk test in M improved (455 m vs 335 m at baseline, +36%). In M, after the introduction of cinacalcet at 3 months, calcium and PTH levels decreased without normalization and minimal effects on phosphorina and TmP/GFR were observed. During 6 months in M we increased Buromab dose to 1.2 mg/kg/28 days and the patient showed further improvement of symptoms at 9 months (pain assessed through VAS score decreased from 3 at 6 months and 5 at baseline to 2), despite persistent hypophosphatemia (phosphorina 2.28 mg/dl, TmP/GFR 0.5 mg/dl).

Conclusions

Buromabum, in XLH complicated with THPT, ameliorates the symptoms, without normalizing phosphorina, and in this subset of patients a higher dose may be needed. Clinical improvement despite hypophosphatemia could suggest a direct role of FGF-23 in the development of symptoms.

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P558

Clinical and biochemical response to Buromabum treatment in two patients with X-linked hypophosfatemic rickets and tertiary hyperparathyroidism

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Introduction

In X-linked hypophosfatemic rickets (XLH) mutations of PHX3 lead to elevated FGF23 levels. Phosphate salts and calcitriol represented the only treatment option. Tertiary hyperparathyroidism (THPT) is a complication of XLH worsening the clinical features and constituting a contraindication to conventional treatment. Buromabum, a monoclonal antibody anti-FGF23, was recently approved in XLH. No data about Buromabum treatment in patients with XLH and THPT are available.

Patients

two patients (M 61, F 67 yrs) affected with XLH and THPT were treated with Buromabum (standard dose 1 mg/kg/28 days). Its compassionate use was approved by local Ethics Committees (Fondazione Ca’Granda Milan and Papa Giovanni XXIII Bergamo, Italy, for patients M and F, respectively).

Results

dates at baseline in M and F, were, respectively, phosphorina 1.4 and 1.4 mg/dl, Ca ++ 1.53 and 1.39 mmol/l (1.13-1.32), PTH 76.4 and 91.75 ng/l (6.5-36.8), 25OHvitamin D 31.8 and 46.4 µg/l, creatinine 1.14 and 0.87 mg/dl, TmP/GFR 0.33 and 0.35 mg/dl, ALP 78 and 110 U/l, CTX 846 and 902 ng/l. At 1 month: phosphorina 2.27 and 2.2 mg/dl, Ca ++ 1.57 and 1.45 mmol/l, PTH 95.2 and 70 ng/l, TmP/GFR 0.63 and 0.59 mg/dl, ALP 78 and 130 U/l, CTX 2250 and 1405 ng/l. At 6 months: phosphorina 1.74 and 2.1 mg/dl, Ca ++ 1.55 and 1.39 mmol/l, PTH 75 and 65 ng/l, TmP/GFR 0.41 and 0.52 mg/dl, ALP 78 and 130 U/l, CTX 1910 and 1605 ng/l. In both patients an improvement in myalgias, arthralgias and mood was noticed. At 6 months six-minute walk test in M improved (455 m vs 335 m at baseline, +36%). In M, after the introduction of cinacalcet at 3 months, calcium and PTH levels decreased without normalization and minimal effects on phosphorina and TmP/GFR were observed. At 6 months in M we increased Buromab dose to 1.2 mg/kg/28 days and the patient showed further improvement of symptoms at 9 months (pain assessed through VAS score decreased from 3 at 6 months and 5 at baseline to 2), despite persistent hypophosphatemia (phosphorina 2.28 mg/dl, TmP/GFR 0.5 mg/dl).

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P559

Extreme hypercalcemia due to primary hyperparathyroidism - a look-back on over a decade in a tertiary care center

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Background

Extreme hypercalcemia is an endemic emergency. Given parathyroid hormone (PTH)-dependent cause, carcinoma should be suspected as a possible etiology. The prevalence of parathyroid carcinoma among patients presenting with extreme hypercalcemia is not well elucidated.

Aim

Establish proportion of patients with parathyroid carcinoma among those presenting with severe hypercalcemia and compare clinical and laboratory features between benign and malignant etiologies.

Methods

Admissions during 2009-2021 with serum calcium ≥14 mg/dl were identified via MD-clone platform. Cases with PTH < mid-reference range or serum creatinine
Severe hypercalcemia is uncommon and PTH-dependent etiologies constitute a minority of those. Benign parathyroid disease was the most common etiology of severe PTH-dependent hypercalcemia. Due to the extreme rarity of parathyroid malignancy, significant clinical or laboratory predictors were not identified.

Conclusions

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Context

Normocalcemic hyperparathyroidism (NHPT) is considered as an earlier or milder phenotype compared to traditional primary hyperparathyroidism (PHPT).

To make a correct diagnosis, secondary hyperparathyroidism due to low calcium intake must be excluded. Whether calcium intake might affect presentation of PHPT vs NHPT has never been addressed consistently.

Objective

To describe patients with a diagnosis of NHPT or PHPT in relation to their calcium intake, through three standard validated questionnaires.

Design

Cross-sectional study.

Setting

Outpatient, single academic medical center.

Patients

44 consecutive women recruited from March through December 2021. 22 patients with mild primary hyperparathyroidism (PHPT or NHPT) were age-matched with 22 women undergoing bone mineral evaluation for the first time due to recently diagnosed hormone-positive breast cancer. NHPT diagnosis was based on multiple determinations of both total calcium and albumin-corrected calcium within normal limits, as per current international guidelines.

Interventions

Administration of all the following: a validated local food-frequency questionnaire (LOC), International Osteoporosis Foundation Calcium Calculator (IOF) and National Osteoporosis Foundation Calcium Calculator (NOF).

Main outcome measures

Any association with biochemicals or clinical features.

Results

All three questionnaires confirmed that NHPT patients had similar calcium intake as compared with PHPT or controls. Calcium intake evaluated with all three questionnaires was not correlated with any biochemical index in NHPT nor PHPT, although it showed an association with hip T-scores in PHPT patients (r = 0.821, P = 0.027 for total hip T-scores). Maximum serum calcium reached over time (CaMax), SCa ranges and 24-Hour Urinary Calcium were significantly greater in PHPT than in NHPT. The remaining biochemistries and bone turnover markers were similar, even when compared with controls. Age positively correlated with calcium intake only in PHPT patients (r = 0.630, P = 0.038).

Multivariate analysis investigating predictors of CaMax (age, BMI, albumin-corrected SCa, serum phosphate, GFR, calcium intake, PTH and 25(OH)vitamin D) showed that only albumin-corrected SCa predicted CaMax. GFR was a much milder positive predictor.

Conclusions

NHPT appears to represent a milder phenotype of PHPT. Presentation of NHPT is independent of calcium intake, when this is sufficient. The setpoint of albumin-corrected serum calcium probably determines the subtype of primary hyperparathyroidism, with greater values having greater chances of reaching calcium levels above normal, independent of other biochemistries.

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P562

Serum 25-hydroxyvitamin D (25(OH)D) levels in Pregnant women with gestational diabetes mellitus

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1Tameside and Glossop Integrated Care NHS Foundation Trust, United Kingdom; 2The University of Manchester, Manchester, United Kingdom

Background

The importance of vitamin D supplementation in pregnancy is well known. Hypovitaminosis D is associated with adverse maternal and foetal outcomes such as pre-eclampsia, gestational diabetes mellitus, bacterial vaginosis, increased incidence of caesarean section delivery, intra-uterine growth restriction and reduced bone and muscle mass in childhood. The recommendations for vitamin D supplementation vary widely, with NICE guidelines suggesting a daily replacement dose of 400 IU day. The aim of this study was to determine whether the recommended replacement dose of cholecalciferol of 400 IU/day was sufficient to maintain normal vitamin D level (25(OH)D > 50 nmol/l) in pregnant patients.

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P560

Syringomyelia and neurologic symptoms as rare complications in untreated adult with X-linked hypophosphatemic rickets

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X-linked hypophosphatemia is a rare inherited disorder, yet the most common among the inherited causes of rickets. It is caused by different mutations in the PHEX gene leading to an impaired regulation of fibroblast growth factor 23 (FGF 23) and renal phosphate wasting. Patients with XLH show multiple musculoskeletal complications which usually can lead to early diagnosis in childhood. Nevertheless XLH is a lifelong disease, with multisystemic manifestations, including entheseopathies, dental and periodontal recurrent lesions, hearing loss, fractures and pseudofractures, muscle pain and diminished quality of life.

We describe the case of a 21 years old male patient, misdiagnosed as vitamin D deficient rickets in infancy, with short stature, progressive bone deformities, leg bowing and waddling gait which required multiple orthopedic interventions. As a particular manifestation he accused episodes of moderate occipital headaches, aggravated with Valsalva maneuvers, and mildly impaired lower limb proprioception. MRI imaging showed a syringomyelic cavity at C5-T1, but with cerebellar tecta above the foramen magnum. A few months later, episodes of bilateral upper limb paresthesia have appeared, so that repeated MRI monitoring is required and a neuroradical approach should be considered. With this case we want to draw attention to the severe and rare neurological complications of this rare condition, and to the importance of long term follow-up with a multidisciplinary approach.

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Methods
Serum 25-hydroxyvitamin D (25(OH)D) levels of 129 pregnant women who attended the joint antenatal and diabetes clinic between 17/02/21 to 27/04/21 were analysed. All the patients were on standard vitamin D supplement of 400 IU/day (pregnancay) from the time of antenatal booking. Blood was collected for 25(OH)D at the time of oral glucose tolerance test at 26-28 weeks of gestation.

Results
The mean 25(OH)D level was noted to be suboptimal across the study population (47.92 nmol/L), with the mean in South Asians (43.99 nmol/L, n = 37) lower than their Caucasian counterparts (49.50 nmol/L, n = 92) (P = 0.0487). Low 25(OH)D level (<50 nmol/L) was observed in 58.91% of the patients, more prevalent in South Asians (67.57%), compared to Caucasians (55.43%). Significantly reduced 25(OH)D (<30 nmol/L) was noted in 15.5% of the patients, also more prevalent among South Asians (21.62%) compared with Caucasians (13.04%).

Table 1: Distribution of Serum 25(OH)D levels among Caucasian and South Asian Pregnant Women.

<table>
<thead>
<tr>
<th>Serum 25(OH)D (nmol/l)</th>
<th>Caucasians (n=92)</th>
<th>South Asians (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>Number of women</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>30-50</td>
<td>12</td>
<td>13.04</td>
</tr>
<tr>
<td>&gt;50</td>
<td>41</td>
<td>44.57</td>
</tr>
</tbody>
</table>

Conclusion
Our study suggested that vitamin D supplementation of 400 IU/day in pregnant women resulted in suboptimal 25(OH)D levels, more pronounced in South Asians compared to Caucasians. The results suggest the need to revise the guidelines for higher dose of vitamin D supplementation during pregnancy. Larger studies are required to validate the findings.

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P563
Analysis of bone mass and body composition in transgender men at 1 year: a follow up study
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University Center São Camilo, Brazil

Introduction
Sex steroid hormones play a key role in bone health, however medical therapies for gender dysphoria lead to hormonal changes.

Purpose
Understanding the change in bone mass and body composition is extremely important, because this treatment will be carried out over a long period of time Methods

In a prospective study, we included 19 transgender men (female-to-male trans persons) before treatment and after 1 year of treatment with undecanoate (1000 mg i.m./12 weeks). Bone densitometry model Hologic-Discovery performed at baseline and after 12 months of therapy. All participants signed the TCLE, project approved by CEP-CAAEE: 36823220.6.0000.0062.

<table>
<thead>
<tr>
<th>Number of participants: 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline 6 months 12 months p value</td>
</tr>
<tr>
<td>Lumbar spine BMD ± SD (mg/cm²)</td>
</tr>
<tr>
<td>Z-Score ± 0.1 ±1 0.107 0.80</td>
</tr>
<tr>
<td>SD ± -0.4 ±0.9 0.35 0.53</td>
</tr>
<tr>
<td>Femoral neck BMD ± SD (mg/cm²)</td>
</tr>
<tr>
<td>Z-Score ± 0.3 ±0.2 0.55</td>
</tr>
<tr>
<td>SD ± 0.7 ±1.6 0.45</td>
</tr>
</tbody>
</table>

P564
Quantification of cerebral calcification and nephrocalcinosis in patients with hypoparathyroidism
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Introduction
Various methods to quantify calcified coronary plaque have been used in common clinical practice in the past few decades to compliment cardiovascular risk assessment. The estimation of calcium load in other organs and conditions has been at best semi-quantitative. Patients with long-standing hypoparathyroidism are known to suffer with nephrocalcinosis and basal ganglia calcification. We attempted to quantify end-organ calcium burden in a series of patients with various forms of hypoparathyroidism by use of a modified Agatston score.

Patients and Methods
Five patients (4 females and one male, median age 30 years) with various forms of permanent hypoparathyroidism who had a noncontrast CT scan of the brain and/or kidneys as part of usual clinical care in the past three months were included. All CT imaging were performed on a GE Optima 660 scanner. The CT protocol included helical scanning with 0.625 mm slice thickness. The areal detection of 0.1 mm² Images were analyzed on a Philips workstation irrespective of whether calcium deposits were visible. The Agatston score algorithm (HeartBeat-CS, v4.1.7.22037) was modified to identify calcium-based stones using an attenuation threshold of 90 HU within the regions of interest (basal ganglia and renal medulla).

DOI: 10.1530/endoabs.81.P564

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Results

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age</th>
<th>Condition</th>
<th>Duration</th>
<th>Treatment</th>
<th>Score Renal Medulla</th>
<th>Score Basal Ganglia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>Mild Surgical hyperparathyroidism</td>
<td>4 years</td>
<td>Calcium 500 mg bid &amp; vitamin D3 50,000 IU bimonthly</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>87</td>
<td>Idiopathic hypoparathyroidism</td>
<td>lifelong</td>
<td>Alfacalcidol 0.5 mcg/d</td>
<td>0.04</td>
<td>0.24</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>Severe Surgical hypoparathyroidism</td>
<td>10 years</td>
<td>rhPTH(1-84) 75 mcg/d</td>
<td>9.4</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>Pseudohypoparathyroidism Type 1a</td>
<td>lifelong</td>
<td>vitamin D3 50,000 IU bimonthly</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>Severe Idiopathic hypoparathyroidism</td>
<td>7 years</td>
<td>rhPTH(1-84) 75 mcg/d</td>
<td>NA</td>
<td>260.3</td>
</tr>
</tbody>
</table>

NA: not performed

Conclusions

Application of an appropriately modified Agatston score may offer a practical means to accurately diagnose and follow changes in end-organ calcifications in patients with hyperparathyroidism at the point of care.

References


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P565

A case of severe hypercalcaemia secondary to primary hyperparathyroidism responding to steroids

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Case History

A 57 year old male, who was known to have primary hyperparathyroidism was admitted to hospital due to hypercalcaemia on routine blood tests (adjusted S. calcium - 3.44 mmol/l). He had no symptoms due to hypercalcaemia. This was his 5th admission since the diagnosis 18 months ago, each admission requiring treatment with IV fluids and IV bisphosphonates. SESTAMIBI and ultrasonic scans of the thyroid and parathyroids had previously localised a likely right inferior parathyroid adenoma. Myeloma screen was negative. His past medical history included schizophrenia, vitamin D deficiency and psoriasis.

Treatment

He was initially treated with intravenous fluids, zolendronic acid and cinacalcet. Due to persistent hypercalcaemia, the dose of cinacalcet was increased to 60 mg TDS and intravenous calcitonin was added on. However, adjusted calcium remained around 3.44 mmol/l. He was hence re-referred to ENT surgeons for urgent parathyroidectomy. Unfortunately, he contracted COVID, which delayed the surgery. At this point, he was symptomatic with confusion, agitation, nausea, dehydration and abdominal cramps. He had repeat IV zolendronic 4 weeks from the previous dose and was also prescribed IV hydrocortisone 100 mg IV QDS 6 weeks into the hospital stay. The corrected calcium level reduced from 4.2 mmol/l to 2.2 mmol/l within a week. With the resolution of hypercalcaemia, his confusion resolved. He was switched to oral prednisolone 40 mg OD, which was slowly weaned down. His adjusted calcium levels started rising again shortly after the prednisolone was weaned. Three weeks later he had parathyroidectomy. Following this, his PTH level normalised from a peak pre-operative level of 660 pg/ml to 22 pg/ml post operatively. Two days following parathyroidectomy, he became hypocalcaemic with adjusted serum calcium of 1.92 mmol/l. He was discharged on 3000 mg of calcium carbonate and 1600 units of vitamin D3 daily. He was asymptomatic on follow-up.

Follow-up

The histopathology was suggestive of parathyroid carcinoma. He remains under endocrine and ENT follow-up.

Discussion

Parathyroid carcinoma should be suspected in cases with significantly raised PTH and resistant hypercalcaemia. Emergency parathyroidectomy should be considered in severe cases of hyperparathyroidism unresponsive to medical management. A trial of steroids may be useful as an adjunct in cases of severe resistant hypercalcaemia due to primary hyperparathyroidism, but remains an exception rather than the rule. The mechanism of action remains unknown. Potentiation of the action of calcitonin by upregulation of calcitonin receptors on osteoclast by steroids may be a plausible explanation.

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P566

High prevalence of thoracic vertebral fractures in patients with medullary thyroid cancer

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Medullary thyroid cancer (MTC) is a rare malignancy of the thyroid gland. MTCs originate from thyroid-C cells and account for 2-4% of all thyroid neoplasms. Originating from thyroid-C cells, the main secretory product of MTCs is calcitonin, used as sensitive and specific MTC-biomarker. Calcitonin is a hormone known to participate in calcium-bone metabolism suppressing bone-resorption by inhibiting the activity of osteoclasts, and inhibiting the kidney reabsorption of calcium and phosphorus. Despite these well recognized effects, little is known about skeletal health of patients affected by MTCs. Vertebral Fractures (VFs) are one of the most relevant clinical manifestations of skeletal fragility. To date, no data are reported in literature about VFs prevalence in patients affected by MTCs. The aim of our study was to investigate the VFs prevalence in patients with MTCs and in control-matched patients. VFs were detected on lateral chest X-rays using a qualitative and quantitative evaluation of vertebral shape. X-rays were performed prior the thyroid surgical treatment in MTC patients and at hospitalization for infectious respiratory disease in control patients. MTCs and control patients were matched in a 1:1 ratio for age, sex and comorbidities, excluding those with comorbidities and therapies influencing bone metabolism. Sixty-two patients were included in the study, 31 affected by MTCs and 31 in control group. Median (IQR) age was 51 (38-66) years and 24 were male (29%). No statistical differences regarding age and sex were observed between the MTCs and control groups (P = 0.84, P = 1, respectively). VFs were detected in 9 (29%) MTCs patients and 2 (6.5%) control patients (P = 0.043). In MTCs group, no statistical difference was observed regarding age between patients with and without VFs (P = 0.27), and VFs were observed more frequently in male patients compared to female (50% vs 16%, P = 0.044). No statistical associations were found between calcitonin levels and VFs occurrence. For the first-time to our knowledge, we have reported a high prevalence of VFs in patients affected by MTCs. It can be hypothesized that constantly elevated calcitonin levels directly or indirectly through changes in other parameters of bone metabolism may negatively impacts skeletal health.

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P567
Remote management of osteoporosis in the first wave of the Covid-19 pandemic
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We conducted a survey during the first pandemic wave of coronavirus disease 2019 (COVID-19) on a large group of osteoporotic patients to evaluate the general conditions of osteoporotic patients and the impact of the pandemic on the management of osteoporosis, finding high compliance to treatments and low COVID-19 lethality. In a telephone survey conducted from April to May 2020, patients from the Osteoporosis Center, Clinic of Endocrinology and Metabolic Diseases of Umberto I Hospital (Ancona, Italy) were interviewed.

Results
Of a total of 910 interview subjects, 892 provided consent to participate in the survey (response rate 98%), including 785 women (88%) and 107 men (12%). Among the 892 patients interviewed, 77.9% were taking osteoporosis treatment and 94.6% vitamin D supplementation as prescribed at the last visit. COVID-19-like symptoms were reported by 5.1% (44 subjects), whereas confirmed cases were 1.2% (10 patients). A total number of 33 patients had been in hospital and the hospitalization rate of those who had not discontinued vitamin D supplementation was less than 4%. There were eight deaths, two with a concomitant COVID-19 diagnosis. The COVID-19 patients (10, all female) were significantly older than non-COVID-19 subjects (79.9±8.1 vs 70.8±11.4 years, P<0.01) but showed no significant differences in terms of comorbidities. The 2 patients who died of COVID-19 infection were both female; their family members said they were taking vitamin D, although dosing just before the lockdown indicated vitamin D deficiency. The prevalence of severe osteoporosis was 50% in total COVID-19 patients and 87.5% in deceased COVID-19 patients. The overall COVID-19 mortality was 0.2%; lethality was 20%, lower than the national rate of the same age group. According to the logistic regression model considering only vitamin D supplementation, the supplement had a protective effect against the risk of hospitalization (OR 0.31, CI 0.11-0.84, P<0.05).

Conclusions
Our frail patients followed up by phone felt reassured, they showed high treatment compliance, and experienced a lower COVID-19 lethality rate than patients of the same age; those who had not discontinued their vitamin D supplement also had a lower COVID-19 lethality rate than patients of the same age group. According to the logistic regression model considering only vitamin D supplementation, the supplement had a protective effect against the risk of hospitalization (OR 0.31, CI 0.11-0.84, P<0.05).

P54
Glucose prediction model based on continuous glucose monitoring in patients with type 1 diabetes mellitus: GlucoseML study preliminary results
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1University Hospital of Ioannina, Department of Endocrinology, Ioannina, Greece; 2University of Ioannina, Unit of Medical Technology and Intelligent Information Systems, Department of Materials Science and Engineering, Ioannina, Greece; 3University of Ioannina, Department of Biological Applications and Technology, Ioannina, Greece; 4University Campus of Ioannina, Biomedical Research Institute, FORTH, Ioannina, Greece

Introduction
Current guidelines emphasize the important role of Continuous Glucose Monitoring (CGM) for type 1 diabetes mellitus (T1DM) management. The aim of the GlucoseML study is the development of a mobile health system for T1DM self-management based on CGM data, physical activity, food intake and insulin dosage. We herein present the development and evaluation of a univariate Autoregressive Moving Average (ARMA) prediction model of interstitial glucose concentration for prediction horizons of 30-, 45- and 60-minutes.

Methods
CGM data (GlucoMen Day, Menarini) from T1DM patients over a 4-week monitoring period under real life conditions were included in the analysis. Ambulatory Glucose Profile (AGP) report was computed for every patient. Categorical variables are expressed as number (percentage). Continuous variables with or without normal distribution are expressed as mean (standard deviation) or median (range), respectively. An ARMA (p, q) model, where p and q denote, respectively, the order of the AR and MA model of the ARMA equation, was identified upon the glucose data. The partial autocorrelation plot and the Akaike information criterion (AIC) were used to estimate the appropriate values of p and q orders in the model. The root mean square error (RMSE) and the mean absolute error (MAE), were used to evaluate the predictive performance of our models.

Results
Data were included for 29 T1DM patients (38% women) aged 38 years (12). Age at diagnosis was 15 years (2-45) and diabetes duration 20 years (11). Most patients were on insulin treatment with multiple daily injections [19 (66%)] compared to continuous subcutaneous infusion [10 (34%)]. Glycosylated haemoglobin was 7.4% (5.8-10.4). Based on AGP report, time below range (glycose<5.4, <7.0 mg/dl), time in range (70-180 mg/dl) and time above range (>180, >250 mg/dl) were 1.4% (0-10), 4% (2), 62% (21-82), 22% (6) and 8% (0.9-49), respectively. Average glucose was 150 mg/dl (130-247), glucose management indicator 6.9% (6.4-9.2) and glucose variability 39% (32-51). The RMSE for examined prediction horizons of 30-, 45- and 60-minutes was 9.04 (2.22), 11.84 (3.18) and 14.82 (3.87) mg/dl, respectively. Similarly, MAE was 6.48 (1.7), 9.04 (2.56) and 11.62 (3.38) mg/dl, respectively.

Diabetes, Obesity, Metabolism and Nutrition
P53
The investigation of serum and saliva phoxin levels in patients with type 2 diabetes mellitus
Mbahmed Burak Oz1, Kader Ugur2, Zeynep Dila Oz3, Ramazan Fazil Akkoc4 & Süleyman Aylin1
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Purpose: Diabetes is one of the most common metabolic disease which has got many peptide hormones have in its etiology. Phoxin (PNX), a recently discovered neuropeptide appears to have a role in energy management and many peptide hormones have in its etiology. Phoenixin (PNX), a recently discovered neuropeptide appears to have a role in energy management and many peptide hormones have in its etiology.

Materials and methods
A total of 100 participants were included in the study, with 80 patients divided into four groups based on HbA1c: Group 1 (5.7-6.4 % (n=20), Group 2: 6.5-8.4 % (n=20), Group 3: 8.5-9.9 % (n=20), and Group 4: 10 % and above (n=20) and a control group of 20 healthy individuals. After at least 8 hours of fasting, venous serum and saliva samples were obtained from the patient and control groups, and HbA1c were measured. The levels of phoxin in serum and saliva were determined by using the enzyme-linked immunosorbent assay (ELISA). The statistical analyses were performed with the SPSS 22 package program and also one-way Anova test and Pearson’s correlation test were used. The significance value was taken as p≤0.05.

Result
When PNX serum levels were analyzed, it was shown that the prediabetic group (Group 1 (5.7-6.4 %)) had statistically higher levels than type 2 diabetes mellitus patients (p<0.05). PNX salivary levels were found to be significantly higher than serum levels in the control and type 2 diabetes mellitus groups.

Conclusion
The PNX molecule is a neuropeptide that may be found in saliva and serum. It’s thought that the prediabetic groups’ higher serum PNX level is attributable to the effect of hyperinsulinemia, and when overt diabetes occurs, it will be detected at a lower level in the serum related to relative insulin insufficiency. This leads us to believe that PNX is increased in order to control the higher glucose levels in the prediabetic group. Saliva PNX is expected to be favoured over serum PNX in future investigations on PNX metabolic pathways, as serum PNX is an invasive procedure.

Key words
Diabetes mellitus, peptide molecules, phoxin, HbA1C

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Conclusions
The predictive performance of the identified ARMA models compares favourably with that of existing models of similar or higher computational complexity. More advanced multivariate adaptive deep learning models are currently under way as part of the GlucoseML study. Further analyses are required, to test the model’s predictive capacity in the critical region of hypoglycaemia.

DO: 10.1530/endoabs.81.P56

P55
Prevalence of undiagnosed depression in patients with type 2 diabetes in central India
Bharat Saboo & Shweta Saboo
Prayas Diabetes Center, Indore, India

Introduction
Type 2 Diabetes Mellitus (T2DM) is the most common type of diabetes in adults. People with Diabetes usually have depression which is many times undiagnosed. Significant data suggest that depression in the context of diabetes is related to a variety of negative outcomes, including poor treatment adherence, decreased quality of life, deranged blood sugars and HbA1c levels, and increased health costs.

Method
40 patients who consented to be part of the study were surveyed with Patient Health Questionnaire (PHQ-9). Patients with T2DM, between the age of 20 and 65 years and residing in Central India were included in the study. Exclusion criterion: Patients with type 1 DM, the previous history of psychiatric illness or on psychiatric treatment, a family history of depression. The responses were analyzed using MS excel.

Result
The overall depression prevalence PHQ-9 score ≥ 10 was 23%, with a higher prevalence of depression in T2DM females than males (25.5 vs. 21.5%, P < 0.0001). We found a significant association between depression prevalence in T2DM patients and their education level more prevalent in lower education (P<0.0001) and employment status those not employed had higher rates of depression (P<0.0001).

Conclusion
This study is the first to examine depression in patients with T2DM in Central India.

Finall, new policies need to be established to focus on the mental health issues of patients with Diabetes. Which can lead to a better outcome in terms of Quality of life and disease outcomes.

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P56
“Correlation of biomarkers of early diagnosis of diabetic retinopathy”
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Tashkent Medical Academy, Tashkent, Uzbekistan

The purpose of the study is to assess the relationship of the level of growth factor level (VEGF) in blood serum with retinal microcirculation indicators according to oct-A data in patients with type 2 diabetes mellitus (DM2), with different stages of diabetic retinopathy (DR).

Material and research methods
252 people were examined (n=504), of which 168 patients with type 2 and 84 practically healthy persons. The main group (n=174) with DM2, divided into subgroups, depending on the stage of DR: Easy non-proliferative DR (NDR), moderate NDR, severe NDR and PDR. As a comparison group (II; n=162), patients are included without clinical manifestations of others (III; n=168) - the control group was almost healthy faces without significant ophthalm and somatic pathology. All patients conducted a standard and specialized ophthalmological examination. Optical coherer tomography in the angio mode is made using an Optical Cherenk Tomograph RevOFC with an angiography module with a 3X3 mm scan area. The level of VEGF in serum was evaluated by solid-phase immunoassay analysis using Quantikine ELISA sets.

Results
VEGF levels in blood serum in the studied groups showed a significant tendency to increase from 100.47 ± 49.66 pg/ml (control group) to 463.18 ± 78.69 pg/ml PDR (P<0.001). The increase in the VEGF indicator in the blood serum was revealed before the DR occurred clinically 137.29 ± 84.45 pg/ml (comparison group). The average levels of VEGF at easy NDR (177.07 ± 35.37), moderate NDR (255.29 ± 65.67), heavy NDR (424.34 ± 56.67) also showed a tendency to increase. It was statistically established that the difference between all groups was significant (P < 0.05). It was found that the VEGF level correlates with Oct-A (P<0.05).

Conclusions
The earliest marker of DR is to increase the average level of VEGF growth factor in the blood serum of patients 137.29 ± 84.45 Pg/ml, which comes before the appearance of a clinical picture.

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of women with positive O’Sullivan test) versus 37 in 2020 (13.8%), \( P = 0.489 \), 10 of the women with GDM were diagnosed before week 24 in 2019 versus 17 in 2020 (15.4% vs. 17.7%; \( P = 0.699 \)); 31 of the women with GDM were diagnosed after week 24 in 2019 versus 19 in 2020 (16.1% vs. 11.1%; \( P = 0.165 \)). There were no differences between groups with regard to treatment modality during these comparison periods (\( P = 0.454 \)).

**Conclusion**

GDM diagnostic rate was similar using 100-g OGTT criteria (2019) and basal glycaemia/HbA1c criteria due to the COVID-19 pandemic (2020). Besides, there were no differences between periods concerning the number of patients that required pharmacological treatment.

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**P58**

**Study of change in physical activity behavior of diabetic patients after regular awareness sessions by primary care physicians**

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**Background**

Humans have been increasingly spending more time in sedentary behaviors such as prolonged sitting. Regular physical activity is associated with enhanced physical and mental health. Studies have shown that regular physical activity reduces the risk of cardiovascular diseases, diabetes mellitus, osteoporosis, depression and obesity. Patients frequently identify their family physicians as an important source of constant encouragement for physical activity.

**Purpose**

We wanted to assess the impact of regular awareness sessions about physical activity by Primary care physicians in diabetic patients.

**Methods**

73 diabetic patients between the age group 30 to 60 years were recruited in this single center study in rural India.70 participants completed this 6-month intervention study whereas 3 participants dropped out of study. Once in a month audio visual awareness session of one hour were conducted from August 2017 to January 2018 by primary care physicians to educate the diabetic patients about ill effects of sedentary lifestyle and benefits of regular physical activity. Pre and post intervention data were collected by using validated Godin leisure time exercise questionnaire from all 70 participants. Paired t test and Wilcoxon test were used to compare pre- and post-intervention data. Percentage increase in physical activity score was also calculated.

**Results**

In this study baseline Godin score pre intervention was 38.82 ± 12.22 (Mean ± SD) and post intervention was 65.98 ± 11.25 (Mean ± SD). Diabetic patients significantly improved Godin score post intervention which was statistically significant (\( P < 0.001 \)). Compared to baseline pre intervention score, there was 170% increase in physical activity score post intervention.

**Conclusions**

Regular awareness sessions using modern technology by primary care physicians definitely showed positive change in physical activity behavior in diabetic patients. These regular sessions also helped to change the attitude and behavior about physical activity. Primary care physicians can play a significant role in counseling patients and promoting physical activity. Active involvement of primary care physician in this intervention further helped in establishing and continuing physical activity behavior. As primary care physicians have direct regular contact with their patients and their families, their role in promotion of physical activity will have more impact and long-lasting effect on diabetic patient’s behavior. Similar studies are needed to assess impact of physical activity awareness sessions in diabetic patients.

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**P59**

**Impaired glucose homeostasis in a tau knock-in mouse model**

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**Introduction**

Alzheimer disease (AD) is the leading cause of dementia. While impaired glucose homeostasis has been shown to increase AD risk and pathological loss of tau function, the latter has been suggested to contribute to the emergence of the glucose homeostasis alterations observed in AD patients. However, the links between tau impairments and glucose homeostasis, remains unclear.

**Objective**

In order to better understand the links between tau and glucose homeostasis, the present study aimed at investigating the metabolic phenotype of a new knock-in (KI) mice model.

**Method**

Males and females Tau KI mice model expressing a human tau protein bearing the P301L mutation under the control of the endogenous mouse Mapt promoter and their non-transgenic littermates (referred as WT) were used. A complete metabolic phenotyping was explored under high fat diet (HFD) versus CHOW diet in both sexes. Also, glucose-stimulated insulin secretion (GSIS) was studied using isolated islets from tau KI and tau knock-out mice and mouse β pancreatic cell line (MIN6).

**Results**

While under chow diet tau KI mice do not exhibit significant metabolic impairments, we could observe that under HFD male, but not female tau KI animals exhibited glucose homeostasis alterations as compared to control littermates. Interestingly, using immunofluorescence, tau protein was found colocalized with insulin in the β cells of pancreatic islets. Additional experiments performed on isolated islets from tau KI and tau knock-out mice revealed that both exhibit impaired insulin secretion, an effect recapitulated in the mouse β pancreatic cell line (MIN6) following tau knock-down.

**Conclusion**

Altogether, our data suggest that loss of tau function in pancreatic β cell might favor the development of glucose homeostasis impairment and could contribute to metabolic changes observed in AD.

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**P60**

**Performance of EFKC, FAS and 2021 CKD-EPI equations for estimating glomerular filtration rate in people with type 2 diabetes**

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**Background**

Diabetes mellitus (DM) is the leading cause of chronic kidney disease (CKD) worldwide. In clinical practice, kidney function is routinely assessed through glomerular filtration rate (GFR) estimated by equations. However, the accuracy of current equations has been questioned for people with diabetes mellitus (DM).

**Aim**

To evaluate the performance of the European Kidney Function Consortium (EFKC), the Full Age Spectrum (FAS) and the 2021 Chronic Kidney Disease Epidemiology Collaboration (2021 CKD-EPI) equations based on serum creatinine to estimate GFR in healthy and type 2 DM participants.

**Methods**

This cross-sectional study evaluated three creatinine-based equations in two different populations: healthy adults (eligibility criteria: BMI ≤30 kg/m²) and people with type 2 DM (eligibility criteria: mGFR ≥ 60 ml/min/1.73 m²). GFR calculated by the equations was compared with measured GFR (mGFR) by the plasma clearance of 51Cr-EDTA as the reference method.

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Introduction
Type 2 diabetes is one of the main risk factors for severe COVID-19 infection. Inadequate glycemic control is related to high inflammation, hypercoagulability, and mortality in COVID-19 patients. Glucose lowering medications commonly used in type 2 diabetes mellitus (DM) might have effects on COVID-19 pathogenesis. Overall, evidence is conflicting as to which glucose-lowering drugs are associated with the most favourable outcomes in patients with COVID-19. The aim of our study was to evaluate association of COVID-19 severity with different types of DM therapy.

Patients and Methods
The retrospective study included 95 patients with type 2 DM and COVID 19: 25 (26.9%) received metformin, 16 (16.5%) metformin and sulfonylureas, 12 (12.7%) metformin and dipeptidyl peptidase type 4 inhibitors (DPP-4), 8 (8.5%) metformin and glucagon-like peptide receptor agonists (GLP-1 RA), 13 (13.8%) metformin and basal insulin, 10 (9.5%) premix insulin and 11 (11.8%) basal and bolus insulin. Clinical presentation, ICU admission and death rate has been compared in patients with different types of DM therapy.

Results
Clinical presentation was mild in patients with metformin, metformin and DPP-4, metformin and GLP-1 RA and more pronounced in patients with premix insulin and basal bolus insulin. The three most common symptoms were: fever, cough and fatigue. Glycemic at admission were highest in patients with premix insulin (13.6±4.58 mmol/l), and the lowest in patients with metformin and DPP-4 (7.5±4.23 mmol/l). Our studies showed that inflammatory response and ICU admission rate were the highest in patients with premix insulin therapy and the lowest in metformin group (12.3 vs 7.1%). A total of 16 patients died (16.8 %) during hospitalization. The highest rate was in patient who received premix insulin 6 (50%) and the lowest in patients who received metformin 2 (2.1%).

Conclusion
Our results had showed that therapy with premix and basal bolus insulin had link with severe clinical presentation, ICU admission and death.

Key words
COVID 19; type 2 diabetes mellitus, metformin, insulin

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The bidirectional relationship between testosterone and metabolic disorders: testosterone deficiency as an early marker of cardiovascular risk in young men

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In the last years an increasing incidence of cardiovascular diseases (CVD) has been reported in young adults (18-45 yrs), probably accounted by the significant increase in CV risk (CVR) factors. Observational and interventional studies, mainly focused on middle-aged and elderly men, demonstrated that metabolic CVR (mCVR) factors and CVD manifestations are common in hypogonadal men and, conversely, testosterone deficiency is highly prevalent in metabolic disorders; the lack of corresponding robust evidence in younger adults requires more focused investigation. The current single centre, observational, cross-sectional study aimed at better defining the mutual relationship between the prevalence of mCVR factors in a large cohort of 720 young (18-35 yrs) adult men, submitted to physical examination and fasting morning venous blood sampling for the assessment of anthropometric, metabolic and hormonal parameters. Body weight, BMI and waist circumference (WC) significantly decreased across total testosterone (TT) (P < 0.0001), SHBG (P < 0.01; P < 0.001) and calculated free testosterone (cFT) (P < 0.05) tertiles, whereas systolic blood pressure (SBP) and triglycerides (TG) significantly decreased across TT (P < 0.05; P < 0.01) and SHBG (P < 0.05; P < 0.001) tertiles, and diastolic blood pressure (DBP) across SHBG (P < 0.05) tertiles. Spearman correlation analysis revealed a negative association of TT, SHBG and cFT with BMI (r = -0.20, P < 0.001), WC (r = -0.165; P < 0.005), TG (r = -0.172; P < 0.005) and with TT and SHBG with WC (r = -0.234; P < 0.001), SBP (r = -0.112; P = 0.049) and DBP (r = -0.142; P < 0.05) and TG (r = -0.17; P < 0.01) and SHBG (r = -0.204; P < 0.001), whereas a positive association of TT and SHBG with HDL-cholesterol (r = 0.167; P < 0.05) and TG (r = 0.251; P < 0.001) was demonstrated. In multiple linear regression analysis in models adjusted for age, BMI, and WC, TT and SHBG were strong independent predictors of serum HDL-cholesterol (β = 0.151; P = 0.011) (β = 0.186; P < 0.01) and SHBG was an independent predictor of SBP and DBP (β = 0.177; P < 0.05) (P = 0.006; β = 0.204). Lastly, in the subgroup of men with hypotestosteronemia (TT ≤ 12.1 nm), the prevalence of normal weight was significantly lower and that of obesity, visceral obesity (WC > 102 cm), hypertension and metabolic syndrome was significantly higher, compared to normal-testosterone subgroup. Consistently, in the subgroup of overweight/obese men, the prevalence of hypotestosteronemia was significantly higher than compared to normal weight subgroup. In conclusion, the current study demonstrated that in young adult men a bidirectional relationship between testosterone deficiency and metabolic disorders exists, and that a worse androgenic status is associated to a worse cardiometabolic profile and might represent a strong early predictor of mCVR factors, potentially associated to the onset of future CVD.

Aim
Evaluate risk of hypoglycaemia in patients on VRIII with concurrent use of balanced electrolyte solution

Methods
This was an observational study and we included patients who were admitted to medical or surgical wards over a six-week period and who were on a VRIII. Relevant data was collected from patients’ paper notes, observation nursing charts and electrolyte charts. The data was collected for the entire duration patients were on the VRIII. Our hospital has guidelines for the management of patients on VRIII including recommendations on frequency of glucose monitoring and choice of concurrent IV fluids. The recommended balanced solution with carbohydrate substrate used in our hospital is combined 0.18% sodium chloride with 4% glucose (0.18% NaCl+4% glucose). Hypoglycaemia is defined as when the capillary blood glucose falls below 4 mmol/mol.

Results
We included a total of 16 patients in our study with a mean age of 59 years with the majority of patients having type 2 diabetes (87.5%). 0.18% NaCl+4% glucose was used concurrently with the VRIII in 75% of patients. For all the patients that were included in the study a total of 434 hours were spent on a VRIII for which there were 324 capillary blood glucose readings with 3 recorded hypoglycaemia events (<1%) with 2 out of 3 occurring in those who were not on a balanced electrolyte solution.

Discussion
Use of concurrent IV fluids (Normal saline or 5% dextrose) is not a new concept, but often this has been prescribed separately and the infusion switched between the two depending on the threshold levels of capillary glucose levels that has been set by the prescriber. This is prone to human error and consequent adverse events. This study demonstrates that with the concurrent use of balanced electrolyte solution such as 0.18% NaCl+4% glucose there is a minimal incidence of hypoglycaemia and its concurrent use is recommended to prevent harm to patients on VRIII. This would be of particular importance in general ward or less intensively monitored settings.

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The role of empagliflozin in palmitate-induced ER stress and apoptosis in H9C2 cells

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Aim/hypotheses
Ectopic lipid accumulation in the heart contributes to the abnormal function of the heart and to the death of cardiomyocytes. Saturated FFA is one of the most important causes of death in cardiomyocytes. Although empagliflozin has been reported to be beneficial for people with diabetic complications and/or CVD, it has not been confirmed as to how it affects cardiomyocytes death by FFA. This study was designed to evaluate the protective effects of SGLT2 inhibitor on palmitate-induced ER-stress and apoptosis in cardiomyocytes.

Methods
We used differentiated H9C2 cells as cardiomyocytes and palmitate as a saturated fatty acid. To clarify the effects of empagliflozin on apoptosis, free fatty acid was treated with or without empagliflozin in cardiomyocytes and several stress signaling pathways were measured, such as inflammation, endoplasmic reticulum (ER)-stress, and insulin signaling using immunoblotting. Inflammation and cardiac metabolism were analyzed in several related genes. Cardiomyocyte apoptosis was detected using DNA fragmentations assay and immunoblotting using cleaved caspase 3 antibody. DAPI staining was also performed.

Results
Palmitate stimulated increment of ROS (reactive oxygen species) and ER-stress markers such as phospho-eIF2a, CHOP, and phospho-JNK. In addition, cleaved caspase 3 and DNA fragmentation was induced by treatment of palmitate. Interestingly, empagliflozin significantly decreased expression levels of ER-stress markers (including phospho-eIF2a, CHOP, and phospho-JNK) [Jpn N-terminal kinases] in PA-treated cells. Empagliflozin significantly decreased the activity of cleaved caspase-3 (a well-known apoptotic induced molecule) and DNA fragmentation. To investigate the protective molecular mechanism of empagliflozin, we measured AMPK activation and upstream signal pathways.
Empagliflozin significantly stimulated phospho-CAMKK2 and phospho-AMPK. In addition, phosphorylation of acetyl-CoA carboxylase, target protein of AMPK, was also activated by treatment of empagliflozin. But, LKB did not change. Beneficial effects of empagliflozin was abolished by compound C. Conclusion/interpretation This data suggests SGLT2 inhibitors protect palmitate induced cardiomyocytes, ER-stress, and apoptosis. Therefore, attempts to use treatment of SGLT2 inhibitor might be a useful strategy for preventing diabetes associated ventricular remodeling and diabetic cardiac complication.

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**P67**

**Leptin increases VLDL triglyceride secretion and reduces hepatic lipid content in lean male subjects**

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**Background**

Leptin reduces hepatic lipid content in lipodystrophic and overweight, relatively hypoleptinemic, NAFLD patients. However, the underlying mechanism is unknown. In rodents, the anti-steatotic action of leptin is mediated by an increase in VLDL secretion and depends on an intact vagal innervation of the liver.

**Methods**

In this randomized, placebo-controlled, crossover trial, we study the effects of a single metreleptin injection (0.1 mg/kg body weight) on VLDL secretion and hepatic energy/lipid metabolism in 13 male, overnight-fasted volunteers. VLDL secretion rate was determined with an intralipid infusion test 4 hours after injection. Hepatic lipid content and phosphorous metabolites were measured with 1H31P MRS at baseline and 3h after metreleptin injection. In an additional cohort of 10 overnight-fasted, male subjects, we assessed hepatic VLDL secretion after modified sham feeding, an established method to stimulate the vagus nerve, where subjects smell, taste and chew, but do not swallow a test meal. Water was served in the control condition.

**Results**

VLDL triglyceride secretion rate was higher after metreleptin than placebo (360 ± 39 mg/kg/h; P = 0.049) without differences in circulating insulin. As a consequence of the prolonged lasting effect, we observed a similar increase in plasma NEFA, ketone bodies and acylcarnitines in both conditions. However, the almost uniform, fasting-associated increase in liver fat in the placebo condition (+10% relative to baseline, P = 0.01) was prevented by the metreleptin injection. VLDL triglyceride secretion correlated with changes in hepatic lipid content (r=0.5, P = 0.02). Hepatic ATP/PI ratio and ATP synthesis rate changed similarly after placebo and metreleptin. For the second cohort, plasma pancreatic polypeptide increased after modified sham feeding (+206 ± 109% vs. -4 ± 35% in the placebo condition) indicating that our test meal stimulated the vagus nerve. Similar to metareptpine, vagus nerve stimulation was associated with an increased hepatic VLDL triglyceride secretion (244 ± 39 vs. 348 ± 32 mg/h; P = 0.02).

**Conclusion**

Our study supports the hypothesis that, in humans, leptin’s anti-steatotic action is mediated by an increase in hepatic triglyceride export independent of food intake via a brain-vagus-liver axis.

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**P68**

**Development and validation of a new gestational diabetes mellitus (gdm) risk algorithm**

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**Background and Objective**

Gestational Diabetes Mellitus (GDM) is associated with life-long adverse outcomes for the mother and the baby. To date there is no rigorous clinical test for the assessment of GDM risk, since estimation of GDM risk is currently primarily based on clinical risk factors. Additional markers are needed to identify women at high risk. Our aim was to develop and validate a risk assessment model to identify women at high risk of GDM through an algorithm that integrates genetic and clinical variables.

**Methodology**

We analyzed a retrospective cohort of 711 women with 425 control pregnancies and 286 GDM cases. The entire cohort was randomly divided into a training/development dataset (70% of the cohort) for algorithm development and a test dataset (30% of the cohort) for validation. A total of 112 SNPs (Single Nucleotide Polymorphisms) were selected for this analysis after exhaustive exploration of the databases published to date of SNPs associated with GDM. The SNPs were selected based on their predictive power and population frequency, with the following criteria: OR > 1.2, RAE > 0.20, P < 1 × 10^-9. SNPs were grouped into glycan traits categories. Genotyping was performed using iPLEX Gold-MassARRAY from Agena Bioscience. In the clinical and genotype data set of the development/training group, significant attribute selection was performed using Feature Selection (FS) techniques. Logistic regression analysis was then applied to obtain prediction coefficients for the selected attributes in the training group data set. Discrimination and calibration of risk scores were evaluated using the receiver operating characteristic (ROC) curve in the training and the validation dataset.

**Results**

An algorithm was developed on the training dataset that provides a risk score for GDM. The algorithm includes 10 SNPs, maternal age, gestational body mass index, and number of previous pregnancies. In the training dataset the AUC was 0.7420. The AUC of the 10 SNPs alone (0.6981) and the clinical variables alone (0.6133) were significantly lower than their combination. AUC in the validation set was 0.7139.

**Conclusions**

a new tool for GDM risk assessment is presented, which suggests that the utilization of genetic markers in combination with clinical characteristics may improve accuracy of GDM risk evaluation and reinforce the adoption of preventive intervention as early as possible. Further clinical validation studies in different patient cohorts are ongoing.

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**P69**

**Evaluating a novel virtual simulation tool for clinical training to improve clinician confidence managing cases in diabetes and endocrinology**

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**Introduction**

The delivery of medical education has transformed from in-person to remote teaching, accelerated by the ongoing COVID-19 pandemic.Simulation is a useful teaching modality increasingly used to develop healthcare professionals’ knowledge and skills while protecting patients from unnecessary risks. Although simulation has traditionally occurred face-to-face, many of its principles can be
adapted for remote teaching. Simulation via Instant Messaging – Birmingham Advance (SIMBA) is a virtual simulation-based learning tool, run by medical students and junior doctors with support from experts, aimed to increase clinician confidence in managing clinical scenarios. We evaluated the effectiveness of SIMBA to improve participants’ confidence and competencies in diabetes and endocrinology.

Methods

Eight sessions were conducted between May 2020 and October 2021 on various endocrine subspecialties (adrenal, thyroid, pituitary, diabetes, metabolic bone, and reproductive). Moderators used standardised transcripts to simulate anonymised, real-life clinical cases via WhatsApp. Following the simulation, specialists chaired interactive Zoom sessions to discuss simulated cases and participant queries. Participants’ self-reported confidence levels in approaching clinical scenarios were measured using a Likert scale, and responses were categorised as confident, unsure, and not confident. Changes in these categories pre- and post-SIMBA were compared using Wilcoxon signed-rank test. Improvements in clinical core competencies were also analysed.

Results

326 international participants completed the pre- and post-SIMBA surveys and were included in the analysis. Significant improvements were observed in clinician confidence following SIMBA (pre- vs post-survey, confident: +40.6%, unsure: -34.3%, not confident: -6.3%; P<0.0001). In 92.6% (n=302/326) participants strongly agreed/agreed that sessions were engaging, while 88.7% (n=289/326) strongly agreed/agreed that SIMBA accommodated their learning style and 80.5% (n=250/306) preferred SIMBA to traditional pedagogy. The overall quality of the sessions was rated as excellent/good by 98.0% (n=320/326) participants. 93.9% (n=305/306) participants strongly agreed/agreed that the simulated topics were applicable to their clinical practice, with 97.4% (n=297/306) strongly agreed/agreed that the content was impactful at personal and professional levels, respectively. Clinicians reported improvements in core clinical competencies: patient care [56.7% (n=185/326)], management [83.4% (n=272/326)], systems-based practice [43.3% (n=141/326)], and practice-based learning [66.9% (n=218/326)].

Conclusion

SIMBA proved to be an effective postgraduate training tool in endocrinology which improved clinician confidence managing various endocrine conditions and was highly accepted among learners. In addition, the ubiquity of online platforms enabled international participation, which transcends geographical and financial barriers and could help standardise endocrine training globally. Further studies are underway to explore the long-term translation of SIMBA to clinical practice.

DOI: 10.1530/endoabs.81.P70

Table 1 The proportion of cause of death in patients with diabetes mellitus

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Total (n=777)</th>
<th>Men (n=467)</th>
<th>Women (n=310)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (%)</td>
<td>Numbers (%)</td>
<td>Numbers (%)</td>
<td></td>
</tr>
<tr>
<td>Infectious disease</td>
<td>218 (28.1)</td>
<td>120 (25.7)</td>
<td>98 (31.6)</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>190 (24.5)</td>
<td>134 (28.7)</td>
<td>56 (18.1)</td>
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<td>Cardiovascular disease</td>
<td>198 (25.5)</td>
<td>116 (24.8)</td>
<td>82 (26.4)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>75 (9.7)</td>
<td>50 (10.7)</td>
<td>25 (8.1)</td>
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<td>Ischemic heart disease</td>
<td>67 (8.6)</td>
<td>35 (7.5)</td>
<td>32 (10.3)</td>
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<td>Heart failure</td>
<td>56 (7.2)</td>
<td>31 (6.6)</td>
<td>25 (8.1)</td>
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<tr>
<td>Kidney disease</td>
<td>63 (8.1)</td>
<td>38 (8.1)</td>
<td>25 (8.1)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>40 (5.1)</td>
<td>25 (5.4)</td>
<td>15 (4.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>14 (1.8)</td>
<td>7 (1.5)</td>
<td>7 (2.3)</td>
</tr>
<tr>
<td>All other causes</td>
<td>54 (6.9)</td>
<td>27 (5.8)</td>
<td>27 (8.7)</td>
</tr>
</tbody>
</table>

*aAll other causes included gastrointestinal bleeding, pulmonary thromboembolism, epilepsy, acute pancreatitis and panperitonitis.*

P71

The neural mechanism of selective activation of kisspeptin neurons in the ARC of the hypothalamus regulate brown adipose thermogenesis in female mice

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Objectives

Overweight and obesity currently burden our public health, and especially with the aging process in the world, the incidence of obesity is significantly higher in women than that in men partly. Recent studies reported that hypothalamic kisspeptin neurons, with obvious changes of number and structure in female during life, play a crucial role in the regulation of central energy homeostasis. But the precise mechanism remains an enigma.

Methods

High-fat fed Kiss1-CreGFP female mice were used in this study. Selectively activated kisspeptin neurons by using Designer-receptors-exclusively-activated-by-designer-drugs (DREADDs) technology and denervation of the sympathetic nerve in iBAT were used to demonstrate the mechanism by which ARC kisspeptin neurons activate brown fat thermogenesis in female mice.

Results

The Kiss1-CreGFP female mice were injected with AAV-DIO-hM3D(Gq)-mCherry virus in ARC through Stereotactic injection. Three weeks later, AAV was successfully transfected and expressed the corresponding receptor, which were greatly activated by CNO, then the expression of neuronal activation marker c-fos was significantly enhanced. Selective activation of kisspeptin neurons resulted in decreased body weight, improved glucose metabolism, increased energy expenditure, increased iBAT (brown adipose tissue), decreased sWAT, gWAT, rWAT (white adipose tissue) in female mice (P<0.05). The norepinephrine(NE) concentration, sympathetic specific indicator tyrosine hydroxylase (TH), the number of brown adipose cells and the expression of thermogenic related genes were significantly increased in activated group (P<0.05). The metabolic improvement effect disappeared in activating kisspeptin neurons after sympathetic nerve denervation of iBAT, and female mice gained weight, impaired glucose metabolism, failed activation of brown fat, and significantly decreased thermogenesis (P>0.05). But the control group of beneficial effects by chemogenetics activation on weight reduction, glucose metabolism improvement and brown fat thermogenesis activation still existed (P<0.05).

Conclusion

Chemogenetics can relatively specifically activate kisspeptin neurons in the ARC of the hypothalamus in female mice, and the activated Kisspeptin has an effect on energy metabolism, mainly reduced weight, improved glucose metabolism,
increased thermogenic and dissipative, increased brown adipose tissue, strengthened sympathetic activity innervating iBAT, and significantly improved high fat induced obesity. iBAT sympathetic denervation experiments confirmed that Kisspeptin10c neurons in female mice modulate iBAT activation through sympathetic nerve to improve systemic energy metabolism.

Keywords
Kisspeptin, Female, Sympathetic Nerve, BAT, Thermogenesis

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P72
Clinical and nutritional risk factors for insulin requirement during gestational diabetes mellitus
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Background and aim
Gestational Diabetes Mellitus (GDM) is the commonest medical pregnancy complication. Nutritional interventions come to the fore as one of the few levers for managing GDM; as many medications are either harmful to the growing fetus, or their toxicity is uncertain. The aim of this study was to assess the potential clinical features and nutritional risk factors of insulin treatment during GDM.

Methods
This was a prospective study including 150 patients with GDM. Patients who failed to achieve glycemic targets, defined according to the American Diabetes Association guidelines 2021, were treated with insulin. Clinical characteristics and dietary intake were compared between the two groups. Dietary intake data were collected by trained nutritionists using a 24-hour recall method.

Results
Among the 150 patients with GDM, insulin use, along with lifestyle interventions, was necessary in 20.3% of patients. Univariate analysis showed that insulin use was significantly associated with a family history of type 2 diabetes in a first degree relative (P = 0.016), history of GDM (P = 0.02), pregestational Body Mass Index superior to 25 kg/m² (P = 0.005) and presence of four risk factors of GDM (P = 0.005). Insulin therapy group had higher protein intake than nutritional therapy group (100.86 ± 38.8 g/d vs 80.28 ± 36.97 g/d, P = 0.025) and lower vitamin B12 levels (3.93 ± 2.84 µg/dl vs 2.59 ± 1.78 µg/dl, P = 0.01). Energy consumption, carbohydrate intake, fat intake and fiber intake did not statistically differ between the two groups (P = 0.7, P = 0.09, P = 0.89, p = 0.6 respectively). The calcium, iron, zinc, magnesium, vitamin B1, B2, B3, B5, B6 and folic acid intakes did not statistically differ between the two groups. Multivariate analysis showed that vitamin B12 level was an independent factor for insulin requirement during GDM (OR 5.52, 95% CI 1.33-22.83, P = 0.018). The cut-off value of vitamin B12 level, determined by ROC curves analysis, was 2.28 µg/dl (sensitivity of 80% and specificity of 52%, P = 0.01).

Conclusion
The association between vitamin B12 levels during pregnancy and the risk of GDM remains unclear with conflicting data. To our knowledge, this is the first study to elucidate the association between vitamin B12 levels and insulin requirement during GDM. More studies are needed to further strengthen this finding and to clarify possible pathogenetic mechanisms.

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P74
Prevalence and predictive factors of factitious hypoglycemia in non-diabetic patients
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Introduction
Spontaneous hypoglycemia in non-diabetic patients is a rare metabolic emergency caused by multiple etiologies. Factitious hypoglycemia, a form of the Munchausen syndrome, is defined as the surreptitious use of insulin or oral hypoglycemic agents to deliberately induce self-harm. It is one of the most challenging diagnoses associated with significant morbidity and mortality. The aim of this study was to assess the prevalence and the associated factors of factitious hypoglycemia in non-diabetic patients.

Methods
This was a single-center, retrospective study including 70 non-diabetic patients who were admitted to our department between 2004 and 2020 for the exploration of a spontaneous hypoglycemia. All enrolled patients fulfilled the Whipple triad. Exclusion criteria were: pregnancy, severe renal failure, hepatic failure, cirrhosis, heart failure, and a history of malignant tumors. Age, gender, epidemiological parameters, medical history, clinical and paraclinical data, and the etiology of hypoglycemia were collected from medical records.

Results
The diagnosis of factitious hypoglycemia was confirmed in 11 patients (9 women and 2 men) corresponding to a prevalence of 16%. It was secondary to an intentional insulin use in 6 patients and to the ingestion of Glibenclamide in 5 patients. Their mean age was 30.27 ± 13.02 years with extremes of 14 and 54 years. Two patients with factitious hypoglycemia had a personal history of psychiatric disorders. Age < 35 years (Odds Ratio = 5.6, P = 0.017), family history of diabetes mellitus (Odds Ratio = 1.29, P = 0.015), attention disorders (Odds Ratio = 12.5, P = 0.017), and fasting glucose level < 0.7 g/l (Odds Ratio = 5.75, P = 0.017) were positively associated with factitious hypoglycemia.

Conclusion
Factitious hypoglycemia is more frequent in middle-aged women with psychosocial issues and a family history of diabetes mellitus explaining the ease to access to insulin and anti-diabetic agents. A psychiatric referral and a supportive follow up are warranted to provide the appropriate guidance for patients and perform an essential role in the long-term management of factitious hypoglycemia.

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P73
Different treatment outcomes (acute dietary restriction vs conventional treatment) in women with new-onset type 2 diabetes (T2DM), with previous gestational diabetes (GDM)
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Some literary data demonstrate that the twin defect of beta-cell failure and insulin resistance that underline T2DM can be reversed by acute negative energy balance alone. The aim of the present work was to assess treatment outcomes in women with new onset T2DM, who were previously diagnosed with GDM treated with acute dietary restriction or conventionally at 32 weeks postpartum (PP).

Methods
In total 174 women with T2DM at 32 weeks PP, were enrolled in the study. Patients were tested at 32, 40 and 48 weeks PP. Patients were divided into two groups (Gr.): Gr.1 - Acute Dietary Energy Restriction - 61 women - 600 kcal/day for 8 weeks, during next 8 weeks- 1 200 – 1 400 kcal/day, Gr.2 - Conventional Therapy - 113 women - 1 400 – 1800 kcal/day and Metformin.

Results
At entry levels of HbA1c, fasting plasma glucose (FPG), insulin, triglycerides and BMI statistically did not differ in Gr.1 and Gr.2. At week 33 PP (one-week post treatment) FPG decreased: Gr.1 - 170.5 ± 18.6 vs. 96.4 ± 9.1 P = 0.000 and Gr.2- 169.9 ± 18.8 vs. 145.7 ± 14.9; P = 0.32, and at week 48 PP. FPG levels decreased in both groups, but in Gr.1 decrease was statistically more evident, than in Gr.2 (P = 0.004). At week 40 PP HbA1c levels decreased in both groups (Gr.1 – by 1.42 ± 0.12 and Gr.2 – 0.68 ± 0.08; P = 0.000), and at week 48 PP HbA1c levels were statistically lower in Gr.1 (P = 0.000). At week 40 PP fasting plasma insulin fell from 16.1 ± 3.6 to 5.2 ± 1.7 (Gr.1 - P = 0.000), and 15.9 ± 3.1 to 12.1 ± 2.3 (Gr.2 - P = 0.3); and at week 48 PP these indices were statistically lower in Gr.1 when compared to Gr.2 (P = 0.000). After 16 weeks of treatment BMI also reduced in both groups (Gr.1 – by 7.8 ± 0.08/kg/m²; and Gr.2 – by 2.61 ± 0.1%); while at week 48 PP statistically lower BMI was observed in Gr.1 (P = 0.055). Triglyceride levels have dropped in Gr.1 and 2 (by 0.60 ± 0.05 and 0.68 ± 0.06 mg/dl, respectively) though this decrease was not statistically evident.

Conclusion
In women with T2DM, who were previously diagnosed with GDM acute dietary restriction at 32 weeks PP significantly reduced plasma fasting glucose, insulin levels, HbA1c, and BMI when compared to traditional dietary management and Metformin. Our data are in complete accordance, that abnormalities underlying T2DM are reversible by reduced dietary energy intake, that is of an utmost importance for young women after pregnancy and breastfeeding.

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Type 1 diabetes technology and quality of life: glucose control and beyond
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Background
Technological advances in continuous glucose monitoring (CGM) and continuous subcutaneous insulin infusion (CSII) should aim to improve glucose control and quality of life in patients diagnosed type 1 diabetes (T1D).

Aim
The aim of our study was to compare different CGM and CSII devices on these targets.

Methods
Sixty-nine T1D patients (mean age 39 ± 12; 31 males) were recruited. 36 were on multiple daily insulin injections (MDI), 33 on CSII devices including Medtronic Minimed 640G and 670G, Theras Omnipod, Roche Insight and Movi Tandem. Glucose monitoring was performed with Dexcom-G6, Guardian sensor and Flash Freestyle Libre. The Diabetes Treatment Satisfaction Questionnaire (DTSQ); the Diabetes Specific Quality Of Life Scale (DSQOLS) and The Short Form (36) Health Survey (SF-36) were used. The quality of life, HbA1c, time in range (TIR), time above the range (TAR) and time below the range (TBR) were investigated as glucose control parameters.

Results
Patients in the CSII group had higher treatment-related satisfaction (84.8% vs 52.8%; P = 0.005), and better disease acceptance (84.8% vs 52.8%, P = 0.012) compared with patients on MDI, despite similar age (MDI mean age 38 ± 12.5; CSII 41 ± 11.6). No differences were observed among devices (P = ns). TIR remained higher in the CSII group than in the MDI group (P = 0.001). The Dexcom G6 group had higher TIR values than the Freestyle (P = 0.03) group, but similar to the Medtronic (P = 0.12) group.

Conclusions
Technological devices may improve quality of life over MDI treatment. Type of glucose monitoring system may also impact glucose control.

P77
Comparison of hyperphagia and problem behaviors in participants with prader-will syndrome (PWS) receiving diazoxide choline extended-release (DCCR) with matched participants in PATH for PWS (PITPP)
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Background
PWS is a rare neurodevelopmental genetic disorder characterized by hyperphagia, obesity, hormonal deficiencies, and problem behaviors for which there are no approved treatment. DCCR administration (100-525 mg/day) up to 52 weeks in participants with PWS improved hyperphagia, behavior, body composition and metabolic markers.

Objective
The objective of this study was to compare changes in hyperphagia (using Hyperphagia Questionnaire for Clinical Trials [HQ-CT]) and PWS-related behaviors (via PWS Profile Questionnaire [PWS-P]) between 114 participants enrolled in DCCR placebo-controlled, double-blind (C001, NCT03440814) and

Methods
This was a placebo-controlled, double-blind, parallel group, superiority, single-center randomized study including 255 patients. The intervention consisted of a 12-week treatment phase with dulaglutide 1.5 mg or placebo injected subcutaneously at a weekly study visit, in addition to standard of care (behavioral counselling and pharmacotherapy with varenicline). Point-prevalence abstinence rate at week 12 as primary outcome was assessed by self-reported smoking status and biochemical confirmation (end-expiratory exhaled carbon monoxide measurement). We further investigated changes in weight and glucose homeostasis at week 12. In a substudy (n=71), we compared behavioral (i.e., nicotine craving measured by a Visual Analogue Scale) and brain activity changes in response to smoking cue videos using functional magnetic resonance imaging at baseline and week 12.

Results
The point-prevalence abstinence rate after 12 weeks of treatment was 80/127 (63%) in the dulaglutide group and 82/128 (65%) in the placebo group (difference in proportions [95%CI] 1.9% [-10.7, 14.4]; P=0.839). We observed an increase in weight in the placebo (+1.8kg [SD 2.4]) and a decrease in the dulaglutide group (-0.7kg [SD 3.3]) between baseline and week 12; baseline-adjusted difference in weight change [95%CI] -2.5kg [-3.3, -1.7], P < 0.001. Craving in response to smoking cue videos decreased from baseline to week 12 (estimated mean difference [95%CI] -3.0 [-3.7, -2.3], P <0.001), with no difference between dulaglutide and placebo (estimated mean difference [95%CI] 0.4 [-1.2, 2.0], P=0.6). Similarly, no difference in whole brain functional activity was seen between the two treatments, at both time points and between baseline and follow up.

Conclusion
In this study, an exceptional high point prevalence abstinence rate in both groups was observed, most probably due to the very close (weekly) supervision of the patients. Our data provides no evidence that dulaglutide modulates nicotine craving or smoking cessation rates. Nevertheless, GLP-1 analogues such as dulaglutide may be a promising treatment during smoking cessation as it may avoid post-cessation weight gain.

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Habit-intervention induces an amelioration of prediabetes cardiometa- tabolic traits by lowering the miR-21/ROS/HNE damaging axis

Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3, Lucia La Sala1,2, Elena Tagliabue2, Simona Mrakic-Sposta3

P78

Habit-intervention induces an amelioration of prediabetes cardiometabolic traits by lowering the miR-21/ROS/HNE damaging axis

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P82
Adipocytokines profile in patients with Graves' orbitopathy and the effect of high-dose corticosteroids
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Aims
To identify and analyze factors influencing the severity of the COVID-19 course among patients with type 1 and type 2 DM, including the glucose-lowering therapy effects.

Materials and Methods
A retrospective cohort study of 5023 Tashkent inhabitants, who had COVID-19 from April to December 2020, was performed. The data were obtained from the single electronic database of registered cases of COVID-19. All data were analyzed by univariate and multivariate logistic regression models using STATA 17.0 software. Further, the matched case-control study was performed for patients with type 2 DM and no DM based on age, gender, and BMI.

Results
Of the 5023 analyzed subjects, 72.63% had no diabetes mellitus (DM), 4.24% had type 1 DM, 15.19% had type 2 DM, and 7.94% was diagnosed with diabetes during the COVID-19 infection. DM, overweight, and obesity were associated with severe COVID-19; the most significant risk of a severe course was found in patients with type 2 DM. The risk of a lethal outcome and the need for prescription of glucocorticoids did not show a significant association with diabetes in Tashkent. The clinical features of COVID-19 were more common in patients with type 2 DM, especially for shortness of breath, chest pain, and atelecthymia. The patients receiving SU have complained of dyspnea significantly more often than matched patients without DM. Metformin and DPP4i were the groups of drugs that were not associated with significantly increased risk of hospitalization of patients because of COVID-19. The matched case-control study did not reveal statistically significant differences in the disease course severity, notably for hospitalization and glucocorticoids, and death depending on the glucose-lowering therapy preceding the onset of COVID-19.

Conclusion
Diabetes, age and overweight/obesity were associated with severe course of COVID-19 in Tashkent. There was no statistical difference in COVID-19 severity depending on initial glucose-lowering therapy.

Keywords
diabetes mellitus, COVID-19, metformin, insulin, complications, mortality

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P83
Menstrual cycle abnormalities as distinctive sign of type 1 diabetes mellitus: results from a meta-analysis
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Aim
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Conclusion
Diabetes, age and overweight/obesity were associated with severe course of COVID-19 in Tashkent. There was no statistical difference in COVID-19 severity depending on initial glucose-lowering therapy.

Keywords
diabetes mellitus, COVID-19, metformin, insulin, complications, mortality

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Background
Type 1 diabetes mellitus (T1DM) management profoundly changed across years, with increasing emphasis on stringent glycaemic control. While it is well demonstrated that the progressive improvement of glycaemic control allows a tighter control of diabetes-related complications, the positive implications thereof on reproductive functions are still unclear. Indeed, it is well known that oligomenorrhea and amenorrhea are more frequently detected in young women with T1DM compared to healthy age-matched controls. However, whether the menstrual abnormalities incidence changed across years is still matter of debate.

Aim of the study
To evaluate the menstrual cycle abnormalities rates in T1DM young women, compared to healthy subjects, and to search for potential T1DM-related factors influencing female reproductive system. Secondary aim was the evaluation of the possible effects of the change in T1DM management, occurred in the late 90's, on menstrual cycle dysfunction.

Methods
A meta-analysis was performed considering all clinical trials in which menstrual cycle abnormalities in T1DM young women were reported, compared to healthy age-matched subjects. Primary endpoint was the rate of oligomenorrhea/amenorrhea and secondary objective was age at menarche. Sensitivity analysis was conducted dividing studies into two groups, i.e. before and after 2000, according to the change in T1DM management. Three meta-regression analyses were performed, considering the influence of diabetes duration, body mass index (BMI) and glycated haemoglobin (Hba1c) serum levels on menstrual irregularities.

Results
From 623 papers initially identified, 12 studies were finally included. Menstrual cycle dysfunction rate was significantly higher in T1DM women compared to controls, also considering only studies published after 2000 (OR:2.08; 95%CI: 1.43,3.05, P<0.001). Age at menarche was significantly higher in T1DM women compared to controls (P<0.001) also when studies published after 2000 were evaluated separately (mean difference:0.51; 95%CI: 0.32,0.74 years, P<0.001). In meta-regression analyses, the menstrual abnormalities rate in T1DM women were inversely related to diabetes duration (R² =0.396,P=0.023), but not to BMI (R² =0.134,P=0.373) and Hba1c serum levels (R² =0.083,P=0.409).

Conclusion
The meta-analytic approach confirmed the high incidence of menstrual cycle dysfunction in T1DM young women. The improvement in T1DM management, introduced after 2000, seems not able to influence this rate, leaving menstrual cycle abnormalities one of the distinctive signs of this chronic condition. Indeed, T1DM-related menstrual dysfunction is associated neither to anthropometrical variables, nor glycemic control. Although actual pathogenetic mechanisms are not fully understood, here we demonstrate a potential association with T1DM duration, suggesting that the process of disease acceptance could underlie these irregularities.

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Effect of an extract of the Andean plant Lampaya on insulin signaling and proinflammatory markers in human adipocytes treated with palmitic acid

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Background

Obesity is strongly associated with a state of chronic low grade systemic inflammation and insulin resistance (IR). IR at the molecular level may be defined as a diminished activation of the metabolic phosphatidylinositol-3-kinase (PI3K) /Akt pathway of insulin. On the other hand, inflammatory response may be activated by NF-κB. Subject with obesity have elevated plasma levels of saturated fatty acids, such as palmitic acid (PA), which triggers insulin and inflammatory signaling disruption in vivo and in vitro. Additionally, protein phosphorylation is an important regulatory mechanism to activate intracellular signaling. The protein tyrosine phosphatase 1B (PTP1B) is well known to regulate PI3K/Akt route and NF-κB inflammatory signaling. Infusions of Lampaya medicinalis Phil. (Verbenaceae) are used in folk medicine of Northern Chile to counteract inflammatory diseases. Hydroethanolic extracts of lampaya (HEL) contain considerable amounts of flavonoids that may explain the biological activity of the plant. The aim of this study was to assess whether HEL exposure protects against PA-induced inflammation and disruption of PI3K/Akt signaling in human adipose cells.

Methods

Cytotoxicity of a range of HEL concentrations (0.01–10 μg/ml) was evaluated by MTS assay in in vitro differentiated adipocytes from the adipose cell line SW872. Adipocytes were incubated or not with PA for 24 h in the presence or not of HEL (2-h preincubation), and thereafter stimulated with insulin or vehicle. Thereby, experimental conditions were: control (untreated cells), 0.4 mM PA, 0.01 g/ml of HEL, 0.01 μg/ml of HEL (2 h before) + 0.4 mM PA for 24 h, in insulin-stimulated (100 nM, 10 min) or basal conditions. Phosphorylation of Tyr-IRS-1, Ser-Akt, Ser-NF-κB and protein expression of PTP1B were evaluated by Western blot.

Results

In SW872 adipocytes, HEL was not cytotoxic at any concentration assessed. Insulin-stimulated phosphorylation of IRS-1 and Akt as well as phosphorylation of NF-κB and PTP1B protein content were not affected by treatment with 0.01 μg/ml HEL compared with vehicle-treated cells. PA-treated adipocytes showed a reduction in insulin-stimulated phosphorylation of IRS-1 and Akt compared to control (P<0.05), while the phosphorylation of NF-κB and PTP1B protein expression were elevated compared to untreated cells (P<0.05). Interestingly, these effects were prevented by HEL treatment.

Conclusion

These findings give new insights about the effect of HEL ameliorating PA-impaired insulin signaling and inflammatory markers in adipocytes. More studies should focus on lampaya, since might represent a preventive approach in individuals whose circulating PA levels contribute to inflammation and IR.

COVID-19 and Steroids- How well are we monitoring blood glucose levels?

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Background

The Covid-19 pandemic has led to various unprecedented challenges and obstacles, especially in the field of Diabetes and Metabolism, many of which are as novel as the pandemic itself. Discovering efficacious therapeutic options resulting in positive outcomes has been a challenge. Dexamethasone has been shown to reduce mortality in patients with Covid-19 pneumonitis who require oxygen therapy and/or ventilation. Exogenous steroid therapy is renowned to cause adverse metabolic side effects, including Hyperglycemia. In addition to this, concurrent Covid-19 infection further exacerbates the issue at hand.

Aims

The main aim of the Quality Improvement Project (QIP) was to improve adherence and compliance of capillary blood glucose (CBG) monitoring in patients with Covid-19 pneumonitis treated with steroid therapy by implementation of educational tools. Our results were compared with the standard of care guidance as set out by the Joint British Diabetes Societies (JBDS). Specific emphasis was placed upon early recognition of Hyperglycaemia, leading to improved Glycaemic control and patient outcomes.

Methods

Phase one of the project involved data collection on a retrospective basis of patients admitted to both the medical and COVID wards. This involved obtaining relevant data from the patient’s medical, nursing, and electronic notes. Changes were implemented in the form of teaching and educational sessions for the nursing staff. Posters focusing on the importance of Blood Glucose monitoring were circulated on the medical wards including the COVID wards. This was followed by discussions emphasising the importance of Blood Glucose monitoring on the board rounds.

Results

Data collection prior to changes showed that out of the cohort of 23 patients, only 5 patients (21.74 %) met the desired standard of care as per the guidance set out by the JBDS. Following implementation of changes, data collection revealed an improvement of compliance from 21.74 % to 56.52 %. Out of 23 patients, the desired level of care was now met in 10 of the patients. The project was carried out over a period of 3 months, commencing in October 2020, and concluded in January 2021.

Conclusions

Hyperglycaemia was associated with worse outcomes. Our QIP improved rates of blood glucose monitoring, followed by early recognition of hyperglycaemic states. This was also reflected in the fact that early recognition led to early therapeutic measures and prevention of diabetic emergencies. Despite significant changes, we aim to instigate further improvement by reinforcing learning among the frontline staff to achieve 100% compliance with the guidelines.

Sodium glucose cotransporter 2 inhibitors treatment in acromegalic patients with diabetes

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Introduction

Acromegaly is a chronic disease generally caused by a GH-secreting pituitary adenoma. GH excess causes insulin resistance and impair β cell function, predisposing patients with acromegaly to develop DM. Treatment of diabetes has been revolutionized since the introduction of sodium-glucose cotransporter inhibitors (SGLT2i). This novel class is widely used in type 2 diabetes mellitus (T2DM) and recently was approved for patients with heart failure with reduced ejection fraction and patients with chronic kidney disease (CKD) without diabetes. Taking into consideration the cardiorenal protection aspects, SGLT2i seems to be also attractive for diabetes management in acromegalic patients with already known increased cardiovascular risk. However, despite the known favorable aspects, SGLT2i is less recommended for acromegalic patients with diabetes due to the increased risk of diabetic ketoacidosis (DKA).

This study aims To report data regarding the use of SGLT2i in patients with acromegaly and diabetes.

Methods

In the present case series, data was collected using an electronic computerized registry at Clalit Medical Health (CMH) Services from Western Galilee and Haifa district between the years 2000-2020. Charts of patients with acromegaly and diabetes were reviewed thoroughly for current and previous anti-diabetic and acromegaly medications. Notably, electronic computerized files enable health care practitioners to follow the monthly treatment dispensing and report drug side effects. Laboratory results for fasting plasma glucose (FPG), hemoglobin A1c, IGF-1, and GH were reported before SGLT2i administration. In addition, actual hemoglobin A1c, body mass index (BMI), duration of diabetes, tumor size was reported for patients with and without SGLT2i treatment.

Results

34 acromegalic patients with diabetes were identified. Treatment with SGLT-2i was documented in nine patients, out of them 5 females and 4 males with a mean
Predictors of persistent abnormal glucose tolerance in post partum in women with gestational diabetes mellitus
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Background and aim
To determine clinical and metabolic predictors of persistent abnormal glucose tolerance in post partum after gestational diabetes mellitus (GDM).

Methods
This was a prospective study including 150 patients with GDM who underwent 75 g oral glucose tolerance test (OGTT) at 4-12 weeks after delivery.

Results
The prevalence of abnormal glucose tolerance in post partum after GDM was 32.8%, inclusive of 3.3% type 2 diabetes and 29.5% pre-diabetes. After univariate analysis, persistent carbohydrate tolerance disorders in post partum were statistically associated with age (34.77 ± 4.02 vs 32.07 ± 6.29 years, p = 0.015) and AB blood group (10.3% vs 0%; p = 0.012). Family history of type 2 diabetes in a first degree relative, personal history of GDM, fetal macrosomia, pre-gestational Body Mass Index and parity did not statistically differ between the two groups. Thirty minutes of moderate physical activity five times per week was a protective factor (P < 0.004) while sedentary lifestyle was associated with impaired carbohydrate tolerance in post partum (P = 0.004). Fasting blood glucose, glycemia at 2 hour in 75 g oral glucose tolerance test (OGTT) > 16 g/dl and insulin use according to a full basal bolus regimen were significantly associated with the persistence of carbohydrate tolerance disorders (respectively: P = 0.005, P = 0.02, P = 0.03). After multivariate analysis, the independent factor associated with abnormal glucose tolerance in post partum was glycemia at 2 hour (OGTT) (OR: 5.18, 95% CI: 1.27-21.16, P = 0.02).

Conclusion
Antenatal characteristics may predict abnormal glucose tolerance in post partum after GDM. High prevalence of persistent carbohydrate tolerance disorders highlights the importance of ongoing screening for all women with previous GDM in order to delay the onset of type 2 diabetes in this high risk population.

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Evening chronotype is associated with hormonal and metabolic disorders in Polycystic Ovary Syndrome
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Objective
Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder. Recently in the context of obesity, which often coexists with PCOS, it has been highlighted the role of chronotype as risk factor for obesity-related cardiometabolic complications. Given the importance of chronotype categories in the context of metabolic diseases and being PCOS characterized by metabolic derangements, we aimed to investigate the prevalence of chronotype categories in women with PCOS compared to healthy controls and their role in determining hormonal and metabolic aspects of PCOS.

Design and methods
In this case-control study, we investigated the chronotype categories in 112 women with PCOS and in 112 age and Body Mass Index (BMI) matched healthy women. Anthropometric (weight, height, BMI, and waist circumference), clinical (Ferriman-Gallway (FG) score), biochemically (fasting plasma glucose (FPG), insulin levels and Homeostasis Model Assessment (HoMA-IR)), inflammatory (C-reactive Protein (CRP)) and hormonal (testosterone levels) parameters were assessed.

Results
Women with PCOS had a lower chronotype score (P < 0.001) and thus a higher prevalence of evening chronotype category (P = 0.037) than controls. Women with PCOS and evening chronotype had significantly higher levels of FPG, insulin levels and therefore HoMA-IR, CRP, testosterone levels and FG score than women with PCOS with neither and morning chronotype. After adjusting for BMI, chronotype score showed significant negative correlations with CRP, testosterone levels and FG score. Linear regression analysis showed that high testosterone levels were among the factors most associated with a lower chronotype score (P < 0.001), followed by BMI (P < 0.001) and HoMA-IR (P < 0.05).

Conclusions
In summary, the current study reports the first evidence that women with PCOS had a higher prevalence of evening chronotype than women without PCOS. In women with PCOS evening chronotype has been associated with a worse hormonal and metabolic profile. Thus, given the importance of chronotype in women with PCOS emerging in our study, the assessment of chronotype should be included in the clinical evaluation of women with PCOS. Moreover, a chronotype-driven lifestyle approach could potentially improve the treatment of women with PCOS thus increasing the number of women with PCOS achieving their therapeutic goals.

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P92
Transforming growth factor beta 1: a new factor reducing hepatic sex hormone binding globulin production during liver fibrosis development
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Low plasma sex hormone-binding globulin (SHBG) levels are present in fatty liver disease, which represent a spectrum of diseases ranging from hepatocellular steatosis through steatohepatitis to fibrosis and irreversible cirrhosis. We have previously determined that fat accumulation reduces SHBG production in different non-alcoholic fatty liver disease (NAFLD) mouse models and that SHBG plays an active role in the development of this disease. In the present work, we are interested in elucidating the molecular mechanisms reducing SHBG plasma levels in liver fibrosis development. To do so, in vivo studies were performed using the human SHBG transgenic mice developing liver fibrosis induced by carbon tetrachloride (CCl4). Our results showed that CCl4 induced liver fibrosis and decreased SHBG production by reducing hepatocyte nuclear factor 4 alpha (HNF-4α). The SHBG reduction could be influenced by the increase in TGF-β1 levels, which were elevated in mice developing liver fibrosis. Results obtained in human SHBG transgenic mice showed that TGF-β1 reduced significantly SHBG mRNA and protein levels through TGF-β1 receptor I via STAT3 signaling pathway, resulting in a transcriptional repression of the SHBG gene. Overall, TGF-β1 is a new factor downregulating hepatic SHBG production in liver fibrosis development.

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P93
Determination of serum and cord blood vitamin D status in women in twin pregnancies using liquid chromatography-tandem mass spectrometry – a preliminary results
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Objective
Vitamin D has a pleiotropic effect on the human body. Besides its classical function as a regulator of calcium and phosphorus metabolism, it influences the secretion of other hormones, modulates the immune response and regulates cell proliferation and differentiation. Because women in twin pregnancies have higher metabolic needs, it can be expected that they might have higher risk of vitamin D deficiency.

Aim of the study and method
The aim is to analyze the serum and cord blood concentrations of vitamin D metabolites in women in twin pregnancies with the use of liquid chromatography-tandem mass spectrometry (LC-MS). Until the submission of this abstract (January 2022) 15 maternal and 30 cord blood samples were tested. We have collected data on supplementation and dietary intake questionnaires.

Results
The mean maternal age was 34.1 years (±3.5). The delivery took place at an average 34.8 week of pregnancy (±3.3). All patients supplemented vitamin D in doses ranging from 200-4000 international units per day. The median concentration of total 25-hydroxyvitamin D (25(OH)D) in maternal serum was 43.9 ng/ml (interquartile range [IQR] 42.0-54.1). Its deficiency was found in one patient. Elevated vitamin D levels were found in 36.4% of the mothers (maximum 73.6 ng/ml). The median concentration of 25(OH)D in cord blood was 25.2 ng/ml (IQR 20.1-28.8). Maternal and cord blood levels were highly correlated (r=0.58).

However, in each case, 25(OH)D level in the cord blood was lower than in the serum of corresponding mother (difference ranging from 7.1-48.2 ng/ml). In each pair of twins cord blood 25(OH)D concentrations were similar (differences: minimum 0.2, maximum 5.8, mean 2.2 ng/ml). In the described group, 25(OH)D levels in mothers were also determined by the commonly used in clinical practice chemiluminescent immunoassay (CLIA). The 25(OH)D levels obtained using the LC-MS method were significantly higher (median 43.9 ng/ml, IQR 42.0-54.1), than in case of CLIA (median 31.3 ng/ml, IQR 23.4-40.2, P=0.003). The differences in individual patients ranged from 5.4 ng/ml up to 36.7 ng/ml. These finding seem particularly important in terms of clinical decision making.

Conclusions
In the studied group of women in twin gestation that supplemented vitamin D, low prevalence of its deficiency determined by LC-MS was found. Maternal and cord blood levels of 25(OH)D were highly correlated. There are large discrepancies in the 25(OH)D concentrations obtained with LC-MS compared to CLIA in maternal samples.

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P94
The prevalence of non alcoholic fatty liver disease among diabetic patients attending the diabetic clinic in a tertiary care institute in colombo
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Background and Objectives
Non-alcoholic fatty liver disease (NAFLD) is the presence of hepatic steatosis in the absence of other causes for secondary hepatic fat accumulation. The incidence and the prevalence of the NAFLD has risen exponentially in the recent past especially in the patients with diabetes. We have studied the prevalence of NAFLD in patients with diabetes attending the diabetes clinic based on the biochemical and ultrasonic criteria, the risk factors for disease development and associated comorbidities.

Methods
A descriptive cross sectional study was conducted from August 2020 to March 2021 at the Diabetes Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting participants who are attending the diabetic clinic for annual end organ screening. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. The diagnosis of NAFLD is made according to the NINAS III criteria and the USS criteria. Categorical and numerical variables were analyzed using Chi-square and independent sample t-tests respectively. Multiple linear regression was used to determine the predictors of NAFLD diagnosis.

Results
The study enrolled hundred and one patients. The mean age was 58.3 years (range 23-80) and 69.3% were females. The mean weight was 65.7 (SD=12.5) kg and BMI was 26.8 (SD=4.7) kg/m². The prevalence of NAFLD according to the biochemical and/or USS criteria was 72.3% (n=73). Out of that 34.7% met both biochemical and USS criteria. Furthermore, 7.9% (n=8) met only the biochemical criteria while 29.7% (n=30) met only the USS criteria. More females were diagnosed with NAFLD compared to males (P=0.009). Pioglitazone use was protective against the development of NAFLD (P=0.000). The younger age (P=0.001), higher HbA1c (P=0.033), higher Body mass index (BMI) (P=0.014) are other statistically significant factors contributing to the development of NAFLD. Multiple linear regression model identified BMI (P=0.002), pioglitazone use (P=0.002), gender (P=0.000) as predictors of diagnosis of NAFLD.

Conclusions
The prevalence of NAFLD is higher in the diabetes patients when compared to the general population. The use of biochemical criteria only identifies a proportion of patients with NAFLD. Early diagnosis with suitable tests will allow early intervention and prevention of long term deleterious complications. Optimization of modifiable factors such as high HbA1c, BMI is paramount in the prevention of the disease development. Further large scale studies including community studies are needed to recognize the current prevalence of NAFLD in the general as well as diabetic populations.

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Perceived stigma in type 2 diabetes patients
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Introduction
Diabetes stigma (DS) refers to the experience of negative feelings such as exclusion, blame, rejection, or judgment due to having a chronic disease. The objective of this work was to measure the DS and its clinical determinants in type 2 diabetic patients.

Patients and methods
Cross-sectional study conducted on 84 type 2 diabetic patients who consulted on an outpatient basis between September and December 2021. DS was assessed using the arabic version of the type 2 Diabetes Stigma Assessment Scale (DSAS-2).

Results
Women represented 42% of the patients. The duration of diabetes was meanly 9.4 ± 6.4 years. The mean glycated hemoglobin was 9.9 ± 2.4. The mean BMI was 27.7 Kg/m² ± 4.7. The mean Total Diabetes Stigma score was 46.9 ± 10.2 (range 19–90). Subscale scores were as follows: Treated differently: 15.4 ± 4.3 (range 6–30), Blame and Judgment: 17.5 ± 4.3 (range 7–35), and Self stigma: 13.9 ± 2.3 (range 6–30). A total of 26 (30%) respondents scored more than the mean total diabetes stigma score, suggestive of potentially problematic perceived diabetes stigma. Higher Total Diabetes Stigma Scores were associated with level of therapeutic education (P = 0.045), social coverage (P = 0.043), diabetes treatment (P = 0.044), HbA1c level (P = NS).

Discussion and conclusion
The results of this work highlights the importance of identifying DS in type 2 diabetics. High levels of DS have been associated with poor glycemic control, poor diabetes self-management and poor quality of life. These data support the need to focus on increasing awareness efforts to educate the public about type 2 diabetes and its management.

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Increased haematocrit mediates lowering of blood glucose in mice exposed to hypoxia or treated with erythropoetin
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Conclusions

In women with PCOS, evening chromosome has been associated with a more severe IR and unhealthiest eating habits. Thus, chromosome assessment could be effective tool to screen the eating habits, and more generally the lifestyle, of women with PCOS.

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P98

VLCKD: a real time safety study in obesity

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Very Low-Calorie Ketogenic Diet (VLCKD) is currently a promising approach for the treatment of obesity. However, little is known about the side effects since most of the studies reporting them were carried out in normal weight subjects following ketogenic diet for other purposes than obesity. Thus, the aims of the study were: 1) to investigate the safety of VLCKD in subjects with obesity; 2) if VLCKD-related side effects could have an impact on its efficacy. In this prospective study we consecutively enrolled 106 subjects with obesity (12 males and 94 females, BMI 34.98 ± 5.43 kg/m²) that underwent to VLCKD. In all subjects we recorded side effects at the end of ketogenic phase and assessed anthropometric parameters at the baseline and at the end of ketogenic phase.

In a subgroup of 25 subjects, we also assessed biochemical parameters. Ninety-nine (93.4%) of the subjects enrolled experienced at least one mild side effect but none of the most severe ones. From the most to the less frequent, the percentages of occurrence of the mild side effects were as follows: 49 (46.2%) lethargy, 49 (46.2%) halitosis, 48 (45.3%) headache, 41 (43.5%) dry mouth, 30 (28%) constipation, 19 (17.9%) hypotension, 17 (16%) dizziness, 16 (15.1%) vomiting, 16 (15.1%) nausea, 15 (13.7%) hair loss, 13 (11.6%) abdominal pain, 11 (10.4%) hyperuricemia, 5 (4.7%) visual disturbances, 1 (0.9%) low blood sugar. No one experienced urolithiasis and gallbladder disease. In addition, 9 (8.5%) subjects stopped VLCKD before the end of the protocol for the following reasons: 2 (1.9%) due to palatability and 7 (6.6%) due to excessive costs. Finally, there were no differences in terms of weight loss percentage (13.5 ± 10.9 % vs 18.2 ± 8.9 %, P = 0.318) in subjects that developed side effects and subjects that did not developed side effects. Our study 2 demonstrated that VLCKD is a safe and effective nutritional tool in the management of subject with obesity.

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P99

A novel successful therapeutic option after a journey of treatment failures in a patient with heterozygous melanocortin-4 receptor deficiency

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Introduction

Obesity is a complex and multifactorial disease with a chronic and relapsing nature, and is associated with over 200 co-morbidities. In a minority of patients, the obesity is caused by gene defects in the leptin-melanocortin pathway. As lifestyle interventions often fail in these patients, additional anti-obesity pharmacotherapy is needed. In this case report, we describe the therapeutic journey of a patient with early-onset obesity and hyperphagia due to heterozygous melanocortin-4 receptor deficiency.

Case presentation

A 33-year-old woman presented herself at our outpatient clinic with severe obesity, hyperphagia, and mild intellectual deficit. She developed obesity at the age of 6 years, resulting from hyperphagia. After regular lifestyle treatment without sufficient effect, a gastric bypass was performed at the age of 26 years leading to -40 kg weight loss, but eventually in greater weight regain. At the age of 33 years, she presented with -29.5 kg weight loss (-15.8%, weight at start 186.4 kg), of which -27.9 kg (-7.3%) was fat mass. Most importantly, her subjectively reported hyperphagia, satiety, and subsequently quality of life improved.

Discussion

To our knowledge, this case report is the first to describe that naltrexone-bupropion can effectively reduce weight and improve subjectively reported hyperphagia and quality of life in a patient with genetic obesity. This extensive journey learns us that in patients with genetic obesity various anti-obesity agents can be initiated and when ineffective terminated and substituted to another anti-obesity agent to find the most efficient treatment with regard to weight loss, hyperphagia, and quality of life. It also demonstrates that genetic screening should be considered in patients with early-onset obesity, hyperphagia, or other specific symptoms of monogenic obesity, prior to bariatric surgery as they are at higher risk for weight regain.

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P100

The triglyceride-glucose index shows a stronger correlation with serum adiponectin levels than HOMA-IR

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Objective

Different methods are used to identify individuals with insulin resistance. The gold standard is the euglycemic-hyperinsulinemic clamp. However, in clinical practice, clamp is not preferred because it is cumbersome, the HOMA-IR index is used more often. The Trigliserid-glucose (TyG) index is a new and practical way to identify individuals with insulin resistance (IR). When compared to HOMA-IR, this index has been shown to be more reliable in determining insulin resistance and more effective to predict common diseases related to IR. In this study, the relationship between TyG index/ HOMA-IR and adiponectin were investigated.

Method

A total of 400 individuals, aged 24-50, were included in the study. Two hundred of participants had normal (Group 1) body mass index (BMI) values (18.5-25 kg/m²), while 200 were either overweight or obese (Group 2) (BMI >25 kg/m²). Demographic characteristics of all participants have been recorded. Height, weight and waist circumference were measured; BMI values were calculated. Body fat content was determined by the electrical impedance method. Glucose, insulin, triglyceride, total cholesterol, LDL, HDL and adiponectin were measured.

Results

There was no difference between groups in terms of gender distribution. Group 1 were younger (33.3 ± 6.8 years vs. 36.4 ± 7.0 years, P < 0.001). BMI, waist circumference, fat weight, fat ratio, plasma glucose levels, insulin, triglyceride, total cholesterol, LDL, HOMA-IR and TyG index values were higher in group 2 (TyG index; Group 1: 8.25 ± 0.51 vs Group 2: 8.58 ± 0.57). HDL cholesterol and adiponectin concentrations were found to be lower in Group 2. There was a stronger correlation between the TyG index and the adiponectin levels in Group 1, Group 2 and whole cohort compared to the HOMA-IR (Group 1, adiponectin-HOMA-IR, r = -0.19, P = 0.006, adiponectin-TyG index, r = -0.37, P < 0.001; Group 2, adiponectin-HOMA-IR, r = -0.26, P < 0.001, adiponectin-TyG index, r = -0.38, P < 0.001; Whole cohort adiponectin-HOMA-IR r = -0.27, P < 0.001, adiponectin-TyG index, r = -0.41, P < 0.001).

Conclusion

The TyG index is correlated with adiponectin levels better than HOMA-IR. This index could be an easy, practical and powerful method to predict unfavorable adipokine profile.

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P101

Hypothyroidism and obesity in a population of Italian women with lipedema and correlation with the clinical stage
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Aim
Lipedema is a painful fat disorder that affects ~11% of the female population, characterized by bilateral, disproportionate accumulation of subcutaneous adipose tissue predominantly in the lower body. The initial manifestations of lipedema arise in phases of hormonal change (puberty, pregnancy, menopause). The pathophysiology of lipedema is unclear. The putative causes proposed include altered adipogenesis, microangiopathy, and disturbed lymphatic microcirculation. The diseases is diagnosed on the basis of its main manifestations: pain, a feeling of tension, and increased tendency to form hematomas in the affected areas. Treatment is symptomatically oriented and based on complex decongestive therapy and nutritional regimen, low carb or ketogenic. There are four stages of lipedema that refer primarily to changes in the skin, based on the progression of fat accumulation and changes to the skin. The fourth stage is a condition characterized by lymphatic complications secondary to the failure of lymphatic system. A higher incidence of endocrinopathies, such as obesity and thyroid diseases, has been described in women with lipedema, but no studies have been done in Italy. The aim of the study was to evaluate the prevalence of these endocrine diseases in an Italian population of women with lipedema.

Materials and methods
Sixty-five women suffering from lipedema, who arrived consecutively at the lymphological clinic, underwent an endocrinological examination, with particular reference to the presence of obesity and thyroid diseases.

Results
The median age was 41.1 ± 13.5 years. Twenty-two women had stage 1 lipedema, twenty-five stage 2 lipedema, fifteen stage 3 lipedema and three stage 4 lipedema. Thirteen women (30%) were normal weight (BMI <25 kg/m2), twenty-two women (33.8%) were overweight (BMI ≥ 25 <30), thirty women (46.2%) were obese (BMI ≥30.0). The prevalence of obesity increases with the lipedema stage (P<0.001): 9.1% in stage 1, 48% in stage 2, 86.7% in stage 3, 100% in stage 4. Hypothyroidism was present in twenty-seven patients (41.5%). The prevalence of hypothyroidism (autoimmune and non-autoimmune hypothyroidism) increases with the lipedema stage (P<0.001): 18.2% in stage 1, 40% in stage 2, 66.7% in stage 3, 100% in stage 4.

Conclusions
The study confirms a high prevalence of obesity and hypothyroidism in patients with lipedema in Italian population and suggests a correlation between these diseases with the lipedema stage. Obesity and thyroid dysfunction should be evaluated in patients with lipedema, especially because for the possible worsening effect on the evolution of lipedema.

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P102

Design of a phase 2, double-Blind, placebo-controlled trial of setmelanotide in patients with genetic variants in the melanocortin-4 receptor pathway
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Introduction
Rare genetic causes of obesity result from disruption of the melanocortin-4 receptor (MC4R) pathway, a regulator of energy balance. Patients with obesity due to variants in multiple genes, including POMC, LEPR, SRI1, and SH2B1, have shown weight and hunger reductions after treatment with setmelanotide, an MC4R agonist. DAYBREAK is a Phase 2 trial of setmelanotide in patients with additional gene variants with suggested relevance to the MC4R pathway (ClinicalTrials.gov identifier: NCT04963231).

Methods
This Phase 2, double-blind, placebo-controlled, 2-stage study will enrol ~500 patients in Stage 1 to achieve ~130 qualified patients in Stage 2. Patients (aged 6 to 65 years) with pathogenic, likely pathogenic, or uncertain significance genetic variants based on American College of Medical Genetics criteria in a preselected set (n = 31) of MC4R pathway genes, including LEP, SIM1, MRAP2, and KSR2, and body mass index (BMI) ≥40 kg/m2 (aged ≥18 years) or BMI ≥97th percentile (aged <18 years) according to age and sex are eligible. Exclusion criteria include recent diet or exercise resulting in >3% weight loss, bariatric surgery within 6 months of enrollment, significant features or diagnosis of syndromic obesity, glycated hemoglobin >10.0%, and glomerular filtration rate <60 ml/min. Setmelanotide will be self-administered subcutaneously. Daily dosage will be age dependent: 2 mg will be administered for 14 days, then 3 mg thereafter in patients ≥12 years old or 1 mg will be administered for 7 days, 2 mg for 7 days, and 3 mg thereafter in patients 6-12 years old. Patients will be eligible to enter Stage 2 (randomized withdrawal period) if they have achieved ≥5% weight loss from baseline (≥18 years old) or ≥2.0-point reduction from baseline in BMI Z score (<18 years old) at the end of Stage 1 (16-week open-label run-in). Eligible patients will be randomized 2:1 to daily setmelanotide or matching placebo for 24 weeks. Primary endpoints include proportion of patients achieving ≥10% weight loss (aged ≥18 years) or ≥2.0-point reduction from baseline in BMI Z score (aged <18 years) from baseline at/week 40. Secondary endpoints are initial response to open-label setmelanotide and changes in body weight, waist circumference, hunger, and quality of life. Safety will be assessed by severity and frequency of adverse events.

Results
Patient dosing has been initiated as of January 2022.

Conclusions
The Phase 2 DAYBREAK trial will evaluate setmelanotide for weight loss and hunger reduction in individuals with variants associated with the MC4R pathway.

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P103

The crosstalk between adiposity and bone: a potential role for SIRT1 and sclerostin
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Background and aim
Sirtuin 1 (SIRT1) and sclerostin play important roles in adipose tissue and bone metabolism. SIRT1 pharmacological induction improves bone quality both in murine and human models and--as adiposity increases--its expression decreases both in peripheral tissues and blood. Sclerostin reduces osteoblasts' differentiation and mineralization and is associated with DMT2, obesity and cardiovascular risk. We evaluated the circulating SIRT1 and sclerostin relationship with mass and quality of bone considering the degree of adiposity.

Materials and methods
66 premenopausal women (16 underweight, 25 normal weight and 25 with obesity), aged <50 years, were enrolled. Plasma SIRT1, sclerostin, and DXA body composition (total-fat mass (FM), abdominal visceral adipose tissue, lean mass, trabecular bone score (TBS), lumbar spine and femoral neck-bone mineral density (BMD)) were assessed.

Results
The patients with obesity showed the lowest SIRT1 and TBS values and the highest sclerostin concentrations; BMD increased with FM and BMI and had an inverse association with SIRT1. Sclerostin was negatively correlated with SIRT1 (P =0.37, P=0.002). When spine-BMD, femoral neck-BMD and TBS were standardized for BMI, a positive correlation with SIRT1 and a negative correlation with sclerostin were seen (P<0.005). In a regression analysis, sclerostin was the best independent, negative predictor for BMD and TBS, while SIRT1 directly predicted TBS (P<0.005).

Conclusion
Blood measurement of SIRT1 and sclerostin could represent a snapshot of the bone status that, taking into account the degree of adiposity, may reduce the interference of confounding factors in the interpretation of the bone health parameters.

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P104

Impact of basal bolus insulin therapy on glucose control and mortality in patients with type 2 diabetes hospitalized with COVID-19: a retrospective study
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Introduction

Previous studies have reported that SARS-CoV-2 infection is associated with a more severe disease and worse outcome in patients with diabetes mellitus. Insulin is the mainstay of diabetes therapy in the inpatient setting. However, the treatment of diabetes in patients with COVID-19 remains unclear. In this study, we investigate the influence of different insulin regimens and other antidiabetic medications on glucose control and mortality in COVID-19 patients with type 2 diabetes.

Methods

We conducted a retrospective electronic medical record analysis of 359 type 2 diabetes patients hospitalized with COVID-19 between 01/04/2020 and 31/03/2021 in the Emek Medical Center. The following baseline characteristics included in the study are: gender, age, BMI, GFR, CRP, preadmission diabetes treatment regimens, and comorbidities. We divided the patients into two groups based on their diabetes treatment during hospitalization. The first group included patients treated only with insulin, and the second group of patients were treated with insulin and other classes of antidiabetic drugs. We recorded data of patients' 28-day mortality rates, preadmission diabetes treatment, average blood glucose, diabetes treatment regimens at discharge, and HbA1C levels 6 months before and after hospitalization in both groups.

Results

Of 359 patients, 82 were mechanically ventilated and 110 patients suffered a severe course of COVID-19. The mortality rate on day 28 after admission was similar in patients treated with insulin only and those treated with a combination of insulin and other treatment modalities ($P=0.29$) and remains non-significant after exclusion of mechanically ventilated patients from the statistical analysis. Patients who survived their hospital stay had lower CRP levels at admission (11.5 ± 8.2 vs 16.1 ± 9.7; $P=0.000$). During hospitalization, most of the patients in the combination therapy group received metformin on top of insulin (131 out of 162, 80%), 28 patients (17%) received SGLT-2 inhibitors, 12 (7%) were treated with IDeg Lira, previously uncontrolled on basal insulin and metformin, and follow up for 6 months. Patients were devide in two groups according HbA1c: group I with IDeg Lira in type 2 diabetes.

Conclusion

Basal bolus insulin regimens, as well as a combination of insulin and other classes of antidiabetic medications, were not associated with dissimilar mortality rates in patients affected with SARS-CoV-2. Our study shows that new antidiabetic medications, such as incretin-based therapy and SGLT-2, as well as metformin in combination with insulin may safe, and effectively control glucose levels in hospitalized COVID-19 patients.

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P105

Relationship between change in glycemic parameters and body weight with IDegLira in type 2 diabetes

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Introduction

IDegLira is the first fixed ratio combination of a basal insulin degludec and a glucagon-like peptide-receptor analogue liraglutide. These combination producer-duction in glycated hemoglobin A1c (HbA1c) and help to mitigate the weight gain. The aim of this study was to evaluate relationship between change in glycemic parameters and body weight in patients who began therapy with IDegLira.

Patients and Methods

Retrospective study included 86 patients with type 2 diabetes who began therapy with IDeg Lira, previously uncontrolled on basal insulin and metformin, and follow up for 6 months. Patients were divided into two groups according HbA1c: group I with HbA1c $<9$ (n=50) and group II with HbA1c $\geq 9$ (n=36). We examined glycemic parameters (HbA1c, fasting plasma glucose, FPG) and antropometric parameters (body weight and BMI).

Methods

The analysis showed that patients in group II with higher HbA1c from baseline had higher reduction in HbA1c and FPG (0.9% vs. 0.6%, $P<0.05$ for HbA1c, 1.0 mmol/l vs. 0.6 mmol/l, $P<0.05$ for FPG). Patients in all groups had decreased body weight at the end of study. The higher decreased in HbA1c in group II didn't followed with significance higher weight loss (1.9 kg vs 1.8 kg, $P>0.05$) and higher reduced BMI (0.8 vs 0.7 kg/m², $P>0.05$). We founded in both groups a significant direct correlation between reduction HbA1c and BMI ($r=0.35$, $P<0.05$, $r=0.42$, $P<0.05$), but with no significant difference between groups. At the end of study, no difference had showed in dosage of DLegLira between groups. Patients with poorer glycemic control from baseline were older and obese according BMI, but with no difference in duration of diabetes.

Conclusion

Our results showed that reduced glycemic parameters and weight loss depends on baseline value with IDegLira. The higher reduction glycemic parameters had no relationship with significantly higher weight loss.

Key words: insulin degludec, liraglutide, weight loss, type 2 diabetes.

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P106

Features of the level of amylinemia in patients with latent autoimmune diabetes in adults

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Background

Among the heterogeneous types of diabetes mellitus (DM), latent autoimmune diabetes in adults (LADA) is the most common and attracts the attention of scientists, the pathogenesis of which combines the main mechanisms of classical type 1 (T1DM) and type 2 diabetes mellitus (T2DM). The role of hyperamylinemia in the development and progression of LADA remains out of the researchers’ attention.

The objective of the study was to determine the features of the level of amylinemia in patients with LADA compared to classical types of DM.

Methods

89 patients with diabetes and chronic kidney disease (CKD) were examined, as well as 15 representatives of the control group. The patients were divided into three groups by the types of DM (25 patients with classical T1DM, 36 patients with LADA, 28 patients with T2DM). The LADA group included patients with LADA1 phenotype (antiGAD $\geq 180$ U/ml) and LADA2 phenotype. Serum amylin levels were measured using the ELISA method.

Results

In patients with classical T1DM, the level of amylinemia did not change, whereas in T2DM group it was 10.8 times significantly higher compared to the control and 8.3 times higher than in the group of patients with classical T1DM. In the group of patients with LADA, the amylin content was 9.0 times higher than in control and 6.9 times higher compared to classical T1DM. In the distribution of patients with LADA into phenotypes, in patients with LADA1, the serum level of amylin was 5.9 times higher relative to the control ($P<0.01$), 4.1 times higher relative to classical T1DM ($P<0.01$), but almost half as low as in T2DM ($P<0.01$). In LADA2 group, the above indicator exceeded that in the control group by 13.5 times ($P<0.01$), in the group of classical T1DM – by 9.3 times ($P<0.01$) and in patients with LADA1 – by 2.3 times ($P<0.05$). In patients with LADA, an interdependence was found between the content of amylin and insulin ($r=0.64$, $P=0.000$), C-peptide ($r=0.74$, $P=0.000$), the HOMA-IR index ($r=0.54$, $P=0.001$).

Conclusions

Serum amylin level significantly increase in patients with latent autoimmune diabetes in adults, especially in LADA2 phenotype compared to classical types of diabetes, which indicates the role of hyperamylinemia in the development and progression of this subtype of diabetes.

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P107

The relation between insulin resistance and both growth hormone and insulin-like growth factor (IGF-1) levels in a sample of Iraqi patients with type 2 diabetes

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Introduction

The relation between insulin resistance and both growth hormone and insulin-like growth factor (IGF-1) levels in a sample of Iraqi patients with type 2 diabetes.
Introduction Background
Over the last decade, scientific attention has been drawn to the potential role of growth hormone (GH) and insulin like growth factor-1 (IGF-1) in the pathogenesis and progression of T2DM. Both hormones are interleaved but exert variable effect on glucose homoeostasis. While GH increases blood glucose level, IGF-1 maintain insulin secretion and enhance insulin sensitivity.

Methods
A cross sectional study conducted in the National Diabetes Centre, Baghdad, Iraq, from May 2020 to May 2021. Sixty patients with type 2 diabetes were investigated for fasting plasma glucose (FPG), GH, IGF-1 Hba1c, HOMA-IR, HOMA-B and anthropometric measures. Patients with Type 1 diabetes mellitus, thyroid disease, pituitary disease, chronic kidney disease, hepatic disease and Pregnancy were excluded from the study.

Results
There was no significant difference between gender and other variables of studied sample. There was association between HOMA-IR with Hba1c, IGF-1, fasting insulin, HOMA-B, and with QUICKI. A significant association between IGF-1 and body mass index (BMI), glycated haemoglobin (Hba1c), the duration of type 2 diabetes, quantitative insulin sensitivity index (QUICKI), and the age of patients was found. IGF-1 showed a significant negative correlation with BMI and a significant positive correlation with Hba1c and QUICKI. Fasting GH correlated negatively with waist hip ratio (WHR), fasting insulin, HOMA-IR and positively with age and QUICKI. Hba1c was significant positive correlations with duration of T2DM, WHR, FPG, fasting TG, IGF-1, HOMA-IR and negatively correlated with QUICKI. There was a significant negative correlation between QUICKI index and BMI, WHR, FPG, Hba1c, fasting TG, fasting GH, Fasting insulin, and HOMA-IR. While HOMA-IR was significantly positive correlated with BMI, Fasting Plasma Glucose, Hba1c, Fasting TG and fasting insulin.

Discussion
GH and IGF-1 play a complex role in type 2 Diabetes Mellitus. In this study, IGF-1 in obese patient was low while in uncontrolled diabetes was high. GH decreased upon increased insulin resistance. Targeting IGF-1 in type 2 diabetes can be utilized as a potential therapy in the near feature. However, this needs further well designed randomized controlled trials. Conduct larger scale study to specify the cut off value of HOMA-IR for Iraq.

Conclusion
GH and IGF-1 play a complex role in type 2 Diabetes Mellitus. In this study, IGF-1 in obese patient was low, while in uncontrolled diabetes was high. GH decreased upon increased insulin resistance.

Keywords
Growth Hormone, IGF-1, Type two diabetes, insulin resistance, HOMA, QUICKI.

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P109

Maternal triglyceride levels, and not fructosamine, in early pregnancy are associated with birth weight

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Objectives
Maternal metabolism has a major impact on foetal growth, and the risk of developing obesity, cardiovascular disease and diabetes in later life. Identification of maternal metabolic parameters in early pregnancy that predict birth weight (BW), is pivotal in the prevention of these diseases. We evaluated whether maternal triglyceride (TG) or fructosamine levels in early pregnancy, as possible reflectors of maternal insulin resistance (IR), could predominantly contribute to BW and whether this is sex dependent.

Study design
The data were obtained from the Amsterdam Born Children and their Development cohort study. Non-fasting TG and fructosamine levels were determined in early gestation (median 13 weeks). Associations between maternal TG and fructosamine levels, and BW - small for gestational age (SGA) - large for gestational age (LGA), were analysed for each sex separately.

Results
In total 3514 pregnant women were included. With every increase of 1 mmol/l TG, the BW increased significantly by 81.7 g. This increase was larger with boys (107.3 g, 95% CI 66.0-148) compared to girls (60.5 g, 95% CI 23.6-97.4). However, no association was found with fructosamine. The results were adjusted for gestational age at blood sampling, total duration of pregnancy, maternal height, age, parity, ethnicity, educational level, smoking, alcohol and pre-pregnancy BMI. These covariates were also used in a different statistical test (R-squared), and explained 29.2% of the variance in BW. Adding fructosamine to this model, had no added value in predicting BW (R2 stayed 0.292). Contrary, TG levels raised the R2 from 0.292 to 0.299 (P<0.001). In total 8.3% children in our population were LGA. The odds of a new-born LGA with higher maternal TG levels were increased (OR 1.6, 95% CI 1.3-2.0). No increased odds were found for fructosamine levels (OR 1.0, 95% CI 1.0-1.0).

Conclusions
This study shows that fructosamine levels, measured in the first trimester of a physiological pregnancy, are not significantly associated with BW, in contrast to maternal TG levels. This association is more prominent with boys. Our data suggest that the lipid profile in early pregnancy is more predictive for pregnancy outcomes, like LGA, than glycaemic metabolic parameters, such as fructosamine. This may give a different focus on metabolic variables (TG vs fructosamine) involved in early patterns of maternal IR during a physiologic pregnancy. Additional studies could show whether maternal TG levels should be included in the screening or follow-up of pregnancies with a pronounced IR (e.g. in gestational diabetes).

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P110
Evaluation of a new transition organization for young adults with endocrine or metabolic diseases
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Objective
To evaluate the effect of a new care organisation on multiple outcomes of transition success and its cost-effectiveness in patients with any endocrine or metabolic disease diagnosed during childhood and transferred to adult care.

Design
Non-randomized controlled trial in a French University Hospital.

Methods
Patients transferred to adult care during the control period (04/2014-08/2016) and the intervention period (09/2016-06/2018) were included. The intervention is based on case management involving liaising with pediatric services, personalising care pathways, and liaising with structures outside hospital (general practitioner, educational and social sector). The primary endpoint was the percentage of patients lost to follow-up at 24 months post transfer. Other outcomes were collected from medical files, consultation software, and questionnaires. A cost analysis was performed.

Results
202 patients were included (101 per period), the most represented pathologies were congenital and non-congenital hypopituitarism (respectively n=34 (17%) and n=41 (22%)) and thyroid diseases (n=21, 10%). Patients were aged 22.5 ± 24 months post transfer where 12 were lost to follow up in the control group and 59 in the intervention group (P=0.49). The percentage of honouredom consultation among those planned during 24 months was higher with intervention (P=0.0085). Patient satisfaction, physician trust, transfer delay did not differ between the groups. The incremental cost-effectiveness ratio was €179 per patient not lost to follow-up.

Conclusions
At 24 months post transfer the rate of lost to follow-up does not significantly differ, but indicators of a steadier follow-up are increased and the intervention appears to be cost-effective.

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P111
Analysis of the nutritional status of women in twin pregnancies in terms of key vitamins and microelements – preliminary results
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Objective
Diet and nutritional status during pregnancy are critical for the health of both mothers and the neonates. Women in twin pregnancies have higher metabolic needs compared to women in single pregnancies and it can be expected that they have higher risk of key vitamins and micronutrients deficiencies. However, very scarce data are currently available on this topic.

Aim of the study and method
The main aim is to analyze the nutritional status of women in twin pregnancies in terms of selected vitamins and microelements: iodine, vitamin D, calcium, magnesium, iron, folic acid and vitamin B12. It will be achieved through analysis of the nutritional status of the mentioned nutrients in 100 women with twin pregnancies after 22 weeks of pregnancy. A comparison with a control group of women in single pregnancies is also planned.

Results
Until the submission of this abstract (January 2022) 69 women in twin pregnancies were recruited. The median age in this group was 34 years (interquartile range [IQR] 31-36), whereas median gestational age was 30.4 weeks (IQR 25-33.3). 52.2% of women were in dichorionic diamniotic, 43.5% in monochorionic diamniotic and 31-36), whereas median gestational age was 30.4 weeks (IQR 25-33.3). 52.2% were recruited. The median age in this group was 34 years (interquartile range [IQR]

Conclusions
Until the submission of this abstract (January 2022) 69 women in twin pregnancies after 22 weeks of pregnancy. A comparison with a control group of women in single pregnancies may constitute a high-risk group for the deficiencies of iron, vitamin D and vitamin B12 deficiency.

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P112
Expression of beta2 adrenergic receptors in pancreatic islets of metabolic syndrome induced C57BL/6J Mice
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Background
The global prevalence of metabolic syndrome (MetS) characterized by type 2 Diabetes (T2D), obesity, and cardiovascular diseases, has reached alarming proportions worldwide. The prevalence is rapidly increasing among all the age groups due to calorie dense food intake and sedentary lifestyle. Beta adrenergic receptors (β-ADRs), are known for its role in thermogenesis, lipolysis and glucose metabolism. Ceaarne et al., 2018, reported that pancreas-specific deletion of Adb2 resulted in glucose intolerance and impaired insulin secretion in mice.

Objective
To develop an animal model by feeding high fat simple carbohydrate diet (HFSC) and to study the expression pattern of β2 ADRs in the pancreatic islets.

Methodology
The MetS was induced in male C57BL/6J mice (n=10) by feeding HFSC. The control animals were fed with standard diet. The MetS was confirmed by anthropometrical analysis, fasting blood glucose, total cholesterol, triglycerides, HDL and LDL. At the end of 5th month of feeding, the experimental animals were sacrificed, the pancreas was isolated. The morphology of the pancreas was studied by histology and SEM. The pancreatic islets were isolated by collagenase digestion. The quality of islet was accessed by Dithiozone staining. The total islet protein was extracted by RIPA lysis method and quantified by BCA assay. The protein was separated by SDS PAGE, immune blotted and probed with β2 ADR polyclonal antibody followed by Goat anti rabbit IgG (H+L) cross adsorbed DyLight488. The blots were quantified using Biorad Geldoc XR + with ImageLab sofware.

Results
The metabolic syndrome was developed in male C57BL/6J mice by feeding HFSC diet up to 5th month. Blood glucose (P<0.01), triglyceride level (P<0.0001), total cholesterol (P<0.001), LDL (P<0.01) of HFSC fed mice was significantly increased compared to control. The number of pancreatic islets was reduced in the HFSC fed mice compared to control. In comparison to control mice, HFSC-fed mice’s islets were depleted and had higher lymphatic infiltrates. The expression of β2 ADRs were found to be altered in the HFSC fed mice. Conclusion

Serving as a model, HFSC fed mice more closely resembled human obesity with altered blood glucose and lipid profile. The presence of lymphatic infiltration around the islets of HFSC-fed mice indicates that the inflammatory process may also contribute to islet destruction, which could lead to T2D. Additional changes associated with the β2 ADRs and its downstream signaling will be discussed during the congress.

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P113
Impact of hyperuricemia at metabolic syndrome and diabetic nephropathy, among patients with diabetes mellitus
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Hyperuricemia is a high risk factor for atherosclerotic diseases such as CVD and carotid atherosclerosis, hypertension, type 2 diabetes mellitus (T2DM), metabolic syndrome (MS). There are complex interrelations between hyperuricemia,
T2DM, chronic kidney disease (CKD) and MS. The purpose of our study was to investigate the relationship between hyperuricemia, CKD, MS, and its components.

Materials and methods

179 patients with T2DM were included. The baseline presence of components of metabolic syndrome as defined by the World Health Organization was determined. CKD was defined according to the guidelines by reduction of GFR below 60 ml/min/1.73 m², with a minimum duration of 3 months or renal impairment lasting more than 3 months. Hyperuricemia was determined as serum uric acid level above 7 mg/dl in men and 6 mg/dl in women.

Results

Following the analysis of the studied group, out of the 179 cases, 131 were identified with hyperuricemia and 48 with normo-uricemia. The prevalence of hyperuricemia was 73%. The average age of the patients was 73 years. In patients with hyperuricemia, the mean values of SBP and DBP were statistically significant higher than in patients with normo-uricemia (P<0.003). Triglycerides had statistically significant higher values in the hyperuricemia group (P<0.005).

The mean HDL-cholesterol value being statistically significant lower in the hyperuricemia group (P<0.01). Renal function evidenced by creatinine, blood urea nitrogen and GFR, was statistically significant lower in patients with hyperuricemia (P<0.001). There was statistically significant relation between hyperuricemia and albuminuria (P=0.008), as predictor of diabetic nephropathy.

Conclusions

Among diabetic patients with hyperuricemia, the prevalence of CKD, obesity, hypertension, MS and its components are statistically significantly higher than in patients with normo-uricemia.

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P115

Immunotherapy-induced Diabetes Mellitus is not uncommon

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Background

Lung cancers are one of the leading causes of death worldwide which has resulted in an increase in immunotherapy, particularly immune checkpoint inhibitors (ICIs). Recent studies have shown induced endocrinopathies secondary to ICIs as a result of pancreatic beta cells, thyroid, and pituitary dysfunction.

We aim to present an interesting case of Type 1 Diabetes mellitus secondary to immunotherapy. Pembrolizumab is used to treat melanoma, non-small cell lung cancer, head and neck cancer, Hodgkin lymphoma, stomach cancer, and cervical cancer. Pembrolizumab is a human monoclonal IgG4 antibody that selectively binds to programmed cell death ligand-1 (PD1) receptor on the cell surface, thus blocking PD-1 (Programmed cell Death 1) which prevents T-cells from recognising and attacking cancer cells.

Case

In this case, a 62-year-old lady presented to hospital with polyuria, polydipsia, and weight loss after 8 months of immunotherapy. She was found to be hyperglycaemic and new of type 1 diabetes. Her background includes poorly differentiated adenocarcinoma of right lung diagnosed in March 2017, dermatomyositis, and an ex-smoker. She had received 4 cycles of chemotherapy (Cisplatin/Pemetrexed) between April 2017- June 2017 and then radical radiotherapy which completed August 2017 with good response and then she commenced Pembrolizumab in July 2020. Initial investigations were not consistent with DKA; pH 7.451, serum glucose 29.7 mmol/l, HCO3 26.2 mmol/l and urinary ketones 4+. She was commenced on NovoRapid 4 units 3 times a day and Levemir 10 units in the morning and 4 units in the evening. TSH was 0.90 mU/l and cortisol of 263 nmol/l excluded adrenal insufficiency. She was negative for Ilets-cell antibodies, anti-GAD antibodies, and ZNT8.

Discussion

ICIs are commonly associated with endocrinopathies which are categorized as immune-related adverse events (Ruggeri 2019). New type 1 diabetes mellitus is a frequent toxicity of immunotherapy and can potentially be life-threatening if not diagnosed promptly. Therefore, during immunotherapy treatment, serum glucose should be regularly monitored. The UK National Institute of Health and Care Excellence (NICE) recommends developing an early plan of care, blood glucose management (periodic HbA1c and serum fasting glucose level tests), and managing long-term complications for adults diagnosed with Type 1 Diabetes mellitus. It is also recommended that patients started on ICIs have other endocrine toxicities testing. Current treatment is targeted to replace the specific hormone deficiency, e.g insulin in the case of new T1DM, as well as immunosuppression depending on the severity of the endocrinopathy (Ruggeri 2019).

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P116

Association of uric acid levels with diabetic retinopathy in filipino patients with type 2 diabetes mellitus at a tertiary government hospital: a cross-sectional analytic study

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Objectives

Diabetic retinopathy, is the most frequent cause of new cases of blindness among adults aged 20–74 years in developed countries. In 15 of the 23 studies in developing countries and in ethnic minority groups within developed countries, the prevalence of diabetic retinopathy was over 35%. In developed countries, only 2 of 16 studies reported a prevalence of 35% or over. Variation in neither population demographics nor method of retinopathy assessment appeared to account for these differences in prevalence. Serum uric acid is one of the major
sources of oxidative stress thru generation of free radicals and exhibits pro-inflammatory actions. This study aims to investigate the association of serum uric acid levels and diabetic retinopathy.

Methodology
Consecutive patients at the Diabetes Clinic at East Avenue Medical Center, diagnosed with Type 2 Diabetes Mellitus by the ADA criteria for diabetes from August 2019 to May 2020 were recruited. We excluded patients with pre-diabetes, Type 1 DM, diabetes induced by steroid use and other endocrine diseases, gestational diabetes, significant co-morbidities (cancer, COPD, decompensated heart/liver failure, ESRD on HD), kidney transplanted patients, renal artery stenosis, autoimmune kidney diseases and patients who undergone cataract or any retinal surgeries. Demographic, medical and laboratory data were obtained. Blood examinations were performed in the same diagnostic center by the same trained and calibrated operators to prevent inter-observer variability.

Results
117 (67 with DR and 50 no DR) patients were analyzed. The mean age of patients with diabetic retinopathy was younger (55.73 ± 8.18) than those patients without diabetic retinopathy (56.34 ± 11.31) however the difference between the two groups was not statistically significant (P = 0.736). The mean serum uric acid level was 6.44 ± 1.54 mg/dl in patients with DR whereas it was 6.10 ± 1.50 mg/dl in those without DR. The levels however were not statistically significant (P=0.249). Using the binary logistic regression, duration of DM, presence of anemia as well proteinuria and low estimated glomerular filtration rate (eGFR) were independently associated with DR (P=0.006, 0.008, 0.012 and 0.037, respectively).

Conclusion
Serum uric acid levels were not associated with diabetic retinopathy, but it was shown in this study that there was a higher concentration of uric acid levels in patients with more severe retinopathy. Duration of diabetes, anemia, lower eGFR and presence of proteinuria reflecting chronic kidney disease were independently associated with the presence of diabetic retinopathy.

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P118
Association between hyperuricemia and degenerative complications of type 2 diabetes
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Introduction
Hyperuricemia is associated with increased cardiovascular mortality and morbidity hence the interest in screening for hyperuricemia in the type 2 diabetic population.

Objective
To investigate the association between hyperuricemia and degenerative complications in type 2 diabetics.

Patients and Methods
This is a retrospective study including 130 patients followed in the C department of the National Institute of Nutrition in Tunis.

Results
The average age of our patients was 61 ± 11 years, with a sex ratio M/F=0.63. The average duration of diabetes was 14 ± 8 years. Obesity was present in 63.2% of patients. The incidence of hyperuricemia was 47.1% with a higher incidence in women: 54.4% of these patients were women vs 45.6% of men. In this population, microangiopathic and macroangiopathic degenerative complications were noted in 80.8% and 45% of cases respectively. For macroangiopathic complications, coronary artery disease topped the list with a frequency of 43.1%, followed by obliterator arteriopathy of the lower limbs with a frequency of 25.5% and finally stroke with a frequency of 3.9%. For microangiopathic complications, diabetic retinopathy was noted in 56.9% of cases. The frequency of diabetic nephropathy was 50%, of which 26.3% were at the stage of renal failure. The frequency of diabetic neuropathy was 38.5%. This analysis showed that hyperuricemia was significantly associated with macroangiopathic complications (P=0.006) and microangiopathic complications (P=0.049).

Conclusion
Our study showed a significant association between hyperuricemia and degenerative complications of type 2 diabetes.

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P119
Spontaneous discitis after diagnostic lumbar puncture in a post COVID-19, diabetic patient
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Background
During the COVID-19 outbreak, there are rising concerns about long-term complications of COVID-19. On the other hand, discitis is a rare neurologic diagnosis, often delayed or missed due to the rarity of the disease. Patients usually present at an average age of 69 years with a history of diabetes or with a systemic infection. The lumbar spine is the most frequent site of infection (54%), and the cervical is the least at 10%. This is a case of post-COVID-19, diabetic patient complicated by discitis after a lumbar puncture.

Case presentation
A 77 years old patient presented in our emergency unit with intermittent temperature, headache and nuchal rigidity. Medical history: Patient was diagnosed with Diabetes Mellitus and hypertension 5 years ago. He was being treated with Metformin and antihypertension drugs. He was diagnosed with COVID-19, two months ago, since then he has had temperature between 38.39°C. Laboratory analysis: hyperglycemia and hypoaalbuminemia, in haemogram:

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Conclusions
Managing diabetes in patients with mental health problems can be challenging. It has to be integrated, MDT team (psychiatry and diabetology teams), use of cognitive behavioural therapy (CBT), use of motivational interview. NICE recommends screening for diabetes at baseline, 3-4 months after initiation of anti-psychotic and then annually.
microcytic hypochromic anemia and neutrophilic leukocytosis. CRP/C Reactive Protein) and D-dimer were very high (22 mg/dl and 4 times normal range respectively). Kidney, liver and thyroid gland function resulted normal. In craniothoracic CT: Large multinodular thyroid gland with calcified nodules that slightly compressed trachea. Head and thorax normal. A diagnostic lumbar puncture was obtained but the result excluded meningitis. Because of disequilibrated diabetes and need for thyroid exploration, the patient was hospitalized in Endocrinology Department where insulin, antibiotics (ceftriaxone and moxifloxacin), gastric scintigraphy and human albumin were started. After being hospitalized he complained a severe lumbar pain. CRP firstly, started to fall and then started to raise (10 days later even on antibiotic therapy, CRP was 18 mg/dl again), and immediately CT and then MRI with contrast were performed and confirmed presence of L2-L3 spondylodiscitis. ASLO, C3, C4, RF, and tumoral markers were normal. Infectionist changed antibiotic therapy to Imipenem and Cefiproloxine, 10 days later, CRP level decreased to 6.6 mg/dl, but lumbar pain persisted even under painkiller. Sub febrile temperature kept persisting also. Our patient also achieved better glycemic control under basal-bolus insulin regimen but inflammatory parameters (PCR, D-dimer and Fibrinogen) remained high and actually he is transferred to local hospital for further treatment with intra venous antibiotics.

Conclusion

Post-covid-19 diabetic patients who are immunocompromised, are in higher risk of developing serious infections (like spondylodiscitis) even after diagnostic procedures like lumbar spine diagnostic puncture. Physicians must be careful to prevent.

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P311
Oxidative stress decreased after six months testosterone treatment compared to placebo in ageing men – a randomized, double-blind trial
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Background

High oxidative stress is associated with increased morbidity. The effect of testosterone treatment (TT) on oxidative stress in ageing men with reduced bioavailable testosterone is undetermined.

Aim

To determine the effect of TT compared to placebo on oxidative stress biomarkers.

Methods

Double-blinded, placebo-controlled study in 38 men, aged 60–78 years, with bioavailable testosterone <7.3 nmol/l and waist circumference ≥94 cm, randomized to six-month testosterone gel therapy (n=20) or placebo (n=18). Whole body oxidative stress was assessed at baseline and after 6 months therapy by measuring 24 h urine oxidized derivatives of nucleic acids: 8-oxoguanosine (8-oxoGuo) and 8-oxo-2’-deoxyguanosine (8-oxodG) by ultra-performance liquid chromatography tandem mass-spectrometry. Fat and lean mass were measured by whole body dual x-ray absorptiometry. Changes between TT and placebo groups were compared using Mann-Whitney test. Δ-values for clinical and biochemical markers were calculated as 6 months minus pretreatment level. Bivariate associations of Δ-values of clinical and biochemical data were investigated by Spearman’s Rho correlational analyses. Linear regression analyses was used to adjust for changes in body composition. P-value of <0.05 was considered significant.

Results

At baseline, median (interquartile range) age was 67 (64-72) years, BMI 29.8 (26.6-33.3) kg/m2, total testosterone 12.6 (8.9-16.1) and bio-available testosterone 4.7 (3.7-5.9) nmol/l. Levels of 8-oxoG/24h decreased during TT compared to placebo (P=0.038). Δ-8-oxoGuo/24h was inversely associated with Δ total testosterone (ρ=–0.35, P=0.04) and Δ bio-available testosterone (ρ=–0.37, P=0.03). Δ-8-oxoGuo/24h and Δ-8-oxoGd/24h were associated with Δ-fat mass (ρ=0.47, P=0.006 and ρ=0.40, P=0.02, respectively). Δ-8-oxoGd/24h was inversely associated with Δ-lean mass (ρ=–0.38, P=0.03). In linear regression analyses. The inverse association between Δ-oxidative stress biomarkers and Δ-total testosterone remained significant after adjustment for Δ-fat mass and Δ-lean mass.

Conclusion

Oxidative stress biomarkers decreased during six-month TT compared to placebo in ageing men.

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P312
Gastric dysmotility in diabetes
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The prevalence of diabetes is growing every year. One of the important complications of diabetes is the effect of diabetes on the gastrointestinal tract.

Purpose of the study: to identify the frequency of delayed gastric emptying in patients with diabetes.

Materials and methods

122 patients with type 2 diabetes were examined for complaints from the upper gastrointestinal tract. For this, the GCSI questionnaire was used. After a thorough clinical, laboratory and instrumental examination, 34 patients were excluded. The remaining 88 patients underwent gastric scintigraphy to determine the motor-evacuation function of the stomach.

Results

A comprehensive examination was carried out of 88 patients with type 2 diabetes mellitus. All patients were divided into three groups depending on the age of diabetes: the first group (up to 5 years) - 23 people (27.27%), the second (6-10 years) - 26 (29.5%), the third (more than 11 years) - 39 people (43.2%). The average age was 52.8 ± 6.51 years. Clinical and metabolic compensation of diabetes (HbA1c <7%) was observed in 12 people (13.6%), decompensation of carbohydrate metabolism - in 76 people (86.4%). A labile course of diabetes mellitus was observed in 19 people (11.36%). Dynamic scintigraphy revealed the following data. Accelerated emptying of the first portions of TC into the intestines was observed more often in 37 people (42.3%), in 27 people (30.76%) - there was a delayed intake, in 4 patients (3.84%) - normal. Gastroesophageal reflux was observed in 27 people (30.7%), and duodenogastric reflux in 4 patients (3.84%). The time of maximum accumulation of TC in the stomach, was slow in most patients in all three groups. 15.9% of patients there were no complaints from the organs of the gastroesophageal zone, while 80% of them had a delayed motor-evacuation function of the stomach (T1 / 2av = 81.2 min), in 20% - within normal limits. Mathematical modeling with the construction of 3D graphs made it possible to identify the relationship between the motor-evacuation function of the stomach, the duration of diabetes and the presence of hypoglycemia, namely, with an increase in T1 / 2 (stagnation of food in the stomach), the frequency of hypoglycemia increases, and with an increase in the duration of diabetes, evacuation is even more delayed test breakfast from the stomach.

Conclusion

A comprehensive and targeted examination of 88 patients with type 2 diabetes mellitus showed a high prevalence of pathology of the gastrointestinal tract.

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P313
Obesity and obesity-related diseases as a new clinical features in 3q27.3 microdeletion syndrome involving adipoq gene: a case study
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Introduction

Adipose tissue is recognized as an important endocrine organ, secreting many endocrine factors. Adiponectin is the most abundant peptide released into circulation, encoded by ADIPOQ gene localized in chromosome 3q27.3. Adiponectin decreases intracellular ceramide, implicated in insulin resistance, inflammation and atherosclerosis. It stimulates fatty acid oxidation in skeletal muscle and inhibits glucose production in the liver. Hypo-adiponectinemia plays a central role in obesity and obesity-related disease. Since the advent of Comparative Genomic Hybridization Array (CGH-Array), numerous new microdeletion syndromes have been described. Few cases of autosomal dominant 3q27.3 microdeletion syndrome have been described, mostly characterized by intrauterine growth retardation, marfanoid habitus, cranio-facial

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P314
Diabetes and cervical pathologies: The phenotype and genotype connection
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Cervical cancer is the fourth most common cancer among women globally and second most common in India. As per WHO, almost 90% of new cases and deaths worldwide, occurred in low to middle income countries in 2020. More than 95% of cervical cancers are associated with chronic Human papilloma virus infection (HPV), particularly of the types 16 and 18. High income countries have vaccination and screening programs that are in place for young girls but low-and-middle income countries usually do not have access to such facilities. Another disease that is increasing in incidence and prevalence in such populations is diabetes mellitus. Diabetes is known to be associated with increased incidence of various cancers like endometrial, cervical, breast, stomach and pancreas. It is also observed that cancer patients with diabetes have an overall reduced survival as compared to non-diabetics. We undertook this study to observe frequency and pattern of cervical pathologies (using routine pap smear) among diabetic females from reproductive age group and compared them with non-diabetic females. The idea was to observe if diabetic females have higher prevalence of cervical pathologies which might progress to cervical cancer in future. We found that diabetes was associated with higher occurrence of cervical pathologies like cervicitis (Odds’s Ratio 10.9), vaginitis (OR 1.23), HPV infection (OR 1.4) and malignant changes (OR 1.52). We then attempted to find genetic association between diabetes and cervical pathologies to determine if there are overlapping predisposing genes that can explain higher preponderance of diabetics towards cervical pathologies. This was done by applying gaussian mixture modelling on available genetic data for diabetes mellitus (types 1 and 2), chronic HPV infection, cervical intra-epithelial neoplasia (CIN) and cervical cancer. Some MHC loci like HLA-DQA1, HLA-DQB1 were found to be overlapping, which was expected. Apart from MHC genes, certain genes showed positive association with both spectra (diabetes and cervical pathologies) like INS-IGF2, TERTB, SILC1. The genetic association may help in understanding the connection between the two diseases in a better way and may also help in predicting higher chances of cervical pathologies in populations with higher preponderance towards upregulation of such genes.

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P315
Participation in Diabefly® digital therapeutics program leads to significant improvement in glycemc control and reduction in weight and BMI among people with T2D
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Background
People with chronic metabolic conditions such as type 2 diabetes (T2D) encounter challenges with self-management regimens to improve their glycemc control, weight and as well as to reduce complications associated with diabetes. Optimal management of T2D requires regular monitoring by physician, access to multidisciplinary care and achieving target HbA1c without hypoglycemia. Digital therapeutics (DTx) provide highly accessible, cost-effective, evidence-based solutions for better management of T2D using high-quality software. This study explores the real-world effectiveness of the Diabefly® DTx program in improving glycemc control among people with T2D.

Methodology
The 90 days Diabefly® program offers mobile application enabled real-time digital logging of daily meals, physical activity, and provides access to remote lifestyle coaching from health coaches and experts (psychologist, physiotherapist, and nutritionist). The aim of the study was to evaluate the changes in HbA1c, weight, body mass index (BMI) and waist circumference at the beginning and at the end of the program. All the outcomes were evaluated using paired t-test with P < 0.05 considered as significant.

Results
De-identified data of 205 participants (Mean age: 47.14 ± 12.67 years; Gender: 55.60% female) was analyzed. After the completion of the Diabefly® program, a significant mean reduction in HbA1c by 1.55 ± 1.88% (P < 0.001) from the baseline of 8.59 ± 2.01% was observed. HbA1c levels were reduced in 87.80% (180/205) participants while reduction of > 1% in HbA1c levels was observed in 56.11% (109/180) participants. A significant mean reduction in body weight and BMI was by 2.39 ± 3.25 kg and 0.82 ± 1.14 kg/m² from the baseline of 75.33 ± 15.43 kg and 27.41 ± 4.68 kg/m² was observed respectively (P < 0.001 for both). Reduction in body weight was observed in 68.29% (140/205) participants and a reduction of > 5 kg body weight was observed among 20.71% (29/140) participants. Furthermore, complete data on waist circumference was available for 109 participants which showed a significant mean reduction by 3.49 ± 8.24 cm from the baseline of 98.80 ± 14.08 cm (P < 0.001).

Conclusion
At the end of the program, a significant improvement in glycemc control and reduction in weight and BMI was observed. Thus, the study showed that usage of the Diabefly® program along with standard medical care by a physician can be effective in better management of T2D by providing multidisciplinary care and continuous support to people with diabetes.

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P316
Simultaneous pancreas-kidney transplantation: long-term survival and metabolic profile analysis among functioning pancreatic graft patients – A 20 year experience from a center in Portugal
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Introduction
Simultaneous pancreas-kidney transplantation (SPKT) is the treatment of choice for type 1 diabetic patients with advanced kidney chronic disease (CKD), restoring normoglycemia, insulin independence and improving survival. The
present study aims to analyse survival of patients undergoing SPKT and the post-SPKT metabolic profile of patients with a functioning pancreatic graft.

Methods

Retrospective observational study. T1DM patients with CKD stages 4-5 KDIGO undergoing SPKT at Centro Hospitalar Universitário do Porto from May 2000 to November 2020 were included. Pre-SPKT baseline data collection. Survival analyses were performed using Kaplan-Meier method. Metabolic profile of patients with a functioning pancreatic graft was secondarily investigated in the latest post-SPKT medical visit.

Results

242 patients were included with a mean age at SPKT of 35.4 ± 6.1 years, mean duration of DM and dialysis of 24.1 ± 5.9 years and 25.8 ± 19.5 months, respectively. Patients had mean values of HbA1c total daily insulin dose (TDID) and BMI of 8.5 ± 1.6 %, 38.8 ± 12.5 U/day and 22.4 ± 2.8 kg/m2 pre-SPKT. Cumulative patient survival was 96.3%, 94.4%, 90.1%, 83.4%, and 80.6% at 1, 5, 10, 15, and 20 years post-SPKT. Pancreatic graft survival of 85.5%, 79.4%, 74.5%, 65.0% and 61.8% at 1, 5, 10, 15 and 20 years. Renal graft survival of 93.8%, 88.6%, 80.1% and 73.5% at 1, 5, 10 and 20 years. The main causes of failure were graft rejection and thrombosis. The metabolic profile of the individuals analysed at the most recent post-SPKT consultation included 178 patients with functioning pancreatic graft, with a mean follow-up of 9.3 ± 5.2 years post-SPKT, and of these, 94.4% with functioning renal graft. Mean BMI, creatinine clearance, C-peptide, HbA1c, LDL-cholesterol and non-HDL-cholesterol were 23.7 kg/m2, 63.8 ± 211.2 ml/min/1.73 m2, 3.1 ± 2.0 mg/dl, 5.6 ± 1.7%, 79.0 ± 35.3 mg/dl and 111.3 ± 40.0 mg/dl Intermediate hyperglycaemia was present in 29.8% of patients and 5.1% had HbA1c ≥ 6.5%. Conclusion

Results of our center reinforce SPKT as a valid option in the treatment of T1DM, aiming to improve quality of life, with sustained maintenance of euglycemia, without the need for exogenous insulin, in the medium/long term within a selected group of patients with advanced diabetic kidney disease.

Keywords

Type 1 diabetes mellitus, simultaneous pancreas and kidney transplantation, transplant, transplantation, chronic complications of diabetes, metabolic profile.

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P317

Changing trends in the aetiology of diabetes-related ketoacidosis(DKA)- a blueprint to identify preventable causes

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Introduction

Diabetes-related Ketoadiiosis (DKA) is a commonly-encountered acute endocrine emergency requiring prompt recognition and treatment. DKA is triggered by risk factors that are often preventable. There are limited studies evaluating the precipitating causes of DKA and depicting their trends over the years. The latter is important in the prevention of DKA by ensuring appropriate education and interventions.

Aim

To study the trends of aetiologies that precipitate DKA over the years.

Methods

We conducted a retrospective analysis of all DKA related admissions across six regional hospitals in the United Kingdom between April 2014 to November 2021. DKA was classified as serum glucose ≥11 mmol/l, ketones ≥ 3 mmol/l and pH ≤7.3 or bicarbonate ≤ 15 mmol/l. Precipitating factors were classified as Alcohol-related, COVID-19, Drug-induced, Intercurrent illness, New diagnosis of type-1 diabetes, SGLT-2 inhibitor-associated, Sepsis, Suboptimal compliance to treatment and Trauma respectively. Statistical analysis was done using SPSS version 27. Results are expressed in percentage and proportion.

Results

A total of 1463 DKA episodes were included in the analysis. Intercurrent illness (34.8%, n = 509) and Suboptimal compliance to treatment (28.2%, n = 413) were the most common factors identified. Other notable causes of DKA were: New diagnosis of type 1 diabetes (8.9%, n=130), Sepsis (4.2%, n=62), Alcohol-related (3.9%, n=57). The proportion of these aetiologies has remained consistent over the years. Newer varieties of precipitating causes such as SGLT2 inhibitor-associated (1.3%, n=19) and other Drug-induced (1.1%, n=16) had an increasing trend since 2019. COVID-19 accounted for 5% of the total episodes (n=41). Precipitating aetiology was unclear in 8% (n=187) of the DKA admissions. However, the proportion of unclear causes as precipitating aetiology for DKA has been steadily down trending since 2016 (24.0% in 2016, 19.2% in 2017, 14.5% in 2018, 16.2% in 2019, 12.6% in 2020 and 8.0% in 2021)

Conclusion

Infections and Suboptimal compliance to treatment accounted for a majority of 63% of the DKA cases, suggesting more work needs to be done to minimize these preventable causes. A rise in medication-induced DKA prompts the need to educate patients and clinicians to be aware of the role of these contributory medications. Down trend seen in Unclear Causes of DKA is a welcome result as this can help us prevent recurrences in patients by educating them regarding the known or established precipitating factors so that they could be vigilant in regards to these in future.

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P318

Effect of treatment of gestational diabetes mellitus with insulin on pregnancy outcomes

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Introduction

Gestational diabetes mellitus (GDM) complicates approximately 3% to 9% of pregnancies. Diagnosis and treatment of GDM remain essential to limit maternal and fetal outcomes. The aim of the study was to evaluate the difference in pregnancy outcomes between insulin- and diet-treated Tunisian women with gestational diabetes.

Methods

It was a prospective longitudinal study including 220 patients followed for GDM at the research unit of the C department of the national institute of nutrition in Tunis. The patients were followed during pregnancy and until post partum. Patients were divided into two groups: group 1 (G1): Insulin treated and insulin therapy and group 2 (G2): Patients treated by diet alone.

Results

At the end of our study, 68 patients were treated with insulin, 11 patients developed gestational hypertension or pre-eclampsia. Two thirds of the patients (68%) delivered by cesarean section. Neonatal outcomes were dominated by macrosomia (13.5%) and transient respiratory distress (11.4%), insulin-treated patients had a higher incidence of gestational hypertension (G1: 11.9% vs G2: 2.1%; P=0.03), insulin treatment did not reduces the rate of caesarean section (G1: 64.7% vs G2: 63.2%; P=0.785). Insulin therapy did not reduce fetal outcomes, including intrauterine growth retardation (G1: 0% vs G2: 1.3%; P=0.326), fetal death in utero (G1: 0% vs G2: 1.3%; P=0.306), neonatal hypoglycemia (G1: 0% vs G2: 1.3%; P=0.333), macrosomia (G1: 17.6% vs G2: 11.2%; P=0.203), hydranromosis (G1: 13.2% vs G2: 6.6%; P=0.111), transient respiratory distress (G1: 11.8% vs G2: 10.5%; P=0.781), neonatal jaundice (G1: 5.9% vs G2: 3.3%; P=0.787) and prematurity (G1: 7.4% vs G2: 4.6%; P=0.452).

Conclusion

Our study showed that patients treated with insulin had a higher incidence of pregnancy outcomes. However, treatment of gestational diabetes with insulin did not reduces the rate of caesarean section and neonatal morbidity.

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P319

Feeding and DKA resolution

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Background

Diabetic ketoacidosis (DKA) is a complication of Diabetes Mellitus and is a life-threatening medical emergency usually requiring admission to an intensive care unit. There is no established guideline regarding timing of initiation of oral/enteral feeding in DKA patients. Purpose

To determine if there is a difference in clinical outcomes for DKA patients whose feeding was started early vs patients whose feeding was started beyond 24 hours. Methods

A 10-year retrospective observational cohort was conducted in a single medical center. Subjects consisted of DKA patients admitted in the Intensive Care Unit.
Clinical outcomes were compared among DKA patients who were fed within 24 hours of admission (early feeding) vs those fed beyond 24 hours (late feeding). Primary outcome was DKA resolution. Secondary outcomes were Anion gap closure, Length of hospital stay, Length of ICU stay, and inpatient Mortality.

Results
A total of 68 patients were included in the study – 39 in the early feeding group and 29 in the late feeding group. Baseline characteristics, classification of Diabetes, DKA severity, and complications were comparable among the two groups. The odds of early DKA resolution or DKA within 24H was 4.8x higher in early feeding group compared to the late feeding group (95% CI: 1.2 – 19.6). Time to DKA resolution, time to anion gap closure, and length of hospital stay were also significantly shorter for the early feeding group. There was no significant difference in the ICU length of stay and inpatient mortality between the two groups. The power of the study is 87.34%.

Conclusion
DKA patients benefit from early feeding because it significantly shortens time to DKA resolution and anion gap closure, also length of hospital stay, without significant increase in the rate of DKA complications. Early feeding is also associated with DKA resolution within 24 hours.

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P320

Differences in diabetic neuropathy in type 1 and type 2 diabetes mellitus
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Background
Diabetic neuropathy (DN) is the most common diabetes complication in type 1 (T1DM) and type 2 (T2DM) diabetes mellitus. Due to diagnostic issues, it is the least studied complication with limited and controversial data about the differences of various types of DN between T1DM and T2DM patients.

Aim
To evaluate the differences of diabetic polyneuropathy (DPN) and cardiac autonomic neuropathy (CAN) between T1DM and T2DM patients.

Materials and Methods
Three methods were used to evaluate DPN: clinical examination was done using neuropathy symptom score (NSS) and neuropathy disability score (NDS); neuroemetry (NM) – using Neurometer NervScan™ LLC device; electromyography (ENG) – using Nihon Kohden Neuropack M-1 Electromyogram Machine. CAN was assessed by performing cardiovascular autonomic reflex tests (CARTS) using Cardiosys Extra MDE diagnostic device.

Results
There were 53 T1DM and 63 T2DM patients enrolled in to the study. T1DM patients were significantly younger (P<0.05 for all) (41.6 ± 15.9 vs 60.0 ± 11.7 years), had lower BMI (23.5 ± 3.5 vs 36.0 ± 6.3 kg/m²), systolic and diastolic blood pressure (124.5 ± 16.3 vs 138.7 ± 13.7 and 74.2 ± 9 vs 80.5 ± 8.3 mmHg respectively), incidence of arterial hypertension (35.8% vs 90.5%), heart failure (3.8% vs 20.6%) and coronary artery disease (5.7% vs 20.6%). T2DM patients had significantly higher scores of symptomatic neuropathy compared to T1DM (NSS 4.3 ± 3.3 vs 3.1 ± 3.4, P<0.049), but the severity of pain, evaluated by self reported numerical rating scale did not differ (1.8 ± 2.5 vs 1.4 ± 2.5, P=0.17). The prevalence of DPN did not differ between the groups, however the proportion of DPN depended on method used, being the highest diagnosed with NSS (67.3% vs 61.3%, P>0.05), followed by ENG (40.9% vs 44.1%, P>0.05) and clinical examination (30.2% vs 35.5, P>0.05). Tuning fork vibration perception was the only test of clinical evaluation that showed significantly worse vibration perception in T2DM patients compared with T1DM (impaired in 78.3% vs 57.1%, P=0.023). CARTS showed significantly higher incidence of CAN in T2DM compared to T1DM patients (67.3% vs 32.7%, P=0.011).

Conclusions
There was no difference in the prevalence of DPN between T1DM and T2DM, however significant difference in diagnostically accuracy of different methods was observed. T2DM patients were more likely to have symptomatic polyneuropathy, large fiber damage and CAN.

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P321

Effect of a novel-app based strategy for carbohydrate counting on glucose control in type 1 diabetes
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Background
Carbohydrate counting is often performed inaccurately by patients with type 1 diabetes (T1D). We hypothesized that mobile App ‘Dietrometro’, that estimates CHO content of food figures, would ameliorate glucose control.

Aim
To study the effect of ‘Dietrometro’ on glucose control.

Methods
54 T1D subjects (aged 18-60 years, 26 males), on multiple daily injections (n=23) or continuous subcutaneous insulin infusion (n=31), were randomly assigned to three groups: no counting (group 1; n=19), ‘self-managed’ counting (group 2; n=19) and App-assisted counting (group 3; n=16). Outcomes were one- and three months follow-up TIR (time in range), TAR (time above the range) and TBR (time below the range), estimated by flash or continuous glucose monitoring, and HbA1c.

Results
At the baseline TIR were similar between groups, while HbA1c was lower in group 3 compared to group 1 (6.9 ± 1.06 vs 7.8 ± 0.85%, P<0.05). At one-month follow-up, TIR was higher in group 2 and 3 compared to group 1 (63.58 ± 11.55 vs. 52.32 ± 13.22%, P<0.014, and 71.25 ± 9.75 vs. 52.32 ± 13.22%, respectively; P<0.001). TAR at one-month follow-up was significantly lower in group 3 (31.25 ± 19.18 vs. 22.31 ± 10.89%, P<0.001), while no differences were observed in TBR. At three-months follow-up, groups 2 and 3 had a lower HbA1c than group 1 (7.16 ± 0.64 vs. 6.56 ± 1.91 vs. 7.96 ± 1.0%; P<0.05).

Conclusions
App-assisted CHO counting might improve glucose control. Larger sample size and longer follow-up are needed to define the long-term effect of this system.

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P322

Higher levels of psychological stress are associated with lower levels of the insulin sensitizer FGF-21 in patients with obesity
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Background
Altered signaling of hormones regulating appetite and metabolism is often observed in individuals with obesity (BMI ≥ 30 kg/m²) and related diseases, potentially resulting in increased hunger signaling and metabolic dysfunctions. Previous research indicates that such disturbances may be induced by weight gain itself, but also by other factors such as glucocorticoid excess (e.g. due to stress). However, knowledge regarding the associations between hormonal appetite signals and biological or psychological measures of stress is still limited, particularly in patients with obesity.

Methods
Data were collected from 68 patients with obesity (47 women). We assessed psychological stress perceived over the last month (via the Perceived Stress Scale (PSS)-14, ranging from 0 to 56) and biological stress (using the average of 24h overnight-fasted serum levels of the hormonal appetite regulators leptin, adiponectin, FGF-21, PP, GIP, PYY, CCK and AgRP (pg/ml). To investigate cross-sectional associations between psychological/biological stress and hormonal appetite regulators, we used linear regression analysis with PSS-14 scores or urine cortisol levels as independent variables.

Results
Higher levels of psychological stress were significantly associated with lower levels of FGF-21 (β = -0.24, 95% CI: -0.46 to -0.03, P=0.03) and AgRP (β = -0.22, 95% CI: -0.41 to -0.03, P=0.03). No significant associations were found with PP, GIP, PYY, CCK, leptin and adiponectin. No significant associations were found with biological stress (using average of 24h overnight-fasted serum levels of cortisol).
Results
There was a negative association between PSS-14 scores and log10-transformed FGF-21 levels ($\beta = -0.015$ ($p < .002$; $95\%$ CI, $P < .05$). We did not see any other associations of hormonal appetite regulators with PSS-14 scores, nor with 24h urine cortisol levels.

Conclusion
A 1-point increase on the PSS-14 score was associated with a 3.4% decrease in serum levels of the insulin sensitizer FGF-21. In patients with obesity, FGF-21 levels are often increased compared to normal weight controls, probably to compensate for metabolic challenges associated with the disease. We hypothesize that chronic stress may interfere with FGF-21 actions in these patients by decreasing FGF-21 levels, resulting in a failure to compensate for metabolic challenges. Future studies should further investigate the directionality of this association and its potential implications for eating behaviour and the development of metabolic disorders such as type 2 diabetes.

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P323
Sleep quality in patients with type 1 diabetes: a large cross-sectional study
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Background
Altered sleep quality and duration have been reported in 26-67% of patients with type 1 diabetes (T1D), however, in differences in study designs, populations, and methods of sleep quality assessment have led to heterogeneous results in terms of association with clinical data and blood glucose parameters.

Aims
To investigate the sleep quality of a large cohort of adult patients with autoimmune diabetes under insulin treatment, and to analyze the relationship with clinical and biochemical data.

Methods
We administered the Pittsburgh Sleep Quality Index (PSQI) questionnaire to 553 adult subjects (≥18 years) with T1D or latent autoimmune diabetes of the adult (LADA). We excluded 44 patients without clinical data. Patients were also administrated additional questionnaires: Diabetes Distress Scale (DSD), Diabetes-Related Quality Of Life (DRQOL), Diabetes Treatment Satisfaction Questionnaire (DTSQ), and Hypoglycemia Attitudes and Behavior Scale (HABS). We retrieved biochemical and clinical data at the time of the PSQI administration (+/- 4 months). Glucose metrics up to 3 months before PSQI administration were analyzed in 183/329 patients under continuous glucose monitoring (CGM).

Results
PSQI questionnaires had complete data in 465 patients. Altered sleep quality (PSQI score ≥5) was detected in 150/465 subjects (32.3%). Short sleep duration (<7 hours) was detected in 181/465 patients (38.9%). PSQI score was higher in females vs males (5.3±4.3 vs 4.7±2.9; P=0.031), with higher values of sleep latency (P=0.010), sleep disturbances (P=0.001), and daytime dysfunction (P<0.001). No difference in PSQI score were detected between patients under multiple daily injections (n=390) and insulin pump (n=75;P=0.412), and among subjects under self-monitoring of blood glucose (n=159), intermittently-scanned CGM (n=221) and real-time CGM (n=85;P=0.403), even when analyzed separately by sex. When compared to those with normal values, patients with altered sleep quality had higher glycated hemoglobin (56.4±12.1 vs 60.4±11.5;P=0.001), higher distress (DSD scores 1.9±0.9 vs 2.4±1.1; P<0.001), lower treatment satisfaction (DTSQ scores 29.3±5.4 vs 27.1±5.7; P<0.001) and lower quality of life (DRQOL scores 1.7±0.3 vs 2.0±0.4; P<0.001), whereas duration of diabetes was not different (P=0.751). No correlation was found between glucose metrics derived from CGM and parameters of sleep quality.

Conclusions
Altered sleep quality was detected in one third of the patients with autoimmune diabetes and was associated with higher glycated hemoglobin levels, rather than altered parameters of glycemic variability, irrespective of the specific treatment for diabetes. Higher distress and lower quality of life were detected in patients with altered sleep quality.

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P324
Characterization of the somatostatin and ghrelin hormonal systems revealed their potential therapeutic role in chronic liver disease
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Hormonal signalling plays a key role in the progression of metabolic (dysfunction)-associated fatty liver disease (MAFLD) to hepatocellular carcinoma (HCC). However, the role of somatostatin (SST), cortistatin (CORT), neurostatin (NST) and ghrelin systems in MAFLD progression has not yet been elucidated. We characterized the role of SST/CORT/NST and ghrelin systems in chronic liver diseases and evaluated their clinical potential. The expression of the components of the SST/CORT/NST/ghrelin systems (ligands, receptors and accessory proteins) was analysed in different mouse models of MAFLD (non-alcoholic steatohepatitis (NASH))/cirrhosis, in two retrospective human cohorts (cohorts 1: HCC vs. adjacent (n=93); cohort 2: HCC vs. adjacent (n=58), cirrhosis (n=39), and healthy livers (n=51), in different silico MAFLD and HCC human cohorts (mRNA/protein), and in three liver-derived cell lines (HepG2, Hep3B and SNU-387). Proliferation after treatment with natural (SST/CORT/NST) and synthetic (Lanreotide, Octreotide, Pasireotide) peptides was evaluated in cell lines and human liver primary cultures. Our results revealed that MAFLD mouse models showed a damage-dependent differential expression pattern of SST/CORT/NST components. Indeed, early MAFLD stages were characterized by a decreased expression of CORT, Sstr1, Sstr2, Sstr3 and the truncated Sstr5 md3 receptor, while there was a marked increase in the expression of Sstr5, Son4, Sstr5 and Son5 null in advanced stages. Some of these observations were validated in a human in silico cohort of MAFLD (i.e. SSTR5 overexpression and CORT downregulation), confirming CORT dysregulation as an early event in MAFLD. In tumoral stages, retrospective cohorts revealed a decreased expression of CORT, SSTR1, SSTR2 and ghrelin receptor and the overexpression of SSTR5 and the NST receptor (GPR107) in tumoral tissues. These alterations were validated in silico cohorts of HCC. Besides, the decreased expression of CORT was associated with the dedifferentiation of the tissue while GPR107 overexpression was associated with key aggressiveness parameters (survival, recurrence, tumoral diameter, etc.) in the retrospective and in silico cohorts. In vitro assays revealed a decreased proliferation after treatment with SST, CORT, NST and the synthetic analogues, which was dependent on the expression of the receptors. Specifically, NST reduced proliferation of the most aggressive cell lines, Hep3B and SNU-387. Altogether, this study demonstrates an profound alteration in the expression levels of the SST/CORT/NST and ghrelin systems in human, animal, and cellular models of chronic liver disease, and suggests a potential prognostic and therapeutic role of certain components of these hormonal systems in chronic liver disease.

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P325
Association between the coefficient of glycemic variation and time in range, below and above range in continuous monitoring glucose systems in type 1 diabetes
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Introduction
Glycemic variability (GV) is a major consideration when evaluating quality of glycemic control. Coefficient of glycemic variation (%CV) is the metric of choice to define GV. International consensus on continuous glucose monitoring (CGM) recommends a %CV < 36. Additional studies suggest that low %CV minimize hypoglycemia events <54 mg/dL.

Aims
The aim of this analysis is to examine the expected relationship between the coefficient of glycemic variation and time in range (%TIR), time below range (%TBR) and time above range (%TAR) in continuous glucose monitoring systems.
Methods
We analysed a subset of 71 patients with type 1 diabetes followed at our endocrinology outpatient clinic using a continuous glucose monitor system that uploads data to a database accessible for clinicians. 16 out of 71 patients were excluded, 11 patients because they had less than 70% of data captured by the sensor in the previous 2 weeks and 5 patients because they had a diagnosis within the previous year. A bivariate analysis was performed to evaluate the relation between %CV and TIR, %TBR and %TAR in 55 patients. Time in range is defined as between 70 and 180 mg/dl. Furthermore, a bivariate analysis was performed to evaluate the relation between %CV and the subgroup time below 54 mg/dl (%TBR 54).

Results
Patients were between 22 and 66 years old (mean 43, SD 12) and 42% were male. The %CV showed a strong positive correlation and statistically significant with %TBR ($r=0.708$, $P<0.0001$) and a weak negative correlation, but statistically significant with TIR ($r=-0.398$, $P=0.003$). There was no correlation between %CV and %TAR. Both correlations are independent of age and sex. Moreover, the %CV showed a strong positive correlation and statistically significant with %TBR 54 ($r=0.664$, $P<0.0001$).

Conclusions
The coefficient of glycemic variation is an important metric to evaluate the risk of hypoglycemia, in our analysis it is closely correlated with time below 70 mg/dl and also with time below 54 mg/dl. These results are consistent with results from other studies. Although weak it is important to note the negative correlation between coefficient of glycemic variation and time in range, as the latest is an indicator for evaluating the efficacy of glycemic control and predicting diabetic complications. Our analysis highlights the importance of %CV in the management of type 1 diabetic patients.

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P326
Personalized glycemic response based Diabefly-Pro® digital therapeutics improves dietary patterns, glycemic control and reduces postprandial hyperglycemia in real-world settings
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Background
CGM based monitoring can help in development of personalized digital therapeutics programs based on the understanding of the effect of diet, physical activity and medications on everyday blood glucose excursions. The variation in intra-individual glycemic response to the same food has been reported in many studies. Thus, understanding of personalized glycemic response (PGR) of each individual becomes important for effective diabetes management.

Methods
De-identified data of 108 participants (Average Age: 40.86 ± 12.08 years, 36.11% females) with T2D in Diabefly-Pro® program was analyzed. The program provided 90 days PGR based lifestyle management support via digital meal logging through mobile application and remote health coaching. CGM data was collected in week 1 and week 2 with a modified lifestyle plan being introduced from week 2 of the program. All the parameters were analyzed for week 1 (baseline) and week 2 of the program. Net area under the curve (AUC) for 0-24h was calculated using trapezoidal rule. The incremental area under the curve (iAUC) was calculated at 1h-post breakfast. Paired t-test and spearman correlation method was used for statistical analysis with $P<0.05$ considered as significant.

Results
A significant reduction in AUC by 44.71 ± 17.40 % was observed from an average week 1 AUC of 738.29 ± 526.79 mg/dl*h ($P<0.0001$). AUC post breakfast showed a significant reduction by 42.33 ± 22.90 % from a baseline average of 340.52 ± 202.19 mg/dl*h ($P<0.0001$). The comparison of dietary recall in week 1 and week 2 showed that participants showed reduction in intake of calories (70.29 kcal; $P=0.04$) and carbohydrate (12.66 g; $P=0.002$). The percentage reduction in AUC showed a significant correlation with the reduction in the amount of carbohydrate intake ($r=0.24$, $P=0.01$). Time-in-range (TIR) improved significantly from a baseline of 67.35 ± 25.56 % to 70.05 ± 25.55 % ($P=0.03$) in week 2. Time-above-range (TAR) reduced significantly from a baseline of 27.13 ± 27.64 % to 22.13 ± 27.25 % ($P<0.0001$). Reduction in TAR showed significant correlation with percent reduction in AUC ($r=0.32$, $P<0.001$).

Conclusion
Diabefly-Pro® program led to significant reduction in postprandial hyperglycemia while improving TIR and dietary behavior in people with diabetes after 7 days of modified lifestyle plan. PGR-based coaching can play an important role in achieving better glycemic control in the long-term.

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P327
Retrospective observational study of Italian patients with diabetes mellitus in Covid-19 era: a big data approach
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Introduction
The prevalence of diabetes mellitus (DM) in patients with coronavirus disease (COVID-19) varies widely, depending on population characteristics, country, age and disease severity. Moreover, pre-existing DM seems to double the risk of both critical COVID-19 and mortality.

Aim
To evaluate incidence and mortality risk of COVID-19 in a large diabetic population in Northern Italy.

Methods
A retrospective, observational, big data cohort study was carried out, including subjects with type 1 and type 2 DM living in the Province of Modena, submitted to at least one swab for SARS-CoV-2 between March 2020 and March 2021. Data were extracted from the Hospital data warehouse.

Results
9553 diabetic patients were enrolled (age 68.8±14.1 years). COVID-19 was detected in 2302 patients (24.1%) with death in 8.9% of cases. No differences in COVID-19 prevalence were detected considering sex. Mean age (67.6±13.7 yr vs 69.8±14.1 years) was significantly lower in infected than uninfected patients and COVID-19 was more frequent in youngest people, according to quartile of age ($P<0.001$) and retirement age of 65 years ($P<0.001$). Moreover, DM duration was lower in infected than uninfected patients (11.2±6.6 vs 11.8±6.7 years, $P<0.001$), but higher HbA1c was found in infected compared to uninfected patients (58.7±16.7 vs 56.7±15.9 mmol/mol, $P<0.001$). Accordingly, COVID-19 was less frequent in patients treated with anti-diabetic drugs compared to those not treated ($P<0.0001$). Logistic analysis confirms these results and identifies 3 risk factors for COVID-19: age (odds ratio-OR 1.013, 95% confidence interval-Cl:1.008-1.017), DM duration (OR 1.007, 95%Cl:1.001-1.013), and HbA1c (OR 1.009, 95%Cl:1.002-1.016). As regards COVID-19 mortality, logistic analysis demonstrated that death was predicted by DM duration (OR 1.010, 95%Cl: 1.005-1.015) and HbA1c (OR 1.005, 95%Cl:1.002-1.009). Three ROC analyses were generated setting death as test variable, showing that the worse prognosis could be predicted by DM duration longer than 10.9 years (AUC=0.639, 95%Cl:0.601-0.676) and age older than 74.4 years (AUC=0.797, 95%Cl:0.767-0.827).

Conclusion
Our big data analysis confirms the correlation between COVID-19 mortality and DM. In particular, although COVID-19 was more frequently detected in youngest patients, a poor glycemic control worsens outcomes, confirming the importance of strict glyco-metabolic control, especially in older diabetic people with long DM duration. Thus, diabetic patients should undergo careful monitoring of blood glucose
glucose. In particular, patients with DM and COVID-19 should be followed carefully when older than 74 years and with long DM duration.

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**P328**

DKA registry: A step towards harmonising management of diabetes-related ketoacidosis in the United Kingdom-initial findings

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Background

Diabetes-related ketoacidosis (DKA) is a common and potentially life threatening complication in people with diabetes. Despite national and international guidelines, interhospital guideline variation and mismanagement during admission are important contributory factors to increased DKA duration and length of stay.

Aim

To establish a common DKA registry to identify gaps in management, assess outcomes and share best practises across centres.

Methods

Retrospective analysis of all DKA admissions between 1st January 2021 to 1st December 2021 across six hospitals in the United Kingdom was undertaken. People aged < 18 years, admission pH > 7.3 or self-discharged before treatment completion were excluded. Information on fluid and insulin prescriptions, glucose and ketone monitoring, DKA duration and length of hospitalisation was collected. Comparison between hospitals was performed using the Independent-Samples Kruskal-Wallis Test. Data was analysed using SPSS version 27.0 and presented in median interquartiles, frequencies and proportion as appropriate.

Results

Since the objective is to identify best practice and not to compare, hospital names are coded A to F to ensure anonymity. A total of 465 DKA episodes across the six hospitals were included. There were differences observed in the DKA duration (median in hours; A- 13.1, B-11, C-9.7, D-15.7, E-19.5, F-15.2; are coded A to F to ensure anonymity. A total of 465 DKA episodes across the six hospitals were included. There were differences observed in the DKA duration (median in hours; A - 13.1, B - 11, C - 9.7, D - 15.7, E - 19.5, F - 15.2; P value < 0.001) and length of hospitalisation (median in days; A - 4.6, B - 5.4, C - 2, D - 3.9, E - 4.5, F - 3.5; P value < 0.001) across hospitals. Similarly, variations were noticed in the appropriateness of fixed rate intravenous insulin infusion (A - 100%, B - 100%, C - 100%, D - 100%, E - 100%, F - 133.3%; P value < 0.001), appropriateness of ketone monitoring (A - 61.3%, B - 83.6%, C - 91.5%, D - 67.3%, E - 62.6%, F - 69.6%; P value < 0.001) and fluid prescription (A - 83.6%, B - 80.0%, C - 102.8%, D - 100%, E - 100%, F - 19.0% [IQR: 13.0–14], P value: 0.023) across hospitals. No significant differences were noted in the appropriateness of fixed rate intravenous insulin infusion (A - 100%, B - 100%, C - 100%, D - 98.8%, E - 98%, F - 100%; P value: 0.156).

Conclusion

With the exception of fixed rate intravenous insulin infusion, significant interhospital variation in other individual parameters were observed. A centralised DKA registry can abet identifying gaps in DKA management and dissemination of best practises across centres to aid improved patient outcomes.

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**P329**

The relationship between clinically significant neonatal hypoglycemia and cord blood c-peptide levels in neonates of mothers with type 1 diabetes

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Introduction

Neonate of patients with type 1 diabetes (T1D) are at increased risk for neonatal hypoglycemia. It is hypothesized that this is a result of maternal hyperglycemia and subsequent fetal hyperinsulinemia.

Aim

The aim of this study was to determine the relationship between clinically significant neonatal hypoglycemia (CS-hypo) and cord-blood c-peptide (CBCP) concentrations in patients with T1D.

Materials and methods

This was a prospective cohort study including patients with T1D followed at a single tertiary center. Clinical variables and glucose control data during pregnancy were prospectively recorded. Cord-blood of neonates was collected, and CBCP concentration was determined. The correlation between CS-hypo (neonatal hypoglycemia requiring IV glucose treatment) and CBCP concentrations was determined.

Results

This analysis pertains to 54 pregnancies. Mothers to neonates that experienced CS-hypo had longer diabetes duration (19 vs. 13 years, P = 0.023), higher HbA1c at conception (7.3 [6.3–8.8] vs. 6.5 [6.0–7.0], P = 0.042) and higher rates of caesarian section (73.3% vs. 28.2%, P = 0.005) than mothers to neonates who did not. No differences were observed between the groups in BMI, age, and other maternal complications, nor in glucose control indices (Table 1). CBCP levels were significantly higher in neonates with CS-hypo than in those who did not (3.3 mg/dl vs 1.9 mg/dl, P = 0.002). After adjustment for age at conception, BMI, diabetes duration, neonatal birth weight and 3rd trimester HbA1c, every 1 unit higher in CBCP level was associated with a 1.46 (1.02–2.09, P = 0.035) fold greater risk CS-hypo.

Conclusion

In neonates of patients with T1D, higher CBCP levels are associated with a higher risk CS-hypo.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Neonatal – CS-hypo</th>
<th>No neonatal CS-hypo</th>
<th>P for comparison</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td>30.0 [26.0–34.0]</td>
<td>29.0 [25.7–35.2]</td>
<td>0.905</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>23.1 [21.2–30.1]</td>
<td>25.4 [23.1–27.8]</td>
<td>0.333</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of T1D</td>
<td>19.0 [13.0–23.0]</td>
<td>14 [9.5–18.0]</td>
<td>0.023*</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C at conception</td>
<td>7.3 [6.3–8.6]</td>
<td>6.5 [6.0–7.0]</td>
<td>0.042*</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C at 1st trimester</td>
<td>6.7 [5.5–7.3]</td>
<td>5.9 [5.5–6.4]</td>
<td>0.136</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C at 2nd trimester</td>
<td>5.8 [5.2–6.1]</td>
<td>5.5 [5.2–6.0]</td>
<td>0.347</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C at 3rd trimester</td>
<td>5.7 [5.3–6.0]</td>
<td>5.7 [5.3–6.1]</td>
<td>0.969</td>
<td></td>
</tr>
<tr>
<td>[Median, [IQR]]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean average blood-glucose [Median, [IQR]]</td>
<td>126 [119.7–156.7]</td>
<td>127 [111.5–138.3]</td>
<td>0.591</td>
<td></td>
</tr>
</tbody>
</table>

Endocrine Abstracts (2022) Vol 81
Background The incidence of gestational diabetes mellitus (GDM) is increasing worldwide, with considerable impact on the health of both mother and newborn. There is no doubt that screening for GDM between 24 and 28 gestational weeks (GWks) is important to reduce the risk of adverse outcomes; however, there is no clear consensus about the diagnosis and treatment of GDM in early pregnancy.

Aims To evaluate the effect of time of GDM diagnosis (early onset (EO, 16–18 GWks) vs late onset (LO, 24–28 GWks)) on fetal outcomes.

Materials and methods We retrospectively evaluated 1369 women with GDM followed at our Center. Diagnosis of GDM was performed by an oral glucose tolerance test (OGTT) at 16–18 GWks (n = 321) or at 24–28 GWks (n = 1048). Neonatal outcomes were macrosomia, neonatal intensive care unit (NICU) admission, neonatal hypoglycemia and neonatal cardiac hypertrophy. Self-monitoring of blood glucose (SMBG) data and insulin therapy at last visit were also assessed.

Results No differences between groups were found in the need for insulin therapy (EO 48.5% vs LO 33.4%, P = NS) or in SMBG parameters. Considering all pregnancies, 18.3% were complicated with macrosomia; 10.7% of newborns had neonatal hypoglycemia and 20.5% had cardiac hypertrophy, while no NICU admission was observed in either group. In both groups, neonatal hypoglycemia correlated with poor glucose control at the last visit (less than 50% of SMBG measurements in target). In the EO group, we found a higher risk to develop macrosomia (P = 0.003) or cardiac hypertrophy (P = 0.001) compared to EO group. Interestingly, we observed that 23% of women in EO group presented the risk factors suggesting to perform an early OGTT, that was lost for different reasons. In this subgroup, 63% of women had at least one neonatal adverse outcome.

Conclusions High risk women should be screened as early as possible and an early treatment may have a significant effect to improve fetal outcomes.

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P331

Increasing overrepresentation of diabetes in non-traumatic lower limb amputations

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Background and Aim Recent international studies indicate a secular decrease in the proportion of patients with diabetes who undergo lower limb amputations (LLA), and the same trend is observed in the national quality indicator. The validity of electronic databases and quality indicators are limited by multiple discharges and precision of coding. Furthermore, amputation codes included in the quality indicator do not include all amputations. We therefore aim to investigate the recent incidence of LLA in the catchment area of a middle-sized Norwegian hospital, and to compare it with data collected during 1990–99.

Methods Medical records for all patients identified with LLA by the electronic discharge registers at Innlandet Hospital, Elverum, from 2013 through 2019 were retrieved. All codes for amputations and exarticulations were included, and amputations were verified by manual review by two of the authors. Traumatic and cancer-related amputations were excluded. Both minor and major amputations were included in further analyses. Diabetes was defined by the WHO criteria. The prevalence of diabetes was calculated using data from the Norwegian Prescription Database and Statistics Norway.

Results We identified 169 non-traumatic, non-cancer related amputations in 127 patients, of which 77 had diabetes. The proportion of amputees with diabetes has increased from 44% in the previous period to 61% in the recent data. Ten percent had type 1 diabetes compared to 4% during 1990–99. We estimated that 0.23% of individuals on antidiabetic drugs in the catchment area, underwent an amputation per year in the period 2013–19, compared to 0.31 % in 1990–99. The average absolute number of diabetics undergoing an LLA per year was 11 in both periods. Multiple amputations were common both in persons with and without diabetes and was present in 26% of the amputees, even though a high proportion in both groups underwent vascular surgery before amputation. Detailed information and further results will be provided.

Conclusion Our findings suggest that the proportion of diabetics among patients undergoing non-traumatic, non-cancer related lower limb amputations has increased over the past decades. Multiple amputations are still common, despite comprehensive preoperative investigations and other surgical interventions.

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P332

COVID-19 pneumonia patients with 25(OH)D levels lower than 12 mg/ml are at increased risk of death

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Objectives There is no consensus about specific serum 25(OH)D levels associated with higher risk of severe outcomes in COVID-19 patients. According to the literature patients with serum 25(OH)D levels < 12 mg/ml are clearly deficient at all ages.

Mean average glucose (Sensor, Median, [IQR])

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>[0.0] 3 [7.7]</th>
<th>0.5</th>
<th>3 [5.6%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm delivery</td>
<td></td>
<td>6 [40.0]</td>
<td>6 [15.4]</td>
<td>0.06</td>
</tr>
<tr>
<td>Cesarian section</td>
<td></td>
<td>11 [73.3]</td>
<td>11 [28.2]</td>
<td>0.005*</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td>3 [20.0]</td>
<td>2 [5.1]</td>
<td>0.124</td>
</tr>
<tr>
<td>OGGT</td>
<td></td>
<td>115 [106.7–126.4]</td>
<td>0.785</td>
<td></td>
</tr>
</tbody>
</table>

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Our aim was to assess COVID-19 mortality in the settings of severe 25(OH)D deficiency.

Methods
A cohort study of 357 COVID-19 patients was conducted. Subjects were monitored until discharge or in-hospital death. At admission, severity parameters (CRP, IL-6, Charlson Comorbidity Index etc.) were assessed. These parameters were compared regarding 25(OH)D levels threshold 12 ng/mL, where values below 12 ng/mL were considered absolute vitamin D deficiency.

Results
25(OH)D levels at the time of admission were independently associated with mortality (P < 0.05). Non-survivors (n = 168) had lower 25(OH)D levels, SO2, higher age, CRP, viral load, and Charlson Comorbidity Index in comparison to survivors. Patients with serum 25(OH)D levels < 12 ng/mL had higher mortality (55% vs. 45%), viral load (21.5 vs 23.1) and Charlson Comorbidity Index (5.3 vs 4.4) in comparison to those with serum 25(OH)D levels > 12 ng/mL (P < 0.05).

Conclusions
COVID-19 patients with serum 25(OH)D levels < 12 ng/mL have higher mortality. Among other factors, severe vitamin D deficiency likely leads to poor outcome. DOI: 10.1530/endoabs.81.P332

P333
REAL Life study of SEMaglutide in Patients with Type 2 diabetes in SPain (REAL-SEM-SP): Retrospective clinical study on the efficacy, adherence, and safety with Semaglutide
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1Hospital Universitario Fundacion Jimenez Diaz, Endocrinology, Madrid, Spain; 2Hospital Universitario Infantil El Encanto, Spain; 3Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain, 4General Hospital Villalba, Spain

Introduction
Real-world data on glucose and weight control effectiveness in patients with Type 2 diabetes mellitus (T2DM) on treatment with semaglutide is scarce. We aim to assess it in a cohort of patients from a real-world setting in Spain.

Materials and methods
We identified 830 patients with T2DM that were prescribed Semaglutide once-weekly since May 2019 to December 2020, in 4 hospitals in Madrid-Spain. At 6±3 months, 435 GLP1-naïve and 317 GLP1-experienced patients continued on treatment. Semaglutide withdrawal occurred in 78 patients (9.4%), mainly due to gastrointestinal adverse events. At 12±3 months, 317 GLP1-naïve and 265 GLP1-experienced patients continued on treatment. Semaglutide withdrawal occurred in 24 patients (3.3%), mainly due to gastrointestinal adverse events. The changes in HbA1c, weight, fat mass and skeletal-mass at 6 and 12 months of follow up, adjusted by basal HbA1c, age, T2DM duration, BMI sex, and change in Metformin, DPP-4, SGLT-2, Sulfonylurea, Repaglinide, Insuline and Thiazolidinedione status was assessed (multiple linear regression model).

Results
Baseline characteristics and T2DM treatments are shown in Table 1. There was a significant reduction in HbA1c, weight, and fat mass after Semaglutide treatment at 6 and 12 months of follow-up (Table 2). The proportion of patients that achieved a HbA1c ≤ 7% was significant higher in both groups. After adjustment the baseline-HbA1c was the only predictor for HbA1c change at 6 and 12 months.

Conclusion
Treatment with semaglutide once-weekly is an effective glucose and weight lowering treatment in GLP1-naïve and GLP1-experienced patients with T2DM.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>GLP1-naïve</th>
<th>GLP1-experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>55.6</td>
<td>56.8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.6(10.5)</td>
<td>61.3(9.1)</td>
</tr>
<tr>
<td>T2DM duration (years)</td>
<td>9.0(7.5)</td>
<td>11.3(6.8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>99.9(19.3)</td>
<td>98.2(16.2)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>38.4(5.5)</td>
<td>35.6(5.4)</td>
</tr>
<tr>
<td>Baseline-HbA1c</td>
<td>7.8(1.5)</td>
<td>7.3(1.2)</td>
</tr>
<tr>
<td>Baseline-eFGR</td>
<td>85.9(20.8)</td>
<td>82.9(20.1)</td>
</tr>
<tr>
<td>HbA1c &lt; 7%</td>
<td>36.6</td>
<td>43.9</td>
</tr>
<tr>
<td>T2DM treatment (%)</td>
<td>82.8</td>
<td>91.1</td>
</tr>
<tr>
<td>– Metformin</td>
<td>40.7</td>
<td>2.2</td>
</tr>
<tr>
<td>– DPP-4 inhibitor</td>
<td>31.5</td>
<td>48.9</td>
</tr>
<tr>
<td>– Sulfonylurea</td>
<td>9.9</td>
<td>5.7</td>
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<tr>
<td>– Repaglinide</td>
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<td>11.4</td>
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<tr>
<td>– Insuline</td>
<td>31.5</td>
<td>42.6</td>
</tr>
<tr>
<td>– Thiazolidinedione</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>– GLP1 agonist</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Total change (%)</td>
<td>-4.93**</td>
<td>-6.71**</td>
</tr>
<tr>
<td>% with HbA1c &lt; 7%</td>
<td>44.3**</td>
<td>55**</td>
</tr>
<tr>
<td>% with weight loss &gt; 5%</td>
<td>14.8**</td>
<td>26.3**</td>
</tr>
<tr>
<td>% with weight loss &gt; 10%</td>
<td>-2.02**</td>
<td>-3.1**</td>
</tr>
<tr>
<td>Fat mass (%) change</td>
<td>-0.48**</td>
<td>-0.89**</td>
</tr>
<tr>
<td>Skeletal muscle mass (kg) change</td>
<td>-0.48**</td>
<td>-0.47**</td>
</tr>
</tbody>
</table>

** P < 0.01; * P < 0.05; m = months

DOI: 10.1530/endoabs.81.P333

P334
Health outcomes following engagement with a digital health tool GroHealth app amongst people with type 2 diabetes
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Introduction
Diabetes is a chronic condition causing morbidity and mortality globally, with a growing economic burden on healthcare systems. In the UK, 1 in 14 people have diabetes, with type 2 accounting for 90% of cases (1). Complications from poorly controlled diabetes are associated with increased socioeconomic costs and a reduced quality of life. Research has shown education and self-management are crucial in helping diabetic patients achieve metabolic control (1). Smartphones

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have become an influential platform providing feasible tools such as health-apps to deliver tailored support to enhance diabetic patients’ ability for self-management. GroHealth is a NHSX-certified digital health tool used to deliver educational and monitoring support to facilitate the development of skills and practices for maintaining good health.

Objectives

To assess self-reported outcomes of the GroHealth app amongst diabetic and prediabetic users.

Method

The EuroQol-5D (EQ-5D) questionnaire is a standardised tool used to measure health status for clinical and economic appraisal. GroHealth users completed the EQ-5D at baseline and 6 months after using the app. Users provided informed consent for use of their anonymised data for research purposes. Health index scores (HIS) and visual analogue scale (VAS) scores were calculated at baseline and 6 months for individuals with prediabetes and type 2 diabetes (T2DM). Descriptive statistics and multiple-regression models were utilised to assess changes in outcome measures and determine the driving variables for change in HIS.

Results

HIS are average values that reflect people’s preferences about their health state (1 = full health, 0 = moribund). There was a significant and clinically meaningful increase in mean HIS amongst app users between baseline (0.746 [SD 0.234]) and follow-up (0.792 [SD 0.224], P < 0.001). The greatest change was observed in mean VAS score with percentage change of 18.3% improvement (baseline: 61.7 [SD 18.1]), follow-up:73.0 [SD 18.8]), P < 0.001). These VAS score improvements remained significant across age, gender, ethnicity, income, and diagnosis (prediabetes/T2DM). Baseline HIS, ethnicity and education variables were associated with significant changes in follow-up HIS (P < 0.001).

Conclusion

This study provides evidence of significant positive effect on self-reported quality of life amongst people living with T2DM engaging with a digital health intervention. The improvements in the five dimensions of health, as described by the EQ-5D, are facilitated through access to education and monitoring support tools within the app. This provides an opportunity for healthcare professionals to incorporate NHS certified digital tools, such as GroHealth as part of the holistic management of patients.

References

(1) Bene. BA et al. BMJOpen2019;9:e025714
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P335
Prevalence of amputation in a group of long-standing type 1 diabetic patients
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Background

Amputation is the major complication of diabetic foot. The aims of our study were to assess prevalence of amputation in a group of long-standing type 1 diabetic patients and to determine its risk factors.

Methods

We conducted a cross-sectional study including type 1 diabetic patients followed at the National Institute of Nutrition of Tunis. All patients had a duration of diabetes ≥ 20 years. Clinical and biological data were collected from medical observation records.

Results

One hundred and fifty five patients with mean age 39.7 ± 9.8 years were included in the study. About 30% of them were male. Age at diagnosis of diabetes was 12.7 ± 7.47 years. Mean duration of diabetes was 27.33 ± 6.38 years. The average of the last four glycated hemoglobin (A1c) was 9.45 ± 1.62%. The prevalence of amputation was 7.1%. It was associated with low socioeconomic status (P = 0.002), low level of education (P = 0.045), unemployment (P = 0.012), age at diagnosis of diabetes (P = 0.039) and anemia (P = 0.031).

Conclusion

Amputation is a serious complication of diabetes. It is more associated with socioeconomic factors than with diabetes-related factors.

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P336
Is there a relationship between nonalcoholic fatty liver disease (NAFLD) and atheroma disease?
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Introduction

Over the last few years, there are some studies that suggests a close connection between Nonalcoholic Liver Disease (NAFLD) and increased cardiovascular (CV) risk in population with obesity. Indeed, these two conditions share common drivers, most notably insulin resistance and other elements of the metabolic syndrome. Notwithstanding the above, this affirmation does not have solid scientific evidence. The proliferation of Vasa Yasorum (VV) in the adventitial layer of the carotid is proposed as an early alteration of atheromatous disease, which precedes the intima-media thickness. However, there is not any study that evaluates the association between NAFLD and VV.

Methods

A cross-sectional study was performed with 54 subjects undergoing bariatric surgery. Before surgery, all patients were subjected to a contrast-enhanced ultrasound study to evaluate carotid density of VV, to measure the thickness of intima-media and to verify the presence of atheromatous plaque. Whilst surgery a liver biopsy was performed.

Results

From liver biopsy, we regarded that 42 subjects had simple steatosis and 12 had steatohepatitis. The mean density of VV was similar between subjects with steatosis and subjects with steatohepatitis (0.742 ±0.173 vs. 0.781 ±0.136 arbitrary units (AU), P = 0.481). In addition, there were no difference in carotid intima-media thickness (0.742 ±0.173 vs. 0.781 ±0.136 AU, P = 0.481). We did not find any significant linear correlation between mean density of VV and the carotid intima-media thickness (r = 0.036, P = 0.790), as well as there was not correlation with clinical parameters such as age (r = -0.128, P = 0.346), BMI (r = 0.066, P = 0.627), fasting plasma glycaemia (r = 0.118, P = 0.390), HbA1c (r = 0.134, P = 0.342), the ‘fatty liver index’ (r = 0.024, P = 0.863) nor levels of GOT (r = 0.087, P = 0.623), GPT (r = 0.099, P = 0.945) and GGT (r = -0.099, P = 0.467). From the multivariate analysis, we did not observe any clinical or analytic variable that correlates with the adventitial VV density in an independent way. Nevertheless, when carotid intima-media thickness was the dependent variable, we found that age correlated independently in the multivariate study, whilst the other variables did not correlate.

Conclusion

NAFLD disease is a comorbidity associated with severe obesity almost inevitably. However, there is insufficient evidence to suggest that NAFLD plays a key role in the initial development of obesity-associated cardiovascular disease.

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P337
Roux-en-Y gastric bypass and vertical sleeve gastrectomy showed similar efficacy in achieving cardiometabolic composite target in subject with type 2 diabetes undergoing bariatric surgery
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Introduction

The American Diabetes Association (ADA) produced a triple composite outcome that summarizes the therapeutic targets of the three most prevalent complications of obesity: type 2 diabetes (T2D), hypertension and dyslipidemia (HbA1c < 7.0%; LDL cholesterol <100 mg/dL and systolic blood pressure <130 mmHg). The present study primarily investigates the difference between VSG and RYGB in achieving the composite target one year after the surgery. The secondary outcome assessed the success rate in achieving the separate components’ target at months 6, 12 and 24 post-surgery, the 2-year remission of DT2 and postoperative adverse events.

Methods

This retrospective observational study evaluated 103 patients with obesity and T2D (75/28 F/M). Sixty-two (60%) underwent VSG and 41 (40%) RYGB. Patient data

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were collected before surgery and subsequently during the follow-up visits at 6, 12 and 24 months post-surgery. At each visit, anthropometric measurements were recorded, and the metabolic and lipid profile was evaluated. Pharmacological therapies for diabetes, hypertension, dyslipidemia and any adverse events were also collected.

**Results**

Twelve months after surgery, patients undergoing RYGB did not show a significant difference compared to those undergoing VSG in achieving the composite target [RYGB vs VSG OR 2.21 (95% CI: 0.61–8.05), P = .57]. Patients undergoing RYGB showed greater LDL target achievement (< 100 mg/dL) at 6 months post-surgery than the VSG group (P = .005). Total cholesterol and LDL cholesterol were significantly reduced over time (months 6–12–24 post-surgery) in the RYGB compared to the VSG group (P = .023 and P = .010 respectively). No significant differences were observed in the TZD remission rate and the use of anti-diabetic, cholesterol-lowering and antihypertensive drugs between the two groups at months 6–12–24 post-surgery. There was a significant increase in the frequency of constipation episodes in the VSG compared to the RYGB group (P = .002).

**Conclusion**

Roux-en-Y Gastric Bypass and Vertical Sleeve Gastrectomy showed similar efficacy in reaching the cardiometabolic ADA composite target in subjects with T2D undergoing bariatric surgery. Patients undergoing RYGB showed a greater achievement of the LDL target < 100 mg/dL at 6 months after surgery and also a significant reduction over time in LDL and total cholesterol compared to the VSG group. More extended randomized studies are needed to evaluate the effectiveness of the two surgical procedures in the improvement and remission of cardiovascular risk factors associated with obesity.

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**Effect of dietary protein source on body composition and cardiometabolic risk in young adults with obesity during anti-inflammatory weight management program**

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1Teaching Institute of Public Health of Primorsko-goranska County, Department of Health Ecology, Rijeka, Croatia; 2Clinical Hospital Centre Rijeka, Croatia. Dietary protein intake was estimated from fasting blood samples were measured and their correlation with dietary protein intake from animal or plant origin was examined.

**Introduction**

Many studies have shown that dietary protein content may play a role in weight management. Moreover, it has been found that diets high in protein (either animal or plant) significantly reduced markers of insulin resistance and hepatic non-alcoholic steatohepatitis independently of body weight change. This study aimed to examine the effect of dietary protein source on body composition and cardiometabolic risk factors in young adults with obesity during anti-inflammatory weight management program.

**Methods**

A total of 56 participants (93% female, mean age 44 years, mean BMI 35.4 kg/m2) were enrolled in the study, and 42 of them completed the 24-week anti-inflammatory weight management program in the Obesity Outpatient Clinic at the Clinical Hospital Centre Rijeka, Croatia. Dietary protein intake was estimated from six-day food diaries. The inflammatory potential of diet was assessed with the Dietary Inflammatory Index (DII). Body composition parameters were assessed by bioelectrical impedance analysis (Seca mBCA 515, Hamburg, Germany). Serum concentrations of glucose, insulin, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and high sensitivity C-reactive protein from fasting blood samples were measured and their correlation with dietary protein intake from animal or plant origin was examined.

**Results**

On average, participants lost 7.1 kg (P < .001) over the 24-week period, and reduced high sensitivity C-reactive protein concentration by 30% (P < .001). The inflammatory potential of their diet was significantly improved toward more anti-inflammatory potential (P < .01). The total (P < .001), animal (P < .001) and plant (P = .001) protein intakes were significantly reduced, but its energy fraction was significantly increased (P < .001). The plant protein intake was strongly negatively correlated with serum triglycerides (r = -.099, P = .002) at the beginning of the program, and total body fat mass (r = -.099, P = .002) after its completion. There was no correlation between animal protein intake with any of the considered parameters.

**Conclusion**

The study results suggest that change of the dietary protein source toward plant origin can improve body composition and cardiometabolic risk profile in young adults with obesity.

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**Autoimmune thyroiditis: What impact on diabetic retinopathy?**

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**Introduction**

Data from literature suggest that combination of autoimmune diseases may have a major physical and psychological impact on type 1 diabetic patients. The aim of our study was to assess the impact of autoimmune thyroiditis on diabetic retinopathy.

**Methods**

We conducted a descriptive observational retrospective study of type 1 diabetic patients, followed at the National Institute of Nutrition and Food Technology of Tunis, between December 2019 and April 2021. All included patients had a diabetes duration of more than 20 years. Clinical and biological data were collected from medical observation records. The diagnosis of diabetic retinopathy was based on fundus examination, associated with retinal angiography in case of abnormality.

**Results**

The study included 155 patients. The mean age of patients was 39.7 ± 9.8 years. The sex ratio M/F was 0.49. Mean duration of diabetes was 27.33 ± 6.38 years with extremes ranging from 20 to 48 years. Autoimmune diseases associated with type 1 diabetes were dominated by autoimmune thyroiditis (22.4%) followed by celiac disease (6.8%) and adrenal insufficiency (4.3%). Diabetic retinopathy was present in 74.3% of the participants with a mean duration of 22 ± 5.9 years. The univariate study showed that autoimmune thyroiditis was present in 16.3% of patients with diabetic retinopathy compared with 35.1% of those with a normal fundus (P = 0.016).

**Conclusion**

Our study highlights the possible protective effect of autoimmune thyroiditis on diabetic retinopathy. Further research are needed to confirm this effect and determine the factors involved in this association.

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**Excellent disease control in Berardinelli Seip type 1 patient through dietary therapy alone: only an exception?**

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**Background and Objective**

Severe metabolic complications generally manifest at an early age in Berardinelli – Seip congenital lipodystrophy (BSCL) and their management is especially
This report proves how a personalized low-fat diet is of great help in the treatment of BSCL type 1 (homozygosity for c.493–1G > A mutation in AGPAT2 gene) and shows undetectable circulating levels of leptin (< 0.2 mg/l).

Conclusions
This report proves how a personalized low-fat diet is of great help in the management of BSCL and its complications; furthermore, a specific hypolipemic diet may be used alone as an effective long-term treatment in selected cases with high compliance and, probably, a milder phenotype.

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Children’s Clinical University Hospital in Riga, Latvia, Latvian Association of Endocrinology, and Latvian organizations of patients with diabetes.

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P341
Impact of the mode of insulin delivery on the quality of life of type 1 diabetes patients
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Background
Insulin pump therapy is an alternative to multiple daily injections and can improve glycemic control and quality of life (QoL) in Type 1 diabetes mellitus (T1DM) patients. The aim of this study was to assess the differences and factors related to the T1DM-specific QoL of T1DM patients in Latvia.

Methods
87 adult patients with T1DM were included. Of them, 20 were pump users and 67 were users of injections. All recruited patients participated in the quantitative part of the study; 8 pump users and 13 injection users participated in the qualitative part. Patients were invited to participate using a dedicated digital platform.

Specially developed questionnaires adapted to Latvian conditions were used for assessment of QoL and self-management habits. Association between social and self-management factors and patients’ QoL was investigated using multiple logistic regression models. Qualitative analysis of answers was performed according to major theme of transcripts.

Results
Compared to injection users, insulin pump users were younger (median age 42.1 vs 49.0 years, P < 0.01) and reported higher HbA1c levels (8.1 ± 1.0 vs 7.3 ± 1.2%, P < 0.01). There were no differences in BMI, physical activity, or metabolic deterioration. However, the interpretation of IGF-1 serum measurement is limited by a poor standardization of its normal values, as they vary significantly with sex, age and BMI.

Objective
To calculate a surrogate marker of serum IGF-1 concentration, normalized for age and sex, expressed as IGF-1 standard deviation score (IGF1-zSDS), in a cohort of 2032 individuals with obesity and to investigate its association with the presence of MS.

Methods
We conducted a cross-sectional study on adult Caucasian patients entering our third-tier obesity centre from 2010 to 2022. Anthropometric parameters, routine laboratory assessments, markers of glycolipid metabolism and serum IGF-1 levels were obtained.

Results
A total of 2032 patients (1551 females and 481 males) were enrolled. IGF-1 means and SDs obtained were specific for the obese population. Overall, male subjects had both a higher BMI (39.1 ± 7.2 vs 37.8 ± 7.1, P < 0.001) and a higher prevalence of MS (64.7% vs 45.7%, P < 0.001) than their female counterpart, suggesting that women may seek medical attention earlier or may be less likely to develop MS. The IGF1-zSDS in the overall population was 0.13 ± 0.8 and was significantly lower in patients with MS than in noMS. A MLA showed that for each decrease in IGF1-zSDS units, the chance of having MUO increased by 30%.

Conclusions
In a large population with obesity, lower IGF1-zSDS is associated with a higher chance of suffering from MS. Our results obtained with classical statistical analysis confirm preliminary results proposed by artificial intelligence. We suggest to use specific IGF-1 reference values to calculate IGF1-zSDS in obese Caucasian patients.

Keywords
metabolic syndrome, insulin-like growth factor 1

P342
IGF1-zSDS in patients suffering from obesity with or without metabolic syndrome: a cross-sectional study in 2032 subject
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Background
Metabolic syndrome (MS) is associated with increased mortality, and the key factors predictive of its development among patients with obesity are still unclear. We recently demonstrated with a machine learning approach that insulin-like Growth Factor 1 (IGF-1) is a novel marker of metabolic health and that in individuals with obesity, lower IGF-1 levels are associated with increased metabolic deterioration. However, the interpretation of IGF-1 serum measurement is limited by a poor standardization of its normal values, as they vary significantly with sex, age and BMI.

Objective
To calculate a surrogate marker of serum IGF-1 concentration, normalized for age and sex, expressed as IGF-1 standard deviation score (IGF1-zSDS), in a cohort of 2032 individuals with obesity and to investigate its association with the presence of MS.

Methods
We conducted a cross-sectional study on adult Caucasian patients entering our third-tier obesity centre from 2010 to 2022. Anthropometric parameters, routine laboratory assessments, markers of glycolipid metabolism and serum IGF-1 levels were obtained. Adult treatment panel III criteria were adopted for the clinical diagnosis of MS. IGF1-zSDS was calculated both in men and in women age-grouped as follows: 18–22; 23–30; 31–50; 51–65; > 65 years, according to the equation IGF1-zSDS = (IGF1 – mean)/SD. Student’s t-test was used to assess differences between patients with MS and groups of obese patients without MS (noMS) matched for age. A multinomial logistic analysis (MLA) was performed to assess the association between IGF1-zSDS and the probability of being diagnosed with MS.

Results
A total of 2032 patients (1551 females and 481 males) were enrolled. IGF-1 means and SDs obtained were specific for the obese population. Overall, male subjects had both a higher BMI (39.1 ± 7.2 vs 37.8 ± 7.1, P < 0.001) and a higher prevalence of MS (64.7% vs 45.7%, P < 0.001) than their female counterpart, suggesting that women may seek medical attention earlier or may be less likely to develop MS. The IGF1-zSDS in the overall population was 0.13 ± 0.8 and was significantly lower in patients with MS than in noMS. A MLA showed that for each decrease in IGF1-zSDS units, the chance of having MUO increased by 30%.

Conclusions
In a large population with obesity, lower IGF1-zSDS is associated with a higher chance of suffering from MS. Our results obtained with classical statistical analysis confirm preliminary results proposed by artificial intelligence. We suggest to use specific IGF-1 reference values to calculate IGF1-zSDS in obese Caucasian patients.

Keywords
metabolic syndrome, insulin-like growth factor 1

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**P343**

Exposing the crosstalk between obesity and prostate cancer: miR-191–5p as personalized diagnostic and therapeutic tool

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Abstract

**Background**

Identifying diagnostic and therapeutic targets for prostate cancer (PCa) is of great importance due to the high prevalence of the disease, particularly in obese patients. A previous study from our group demonstrated that miR-191–5p is dysregulated in PCa cells (compared to non-tumor cells). Moreover, in vitro obese cells (BMI > 30 kg/m²) also dysregulated in PCa cells (compared to non-tumor cells). Additionally, in silico and in vitro assays in normal and tumor prostate cell lines were performed. Results from the array revealed that the expression of 104 miRNAs was significantly altered (P < 0.001) exhibiting an AUC of 0.67. Remarkably, miR-191–5p significantly outperformed the ability of prostate specific antigen (PSA) to distinguish between control and PCa patients, especially in the ‘grey zone’, which represents the range where PSA levels are less accurate to diagnose PCa. Interestingly, the diagnostic capacity of miR-191–5p was even stronger in obese patients (BMI > 30 kg/m²). Furthermore, we found that miR-191–5p levels were also dysregulated in PCa cells (compared to non-tumor cells). Moreover, in vitro overexpression of miR-191–5p significantly increased cell proliferation and migration in DU145 and PC-3, two of the most aggressive PCa cell models. Finally, these functional effects were associated with the alteration in key cellular elements that are critical in PCa and obesity pathophysiology. Altogether, our data demonstrate that miR-191–5p might represent a novel personalized diagnostic biomarker in PCa, especially in patients with obesity, as well as a potential therapeutic tool in PCa.

**Materials and Methods**

In this study, we selected PCa cell lines with high BMI and compared them to normal cell lines. We performed a miRNA array on these cell lines, and the main changes were validated in an independent cohort of patients. The diagnostic capacity of miR-191–5p was evaluated in a cohort of patients demonstrating that miR-191–5p was one of the most profoundly altered miRNAs in PCa patients compared with healthy controls. Of note, 6 of these miRNAs also exhibited a significant ROC curve to distinguish between healthy and PCa patients with an AUC = 1. The validation using an independent cohort of patients demonstrated that miR-191–5p was one of the most profoundly altered miRNAs in PCa (P < 0.0001) exhibiting an AUC = 0.67. Remarkably, miR-191–5p significantly outperformed the ability of prostate specific antigen (PSA) to distinguish between control and PCa patients, especially in the ‘grey zone’, which represents the range where PSA levels are less accurate to diagnose PCa. Interestingly, the diagnostic capacity of miR-191–5p was even stronger in obese patients (BMI > 30 kg/m²). Furthermore, we found that miR-191–5p levels were also dysregulated in PCa cells (compared to non-tumor cells). Moreover, in vitro overexpression of miR-191–5p significantly increased cell proliferation and migration in DU145 and PC-3, two of the most aggressive PCa cell models. Finally, these functional effects were associated with the alteration in key cellular elements that are critical in PCa and obesity pathophysiology. Altogether, our data demonstrate that miR-191–5p might represent a novel and useful personalized diagnostic biomarker in PCa, especially in patients with obesity, as well as a potential therapeutic tool in PCa.

**Funding**

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**References**

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**P344**

Case Report: A triad of Diabetic Ketoacidosis, hypertriglyceridaemia and acute pancreatitis as a first presentation of diabetes mellitus

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Objective

We present a case of hypertriglyceridaemia induced acute pancreatitis (HTG-AP) and concurrent diabetic ketoacidosis (DKA) as a first presentation of Diabetes Mellitus in an adult patient. This uncommon triad has been previously described in the literature; however, it is rare to be observed in a previously undiagnosed patient with diabetes. The purpose of this poster is to describe the potential mechanisms for this and discuss management strategies.

Case Presentation

A previously fit and well 30-year-old South Asian man presented to the emergency department with a 3-day history of vomiting and abdominal pain. He had a BMI of 36 kg/m² and there was a maternal history of Type 2 Diabetes Mellitus. His initial panel of investigations demonstrated severe metabolic acidosis with ketonaemia. Admission venous blood gas showed a pH of 7.152, glucose 20.4 mmol/l, lactate 1.3 mmol/l, bicarbonate (HCO₃⁻) 5.8 mmol/l as well as blood ketones of 6 mmol/l. A subsequent CT scan showed acalculous acute pancreatitis (severity = Glasgow Score 2, Balthazar Score 2). Diabetic antibodies (GAD65, IA-2, ZnT8) were negative for Latent Autoimmune Diabetes of Adulthood (LADA). Triglycerides were 44.22 mmol/l and Haemoglobin A1C (HbA1C) was 118 mmol/mol. He was treated in a high dependency unit with aggressive fluid resuscitation, intravenous and subcutaneous insulin as well as fibrins.

Conclusion

While acute pancreatitis (AP) and DKA are common presentations in the Emergency Department, it was unusual as a de novo diabetic presentation and required Multidisciplinary Team discussion with the Diabetology team as well as the Intensive Care Team. AP is a complication in around 11% of patients with DKA and hypertriglyceridaemia (HTG) commonly occurs as a result of inhibition of lipoprotein lipase. It has been hypothesised that DKA could be the inciting event leading to HTG and ultimately AP. The correction of DKA is the crux of management, involving aggressive fluid resuscitation, intravenous insulin infusion and diligent monitoring of glucose, ketones and electrolytes. In the case of severe hypertriglyceridaemia, clinicians should be aware of interventions such as fibrins or therapeutic plasma exchange.

**Acknowledgements**

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**References**

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Understanding and improving the management of hyperosmolar hyperglycaemic state

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**Background**

Hyperosmolar hyperglycaemic state (HHS) is an acute metabolic complication of diabetes that can lead to significant morbidity and mortality if managed incorrectly. With <1% prevalence, there is limited published literature available on HHS and most management guidelines worldwide are based solely on expert advice and opinions.

**Aims**

To study the precipitating causes and identify baseline practises of HHS management, to highlight areas for improvement.

**Methods**

This retrospective study included all patients who meet the diagnostic criteria of HHS from May to November 2021 in six hospitals across the West Midlands region of the United Kingdom. The criteria for HHS diagnosis was defined as serum osmolality > 320 mOsmol/kg and glucose > 25 mmol/l whereas HHS resolution was defined as either serum osmolality < 300 mOsmol/kg, when fixed rate intravenous insulin infusion (FRIII) was stopped or when the clinical team documented resolution time, whichever came earliest. Osmolality was calculated using the formula: [(2x sodium) + (2x potassium) + glucose + urea, all values in mmol/l]. Data regarding precipitating causes, insulin and fluid administration, glucose and osmolality measurements, total duration of HHS and length of admission were collected. The data was then analysed using SPSS 28.0 and results were presented as frequencies, median and interquartile range (IQR) where appropriate.

**Results**

A total of 31 HHS episodes were identified. From these, 64.5% had the diagnosis of HHS documented in hospital records and 48.4% had serum osmolality measured. The most common precipitating causes were intercurrent illness (38.7%), suboptimal compliance to treatment (12.9%) and new onset of diabetes (9.7%). The median calculated serum osmolality at diagnosis was 343.2 mOsm/kg (IQR: 330.1–363.9). Patients with HHS received a median of 4500 ml (IQR: 1825–8574) of fluid until resolution. 38.7% of patients had FRIII commenced within the first hour of diagnosis and 54.8% were given basal insulin alongside FRIII. The median duration of HHS was 26.7 hours (IQR: 6.7–46.8) and these people were admitted for a median of 9.0 days (IQR: 4.7–11.8). While the length of stay was similar for HHS across included hospitals, there was a significant difference in HHS duration between sites (P < 0.001).

**Conclusion**

Our findings suggest there is an unmet need to improve the awareness of HHS identification and its management. With the difference in HHS duration between

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Introduction Mitochondrial diabetes (DM) is a monogenic form of maternal transmission diabetes that is caused by mutations in the mitochondrial genome. These mutations affecting mitochondrial function may be the cause of initiation of the phenomenon of apoptosis itself having an aggravating role of the phenotype in patients with mitochondrial diabetes.

Materials and Methods This study involved 43 patients with mitochondrial diabetes (20 non-syndromic and 23 syndromic) for whom mutations were identified in the mitochondrial genome in addition to 100 controls of the general Tunisian population. An analysis of apoptosis was carried out on muscle biopsy using TUNEL, immunohistochemistry and western blot cytochrome C expression. The analysis of 11 SNPs in 10 apoptosis genes (TP53, BCL2, BAX, BAK1, FASIL, CASP8, CASP10, CASP3, CASP7) was carried out by genotyping on the DNA of patients and controls.

Results Our results confirmed the presence of apoptosis by the TUNEL approach on muscle biopsy and by the study of the expression of the cytochrome C protein by western blot. This apoptosis is most accentuated in patients with a severe phenotype suggesting possible involvement of genetic factors. To study this hypothesis, we carried out a genotyping analysis of 11 functional SNPs in 9 genes involved in the pathways of apoptosis to evaluate their association with the development of apoptosis in patients with DM compared with controls. Results showed that mitochondrial (TP53) apoptosis and effector pathway (PSAP3) SNPs were significantly associated with a high risk of developing apoptosis (TP53 rs 1042522 OR 3.57, PSAP3 rs1405937 OR 4.33). In addition, this risk is increased (TP53 rs 1042522 OR 6.07, CASP3, rs1405937 OR 4.8) in patients with syndromic DM and pathogenic mitochondrial mutations.

Conclusion Apoptosis initiated by mtDNA mutations is aggravated by SNPs of the apoptosis genes in particular Tp53, and CASP3 in patients with DM in comparison with controls of the general population.

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Uncommon side effect of a common drug: doxycycline induced hypoglycaemia

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Introduction Doxycycline is a broad-spectrum antibiotic that is used to treat gram negative, gram positive and atypical bacterial infections. It is a member of the second-generation tetracycline class of antibiotics.

Case We describe a case of a (non-diabetic) male patient who developed hypoglycaemia following treatment with doxycycline. A 73-year-old male presented to the emergency department following a witnessed collapse at 9am on the 4th of September 2021. He was found to have a blood glucose level of 2.6 mmol/l with the London Ambulance Service. He had a past medical history of asthma, prostatic cancer, GORD and spondylosis. He had recently been prescribed doxycycline by his GP for treatment of a possible lower respiratory tract infection. He took an initial dose of 200 mg of doxycycline followed by 100 mg once daily for 11 days. It was on day 11 that he collapsed. During admission he received a Computed Tomography (CT) Head scan due to head injury which was reported as normal. His cortisol levels were normal at 346 nmol/l and he did not have any further episodes of hypoglycaemia after stopping doxycycline. Following discharge, he was reviewed at an endocrine clinic and endocrine causes of hypoglycaemia were investigated with a prolonged fasting glucose (15 hours) showed normal glucose and a repeat hormonal profile for RIF-1, IGF-2 and cortisol all of which were normal.

Discussion Medications can frequently cause hypoglycaemia especially in the elderly. Anti-diabetic medications are usually the culprit however many other non-diabetic medications used routinely can also cause hypoglycaemia and the list of these medications is expanding. Doxycycline has a number of side effects. Commonly known side effects include gastrointestinal irritation such as vomiting, diarrhoea and oesophageal ulceration. It is also known to cause photosensitivity and phototoxicity. A rare side effect of doxycycline that is not well known is hypoglycaemia A Study of the FDA Adverse Event Reporting System (FAERS) on hypoglycaemia associated with antibiotics alone and in combination with sulfonylureas and meglitinides showed that many patients developed hypoglycaemia while on antibiotics with or with sulfonylureas and meglitinides.

Conclusion Hypoglycaemia due to doxycycline is rare. The mechanism for doxycycline-induced hypoglycaemia is still unclear but it may be related to augmented insulin sensitivity, direct hepatotoxicity, inhibition of insulin degradation in the liver as well as inhibition of glycogenolysis. Paying attention to this potential adverse event is important as this medication is commonly prescribed antibiotic, especially in outpatient setting.

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The effect of intermittently scanned continuous glucose monitoring on the glycemic control and treatment satisfaction in Korean type 2 diabetic patients

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Background In recent years, continuous glucose monitoring (CGM) has emerged as a method for the assessment of glycemic control. Also CGM enables diabetic patients to understand their own blood glucose status and change their lifestyle.

Aims We investigated the effect of CGM on the glycemic control in Korean type 2 diabetic patients.

Methods We enrolled type 2 diabetic patients who met all the following criteria: 1) use of oral antidiabetic drug (OAD) or lifestyle change for diabetes control, 2) no change of OAD before the previous 3 months, 3) HbA1c levels, 7.0–8.9%, and 4) age, 30 to 73 years old. After informed consent, we applied the CGM (Freestyle Libre) to the participants for 2 weeks. Participants were asked to record their diet and exercise while wearing the CGM on the apps. We educated the participants how to interpret the glucose profile and manage glucose. The participants were randomly assigned CCGM or CCGM + short message service (SMS) group. We sent educational feedback message for the each CGM glucose profile and lifestyle to the participants for 2 weeks. Participants were asked to record their diet and exercise while wearing the CGM on the apps. We educated the participants how to interpret the glucose profile and manage glucose. The participants were randomly assigned CCGM or CCGM + short message service (SMS) group. We sent educational feedback message for the each CGM glucose profile and lifestyle to the CCGM + SMS group. We compared the change of HbA1c, lifestyle, and diabetes treatment satisfaction questionnaire after 10 to 12 weeks.

Results Fifty seven diabetic patients consented to the study. But 11 participants did not apply the CGM (no wearing CGM group). Twenty four were assigned to the CGM group. Twenty two were assigned to the CCGM + SMS group. There were no differences in age (56.4 ± 7.8 vs 58.5 ± 7.3 years, P = 0.429), DM duration (12.5 ± 7.0 vs 12.4 ± 6.5 years, P = 0.946), baseline HbA1c (8.0 ± 0.5 vs 8.0 ± 0.3%, P = 0.926) between wearing CGM (CGM and CCGM + SMS group) and no wearing CGM group. The deltaHbA1c of CGM, CCGM + SMS, no wearing CGM group was −0.35 ± 0.65%, −0.32 ± 0.73%, and −0.04 ± 0.78% (P = 0.478). There was no difference in the scan frequency per day (11.2 ± 5.8 vs 10.9 ± 4.8, P = 0.825) and in walking time per week (219 ± 170 vs 302 ± 180 minutes, P = 0.159) between CCGM and CCGM + SMS group. The self-care for diabetes was improved in both CCGM and CCGM + SMS group, especially in diet, exercise, and glucose monitoring. The DTSQ score was also improved in CCGM (delta 4.0 ± 7.6) and CCGM + SMS group (delta 4.1 ± 5.6). In the logistic regression analysis, time in range in CGM results was related to the prediction of glycemic control in this study.

Conclusions CGM can be used as a motivational tool for diabetes management when integrates with diabetes education. It is presumed that the intuitive ambulatory glucose profile had an effect on diet and diabetes management.

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P349
User acceptance and satisfaction with the eversense XL CGM in patients with type 1 diabetes
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Objectives
Eversense XL is a fully implantable sensor for continuous glucose monitoring (CGM) that lasts for up to 180 days. Our objective was to perform a survey on user acceptance and satisfaction among our type 1 diabetic patients who had been using the Eversense XL CGM for at least 3 months.

Methods
A questionnaire was devised in which the patients were asked about their experience with the Eversense XL CGM, including:
- Comparison with blood glucose strips and previously used glucose sensors if available.
- Perceived accuracy, comfort and ease of use.
- Perceived changes in quality of life, and ability to perform their daily activities including sports.
- Overall satisfaction with the device.

Visual analogue scales were used for quantitative data. The questionnaires were collected anonymously and with informed consent from the patients. All our type 1 diabetic patients who had been using the Eversense XL monitor for at least 3 months gave their consent and fulfilled the questionnaire.

Results
Thirteen patients were included in the survey, mean age 34 ± 5 years, 61.5% male. Five of them (38.5%) had previously used a glucose monitor (Abbott Freestyle Libre in all cases). All patients were more satisfied with the Eversense XL than with blood glucose strips (by 49.3 ± 11.4%) and their previous glucose monitor (by 13.4 ± 2.5%) 9 patients (69.2%) perceived the Eversense XL as more accurate than blood glucose strips (change 13.6 ± 5.8%) and 3 patients (60%) as more accurate than the previous sensor (change 7.3 ± 4.7%). The Eversense XL increased the perceived overall quality of life of 11 patients (84.6%, change 23.2 ± 7.3%), and the perceived ability to perform their daily activities in all patients (change 32.7 ± 9.6%); all the 9 patients who regularly performed sports activities improved their ability to do so (by 63.7 ± 15.6%). Comfort was rated 72.0 ± 15.5%, and ease of use 45.8 ± 29.7%.

Conclusions
The user acceptance and satisfaction with the Eversense XL CGM was high among our type 1 diabetic patients. The general impression was an improvement in their quality of life, and in their perceived ability to perform their daily activities. In particular, their ability to perform sport activities was markedly enhanced.

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P350
Prevalence of autoantibodies in paediatric and adult patients with type 1 diabetes mellitus – a study of a Portuguese cohort
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Introduction
Almost all type 1 diabetes mellitus (T1DM) patients have autoantibodies (ab) at disease onset. These ab prevalence varies according to patients’ age, origin and disease duration.

Aim
Determine diabetes mellitus ab prevalence in a paediatric and adult T1DM Portuguese according to their age on diagnosis, gender and diabetes duration.

Methods
Retrospective review of T1DM ab (glutamic acid decarboxylase 65 autoantibodies – GAD, islet cell autoantibodies – ICA, insulin autoantibodies - IAA, tyrosine phosphatase-like insulinoma antigen-2 antibodies - IA2) evaluated from 2018 to 2021. Considering the age at ab assessment, patients were divided into prepuberty (0-12 years) or postpuberty (≥ 13 years) and further subdivided into G1 and G2 when the assessment was at diagnosis or during follow-up, respectively.

Results
Included 156 patients (56.4% men; mean age 21.9 ± 15.5 years). Of these, 101 (64.7%) belonged to G1 and 55 (35.3%) to G2 (mean age at diagnosis 15.1 ± 10.2 vs. 20.7 ± 12.1 years; P=0.004). In G1, 65 (64.4%) were men and 45 (44.6%) were prepubertal. In G2, 23 (41.8%) were men and TIDM mean duration was 13.4 ± 14.2 years. The overall prevalence of positive ab was 83.2% in G1 and 69.1% in G2 (P=0.042), without differences between genders. There was a higher prevalence of GAD (P=0.023), IA (P=0.009) and ICA (P=0.006) in G1 and IAA (P=0.17) in G2. In G1, the mean number of positive ab was 1.6 and in G2 was 1.1 (P=0.017). In prepubertal G1 patients, positive ab prevalence was 88.9% (highest rate between 6–12 years) and in postpubertal was 78.6%, without significant difference regarding each ab prevalence in pre or postpuberty. In G2, patients diagnosed in postpuberty had a higher prevalence of ab, with a significant difference for GAD (P=0.011) and ICA (P=0.025). Patients with all ab negative (30.9%) had TIDM duration of 19.2 ± 13.1 years, while patients with at least 1 positive ab (69.1%) had TIDM duration of 10.7 ± 14 years (P=0.039). Spearman’s correlation test indicated that there was a negative and moderate correlation between the number of positive ab and the diabetes duration (r=-0.5, P=0.001).

Conclusions
In our cohort, more than 80% of T1DM patients had positive ab at diagnosis. GAD and IA were the most prevalent ab, contributing to T1DM diagnosis both in pre and postpubertal patients. There was no difference between genders and ab prevalence. The number of positive ab decreased with disease duration.

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Glucokinase (GCK) diabetes
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Background
Glucokinase (GCK) is a gene which plays an important role in recognising how high the blood glucose is in the body. It acts as the glucose sensor for the pancreas. Changes in the GCK gene can lead to increases in blood glucose and affected people may be diagnosed with diabetes although this rise in blood glucose is mild and does not need treatment. Glucokinase diabetes is one of familial diabetes types that called MODY (maturity onset diabetes of the young). We report a case was diagnosed with type 1 diabetes during her second pregnancy in 2006 and she was on insulin since. However, her genetic test in 2021 confirmed Diabetes - MODY2 – Heterozygous mutation in GCK.

Case report
50-year-old female diagnosed with type 1 diabetes during her second pregnancy in 2006 and at that time her ketone levels were high and therefore she was started on insulin. She was commenced on a basal bolus regime during her pregnancy. After pregnancy, she was only on Insulatard twice a day. Her insulin requirements were low so the type of diabetes was revisited in 2010 and at that time the islet cells antibodies were positive and therefore it was agreed to continue to treat her as type 1 diabetes. She was on a small dose of Insulatard and still having hypoglycse and therefore the insulin was stopped in January 2020. Before that she had another set of blood tests done in November 2019 and at that time her islet cell, IA2 and GAD antibodies were all negative. The C peptide level was still in the middle of the range at 0.76 nmol/l. Her HbA1c remained between 39 and 47 mmol/mol since 2009. When she was on insulin always in the normal range. Her MODY probability score shows the probability of MODY being 15.1%. Her genetic test results show a pathogenic GCK missense variant consistent with MODY2. Her daughter genetic test also confirmed the same variant. It was explained to her that there is no need for any treatment.

Conclusions
Patients with GCK gene variants generally have a mildly raised fasting blood glucose (typically 5.5- 8 mmol/l) and small increment at 2 hours (4.5 mmol/l) and does not need treatment. Glucokinase diabetes is one of familial diabetes types that called MODY (maturity onset diabetes of the young). We report a case that was diagnosed with type 1 diabetes during her second pregnancy in 2006 and she was on insulin since. However, her genetic test in 2021 confirmed Diabetes - MODY2 – Heterozygous mutation in GCK.

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P352
The effects of an acute metreleptin injection on hepatic lipid metabolism in patients with lipodystrophy
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Higher glucocorticoid receptor sensitivity is associated with less favorable body mass with obesity

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Background

Mounting evidence points to an association between increased glucocorticoid (GC) action and weight gain. However, the response to GCs is not only determined by GC serum concentrations, but also by individual differences in tissue-specific sensitivity, influenced by genetic and acquired (e.g. disease-related) factors. The extent to which differences in GC sensitivity may influence development of (abdominal) obesity, or vice versa, is poorly understood. In this study we investigate the relation between GC sensitivity and (abdominal) obesity.

Methods

Anthropometric data (BMI, weight, waist circumference and dual-energy X-ray absorptiometry (DXA) scans) and peripheral blood mononuclear cells (PBMCs) were obtained at baseline (T0) and completion of 10 weeks of treatment (T1) from 300 overweight or obese subjects (BMI > 30 kg/m^2) undergoing a combined lifestyle intervention with cognitive behavioral therapy. The half maximal effective concentration of dexamethasone (DEX), mediating the transactivation (EC50) or transrepression (IC50) of responsive genes GC-induced leucine zipper (GILZ) or corticosteroid-induced gene (CIG) was measured. IC50 and EC50 quantifies the effective concentration of DEX, mediating a 50% decrease or increase in response to DEX.

Results

A lower IC50 of DEX-mediated transrepression of IL-6 at inclusion (higher sensitivity) was associated with higher DXA fat mass (% of total body mass) (β = -0.52, 95%CI = -0.86 to -0.19) and lower DXA lean mass (% of total body mass) (β = 0.52, 95%CI = 0.18 to 0.86). Interestingly, the lower the IC50 for DEX-mediated transrepression of IL-6 at inclusion, the higher the weight loss in the first 10 weeks of lifestyle intervention (T1, β = 0.32, 95%CI = 0.04 to 0.60). Similar, but non-significant, associations were observed for IL-2. However, there were no associations between EC50 of DEX-mediated transactivation of GILZ and any of the above-mentioned anthropometrics variables.

Conclusion

This study suggests that increased GC sensitivity is associated with a less beneficial body composition in patients with obesity. Although, increased GC sensitivity at baseline was associated with weight loss at T1, further analysis of the data is in progress to determine whether this seeming contradiction is related to changes in GC sensitivity after lifestyle intervention.

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Evaluating obesity among second and third age premature children

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Introduction

Premature newborns are defined as babies born before 37 weeks of pregnancy and after 22 weeks of pregnancy as a viability limit. This study aimed to analyse growth characteristics at the age of second and third and the prevention of metabolic diseases that may occur in adult age at an early phase.

Methods

This study was conducted as a retrospective cohort study between May 2021 and October 2021 in 18 different Outpatient Clinics in Patna, Bihar. All participants were at least 3 years old and their follow-up visits were made by the same family physicians for 3 years.

Results

The findings showed that 55% of the babies were males and 46% of them were females i.e., 123 participants were males and 102 participants were females. The evaluation of the body mass index showed that 19.8% were overweight (43 babies), 16% of the participants were obese (36 babies) at the age of 2. 20% of the participants were overweight (45 babies), 13.33% of the participants were obese (30 babies) at the age of three. Mean Hb levels of the mothers showed that those mothers whose children were obese at the age of two were statistically low as compared to those who were not obese.

Conclusion

The worldwide prevalence of childhood obesity and overweight was 6.70% in the year 2010. In 2020, it was expected to reach 9.10%. When reasons for high obesity and overweight were searched, not much significant difference had been seen between feeding patterns and maternal factors. A significant relationship was however seen between maternal anemia and obesity or overweight.

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GLP-1 receptor agonists and erectile dysfunction in diabetic men with and without hypogonadism: a 1-year retrospective observational study

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Prevalence and awareness of complications in type 2 diabetes mellitus: a hospital based comparative cross-sectional study
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Introduction
Diabetes Mellitus appears to be globally pandemic and is drawing attention as a major public health concern. Chronic complications of this disease can lead to poor quality of life with significant financial burden to family and country as well. The current study aims to assess prevalence of such complications and its awareness in type 2 diabetes population.

Methods
This descriptive cross-sectional study was conducted during one year period in Endocrinology Outpatient Department of Koshi Hospital, Biratnagar, Nepal from 1st January 2021 to 31st December 2021. Consecutive sampling was applied and face to face interview was conducted to collect the information after informed verbal consent. Various factors related to awareness level were noted and compared.

Results
Out of 495 participants, 294 (59.4%) were male and 201 (40.6%) were female. The mean age of the participants was 52.07 ± 11.35 years. Of total participants 49.7 percent had diabetes related complications. Out of them 30.9 percent had one, 13.9 percent had two, 4.2 percent had three and 0.6 percent had four complications pertaining to their primary condition i.e. Diabetes Mellitus. Peripheral neuropathy was high (27.5%) followed by Diabetic retinopathy (17.6%), Diabetic Kidney Disease (16.2%), Ischemic Heart Disease and/or Heart failure (4.8%), sexual problems (3.8%) and Cerebrovascular disease (3.4%). Regarding awareness, only 45.5 percent had good awareness on microvascular and macrovascular complications related to Diabetes. Among the 49.7 percent patients who had complications, only 48.3 percent patients with retinopathy were aware that their retinopathy was secondary to Diabetes Mellitus. Similarly it was 75 percent awareness in case of cardiovascular complications, 52.9 percent with Cerebrovascular disease, 43.4 percent with Diabetic Kidney Disease. Among the 60 ml/min per 1.73 m2 were excluded. As per protocol, men with HbA1c < 7.2 % received metformin (2000 mg per day) while those with serum HbA1c > 7.2% received a GLP-1RA as an add-on to metformin (52% liraglutide, 1.2 mg/day; 48% dulaglutide, 1.5 mg/week) for one year. ED was diagnosed and classified by the International Index of Erectile Function 5 (IIEF5) score. Hypogonadal men were identified according to standardized parameters from the European Male Aging Study (EMAS).

Results
Forty-eight men with hypogonadism (HP) and 62 euogonadal individuals (EP) complaining of ED were retrospectively eligible for analyses. Mean age ranged 51–64 years; T2DM evolution ranged from 5–10 years. Around 6% of participants had established cardiovascular disease. Twenty-eight HP were on metformin plus a GLP-1RA (HPs), and 20 HP were on metformin alone (HPc); thirty-eight EP received metformin plus a GPL-1RA (EPs), and 30 were on metformin alone (EPc). After 12 months of treatment, both HPs and EPs significantly reduced serum HbA1c compared to baseline (all P < 0.01). HPc and EPc slightly increased HbA1c (0.3% and 0.4%).

Conclusions
Liraglutide and dulaglutide seem to have a favorable effect on ED in T2DM men with and without baseline hypogonadism. Further controlled studies are needed to confirm those preliminary results.

References
3. Bajaj HS et al., Lancet Diabetes Endocrinol. 2021, 9(8), 484–90

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assess the sexual quality of life (SQOL) of women with long-standing type 1 diabetes.

Methods
We conducted a cross-sectional study of women followed at the National Institute of Nutrition and Food Technology of Tunis. We included women with type 1 diabetes for 20 years or more. Women who were not sexually active and those who were pregnant or breastfeeding were not included. The Audit Diabetes Dependent Quality of Life (AIDQOL) scale was used to assess quality of life. This scale assesses overall quality of life, quality of life without diabetes and 19 life domains, including sexual life. SQOL was impaired if its relative score was less than (-3).

Results
We included 39 patients with mean age 40.77 ± 7.9 years [ext: -29-60 years]. Participants had been sexually active for a mean of 11 ± 8.9 years. All women included had only one partner. The mean glycated hemoglobin (Alc) was 9.3 ± 1.3%. The mean QOL score was (-3)±3 with extremes ranging from (-9) to 0. SQOL was impaired in 64.1% of the population. Univariate study showed that impaired SQOL was associated with history of in utero fetal death (P = 0.012) and number of abortions (P = 0.015). SQOL was associated with quality of life without diabetes (P = 0.012). Overall quality of life, glycaemic control, and chronic complications of diabetes were not associated with SQOL.

Conclusion
The results of our study highlight the impact of previous pregnancies on the SQOL of long-standing type 1 diabetic patients. Hence the importance of psychological support for all these women, especially those who have experienced an early or late abortion.

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P359
New insights into obesity treatment provided by smart technologies and telemedicine
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Introduction
Obesity represents a major public health challenge and is linked with increased risk of multiple medical conditions including atrial fibrillation (AF). We have recently published the study protocol of the ‘The Effect of complex weight-reducing interventions on rhythm control in obesity’ (HOBIT-AF) trial. Here we communicate the preliminary results with the focus on the use of smart technologies and telemedicine.

Methods
HOBIT-AF is a single-blinded, parallel-group, randomised controlled trial with 18-month follow-up to assess the effect of complex weight-reducing interventions supported by the use of smart technologies on the arrhythmia burden in obese individuals following catheter ablation for AF. Participants are randomised in a 1:1 fashion to undergo a structured weight reduction programme and optional sleeve gastrectomy aiming to achieve greater than 10% weight reduction (intervention group) or standard post-ablation medical care (control group). All participants are provided with the Apple Watch Series 5 and iPhone (Apple Inc, Cupertino, CA, USA). Daily initial settings for the intervention group are as follows: 5000 steps, 30 minutes of physical activity, energy expenditure of 900 kCal daily, home self-monitoring of blood pressure, heart rhythm, body weight, waist circumference etc. Control group have no goals set and use smart technologies solely for the heart rhythm monitoring. Individual patient goals and settings are monitored by healthcare team by a custom made software iKEMOnlineFit.

Results
Thus far 75 patients have been enrolled into the trial of which 50 are male. Mean baseline characteristics are as follows: age 56 years, weight 118 kg, BMI 37 kg/m2, waist circumference 128 cm. 69 % patients suffer from paroxysmal AF, baseline characteristics are as follows: age 56 years, weight 118 kg, BMI 37 kg/m2, waist circumference 128 cm. 69 % patients suffer from paroxysmal AF, 3 with extremes ranging from (-9) to 0. SQOL was impaired in 64.1% of the population. Univariate study showed that impaired SQOL was associated with history of in utero fetal death (P = 0.012) and number of abortions (P = 0.015). SQOL was associated with quality of life without diabetes (P = 0.012). Overall quality of life, glycaemic control, and chronic complications of diabetes were not associated with SQOL.

Conclusion
The results of our study highlight the impact of previous pregnancies on the SQOL of long-standing type 1 diabetic patients. Hence the importance of psychological support for all these women, especially those who have experienced an early or late abortion.

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P360
Functional analysis of melanocortin-4 receptor variants linked to obesity
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Introduction
Melanocortin-4 receptor (MC4R) is a G-protein-coupled receptor expressed in regions of the hypothalamus regulating appetite and energy expenditure. Extensive evidence from genetic and biological studies show that MC4R is a key player in the homeostatic regulation of body weight. MC4R loss of function (LoF) variants are the most common cause of monogenic obesity. We have identified 13 heterozygous MC4R variants in patients with obesity at our academic Obesity Center COG, Erasmus MC. However, it is unknown whether these variants affect MC4R signaling and are causing obesity. Here, we functionally characterized these variants by analyzing the effects on cell surface expression, MSH-induced cAMP production and β-arrestin 2 (βarr2) recruitment.

Methods
HEK293 cells were transiently transfected with expression plasmids encoding WT or variant MC4R and stimulated with MSH. cAMP response was measured using GloSensor cAMP bioluminescence assay. NanoBIT complementation luminescence assay was used to measure βarr2 recruitment, and the cell surface expression was measured using IBBIT Detection System.

Results
Thirty variants were identified by sequencing the MC4R gene of adult and pediatric patients with obesity using an obesity gene panel. Eight of these variants have not been previously reported in literature. The median age of onset obesity for the adult patients was 1.0 years and for the pediatric patients was 1.9 years. Furthermore, the median BMI of the adult patients was 48.8 kg/m² (range 36 - 58.8) and the median BMI-SD of the pediatric group was +4.2 SD (range +3 SD - +7 SD). Eleven out of 13 patients presented with hyperphagia. MC4R variants had differential effects on cAMP production, βarr2 recruitment and cell surface expression. Eight of the 13 MC4R variants caused partial or complete LoF for both cAMP production and βarr2 recruitment; out of those eight variants, three showed no cell surface expression. Surprisingly, two of the 13 MC4R variants resulted in a gain in function of cAMP production, and two other variants showed a normal cAMP response as well as βarr2 recruitment.

Conclusion
We show that the MC4R variants identified in our patients with obesity affect MC4R signaling differently, through modulation of cell surface expression, cAMP and/or βarr2 signaling pathways. Therefore, this study demonstrates the value of examining different aspects of MC4R signaling to understand possible biased effects of mutations on these pathways. Overall, our results show the clinical importance of assessing the function of MC4R variants as these studied variants are likely to be causative of obesity.

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P361
Comparison of glycemic variability in type 2 diabetes mellitus patients on oral anti diabetic drugs (OAD) with and without insulin using ambulatory glucose profile (AGP)
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Introduction
Assessment of diabetes with daily blood glucose fluctuations including peaks and nadirs forms the crux of the modern management. Use of glycemic variability
Introduction
Disease-related malnutrition is one of the main factors associated with morbidity and mortality in cancer patients. Furthermore, maintaining and improving muscle mass and function are important to achieve an optimal nutritional status. In this sense, the role of leucine-enriched essential amino acids supplementation for the therapeutic approach to the promotion of muscle anabolism stands out.

Methods
46 cancer patients with malnutrition receiving systemic treatment were randomized to receive for three months leucine-enriched essential amino acids supplementation or standard supplements. Patients were evaluated before and after three months. Nutritional assessment was performed using bioelectrical impedance analysis (BIA), dynamometry, ultrasound of rectus femoris muscle and subcutaneous fat tissue, functional tests and laboratory parameters.

Results
54% women. Mean age: 65 years. Median BMI: 24 kg/m². 19.6% with colorectal cancer. Regardless of primary tumor origin, 63% of patients received combined modality therapy consisting of surgery along with chemotherapy and/or radiotherapy. 80% of patients were classified as malnourished according to the GLIM criteria and 67% of patients presented decreased standardized phase angle (SPA) in the first morphofunctional assessment (Median 4.5° IQR 3.6–5.9). Positive correlation between 'Timed-Up-and Go' test (TUG), dynamometry and SPA was demonstrated (P < 0.05). Nutritional supplementation increased prealbumin levels and decreased CRP values. Malnutrition was resolved in three months later in 16% of patients. There were no significant differences between nutritional supplements in ultrasound parameters, body composition, functional test or prevalence of malnutrition after intervention.

Conclusion
In a third of patients disease-related malnutrition was resolved despite being in treatment with combined therapy. There were no differences between nutritional supplements, probably because of the short duration of nutritional treatment. DOI: 10.1530/endoabs.81.P362

P363
Evaluation of the Ankle-brachial index in a group of long-standing type 1 diabetic patients

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Background
Lower extremity artery disease (LEAD) is a common complication of diabetes, with increasing prevalence with duration and/or the coexistence of other cardiovascular risk factors. The Ankle-brachial index (ABI) is the first diagnostic step after clinical examination, for screening and diagnosis of LEAD. The aim of our study was to evaluate the ABI in a group of long-standing type 1 diabetic patients.

Methods
We conducted a cross-sectional study at the National Institute of Nutrition of Tunis. We included type 1 diabetic patients who had diabetes for more than 20 years. We measured the brachial systolic pressure using the tourniquet and the Doppler probe and the posterior tibial systolic pressure. A high ABI (>1.30) suggests the presence of mediaaoclastic. An ABI ≤0.90 indicates the presence of LEAD.

Results
We included 155 type 1 diabetic patients with mean age 39.7 ± 9.8 years. The population was predominantly female (67.1%). Mean duration of diabetes was 27.33 ± 6.38 years [ext = 20–48 years]. Mean glycated hemoglobin (A1c) was 9.45 ± 1.62%. The mean ABI was 1.22 ± 0.25 with extremes ranging from 0.76 to 2.18. The majority had an ABI between 0.9 and 1.3. An ABI >1.3 was found in 18.6% of patients. Only 5.2% of patients had an ABI <0.9. The ABI was correlated with age (r=0.360; P<0.001) and duration of diabetes (r=0.398; P<0.001). It was inversely correlated with insulin dose (r=-0.278; P=0.006).

Conclusion
Most patients with LEAD are asymptomatic. Patients with diabetes are at higher risk of chronic limb-threatening ischaemia as the first clinical manifestation of LEAD, supporting regular screening with ABI measurement for early diagnosis. DOI: 10.1530/endoabs.81.P363

P364
Acute hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency during treatment of diabetic ketoacidosis in an African American patient diagnosed with Ketosis-prone diabetes

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Background
Diabetic ketoacidosis (DKA) has been associated with severe hemolysis in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency after restoration of euglycemia. Less than 30 cases have been reported so far. The exact mechanism is not fully understood.

Case presentation
A 35-year-old African American man presented to the emergency department with polyuria, polydipsia, abdominal pain and weight loss the last 15 days. Physical examination revealed an afibrile man with severe dehydration, tachypnoea and tachycardia. Diagnosis of DKA was confirmed by laboratory tests. Remarkably, he had no previous history of precipitating factors but he reported use of cannabis twenty days ago, which was confirmed by toxicological testing. He was treated with hydration and intravenous insulin infusion, with a remarkable clinical and biochemical improvement. One day after he was switched to subcutaneous insulin therapy, a significant reduction in hemoglobin (9.2 g/dl)
accompanied by an increase in indirect bilirubin (1.59 mg/dl) was observed. Direct Coombs was negative and haemoglobin was <7.38 (20–200) mg/dl. Examination of peripheral blood smear revealed blisters, indicative of hemolysis. Medical history was negative for common hemolytic causes. Considering that African American men are commonly affected with G6PD deficiency, with a prevalence of approximately 10%, deficiency of this enzyme was suspected and confirmed by its low level (3 IU). Hemolysis was resolved after several days, and the patient left the hospital on intensive insulin regimen. During follow-up, gradual reduction of total daily insulin requirements was observed, with permanent discontinuation 10 weeks later. C-peptide stimulation test showed a peak c-peptide up to 1.1 mg/dl, suggesting residual pancreatic b-cell function. Antibodies to insulin, islet cell, glutamic acid decarboxylase and protein tyrosine phosphatase were negative. The diagnosis of Ketosis-prone diabetes (KPD) Aβ+ subtype was established. During annual follow up, patient was euglycemic without any antidiabetic treatment.

Discussion
KPD is a heterogeneous syndrome characterized by varying degrees of insulin deficiency. It is classified into four subgroups according to AβKPD classification system: 'A' is referring to the presence or absence of islet autoantibodies and 'β' is referring to the presence or absence of b-cell functional reserve, measured 6–8 weeks after DKA episode. Recent data suggest that alterations in genes referring to the presence or absence of b-cell functional reserve, measured 6–8 weeks after DKA episode. Recent data suggest that alterations in genes controlling both insulin secretion and G6PD-mediated antioxidant defences may contribute to the predisposition to KPD in West Africans with G6PD deficiency. The occurrence of hemolysis in these patients during treatment of DKA is increased and should be investigated.

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### P365

**Flash glucose monitoring in patients with DM3c**

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Objective
Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Since November 2020 the use of this system is subsidized in patients with type 3c diabetes (DM3c). Our objective was to describe the characteristics of these patients and their glycemic control expressed as times in range.

Methods and patients
Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM3c in which FGM implementation was subsidized

Results
26 patients included. Mean age: 59.27 ± 12.22 years, with DM diagnosed with a mean age of 51.85 ± 12.19 years. 30.8% women. 76.9% use of pancreatic enzymes in these patients. FGM metrics: A mean use of 91.17 ± 8.57%. 74.83 ± 16.12% time in range, 16.91 ± 11.82% time between 180-250 mg/dl, 3.53 ± 7.50% time above 250 mg/dl, 2.65 ± 2.99% time between 54-70 mg/dl, 0.13 ± 0.34% time below 54 mg/dl. Glycemic CV 31.59 ± 6.61%. 39.1% of patients achieved all clinical targets for FGM metrics.

Conclusion
- The main cause of DM3c in our series was surgical pancreatic resection (38.5% of patients)
- In our series of patients with DM3c and FGM, metabolic control was adequate using the same clinical targets as in DM1. 39.1% of patients achieved all clinical FGM targets.

Table 1.

<table>
<thead>
<tr>
<th>Cause of DM3c</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic pancreatitis (CP) due to alcohol abuse</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>CP w/o alcohol abuse</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>Pancreatic surgery (Tumour)</td>
<td>3</td>
<td>11.5</td>
</tr>
<tr>
<td>Pancreatic surgery (Non tumoral)</td>
<td>10</td>
<td>38.5</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1</td>
<td>3.8</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>11.5</td>
</tr>
</tbody>
</table>

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### P366

**Impact of glucose monitoring on quality of life**

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Introduction
The quality of life (QoL) of patients with Diabetes has been the subject of several studies worldwide. In Portugal, studies have shown that patients under intensive insulin therapy had worse results in QoL questionnaires. The introduction of interstitial glucose monitoring (IGM) appears to reduce the impact of insulin therapy on QoL.

Objective
To assess whether IGM changes the quality of life of patients with diabetes, compared to the assessment of glycemia and its impact on glycemic control of patients.

Methods
Retrospective cohort study of patients with diabetes under intensive insulin therapy and IGM system. The ‘Appraisal of Diabetes Scale’ (ADS) questionnaire was used, which consists of a set of 7 items summed to reflect the patients’ self-appreciation of their diabetes management. A 0 score indicates good management, with minimal impact on quality of life and 35 worse management and a negative impact on quality of life. The ADS was completed in two stages: a questionnaire applied at the time they used blood glucose monitoring and a questionnaire applied when using IGM systems.

Results
29 patients, 80.6% male, mean age 61 years, 58.6% with type 2 diabetes and 41.4% with type 1 diabetes. At the implementation of the IGM system, the mean duration of diabetes was 19.3 +/- 11.2 years, with HbA1c of 8.4 +/- 1.5% and 4.5 +/- 2.6 daily capillary blood glucose tests, on average. The ADS result reported to this date averaged 19 +/- 1.5 points. After the introduction of IGM, for an average period of 13.9 +/- 10.6 months, the mean ADS value was 16 +/- 4, corresponding to a significant reduction of 17% (P<0.0001). The mean HbA1c was 7.8 +/- 1.2%, corresponding to a 7% reduction (P=0.03), with an increase in the number of glucose measurements (12 +/- 11 IGM measurements per day (P=0.004). ADS and HbA1c results were independent of time of IGM use (P=0.2 and P=0.4) and number of daily glucose measurements (P=0.7 and P=0.9).

Discussion
The results demonstrate that the use of IGM, regardless of the number of measurements or the date of placement, has a positive impact both on diabetes control and on patients’ perception of their disease management, with a consequent improvement in QoL.

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### P367

**Metformin: anti-fibrotic molecule?**

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Background and aims
Diabetes causes tissue fibrosis by still poorly understood mechanisms which involve glycation products. Galectin-3 (Gal-3) is an emerging key player in metabolic disorders and a powerful factor in the development and progression of the fibrotic process in target organs in diabetic patients. The plasma level of Gal-3 increases during diabetic cardiomyopathy and diabetic nephropathy. We have studied the correlation between serum Gal-3 level and anti-diabetic treatment.

Methods
We carried out a cross-sectional study with an analytical aim. This work was carried out on type 2 diabetic patients followed in our department whose age range between 35 years and 80 years.

Results
On the therapeutic level, 11 patients (4.2%) were under hygieno-dietetic rules alone, 131 patients (50.4%) on oral anti-diabetics alone, 30 patients (11.5%) on insulin therapy alone and 88 patients (33.8%) on oral anti-diabetics and insulin therapy. For the oral treatment class, 207 patients (79.8%) were on metformin, 64 patients on sulfonylureas (24.6%), 13 patients (5%) on acarbose, 2 patients (0.8%) on glinide. We found a significant negative correlation of Gal-3 with metformin therapy. For the oral treatment class, 207 patients (79.8%) were on metformin, 64 patients on sulfonylureas (24.6%), 13 patients (5%) on acarbose, 2 patients (0.8%) on glinide. We found a significant negative correlation of Gal-3 with metformin treatment (r = -0.042; P = 0.028).

DOI: 10.1530/endoabs.81.P367
Conclusions
We observed a significant inverse correlation between Gal-3 and metformin treatment and this effect was independent of BMI, Hba1c and CRP. Metformin reduces oxidative stress and the formation of AGEs (advanced glycation products). This may help lower serum Gal-3 levels. Metformin has also been shown to reduce Gal-3 in human adipocytes and monocytes indicating a direct effect of metformin against fibrosis. Metformin has been argued to exert a nephroprotective effect by attenuating renal fibrosis, as well as an effect on reducing cardiac remodeling.
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P368
Comparative analysis of clinical, obstetric and perinatal characteristics of pregnant women according to serum levels of vitamin D
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Introduction
Vitamin D is considered a fat-soluble vitamin and a fundamental prohormone in mineral and bone metabolism, with an immunoregulatory and neuroprotective effect, among others. Vitamin D can be found as vitamin D2 or ergocalciferol and vitamin D3 or cholecalciferol. The main source of vitamin D comes from ultraviolet radiation in sunlight, but it is also obtained through food. Vitamin D deficiency is very prevalent in Europe, with a significant peak in Spain among the pregnant and infant population, being associated with adverse maternal-fetal effects such as gestational diabetes mellitus (GDM), deficit of bone mineralization in the newborn and increased risk of preeclampsia.

Material and method
Retrospective observational study that analyzes the data of 148 pregnant women, with a mean age of 33.32 ± 5.29 years, who came to our service to undergo 100g-SOG as a diagnostic test for GDM. Pregnant women were classified into 3 categories based on serum vitamin D levels (≤20 ng/ml, 20–29.99 ng/ml, ≥30 ng/ml), and different clinical, obstetric and perinatal variables were compared. In addition, the correlation of these variables with vitamin D levels was studied.

Results
No statistically significant differences were observed between serum vitamin D levels and the prevalence of GDM. BMI prior to pregnancy, blood pressure, HOMA-IR, total cholesterol, LDL, triglycerides, or newborn weight, among others. However, an elevation of HDL is observed in the pregnant group with higher levels of vitamin D, and an inverse correlation is observed between vitamin D and BMI prior to pregnancy, but not with the rest of the variables.

Conclusions
In our population, no differences were found between clinical, perinatal and obstetric parameters according to vitamin D levels. Vitamin D levels were only inversely correlated with BMI prior to pregnancy.

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P369
A role for somatostatin in regulating weight regain after bariatric surgery in mice
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Hebrew University of Jerusalem, Jerusalem, Israel

Somatostatin is a hormone and neuropeptide expressed in the pancreas, gastrointestinal tract, hypothalamus, and other tissues. It regulates directly the secretion of insulin, glucagon, many of the gastrointestinal hormones, and growth hormone. It is therefore surprising the somatostatin knockout (sst-ko) mice have a very mild phenotype. We subjected sst-ko mice and heterozygous siblings which served as controls to a high-calorie diet, and confirmed that sst-ko mice gain weight normally and have slightly more adipose tissue. Continuous glucose measurement of these mice has shown they have lower glycemia than controls. Both groups of mice lost weight and regained weight at the same rate after a short transition to a normal chow diet. However, sst-ko mice did not regain weight following sleeve gastrectomy (SG), a common bariatric surgery. Sst-ko mice maintained low weight 90 days after surgery, while fed on a high-calorie diet and were leaner than heterozygous siblings that had the same procedure. SG-operated sst-ko mice had low fasting insulin levels, and very rapid glucose clearance. Mechanistically, SG sst-ko mice had an exaggerated post-prandial Glp1 secretion. Post-prandial Glp1 levels were higher than in heterozygous controls that had the same surgery. Sham-operated sst-ko mice did not display an elevation in Glp1 secretion. In conclusion, by performing sleeve gastrectomy on sst-ko mice we were able to expose a role for somatostatin in regulation glycemia and weight gain, in part via regulating postprandial Glp1 secretion.
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P370
Differential localisation of the A-ring reductases in human hepatocytes: implications for substrate preference and utilisation
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The 5-reductases are steroid metabolising enzymes that saturate the C4 = C5 bond of the steroid A-ring, and their substrates include androgens, glucocorticoids, and bile acids. 5-reductases (SRD5A1 & SRD5A2) convert testosterone to the more potent androgen 5-dihydrotestosterone, and carry out the first step in glucocorticoid clearance, generating 5-dihydro cortisol from cortisol. 5-reductase (AKR1D1) is also able to carry out the first step of glucocorticoid clearance, converting both cortisol and cortisone to 5-dihydro cortisol and 5-dihydro cortisone but, in contrast to 5-reductases, it converts testosterone to a low activity intermediate, 5b-dihydrotestosterone. In addition, it catalyses an essential step in bile acid synthesis. The subcellular localisation of steroid metabolising enzymes is thought to have a role in determining their activity and substrate preference. In this regard, hepatic SRD5A1 is reported to be

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Body composition in patients undergoing liver transplantation

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Rationale
Liver cirrhosis frequently leads to changes in body composition consisting of a loss of lean mass, increased body water and variable alterations of fat mass. Changes in body composition may occur after liver transplantation (LT). Our aim was to study the changes that occur in body composition after LT (in the postoperative period after LT as well as 1 month later).

Methods
A body composition study was carried out using the bioimpedance InBody S10 in patients undergoing liver transplantation, postoperatively and 1 month after discharge. Several markers were analyzed: appendicular skeletal muscle mass (ASM), percentage of body fat, phase angle (PA) and extracellular water ratio (ECW ratio). Low muscle mass was considered when the ASM/height² was <7 kg/m² in men or <5.5 kg/m² in women; normal PA according to the standardized tables by age and sex and using the cut-off value of 4°; normal ECW ratio between 0.360-0.390; and normal fat mass in men between 10-20% and in women between 18-28%. Means comparison was carried out using the T-student test for paired samples and the comparison of proportions using the McNemar test.

Results
60 patients (78.3% male) were included. The age was 60.8 (7.5) years. The median stay was 10.5 (5-88) days. The time elapsed between both evaluations was 32.8 (11.1) days. The assessment of body composition before and 1 month after discharge from transplantation is shown in the following table. Sarcopenia was present in 2.1% and 12.7% of men at the first evaluation and 1 month later, respectively (p<0.001). No women presented sarcopenia in the immediate post-transplant period vs 23% at one month. Table-2 shows SMI and PA.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>1 month</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Mass</td>
<td>25.3(3.6)</td>
<td>23.6(3.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Index/kg/m²</td>
<td>79.2(30)</td>
<td>74.2(29.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Fat mass %</td>
<td>23.2(7.6)</td>
<td>23.9(7.9)</td>
<td>0.69</td>
</tr>
<tr>
<td>Visceral fat area (cm²)</td>
<td>34.3(8)</td>
<td>32.8(5.8)</td>
<td>0.038</td>
</tr>
<tr>
<td>Extracellular water ratio</td>
<td>0.40(0.1)</td>
<td>0.39(0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body cell mass (kg)</td>
<td>79.2(30)</td>
<td>74.2(29.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>ASM/height² (baseline vs 1 month, p-value)</td>
<td>8.2(1.4) vs 7.8(1.0), p&lt;0.001</td>
<td>4.2(0.9) vs 4.4(1.4), p=0.001</td>
<td></td>
</tr>
<tr>
<td>PA (baseline vs 1 month, p-value)</td>
<td>7.2(1.2) vs 6.3(0.8), p=0.082</td>
<td>3.5(0.8) vs 4.3(0.6), p=0.02</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion
Alterations in body composition in patients with LT are very frequent. One month after LT, there was a decrease in BMI, ASM, cell mass and body water, and an increase in PA. The worsening of muscle mass indicates that this period is critical in these patients. It would be interesting to assess body composition in the longer term. Since impedance meter is altered by excess extracellular water, these findings could be compared with other techniques for assessing body composition.

DOI: 10.1530/endoabs.81.P371
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Introduction
The association of multi-organ autoimmune diseases is described. We report a case of association between Latent autoimmune diabetes in adults (LADA) and systemic scleroderma (SSc), which remains a rarely reported entity in the literature.

Observation
A 38-year-old female patient, followed for systemic scleroderma with digestive and pulmonary involvements. The patient presented a dysphagia to solids with dyspnea installed in the last 2 months, with general state alteration. No polyuropolydipsic syndrome, no diabetic heredity. A generalized cutaneous sclerosis was objectified at the clinical examination. A standard workup showed fasting blood glucose at 1.69 g/l with HbA1c: 8.6%, the patient is treated with insulin-therapy.

Immunology typing test of diabetes: anti GAD, anti ZnT8: positive Skin biopsy: Morphological aspect compatible with scleroderma.

Discussion
Cases of coexistence of autoimmune diabetes with systemic sclerosis are rare. The pathogenesis of this association is not yet well understood. Interferon seems to play a major role as an immunomodulator and inhibitor of collagen production, and hypotheses suggest that it is also involved in the pathophysiology of several autoimmune diseases, including diabetes. And it is well known that autoimmune diseases with the presence of organ-specific antibodies such as autoimmune diabetes or autoimmune thyroiditis can coexist with other non-organ-specific autoimmune diseases such as SSc. In addition, autoimmune diabetes has been shown to be more likely to occur in first-degree relatives of patients with SSc.

Conclusion
The association of autoimmune diabetes and systemic scleroderma could be at the origin of a difficulty to assure insulin injections, which may be responsible for an important blood glucose unbalance.

Bibliography

DOI: 10.1530/endoabs.81.P374

P375
More than 20 years after diagnosis of type 1 diabetes: what about the quality of life?
Emma Bornaz, Haifa Abdesselem, Chaima Sdiri, Kamila Ounaissa, Fatima Boukhayatia, Imene Sebai, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouch
National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Background
Long-standing type 1 diabetes, had many complications which have an impact on both life expectancy and quality of life of these patients. The aims of our study were to evaluate the quality of life of a group of Tunisian patients with type 1 diabetes evolving for more than 20 years as well as to determine the factors associated with its alteration.

Methods
We conducted a descriptive observational cross-sectional study including type 1 diabetic patients who had diabetes for more than 20 years, followed at the National Institute of Nutrition. Quality of life was assessed using the version 19 of the Audit of Diabetes Dependent Quality of Life (ADDQOL-19), translated into Tunisian dialect; which includes, in addition to two general questions, 19 questions specifically assessing 19 life domains. From these 19 questions, a weighted composite score was calculated. We considered that quality of life was impaired if this score was ≤-3.

Results
A total of 155 patients with a mean age of 39.7 ± 9.8 years were included in the study. The diabetes had progressed for 27.33 ± 6.38 years. The sex ratio M/F was 0.49. More than half of the population (53.4%) had an impaired quality of life with a mean composite score of -3.22 ± 2.19. Of the nineteen life domains assessed, thirteen had a mean score ≤-3. Fear of the future, physical ability and freedom to eat, were the most impaired life dimensions. Their mean scores were -4.39 ± 3.4, -4.09 ± 2.9 and -3.91 ± 3.2, respectively. Univariate analysis showed that impaired quality of life was associated with unemployment (P=0.02), low level of education (P=0.049), low socioeconomic status (P=0.009), frequency of hypoglycemia (P<0.001), complicated retinopathy (P=0.037), peripheral neuropathy (P=0.012), disorders of the lower urinary tract (P=0.047) and category of risk of foot ulceration (P=0.028).

Conclusion
Our study highlights that after more than 20 years of the diagnosis of type 1 diabetes, the quality of life is often impaired. Prevention of chronic complications, psychological management, and adoption of therapeutic techniques that preserve dietary autonomy, could improve the QOL of long-standing type 1 diabetic patients.

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P376
Diabetic retinopathy and erectile dysfunction: is there a relationship?
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Background
Erectile dysfunction impairs the quality of life of men with type 1 diabetes. Many factors are involved in this complication. According to the literature, diabetic microangiopathy is associated with erectile dysfunction. The aim of our study was to evaluate the impact of diabetic retinopathy on erectile dysfunction in a group of long-standing type 1 diabetics.

Methods
We conducted a cross-sectional study that included male patients with type 1 diabetes for 20 years or more and followed at the National Institute of Nutrition of Tunis. Diagnosis and severity of erectile dysfunction were assessed by the short version of the International Index of Erectile Function (IIEF-5), translated and validated in Arabic. Diabetic retinopathy (DR) and its degree of severity were diagnosed by fundus examination and retinal angiography if abnormalities.

Results
A total of 51 men with a mean age of 41±9.7 years were included in the study. Diabetes was diagnosed at the age of 14.8±7 years. Mean duration of diabetes was 26.4±6 years. Only one-fifth (21.1%) of the population did not have DR on fundus examination. Two patients had permanent blindness. DR was minimal, moderate and severe in 18.4%, 21.1% and 15.8% of participants, respectively. It was proliferative in 10.5% of patients and complicated in 7.9%. Mean IIEF-5 score was 15.3±5.3. Erectile dysfunction was diagnosed in 85% of participants. It was mild in 39.1%, moderate in 43.5% and severe in 17.4% of cases. Univariate analysis showed a significant association between DR and erectile dysfunction (P=0.014). Severity of DR was associated with severity of erectile dysfunction (P=0.034).

Conclusion
Erectile dysfunction remains under-diagnosed and untreated in many diabetic patients. However, as our study showed, systematic screening in all patients with DR, especially in the advanced stages, should be recommended.

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P568
Study of musculoskeletal manifestations in type 2 diabetes mellitus
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Introduction
Musculoskeletal manifestation is one of the leading cause of morbidity and disability among type 2 diabetics. Also management of these conditions with steroids and non-steroidal anti-inflammatory drugs, adversely impact the glycaemic control of diabetics. Our study aims to look for prevalence of different musculoskeletal manifestation among type 2 diabetes.

Methodology
Our study is a cross-sectional observational study and it is comprised of 200 type 2 diabetes (>1 year duration) and 200 non-diabetic adult (>18 years) populations. All the cases were subjected to GALS screening (Gait, Arm, Leg and Spine). Patients with positive GALS screening were evaluated by REMS (Regional Examination of Musculoskeletal systems). Radiological examinations were done where needed.

Results
Prevalence of musculoskeletal manifestations was 55% (n=1110) among diabetics compared to 22.5% (n=44) among non-diabetics (P<0.001). 8% of diabetic patients with musculoskeletal manifestations were asymptomatic and detected by GALS screening. According to prevalence most common musculoskeletal manifestation among diabetics was cheiroarthropathy (21.5%; n=43) followed by osteoarthritis (19%; n=38), Adhesive capsulitis (11.5%; n=23), dupuytren’s contracture (6.5%; n=13), Rector tenosynovitis (2%; n=4), Charcot joint (2%; n=4) and carpal tunnel syndrome (1.5%; n=3). Presence of musculoskeletal manifestations is found to be significantly associated with long duration of diabetes, glycaemic control and presence of one or more microvascular complications.

Conclusion
Our study showed that the musculoskeletal manifestations are more prevalent among type 2 diabetics compared to non-diabetes population. A significant proportion of diabetics have these manifestations asymptomatic. Early diagnosis of these manifestations and good glycaemic control are important for the management.

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P377
Diabesity showcases the need for intensive care for COVID-19
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Background
Old age is proven to be one of the greatest danger factors for intensively dealing with COVID-19 patients. Stoutness and diabetes are enhancers of dangers among COVID-19 patients. Stoutness and diabetes are enhancers of dangers among COVID-19 patients. Old age is proven to be one of the greatest danger factors for intensively dealing with COVID-19 patients. Stoutness and diabetes are enhancers of dangers among COVID-19 patients.

Methods
A total of 127 Type 2 DM patients were selected. These patients had recovered from COVID-19, on follow up for diabetes care, from eight diabetes clinics that had the ICU facilities. Descriptive statistics, for example, body weight which is an indicator of the Intensive Care Unit (ICU) confirmations will be investigated.

Results
A total of 127 Type 2 DM patients were selected. These patients had recovered from COVID-19, on follow up for diabetes care, from eight diabetes clinics that had the ICU facilities. Descriptive statistics, for example, body weight which is an indicator of the Intensive Care Unit (ICU) confirmations will be investigated.

Conclusion
Our study showed that the musculoskeletal manifestations are more prevalent among type 2 diabetics compared to non-diabetes population. A significant proportion of diabetics have these manifestations asymptomatic. Early diagnosis of these manifestations and good glycaemic control are important for the management.

DOI: 10.1530/endoabs.81.P377

P569
Metabolic dysfunction–associated fatty liver disease and cardiovascular risk characterization
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Objectives
Metabolic dysfunction–associated fatty liver disease (MAFLD) is a new nomenclature for fatty liver disease (FLD). The clinical impact of the change in nomenclature on the ability to identify individuals at risk for cardiovascular disease (CVD) has not yet been elucidated. The aim of this study is to describe the cardiovascular risk and subclinical CVD of the different MAFLD subtypes.

Methods
Retrospective analysis of patients who attended a medical check-up at Clínica Universidad de Navarra between June 2003-December 2006 who had whole-body CT scan and analytics. Exclusion criteria included cerebral vascular diseases, heart disease, excessive alcohol consumption, advanced liver diseases and malignant disease. The cardiovascular risk was assessed through visceral adipose tissue (VAT)/subcutaneous adipose tissue (SCAT) Ratio. The presence of subclinical CVD was assessed by quantifying epicardial adipose tissue adjusted for body surface area (EATI) and Coronary Calcium according to Visual Scale (CAC-V).

Results
A total of 374 patients were included in the analysis: 154 without FLD and 220 with FLD. Mean age was 57.9 ± 9.3 years and 71.4% (267/374) of the cohort were men. Of the FLD cohort: 12.7% (28/220) were patients without metabolic
P570

When and How to Screen for Glucose Dysregulation (GD) in patients with β-Thalassemia Major (β-TM): A retrospective study by The International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescent Medicine (ICET-A)

Vincenzo De Sanctis¹, Ashraf Soliman¹, Shahina Daar², Vincenzo De Sanctis¹, Ashraf Soliman¹, Shahina Daar², Ploutarchos Tzoulis³, Mehran Karimi⁵, Salvatore Di Maio⁶ & Christos Kattamis¹

¹Quissiana Hospital, Ferrara, Italy; ²Hamad Medical Center, Pediatrics, Doha, Qatar; ³College of Medicine, Sultan Qaboos University, Muscat, Oman; ⁴Department of Diabetes and Endocrinology, Whittington Hospital, University College London, London, UK., United Kingdom; ⁵Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Shiraz, Iran; ⁶Children’s Hospital ‘Santobono-Pausilipon’, Pediatrics, Naples, Italy; ⁷National Kapodistrian University of Athens 11527, Greece, Pediatrics, Athens, Greece

To investigate the best criteria and time to diagnose dysglycemia in β-TM patients, the ICETA performed a retrospective study on glycemic abnormalities (GD) in 397 with β-TM patients (aged 5–40 years; 56.3 % males) followed between 1988 to 2021 in a single centre (by VDS) (40 years).

Methods

Fasting blood glucose (FPG) and standard oral glucose tolerance test (OGTT) results were collected over 40 years of follow up and results were categorized following ADA and WHO criteria.

Results

Based on the FPG data, using the ADA criteria, the prevalence of isolated IFG was 23.6 %, while increasing the threshold value of FPG to 110 mg/dl according to WHO criteria, decreased the prevalence to 15.3 %. β-TM patients showed a higher prevalence of GD mainly in the second to third decade of life. Based on the OGTT, 44 of 234 β-TM patients presented with IFG (18.8%), 3 (1.2%) with IGT and 1 with a new diagnosis of thalassemia related DM (Th-RD). In patients with IFG the probability of diagnosing IGT was higher (46.1%) in subjects with FPG between 100 and 109 mg/dl compared to subjects with FPG between 110 and 125 mg/dl (P = 0.0071). Both ADA and WHO criteria for IFG missed the diagnosis of Th-RD in 4 of 91 patients (4.3%) and 11 of 59 patients (18.6 %), respectively. The number of patients with a new diagnosis of diabetes, after OGTT, increased progressively starting from the age of 11 years (Table).

Conclusion

Many β-TM patients who have a normal FPG may present with GD after OGTT. Dysglycemia may occur in very young patients. OGTT screening seems to be cost-effective. ADA criteria used for the diagnosis of IFG identified an additional group of patients with dysglycemia. Diagnostic value of FPG and OGTT in detecting Th-RD in 384 patients with β-TM aged 5–40 years.

Table 1. Comparative characteristics of 2019 and 2020 groups

<table>
<thead>
<tr>
<th>(mg/dl)</th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG (&lt;100)</td>
<td>0/63 (0 %)</td>
<td>2/19 (10.5 %)</td>
<td>18/95 (19.1 %)</td>
<td>3/40 (7.5 %)</td>
</tr>
<tr>
<td>FPG ≥100</td>
<td>0/11 (0 %)</td>
<td>0/47 (0 %)</td>
<td>9/95 (9.4 %)</td>
<td>7/40 (17.5 %)</td>
</tr>
<tr>
<td>New Th-RD</td>
<td>0/78 (0 %)</td>
<td>6/23 (26.0 %)</td>
<td>3/95 (3.2 %)</td>
<td>7/40 (17.5 %)</td>
</tr>
<tr>
<td>OGTT ≥200 mg/dl</td>
<td>0/63 (0 %)</td>
<td>0/78 (0 %)</td>
<td>0/95 (0 %)</td>
<td>3/40 (7.5 %)</td>
</tr>
</tbody>
</table>

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P571

Glycogen hepatopathy - a rare and frequently misdiagnosed hepatic complication of diabetes mellitus

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Introduction

Glycogenic hepatopathy (GH) refers to excessive intrahepatic glycogen accumulation in patients with poorly controlled diabetes mellitus especially type 1 diabetes mellitus. It is a rare and frequently misdiagnosed complication of diabetes mellitus. The patients present with non-specific pain abdomen may be incidentally detected during evaluation of deranged liver function tests (LFT). Case report

A 15 years old female presented with pain abdomen, nausea and lethargy for last ten days. She was a known case of type 1 diabetes mellitus for last two years and was currently on multiple daily subcutaneous insulin injection regimen. However, her glycemic control was very poor due to poor compliance and she had three episodes of diabetic ketoacidosis (DKA) in the past. Clinical review revealed presence of lethargy and dehydration. Hepatomegaly (palpable 5 cm below costal margin) was also seen. Blood investigations revealed presence of DKA. Blood gas analysis showed arterial pH 7.1 and bicarbonate level of 12 meq/l. Her random blood glucose at the time of hospitalization was 435 mg/dl and HbA1c was 12.9 %. Urine analysis confirmed presence of ketonuria (urine ketone + + +). Renal function tests including serum electrolytes were normal. LFT revealed aspartate aminotransferase (AST) 208 IU/ml, alanine aminotransferase (ALT) 108.2 IU/ml, total bilirubin 1.14 mg/dl, direct bilirubin 0.08 mg/dl, albumin 3.5 g/dl, creatinine 0.3 mg/dl, and urinalysis showed presence of ketonuria (urine ketone 3 + +). Abdominal ultrasonography showed hepatomegaly with gross hepatosteatosis without any other organ abnormality. Contrast enhanced computerized tomography also showed significant hepatomegaly with diffuse fatty infiltration. A thorough screening for liver disease markers including viral markers, autoimmune panel, coeliac disease, hemochromatosis and Wilson’s disease was negative. Subsequently, a liver biopsy as per advice of treating gastroenterologist was done and it confirmed presence of classical glycogenic hepatopathy. The parents were counseled regarding nature of disease and advised to maintain strict glycemic control. Subsequently after three months post discharge, revaluation confirmed regression of hepatomegaly and significant normalization of liver function tests.

Conclusion

GH is a very rare metabolic complication of poorly controlled type 1 diabetes mellitus. It may be frequently missed or misdiagnosed if clinical vigil is not high. The treatment of choice for management of GH includes strict glycemic control, periodic follow up and prevention of DKA episodes recurrence.

DOI: 10.1530/endoabs.81.P571
Introduction

The T-Coach® telephone support program for patients with type 2 diabetes (DM2) treated with insulin glargine 300 u/ml, facilitates dose adjustments of basal insulin therapy through regular telephone consultations and offers diabetes education in order to improve empowerment of the patient. Objective: To assess the usefulness of the T-Coach® program in metabolic control and degree of satisfaction in patients with T2DM.

Patients and methods

Observational, descriptive, retrospective, multicenter study, including patients with type 2 Diabetes (T2DM) included in the T-coach® program from October 2016 to December 2020, attended in Endocrinology in the province of Cádiz.

Demographic data, baseline clinical and laboratory parameters, 3 and 6 months after inclusion in the program are analyzed. The degree of patient satisfaction and evolution of the level of knowledge with the use of the platform are evaluated.

Results

286 patients are included, 50.2% (n = 143) women, age 66.05 ± 11.62 years and T2DM evolution time 15.4 ± 8.2 years. 45.4% (n = 71) had microangiopathy and 24.5% (n = 70) macroangiopathy. 19% started long-acting insulin. Average of 7.2 calls per patient. At baseline long-acting insulin dose was 25.5 ± 16.34 U/day after 6 months 36.2 ± 19.26 U/day. At baseline Fasting plasma glucose 188.5 ± 76.45 mg/dl after 6 months 119 mg/dl. The T-Coach® program from October 2016 to December 2020, attended in Endocrinology in the province of Cádiz.

Conclusions

In our setting, the T-Coach® program is shown to be a useful tool for adjusting the dose of long-acting insulin, with the consequent improvement in glycemic control in these patients. The degree of patient satisfaction with the support for insulin dose adjustment is high and the level of knowledge improves with telephone reinforcement of diabetes education.

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P573

Total daily dose of insulin at the beginning of treatment with Continuous Subcutaneous Insulin Infusion system: which is the best formula?

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Introduction

Several formulas are described to calculate the Insulin Dose to start insulin pump therapy. However, there are no data demonstrating their effectiveness in achieving good glycemic control. Aim

To assess the Total Daily Dose of Insulin (TDDI) at 3 months after beginning an insulin pump, and determine which formula most closely matches the TDDI required in cases where good glycemic control is achieved after that period.

Methods

Retrospective study including individuals with type 1 diabetes who started treatment with an insulin pump between 1st of January of 2019 and 30th of September of 2021 at our center. Patients were frequently evaluated until glycemic control was achieved. Glycemic control was assessed at ‘time zero’ (T0) and ‘time 3 M’ (T3 M) through the HbA1c value, % time in target range(%)TIR), % time above(%)TAR) and below the target range(%)TBR). The TDDI at T3 M months was compared with the insulin dose calculated by the different formulas at T0: F1-mean TDDI of the 7 days preceding the beginning of treatment.F2-TDDI calculated by weight(0.5xweight);F3-obtained by 90% of the mean of F1 and F2 (F1+F2)x0.9.

Results

Of the 62 individuals who started treatment, 52 were included(80.6% women; median age 39 years [minimum-maximum:19–70 years]), with a mean of ±22 ± 13.28 years of disease progression. At T3 M, the median %TIR was 63.5%(IQR 24%), the median %TAR 32%(IQR 31), the median %TBR 3%(IQR 6) and the median HbA1c 7.1%(IQR 1.3). The median TDDI at T3 M was 42 U/I (IQR 21.5U) and was similar to TDDI at T0 by F1(40.5U)(IQR 19.2), F2=0.723 but with a significantly lower percentage of basal insulin 38% vs. 49.3%, P < 0.001. The median TDDI at T3 M was significantly superior than TDDI obtained by F2(42U/I)(IQR 21.3I)(P < 0.001) and by F3(34U/I)(IQR 13.5), P < 0.001). In the 19 patients with %TIR > 70% at T3 M, the median TDDI at T3 M was not different from the TDDI at T0 calculated by F1(P=0.268) and F2(P=0.427), but major differences were found comparing with F3(37.0U/I)(IQR 23.8Vs.29.4(IQR 12.2), P = 0.05).

Conclusion

The TDDI in use in 3 months after the beginning of an insulin pump in this work was quite similar to the mean TDDI of the 7 days preceding the starting of this treatment. This result was similar in patients with TIR above or below 70% at T3 M. The main difference at T3 M was the percentage of basal insulin which decrease significantly from almost 50% to 40%. These results suggest that the mean TDDI of the 7 days preceding the starting of this treatment can be the best option to begin the insulin pump.

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P574

Impact of whatsapp based Communication on insulin adherence and glycemic control in patients with Diabetes in Indian population

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Introduction

Diabetes treatment requires the involvement of people with diabetes in the form of medication adherence. Insulin treatment is an important aspect of diabetes therapy. Regular and timely insulin infusion is necessary for good glycemic control and complications prevention. Never follow-up techniques, such as WhatsApp based communication are now finding their way into diabetes care and treatment. It can assist diabetes patients to maintain a regular treatment schedule and drug adherence.

Materials and Methods

A total of 342 Diabetic patients aged 15–65 years were selected by random sampling. Inclusion Criteria: 1. Known case of Diabetes mellitus 2. Consent to take part in study. 3. Ability to use WhatsApp messaging Exclusion criteria: 1. Inability to use WhatsApp 2. Not consenting to be a part of the study. They were randomly allocated to two groups of 171 people each. In the first group, the participants were added to a WhatsApp group and were asked to regularly answer a question about whether they have taken insulin or not on that particular day to the clinic over WhatsApp. The other group was treated as usual. The participants were monitored for HBA1C and insulin adherence at 3 and 6 months. The results were analysed using SPSS.

Result

After excluding 4 dropouts the analysis of data shown: HBA1C reduction in the WhatsApp group was 1.8 % as compared to 0.8 % in the routine care group. At the end of 3 months and was 2.3 % in the WhatsApp group and 1.3 % at the end of 6 months. The number of patients achieving the target goal of 7% HBA1C was better in the WhatsApp group (54%) as compared to the routine group (38%) at the end of 3 months and in the WhatsApp group (73%) as compared to the routine group (53%) at the end of 6 months. 82 % of patients in the WhatsApp group were insulin compliant compared to 63 % in the routine group.

Discussion

The strategies and means of communicating with patients have improved with the emergence of modern modes of communication. This has paved the door for the development of innovative messaging systems such as WhatsApp that enable more patient-centric communication. When utilized properly, these tools can help
reduce in-person follow-ups while increasing the connection between caregiver and patient. Additionally, this can result in improved patient outcomes, as well as fewer complications and financial repercussions.

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### P575

**Maturity-onset diabetes of the young in a large portuguese cohort**

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**Introduction**

Monogenic forms of diabetes that develop with autosomal dominant inheritance are classically aggregated in the maturity-onset diabetes of the young (MODY) categories. Despite increasing awareness, its true prevalence remains largely underestimated.

**Aim**

To evaluate the clinical and molecular characteristics of patients with MODY.

**Methodology**

This single-center retrospective cohort study enrolled patients with positive genetic testing for MODY between 2015 and 2021, followed at our Pediatric and Adult Endocrinology Outpatient Clinic. Clinical and molecular characteristics were described.

**Results**

Eighty-two patients were included, mostly female (51.2%), with a median age at diagnosis of 23 years (interquartile range [IQR] 23). The most frequent mutation was in the HNF1A gene (43.9%, n = 36), followed by GCK (32.9%, n = 27), HNF4A (12.2%, n = 10), HNF1B (9.9%, n = 4), PDX1 (2.4%, n = 2), INS (2.4%, n = 2) and APPL1 (1.2%, n = 1). The mean number of family generations affected was 2.3 ± 0.7. The following table summarizes the main characteristics of the four most frequent types of MODY within our sample:

**Conclusion**

Mutations of HNF1A gene were the most common within our cohort, followed by GCK. This study highlights the need to increase accuracy in the diagnosis and characterization of monogenic forms of diabetes. This strategy may contribute to a better understanding of this type of diabetes and a more personalized clinical management and follow-up of these individuals and their families.

**Table 1**

<table>
<thead>
<tr>
<th>MODY</th>
<th>Age at diagnosis (years)**</th>
<th>Symptoms of insulin deficiency</th>
<th>Kidney malformations</th>
<th>Non-insulin hypoglycaemic agents</th>
<th>Insulin HbA1c at diagnosis (%)*</th>
<th>C-peptide (ng/ml)**</th>
<th>Actual HbA1c (%)*</th>
<th>Follow-up (months)**</th>
<th>Diabetes-related complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNF1A</td>
<td>30 (23)</td>
<td>5.6%</td>
<td>None</td>
<td>75%</td>
<td>8.7 ±2.5</td>
<td>1.7 (1.46)</td>
<td>7.1 ±0.9</td>
<td>27 (115)</td>
<td>27.8% microvascular 8.3% macrovascular None</td>
</tr>
<tr>
<td>GCK</td>
<td>10 (8)</td>
<td>None</td>
<td>None</td>
<td>22.2%</td>
<td>6.2 ±0.4</td>
<td>1.4 (0.7)</td>
<td>6.2 ±0.4</td>
<td>15 (41)</td>
<td>20% microvascular 10% macrovascular</td>
</tr>
<tr>
<td>HNF4A</td>
<td>22 (29)</td>
<td>10%</td>
<td>None</td>
<td>50%</td>
<td>6.1 ±1.6</td>
<td>1.1 (0.7)</td>
<td>6.1 ±0.8</td>
<td>17 (62)</td>
<td>20% microvascular 10% macrovascular</td>
</tr>
<tr>
<td>HNF1B</td>
<td>11.5 (13)</td>
<td>50%</td>
<td>100%</td>
<td>None</td>
<td>6.8 ±1.5</td>
<td>2.6</td>
<td>6.9 ±1.4</td>
<td>36.5 (173)</td>
<td>50% microvascular</td>
</tr>
</tbody>
</table>

*Results shown in mean ± standard deviation

**P576**

**Ketosis prone type 2 diabetes in covid times - a missing link?**

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Traditional literature agrees that Diabetic Ketoacidosis is typically associated with Type 1 Diabetes Mellitus, but can be associated with stress including infections in Type 2 diabetes. The authors did a retrospective evaluation of diabetic ketoacidosis presenting to a large district hospital in London. 343 patients were admitted with diagnosis of Diabetic Ketoacidosis during the COVID peaks from January 2020 to January 2021. 57% of these were Type 1 diabetics and 43% were found to be Type 2 diabetics. 23% of the patients admitted with Type 2 diabetes and DKA did not have a previous presentation with ketosis. 68% of both Type 1 and Type 2 diabetics tested negative for COVID 19 on first/second swab (accounting for hospital exposure). 56% of Type 2 diabetics with DKA tested positive for COVID-19 on first/second swab. 32% of Type 2 diabetics were new diagnosis of diabetes. Initial studies agreed a significant increase in ketosis prone DKA in Type 2 diabetics during COVID times however were unable to establish a clear correlation with COVID infection. Our Initial studies did suggest a possible extrapolation with widespread vaccination of a possible emerging cohort of ketosis prone type 2 diabetes. We therefore evaluated the incidence of ketosis prone type 2 DKA in vaccinated individuals with a total of 178 admissions with diabetic ketoacidosis evaluated between August 2021 and December 2021. 58.7% of patients admitted with diabetic ketoacidosis were Type 2 diabetics. 23% of patients presenting with diabetic ketoacidosis were new diagnosis of diabetes (19% Type 1 Diabetes). An overall increase in monthly admissions over five months was noted when compared to previous one year evaluated was noted. The authors suggest that exposure/immunity to COVID 19 may be a contributing factor to increase in ketosis prone diabetic ketoacidosis. Several etiologies may be suggested including viral destruction of beta cells in patients with widespread subclinical infection or possible role of antibodies in vaccinated individuals. More research is needed for the same particularly with emergence of variants and widespread vaccination as this has potential to change the understood epidemiology of Type 2 Diabetes.

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### P577

**Covid-19, Dexamethasone and Diabetes(CODED) study: a single centre experience**


**Endocrine Abstracts (2022) Vol 81**
Background
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Coronavirus (COVID-19) caused by severe acute respiratory syndrome (SARS)-CoV-2, which leads to multi-organ disease. Covid-19 high mortality and morbidity arising from autoimmune destruction of the lungs due to pro-inflammatory cytokines storm, has enabled worldwide collaborative studies aimed at elucidating potential management strategies in order to overcome pandemic. The RECOVERY trial, a multi-centred trial involving 175 United Kingdom based hospitals. The results from this trial revealed that using dexamethasone lowered 28-day mortality rate for patients receiving either invasive mechanical ventilation or oxygen but had no effect on patients not receiving respiratory support. Using dexamethasone can cause manifestation of hyperglycaemia or induce Diabetes mellitus in previously non-diabetic patients. In the present study, we looked at 100 patients (both diabetics and non-diabetics) with COVID 19 on dexamethasone and we monitored their glucose levels.

Aims
1. To assess doctors’ and nurses’ knowledge of dexamethasone related hyperglycaemia and diabetes.
2. To assess doctors’ awareness of guidelines for management of patients with COVID-19 who started on dexamethasone and whether they were using it.
3. To assess if patients who had hyperglycaemia and/or hyperglycaemia related complications were seen by diabetes team when appropriate
4. To improve doctors and nurses’ awareness of proper management of patients with COVID-19 who need to be started on dexamethasone

Methods
Retrospective analysis of paper notes, case notes & electronic records of patient reported outcome (EPRO). Single centre study 100 randomly selected patients with RT-PCR COVID-19 treated with dexamethasone admitted to Queen’s hospital.

Results
100 COVID-19 positive given dexamethasone treatment. 18 were removed and T2DM, 82 were non-diabetic. Of the 100 patients, only 87 had regular glucose monitoring, 67 had monitoring as per BHRUT guidelines. Out of the monitored patients (87) 30 patients had hyperglycaemia which was more frequent in T2DM patients (9; 50%). Of those who developed hyperglycaemia 11 (37%) patients had their hyperglycaemic episodes treated as per national guidelines and 10 diabetic patients (50%) with T2DM required up titration of their medications. One of non-diabetic patients started on insulin.

Discussion/conclusion
Dexamethasone can be associated with hyperglycaemia in non-diabetic and known diabetic mellitus increasing their mortality and morbidity risk. Thus, it is important that these patients be monitored and managed according to national and local guidelines. Therefore, we intend to create new proformas to keep doctors and nurses up to date with the guideline of management of COVID 19 patients on dexamethasone.

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P578
Inflammatory markers in patients with type 1 diabetes and diabetic kidney disease
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Background
Inflammation is involved in the pathogenesis of complications of type 1 diabetes (T1DM). We aimed to assess the differences in the markers of endotoxaemia and faecal calprotectin in patients with T1D different status of diabetic kidney disease (DKD).

Methods
31 generally healthy adults (control) and 74 patients with T1DM and were included. Of the latter, 13 had DKD (defined as microalbuminuria, macroalbuminuria, estimated glomerular filtration rate (eGFR) below 60 ml/min/1.732, end stage kidney disease). In serum, lipopolysaccharide (LPS) activity was measured by Limulus Amebocyte Lysate assay, lipopolysaccharide binding protein (LBP), endogenous anti-endotoxin core antibodies (EndoCAb IgG and IgM), high sensitivity C reactive protein (hsCRP) and faecal calprotectin were measured by ELISA.

Results
The mean age in the T1D group was 42.3±15.2 years and in the healthy participant group 37.3±10.6 years. In the T1D group, the mean diabetes duration was 23.1±12.2 years, the mean HbA1c was 8.2±1.9%. Patients with and without DKD did not differ in age, anthropometric measures, prevalence of cardiovascular hard endpoints. Patients with DKD had longer T1D duration (P=0.04); higher prevalence of arterial hypertension (P=0.08); severe retinopathy (P=0.010); end-stage renal disease (P=0.029), and previous gastrointestinal surgery (P=0.02). The levels of EndoCaB IgG and IgM did not differ between T1D and control. Compared to control group, patients with T1D had statistically significantly lower LPS (LPS: T1D 0.23 ng/ml (0.22;0.31) control 0.38 ng/ml (0.32;0.56), P=0.009) and hsCRP (T1D 894.57 ng/ml (1255.91;1990.92), control 313.29 ng/ml (368.82;1173.07), P=0.01). LBP was higher in T1D compared to control, but the difference did not reach statistical significance (T1D: 1144.50 ng/ml (1107.45;13058.45), control 9776.60 ng/ml (8991.34;12911.32)). None of the markers differed between DKD groups. The level of calprotectin did not differ neither between controls and T1D, nor between T1D patients with and without DKD. Within patients with T1D and DKD, LPS correlated positively strongly with serum creatinine and albuminuria; LBP correlated positively strongly with faecal calprotectin.

Conclusions
In patients with T1D and DKD, markers of serum inflammation are associated with kidney function and HbA1c.

Acknowledgements
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P579
Association between clinical and genetic factors and glycemic and weight loss response to liraglutide in patients with type 2 diabetes
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Background
Previous research suggests an association between specific genetic variations and interindividual variability in response to treatment with glucagon-like receptor agonists (GLP-1 RAs) in patients with type 2 diabetes mellitus (T2DM). We aimed to evaluate the role of CTRB1/2 rs7202877 (T>G) polymorphism in glycemic control and weight loss response to liraglutide among Greek patients with T2DM and to identify clinical factors related to prediction of response to liraglutide administration.

Methods
The medical records of 116 adults with T2DM [51% female, mean Body Mass Index (BMI) 35.4±6.4 kg/m²], who had been on treatment with liraglutide for at least 6 months and were genotyped for CTRB1/2 rs7202877 (T>G) polymorphism, using real-time PCR, were evaluated. Clinical and laboratory parameters were measured at baseline, 3 and 6 months after initiation of liraglutide treatment. The good glycemic response was defined as one of the following: i) achievement of glycated hemoglobin (HbA1c) <7%, either at 3 or 6 months after treatment initiation ii) reduction of the baseline HbA1c by ≥1% after
3 or 6 months of liraglutide use, and iii) maintenance of HbA1c <7% that a patient had before switching to liraglutide, after 3 or 6 months of treatment. Weight loss responders were defined as subjects who lost ≥3% of their baseline weight after 3 or 6 months of liraglutide administration.

Results
97 (84%) patients were homozygous for the wild type rs2202877 T allele (TT) and 19 (16%) patients carried one polymorphic G allele (TG). 81 (70%) and 77 (67%) individuals were classified as glycemic control and weight loss responders, respectively. Heterozygotes had similar responses to liraglutide treatment in terms of glycemic control [odds ratio (OR): 1.25, 95% confidence interval (CI): 0.4, 3.8, P = 0.69] and weight loss (OR: 1.12, 95% CI: 0.4, 3.2, P = 0.84). In the multivariable analysis, higher baseline HbA1c (adjusted OR: 1.45, 95% CI: 1.05, 2.1, P = 0.04) and lower baseline weight (adjusted OR: 0.97, 95% CI: 0.94, 0.99, P = 0.01) were associated with better glycemic response to liraglutide, while higher baseline weight was associated with worse weight response (adjusted OR: 0.97, 95% CI: 0.95, 0.99, P = 0.02). Both glycemic responders and non-responders demonstrated a significant reduction in weight and BMI from baseline to 6 months (P < 0.0001). Both weight responders and non-responders significantly reduced HbA1c after administration of liraglutide (P < 0.0001 and P = 0.008, respectively).

Conclusion
Specific patient features can predict glycemic and weight loss response to liraglutide in patients with T2DM.

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PS580
Hypoglycemia and impaired hypoglycemia awareness: frequency and relevance in type 1 diabetes under continuous subcutaneous insulin infusion
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Introduction
Continuous subcutaneous insulin infusion (CSII) therapy in type 1 diabetes (T1D) reduces the risk of hypoglycemia. Hypoglycemia remains a treatment-limiting factor. Impaired hypoglycemia awareness (IHA) occurs in 25% of T1D cases and seems to be underestimated by continuous glucose monitoring (CGM). Glycemic variability (GV) is a increasingly valued parameter as a predictor of hypoglycemia and risk of chronic complications.

Objective
Analysis of the relationship between impaired hypoglycemia awareness (IHA) and new metrics of glycemic control (estimated A1C (A1Ce), time in hyper- and hypoglycemia, GV) in T1D patients on CSII and CGM.

Methods
Cross-sectional, observational study of patients with T1D under CSII and intermittent-scanning GCM FreeStyle Libre® (active >70% of the time). Glycemic control assessed by the 30-day GCM (AGP report). IHA was defined by a score ≥4 on the Clarke Questionnaire (CQ).

Results
43 cases were analyzed: 61.5% were female; mean age of 33.3 ± 9.7 years. The mean A1Ce was 7.1 ± 0.7% and glycemic variability was 39.3 ± 8.9%. The time spent in hypoglycemia was 35.2 ± 18.7% (8.5 hours/day): 24.0 ± 11.5% between 180–250 mg/dl and 11.2 ± 9.4% above 250 mg/dl. Time spent in hypoglycemia was 7.0 ± 5.9% (1.7 hours/day): 4.6 ± 3.3% between 54–70 mg/dl (level 1) and 2.4 ± 3.2% < 54 mg/dl (level 2). From the Clarke Questionnaire, we obtained a prevalence of 14.3% of IHA and 9.3% of ≥1 level 3 hypoglycemia per year. There was a moderate to strong correlation between glycemic variability and time in hypoglycemia (r = 0.72; P < 0.001), as opposed to time in hyperglycemia which showed no significant correlation (P = 0.41). GV did not show correlation with TID duration but approached statistical significance (P = 0.06). In patients with A1Ce < 7% medians of time in hypoglycemia were significantly higher –7.0% (P < 0.03) and 23.2% (P < 0.03). Impaired hypoglycemia awareness occurred in patients with lower A1Ce values (6.9 ± 0.7% vs 7.2 ± 0.7%) but without significant differences. There was no significant difference in time in hypoglycemia at 30 days in these cases.

Conclusion
Hypoglycemia occurred in a higher frequency than the goals especially for more demanding glycemic controls, correlating with the increase in glycemic variability (GV). GV was higher than desirable in most cases, underlying the difficulty of its optimization. Impaired hypoglycemia awareness in this population had a lower prevalence than the overall estimated prevalence in T1D and did not show a significant correlation with the GCM data, highlighting the complexity of its pathophysiology and its possible underestimation by glycemic control metrics.

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PS581
Comparing global rating scores from simulation-based diabetes andendocrine scenarios between healthcare professionals of high- and low-middle-income countries
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Background
Simulation via Instant Messaging - Birmingham Advance (SIMBA) is an online simulation learning modality designed to recreate clinical scenarios, allowing participants to increase their confidence in a safe environment without compromising patient safety. The global rating scale (GRS) is a commonly used assessment tool in medical schools to assess participant competence and skills. Following SIMBA sessions, an independent assessor anonymously scores participants’ performance of their simulated case using an adapted version of the GRS.

Objective
To study the pattern of GRS score across various domains of endocrine scenarios and the variation by country of residence.

Methods
We included all diabetes and endocrine SIMBA sessions conducted from July 2020 to October 2021. The participants’ responses were divided into various domains and each domain was scored from 1 (poor) to 5 (excellent). Data were pooled during analysis and findings are reported as frequencies. Chi-square test was used to compare the differences between participants’ performance across various domains. Participants were further grouped by the country’s income according to the country of residence based on the 2022 World Bank Report: high-income countries (HICs) and low- and middle-income countries (LMICs).

Results
293 healthcare professionals participated in six SIMBA sessions (thyroid, pituitary, diabetes, metabolic bone, gonadal, and diabetic microvascular complications). The median (IQR) GRS scores for domains are as follows: history-taking: 4.0 (3.0–5.0), physical examination: 4.0 (3.0–4.6), investigations requested: 3.3 (3.0–4.0), results’ interpretation: 2.6 (1.6–3.1), clinical judgement: 3.3 (2.6–4.0) and management and follow-up: 2.6 (2.0–3.3). HICs and LMICs (31.2%, n = 91) scored similarly in history-taking (HIC: 3.81 vs LMIC: 3.79; P = 0.05), physical examination (HIC: 3.67 vs LMIC: 3.68; P = 0.19), investigations requested (HIC: 3.35 vs LMIC: 3.33; P = 0.27), and results’ interpretation (HIC: 2.63 vs LMIC: 2.61; P = 0.74). HICs scored better in clinical judgement (HIC: 3.53 vs LMIC: 3.18; P = 0.008) and providing management and follow-up plans (HIC: 2.66 vs LMIC: 2.64; P = 0.001).

Conclusion
All participants, particularly those from LMICs, scored lower in the categories of investigations, clinical judgement, and management skills. This demonstrates the need for targeted educational programmes which can be both cost-effective and beneficial to all participants independent of country of residence.

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Background and aims
In many developing countries, diabetic foot is considered as a problem only when the patient develops a wound on the foot. Until that moment, the detection of changes in the neurovascular condition of the feet is rarely applied. The aim of this prospective, single centre study was to define factors associated with early cardiovascular mortality in diabetes.

Materials and methods
1345 patients under age 75 were included who were undergoing assessment of their diabetes between January 2008 and May 2010 as part of standard practice in a specialist clinic at a regional teaching hospital in Serbia. Peripheral artery disease (PAD) and peripheral neuropathy was assessed. Evidence of other comorbidities was also collected. Outcome was determined in 2008 and baseline characteristics were compared between those who had and had not suffered cardiovascular death under age 75 years within 10 years of review in two casually selected cohorts.

Results
Those who died (n=70) were more frequently male (60 vs. 45.3%, P=0.08), younger (66.4±7.4 vs. 79.9±3.4, P<0.000), had a shorter period of follow-up (5.6±2.3 vs. 11.2±1.7 years, P<0.000) when compared to those still alive (n=1275). Those who died were also significantly (P<0.01) more likely to have had PAD (48.6 vs. 9.3%), diabetic foot ulcer (25.7 vs. 9.3%), major amputation (17.1 vs. 1.3%) at baseline. Minor amputations were significantly more likely (8.6 vs. 1.5%, P<0.04). Following multivariable logistic regression analysis significant differences between groups remained for only current smoking (123±45 vs. 88.9±16.9 mmol/l, P=0.003) and vibration perception threshold <5 (7.8 vs. [95 CI: 3.7-16.4]), P=0.086), estimated maximum lifetime BMI (3.4 vs. [95 CI: 1.7-6.8]), P<0.000), alcohol usage (4.7 vs. [95 CI: 1.5-14.7]), P=0.005), smoking habit (2.2 vs. [95 CI: 1.1-4.3]), P<0.03) and earlier age of diabetes onset (43.4±12.5 vs. 49.2±9.9, P=0.0029). When the 72 patients with impaired vision sense were compared with 73 with VPT >6 and there were significant differences in and PAD (3.9 vs. [95 CI: 1.8-8.1]), P<0.001) and estimated maximum lifetime BMI (9.4 vs. [95 CI: 3.4-25.7]), P<0.000). Those who had had a previous MI at baseline (n=46) was associated with increased death rate (3.2 vs. [95 CI: 1.5-6.6]), P=0.002) and VAP (2.91 [1.3-6.1]), P=0.007).

Conclusion
Decreased VPT, the presence of PAD on clinical testing and higher maximum estimated lifetime BMI are strongly associated with premature cardiovascular death. Early detection of independent markers of greater risk of reduced life expectancy might improve management of their diabetes.

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P583
Waist-to-height ratio is a predictor of weight loss with Gelesis200 treatment for people with overweight or obesity having prediabetes or type 2 diabetes in the LIGHT-UP study

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Introduction
Methods to predict clinically meaningful weight loss can help tailor treatment for people with overweight or obesity. LIGHT-UP (NCT03058029), is a multicenter, double-blind, randomized, placebo-controlled study over 25 weeks including 254 people with prediabetes or type 2 diabetes (127 each in the Gelesis200 and placebo arms) with a body mass index between 27 and 40 kg/m², which demonstrated that Gelesis200 offers a compelling new potential approach in the management of overweight and obesity. A stepwise logistic regression analysis was conducted on data from the LIGHT-UP study to identify variables at baseline that reliably predict body weight (BW) Responders and Super-Responders (< 5% BW loss and ≤ 10% BW loss, respectively, from baseline at Week 25).

Methods
Two stepwise logistic regression analyses were conducted for each study arm (Gelesis 200 placebo). The dependent variables were the percentage of participants who were Responders and Super-Responders. The independent baseline variables included in the models were the ones hypothosized to potentially predict BW loss at Week 25 (e.g., gender, age, BW, body mass index, height, waist circumference, waist-to-height ratio (WHR), fasting plasma glucose, and fasting serum insulin).

Results
After WHR was included in the model, there were no other variables that were significant in the prediction of Responders or Super-Responders. The final regression model shows that for a 0.1 change in the WHR (e.g., from 0.6 to 0.7), the probability for a Responders increases from 63% to 66%, and the probability for a Super-Responder increases from 24% to 39%. For a 0.2 change in the WHR (e.g., from 0.6 to 0.8), the probability for a Responders increases from 53% to 78%, and the probability for a Super-Responder increases from 24% to 56%. None of the independent variables was a significant predictor of Responders or Super-Responders in the placebo arm.

Conclusion
The results of this study suggest that a higher baseline WHR is predictive of an increased rate of Responders and Super-Responders. The independence baseline variables included in the models were the ones hypothosized to potentially predict BW loss at Week 25 et al.
symptoms (UGS). Endoscopic esophageal and gastric lesions were categorised based on Los Angeles and Sydney classification.

Results
32 patients (56% males) were included with mean age of 52 ± 8.5 years-old and BMI of 41 ± 4.4 kg/m². Mean follow-up was 29.4 ± 9.3 M. 71.9% patients performed BP and 28% GS. At pre-op. 53% had positive HP, 21.9% had UGS and 21% were on PPI treatment. Class A or B esophagitis was diagnosed in 15.7% and erythematous gastritis in 78% of patients. Histologic results confirmed gastritis in 65.8%. 12 M after BS patients had a mean BMI of 28 ± 3.7 kg/m² and 81.3% had no UGS. UGE revealed a total of class A or B esophagitis of 25%, in which 75% of the cases was “de-novo” lesion (83% submitted to GS and 33% had UGS). A significant reduction in erythematous gastritis was achieved in the corpus (18.8% (P = 0.05) but not in the antrum (25% (P = 0.22). 15.6% presented with “de-novo” ulcer (all of them underwent BP). Biopsy confirmed gastritis in 43.7% (P = 0.85). 1 case of Barrett’s esophagus was diagnosed but no cases of dysplasia. No significant association was found between histologic result (P = 0.537) or PPI use (P = 0.654), and BS procedure.

Conclusion
This study illustrates the importance of endoscopic follow-up after patients BS; even if no UGS are present. After 12 M esophagitis was more prevalent, suggesting it was appropriate to maintain PPI use, in particular in those submitted to GS. A tendency to reduction was identified in gastric lesions.

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P585

Improvements in physiological and psychological status of patients with obesity in response to a combined lifestyle intervention with cognitive behavioral therapy are not necessarily related to successful weight loss

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quality of life. Changes in DEBQ, EDE-Q and FCQT scores showed decreases in DEBQ and EDE-Q total score (P < 0.05). However, changes in most immune parameters, parameters of psychological health, and eating behavior did not correlate with the amount of weight loss, except for changes in IL1ra (P > 0.001), IWQoL, PSS (both P < 0.05) and EDE-Q total score (P < 0.01).

Conclusion
We show that the value of a multidisciplinary treatment approach for patients with severe obesity is not only limited to successful weight loss and improvements of body composition itself, but also includes the wide range of improvements in metabolic parameters, immunological, psychological, psychosocial, dietary, and behavioural improvements that may occur independently of weight loss.

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P586

Weight loss variability with SGLT2 inhibitors, GLP-1 receptor agonists and repetitive Transcranial Magnetic Stimulation in Type 2 Diabetes and Obesity: results of a retrospective, comparative study

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Weight loss in individuals with Obesity (O) and Type 2 Diabetes (T2D), may improve glycemic control and weight-related comorbidities, and in some cases, induce diabetes remission. However, body weight control is generally an unmet aim in this population. Thus, there is an increasing need to consider pharmacological approaches to assist weight loss in diabetes-obesity. Glucose-lowering agents as the sodium-glucose co-Transporter 2 inhibitors (SGLT2i) and GLP-1 Receptor Agonist (GLP1-RAs) have been proved to be capable to simultaneously control body weight and glucose levels, and their use has been recommended in individuals with O and T2D. Recently, we demonstrated the efficacy of repetitive Transcranial Magnetic Stimulation (rTMS) in inducing weight loss up to 1 year in O individuals with and without T2D.

Aim of this study was to compare retrospectively the efficacy of SGLT2i, GLP1-RA and rTMS in long-term (up to 1 year) body weight reduction in patients with O and T2D. Data obtained from 31 patients with O and T2D were retrospectively analysed: 11 subjects (bw 98.1 ± 18.3 Kg, BMI 36.8 ± 5.7 Kg/m²) were treated for O with High Frequency tTMS for 5 weeks, 8 subjects (93.4 ± 13.1 Kg, 33.6 ± 3.1 Kg/m2) were treated for T2D with SGLT2i for 1 year, and 12 individuals (98.1 ± 18.3 Kg, 36.8 ± 5.7 Kg/m²) were treated for T2D with GLP1-RA for 1 year. Data relating to bw, BMI, glucose, glycated hemoglobin, cholesterol and triglycerides variations in the 3 groups have been analyzed with ANOVA, after 6 months (FU1) and 1 year (FU2) from the start of treatment. Body weight variation (% between the 3 groups was significant both at FU1 [-13.2 ± 1.8% (SGLT2i) vs -3.5% ± 1.5% (GLP1-RA)] vs -6.2 ± 4.0% (rTMS); P = 0.026] and FU2 [-2.1 ± 2.1% (SGLT2i) vs -2.1 ± 4.2% (GLP1-RA) vs -6.7 ± 4.7% (rTMS); P = 0.017]. As expected, glycated hemoglobin variation was significantly higher in SGLT2i and GLP1-1 RA groups both at FU1 (11.7 ± 25.1% (SGLT2i)) vs -11.9% ± 13.2% (GLP1-RA) vs -8.9 ± 10.4% (rTMS); P = 0.922] and FU2 [-15.9 ± 24.2% (SGLT2i) vs -7.8 ± 11.9% (GLP1-RA) vs -5.6 ± 9.0% (rTMS); P = 0.116], although not statistically significant. In this study, rTMS revealed to be a more effective intervention than SGLT2i and GLP1-RAs in promoting long-term weight loss in a population with O and T2D, probably due to a prevalent effect of rTMS on controlling food craving and appetite at the level of meso-cortico-limbic system. These findings lay groundwork for a potential use of rTMS as an add-on intervention for the treatment of T2D and O.

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P587

GLP-1 and glucagon depict complementary actions on visceral adipose tissue that could mediate metabolic shifts towards catabolism

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Visceral adipose tissue (VAT) metabolic fingerprints differ according to the individual’s BMI and glycemic status. GLP-1 and Glucagon are two hormones that participate in energy homeostasis and glycemic control. Dual GLP-1/Glucagon agonists are a drug class under development for obesity and diabetes treatment. Although the pancreas and the liver are considered major GLP-1 and glucagon targets, these hormones act in other tissues, which could contribute for its effects on glucose balance. Thus, our purpose was to assess how GLP-1 and Glucagon influence VAT metabolic fingerprints according to the individual’s BMI and glycemic status. Subjects (n=19) undergoing ablative abdominal surgery for non-infectious nor oncologic conditions were included in this study. Subjects were allocated into 4 experimental groups according to BMI and glycemic status, namely with obesity and euglycemia (Ob + NGT, n = 5), obesity and pre-diabetes (Ob + Pre-T2D, n = 5), obesity and T2D (Ob + T2D, n = 5). Subjects without obesity or dysglycemia were used as controls (Non-Ob, n = 4). VAT harvested during the surgical procedure was kept in culture media supplemented with insulin (100 nM) and exposed for 48 h to GLP-1 or glucagon at different concentrations (1, 10 or 100 nM). Culture media was then collected for proton nuclear magnetic resonance (1 H-NMR) analysis. In VAT of Non-Ob controls, GLP-1 decreased acetate production (-25.20%, P < 0.05), while in Ob + NGT glucagon increased valine consumption (76.6%, P < 0.05). In VAT of subjects with Ob + Pre-T2D, GLP-1 decreased isoleucine consumption (-99.6%, P < 0.05), but increased alanine (32.6%, P < 0.05) and lactate (43.8%, P < 0.01) production. Glucagon decreased the consumption of isoleucine (−55.2%, P < 0.05) and lactate (−169.2%, P < 0.01), as well as the production of alanine (−28.0%, P < 0.05) and lactate (−54.4%), while increasing pyruvate consumption (10.9%, P < 0.05). VAT of Ob + T2D subjects depicted no changes in metabolite profile after exposure to GLP-1 or glucagon. GLP-1 and glucagon are able to modify VAT metabolic profile, particularly in obesity and pre-diabetes. GLP-1 shifts VAT metabolic profile by decreasing isoleucine consumption and increasing alanine/lactate production, which suggests decreased gluconeogenesis. Glucagon lowers isoleucine and valine consumption, coupled with the decrease in lactate and alanine production, whilst increases pyruvate consumption, which suggests an increase in oxidative phosphorylation. Overall, out data suggests that dual GLP-1/Glucagon agonists’ action in VAT could also contribute for improved glucose balance. Funded by CFT (SFRH/BDE/123437/2016). doi: 10.1530/endoabhs.81.P587

P588

**Influence of diabetes and metabolic risk factors on the outcomes of COVID-19 Vaccination: Scoping Review of the Observational Studies**

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Introduction

Obesity and diabetes are the known risk factors for severity and susceptibility to severe COVID-19 with a poor prognosis. However, there is limited evidence for the implications and association of metabolic factors on COVID-19 vaccination.

Methods

We systematically searched PubMed/Medline and Cochrane library till January 28, 2022, using: (“diabetes OR BMI OR weight OR glucose OR obesity OR metabolic” and “COVID OR Coronavirus OR SARS-Cov-2” and “vaccine OR immunization OR vaccination”). Two independent researchers assessed the literature and conducted the review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines for Scoping Reviews (PRISMA-ScR).

Results

We evaluated four studies (3 from Italy) with cumulative 1380 patients. The mean number of patients was 345 (±521, minimum 21, maximum 1123). One study (n = 84) was only among healthcare workers. COVAC-DM cohort study suggests that humoral immune response to COVID-19 vaccination in diabetes is age dependent but is independent of type of diabetes and glycemia control. CAV.EAT study suggests that hyperglycaemia at the time of vaccination worsens the immunological response and, achieving adequate glycaemic control during the postvaccination period improves the immunological response. Evaluation of the protocols suggests that patients with higher BMI ≤ 30 kg/m² are significantly under-represented in most of the trials. Modulation of the diet to hypocaloric, very-low-carbohydrate diet one week before the mRNA vaccine and blood glucose reduction has a significant positive correlation on the adaptive humoral (anti-SARS CoV-2 antibodies) and cell-mediated responses (IFN-γ). Higher waist circumference, smoking, systemic hypertension and dyslipidaemia are independent confounding variables that lead to lower antibody titres. Diabetes and metabolic risk factors can modulate the immunogenicity of COVID-19 vaccine. Omission or under-representation of participants with higher BMI may cause poorer vaccine coverage for people with higher weight and contribute to greater health inequities.

Discussion

Obesity and hyperglycaemia are associated with a reduced adaptive response to a COVID-19 mRNA vaccine. However, weight loss and metabolic—glycemic improvement may reverse the effect. Inclusion of higher BMI individuals in vaccine trials would yield a comprehensive evidence and help mitigate health inequities and potentially add value for substantial subgroup analysis based on the metabolic parameters and appropriately titrate vaccine dose regimes or earlier vaccine boosters, evaluate safety, and ensure equitable protection for higher weight people against COVID-19.

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P589

Utility of webinars with case-based learning approach in teaching endocrinology to undergraduate medical students during the COVID-19 pandemic

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Background

Conventional methods of one-way teaching may not involve the integration of clinical skills and may become more inefficient and passive [1]. During the COVID-19 pandemic, limited patient interaction and shift to online lectures greatly reduced the clinical exposure and opportunity of developing interpersonal skills for junior medical students. In this study, we hosted online webinars with case-based teaching for medical students so that they can amalgamate clinical skills with patient-based care and systems-based practice.

Methods

Six free webinars were hosted at one-month intervals covering various endocrine topics for first and second-year medical students of Punjab, India. Each webinar started with three endocrine case vignettes containing the patient’s chief complaints, history of present illness, and their clinical course. These anonymised clinical scenarios were derived from real-life patient transcripts. It was followed by a lecture explaining the pathophysiology of that system along with a clinical discussion. Then, students were divided into multiple breakout rooms where the instructors discussed the case vignettes and answered any further queries. Pre-webinar and post-webinar assessment were done using multiple-choice questions which were clinically oriented. Follow-up assessment was also done one month after each webinar to estimate the retention of knowledge by students. Students’ attitudes regarding the usage of webinars and case-oriented teaching as compared to conventional training were ascertained using Likert scale (1 = low, 5 = high) and open-ended questions. Analysis was done using SPSS Statistics v26.0.

Results

72 students filled all the surveys and were included in the analysis. Significantly higher (P < 0.001) improvement in student’s post-session scores after attending each webinar and 1-month follow-up assessment were observed compared to pre-test scores. No significant differences were seen in post-webinar results and one-month follow-up results which is indicative of good retention of knowledge. The majority of the students (67, 93.1%) either strongly preferred or preferred case-based teaching for medical students so that they can amalgamate clinical skills with patient-based care and systems-based practice.

Conclusions

Webinars with a case-based learning approach provide an important utility in simulating endocrinological clinical scenarios and may be used...
as an adjunct/alternative when compared to the traditional one-way teaching methods.

Reference


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P590

Type 1 diabetes on continuous subcutaneous insulin infusion: impact of glycaemic control on quality of life
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Background
In type 1 diabetes (T1D), quality of life (QoL) and the effectiveness of treatment influence each other. QoL has been associated with glycemic control assessed by HbA1c in T1D on continuous subcutaneous insulin infusion (CSI), but data on the relationship between Continuous Glucose Monitoring (CGM) metrics and QoL are scarce.

Objectives
To assess QoL and the association between CGM metrics and QoL in T1D on CSI.

Methods
Transversal observational study of adults with T1D on CSII and CGM. Patients with active CGM time <70%, age >65 years and severe unrelated illness were excluded. QoL was assessed by the 34-item ViDa1 questionnaire, between July-December 2021, after its translation and validation. ViDa1 is divided in 4 independent subscales: 2 positively related with QoL (self-care, wellbeing) and 2 negatively related (interference with life [IWL], concern about the illness). Each score is presented in percentage (0-100%).

Results
56 cases were analysed, with mean age of 34.5 ± 12.6 years, 6.5 ± 5.5 years of CSII and 20.6 ± 10.0 years of diabetes duration. 12.7% had diabetes complications. Mean Glucose Management Indicator (GMI) was 7.2 ± 0.7% (5.8-8.6%). Time in range (TIR) 57.7 ± 14.9%, above range (TAR) 13.8%, below range (TBR) 20.4% for GMI 7-8% and bellow range (TIB) 7.1 ± 5.5%, with mean Coefficient of Variation (CV) of 39.8 ± 7.7%. The obtained QoL subscale’s scores were 71.7 ± 17.0% for self-care, 60.6 ± 19.7% for wellbeing, 27.8 ± 20.4% for IWL and 70.2 ± 20.1% for concern. When questioned, 69.1% reported having overall good QoL. Self-care correlated negatively with GMI (r = -0.42, P = 0.003) and TAR (r = -0.40, P = 0.003) and positively with TIR (r = 0.38, P = 0.004), with higher self-care associated with higher TIR. Wellbeing had similar correlations (r = -0.33, P = 0.011; r = -0.34, P = 0.012 and r = -0.34, P = 0.012), with higher TIR associated with higher wellbeing. Mean IWL differed significantly across GMI range (P = 0.027), scoring 45.5 ± 20.1% for GMI >8% vs 27.7 ± 20.0% and 21.9 ± 18.3% for GMI 7-8% and <7%, respectively. Concern was associated with GMI and TAR, with levels of concern >70% showing significantly higher mean GMI (7.4 ± 0.7% vs 6.9 ± 0.6%, P = 0.034) and TAR (39.1 ± 9.0% vs 28.5 ± 13.8%, P = 0.027). QoL didn’t differ significantly based on TBR or CV. In brief, patients with lower GMI and higher TAR had higher self-care and wellbeing; patients with lower GMI showed lower interference with life and patients with higher GMI and TAR showed higher concern about the illness.

Conclusions
T1D patients on CSII displayed overall satisfactory glycemic control and QoL. Patients with better glycemic control displayed better QoL. TBR wasn’t associated with QoL. These results show that QoL may be more influenced by hyperglycaemia than by hypoglycaemia.

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P591

Systematic review of ongoing clinical trials assessing the comparative therapeutic efficacy and safety of insulin glargine 300 U/ml with insulin degludec
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Introduction
To systematically evaluate the study designs and the outcomes being analysed in the ongoing trials evaluating the efficacy and safety of Insulin Glargine 300 U/ml with insulin degludec.

Methods
We reviewed contemporary protocols of trials that are currently ongoing through WHO-ICTRP (www.who.int/ictrp/search/en), www.clinicaltrials.gov trials registry database. Latest evaluation was on January 28, 2022 with key word ‘insulin glargine U 300’, degludec, for the trials initiated over the last two years (2019-2021). Two researchers independently extracted the protocols and analysed the outcomes.

Results
We evaluated clinical parameters to improve metabolic control and lower risk of hypoglycaemia. We analysed the protocols of the six ongoing trials including, the landmark trials namely PREMIER INSULIN (periperoative non-ICU, n = 180), ULTRAFLIXI (T1DM) are cumulatively recruiting 1416 patients; across Japan (4 trials) and Austria (1 trial) and 1 trial as global multicentric (North America and Europe). The study designs include randomised, parallel, cross-over, designed studies. Three trials are evaluating the comparative efficacy patients in T1DM (n = 110) and other three in T2DM (n = 1300). Insulin glargine U300 along with insulin degludec is being compared with Insulin icercod - a novel once-weekly basal insulin analog. The comparative trials include age range from 7 to 90 years, including a dedicated trial in elderly (n = 30). The mean number of participants being enrolled is 236 (SD ± 425, maximum 1096, minimum 25, 95% CI -210 to 682). The trial duration range from 1 day in post-operative non-ICU setting to 52 weeks. Trials evaluate the glycemic control (Hba1c), time spent in hypoglycaemia in post exercise regimen, mean amplitude of glycemic excursion, nocturnal glucose fluctuation index by flash glucose monitoring, and frequency of hypoglycaemia.

Conclusion
We evaluated emerging outcomes based on clinical, comparative glycemc indices including CGM based precision evaluation parameters, qualitative non-glycemc and quality of life parameters, patient reported outcome comparing Insulin glargine U300 with insulin degludec.

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P592

Risk of developing type 2 diabetes in young adults with a psychiatric disorder: a nationwide population-based cohort study
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Objective
Having a psychiatric disorder may increase the risk of developing type 2 diabetes (T2D) and we aimed to determine whether young adults with a psychiatric disorder have an increased risk of developing T2D.

Research Design and Methods
We conducted a nationwide cohort study to evaluate the association of different psychiatric disorders with the risk of T2D in the young population. Records of 6,457,991 adults aged 20—39 years without a history of T2D were retrieved from database of the South Korean National Health Insurance between 2009 and 2012. Service and followed up for incident T2D cases until December 2018. Five categories of psychiatric disorders were included: schizophrenia, bipolar disorder, depressive disorder, anxiety disorder, and insomnia. Hazard ratios (HRs) and confidence interval (CI) for developing T2D were estimated using Cox proportional hazards regression models.

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Results

Over a median follow-up period of 7.59 years (range 6.47-8.23), a total of 122,603 patients with newly diagnosed T2D were identified. Cumulative incidence of T2D significantly increased with all five psychiatric disorders (P < 0.001). The multivariable-adjusted HRs was 1.146 (95% CI 1.106–1.189) for depression; 1.517 (95% CI 1.319–1.745) for schizophrenia; 1.594 (95% CI 1.413–1.798) for bipolar; 1.226 (95% CI 1.183–1.271) for insomnia; and 1.134 (95% CI 1.07–1.62) for anxiety disorder.

Conclusions

All five psychiatric disorders were associated with increased risk of incident T2D in the young population. There was most significant increased risk of T2D in young adults with schizophrenia and bipolar disorders.

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P593

Hyperglycemia, but not previous diagnosis of diabetes mellitus, is an independent indicator of poor outcome in patients hospitalized for severe COVID-19

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Background

Both diabetes mellitus and hyperglycemia are reported to be strong risk factors for poor outcome(s) in patients hospitalized for COVID-19. However, their relative roles in affecting patient prognosis are under debate.

Aims

To evaluate the independent influence of known diabetes mellitus and hyperglycemia on death/admission to intensive care unit (ICU) in patients hospitalized for COVID-19 during the first wave of SARS-Co-V2 pandemic.

Experimental Design

We retrieved the clinical data/records of the patients admitted with COVID-19 between 23rd February 2020 and 31st March 2020 to the Covid-1 macro-unit of the University Hospital of Parma. Known diabetes was defined by self-reported history, electronic medical records or ongoing medications. The readout of hyperglycemia was fasting plasma glucose at admission. The primary outcome (follow-up: 6 weeks) was a composite of transfer to the Intensive Care Unit or death. Logistic regression analysis was used to identify independent risk indicators of the primary end-point by univariable and multivariable models. We used Receiver Operating Characteristic (ROC) curves to assess the overall predictive power of the different regression models.

Results

757 subjects were included, 143 of whom (19.2%) had known diabetes. Patients with diabetes were older and had more frequently comorbidities associated. The primary outcome occurred in 61.5% of patients with diabetes compared to 43.1% in those without (log-rank test < 0.001). Among variables associated with COVID-19 severity, age, obesity, arterial hypertension, previous CV event, eGFR, glucose levels at admission (but not known diabetes), C-reactive protein and HR-CT visual score of pneumonia extension, were independent risk indicators of poor outcome in logistic regression models undergoing progressively more and more adjustments for potential confounders. The ROC curves showed remarkably good accuracy (up to AUC=0.89) in predicting the primary composite end-point in all models, including the one which used the simplest, most immediate clinical parameters.

Conclusions

Known diabetes indicated poor COVID-19 outcomes, but not when adjusted for other baseline clinical variables and comorbidities, suggesting that its impact was mostly driven by concomitant factors and complications. Fasting hyperglycemia was a powerful and independent predictor of poor outcomes, together with age and biomarkers of inflammation (CRP) and lung tissue damage (HR-CT visual score). The molecular mechanism(s) underlying the tight association between high glucose and poor COVID-19 outcome remain(s) to be elucidated.

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P594

Circulating levels of endothelial progenitor cells (EPCs) and sexual function in fertile women with type 1 diabetes

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Introduction

Female sexual dysfunctions (FSD) are complex conditions characterized by impairment of the female sexual cycle. Higher prevalence of FSD has been found in women with diabetes, as compared with matched healthy controls. Endothelial progenitor cells (EPCs) are circulating mononuclear cells participating in the neoangiogenesis. There is evidence that circulating levels of EPCs are reduced in diabetic patients compared with age-matched subjects. The relationship between EPCs and sexual function during menses in women with diabetes has never been investigated.

Aim

The aim of this study is to assess circulating levels of EPCs in different phases of the menses in young women with type 1 diabetes. The relationship between EPC levels and sexual function will be also investigated.

Materials and methods

Sexually active women, aged 18-30 years, with type 1 diabetes (T1D) and age-matched healthy controls with a stable couple relationship and no oral contraceptive use were included in the study. Blood samples were drawn in the follicular, ovulatory and luteal phases of the same menses to assess sexual hormones levels, including FSH, LH, progesterone and estradiol. EPCs were quantified by flow cytometry. Sexual function was investigated using the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS) during the three phases of menstrual cycle; FSDS was diagnosed by a FSFI score < 26.55 and a FSDS score > 15. Women with hypogonadism, polycystic ovarian syndrome or irregular menses were excluded.

Results

A total of 18 women with T1D and 8 healthy controls were enrolled. Mean age was 25 years and mean BMI was 23.4 Kg/m2. In the overall population FSD prevalence was 7%. There were no differences in sexual hormone levels during the different phases of menses in the 2 groups. The FSFI total score as well as the scores related to desire, arousal, lubrication and pain were lower in diabetic women as compared with those of control subjects. Moreover, circulating levels of CD34+ and CD34+ KDR+ cells EPCs were significantly lower in the ovulatory phase (P<0.05) and ovulatory/luteal phases (P=0.04;P=0.02) respectively in women with diabetes as compared healthy controls. No significant difference was observed in the other EPCs phenotypes.

Conclusion

Young fertile diabetic women showed a worse sexual function and lower levels of EPCs as compared with healthy age-matched women during the different phases of menstrual cycle.

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P595

Somatostatin analogue treatment for hyperinsulinemic hypoglycemia with glucokinase activating mutation (GCK), c.295T>C (p.Trp99Arg)

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Somatostatin analogues (SSA) are used to treat different forms of hyperinsulinemic hypoglycemia (HH) in children and adults and therapeutic effect is achieved by suppressing insulin secretion from pancreatic β-cells by complex mechanisms. These treatments might be associated with several side effects, can even cause the worsening of severity of hypoglycemia. This is a report of the treatment of HH with SSA in patient with Activating Mutation (GCK), c.295T>C (p.Trp99Arg). We
present a 58-year-old male with HH, which was diagnosed at the age of 20 years. However, symptoms of hypoglycemia were present from the postnatal period. Fasting was mainly the trigger for hypoglycemia episodes. Additionally, epilepsy was diagnosed at the age of 10 years and he is currently treated with carbamazepine. At the age of 54 years, the patient underwent genetic testing and a heterozygous variant in Glucokinase (GCK) c.295T>C was confirmed. The severity of hypoglycemia ranged from mild to serious with the lowest glucose of 1.88 mmol/l during fasting. In early adulthood, the patient did not consent to pancreatectomy. At the age of 20 years, diazoxide treatment was introduced. It resulted in decreased both the number and severity of hypoglycemic episodes, however, poor patient compliance was observed in terms of regular medical follow-ups and regular diazoxide intake. In 11.2021 SSA treatment was introduced at the age of 57. At that time, his HbA1c level was 4.1%, fasting glucose level 2.90 mmol/l with c-peptide level 2.1 ng/ml, and insulin level 7 uU/ml. Initially patient received 10 mg short-acting octreotide with a good response. He is now treated with 20 mg octreotide monthly. In self-monitoring mean fasting and after meal glycemia values increased by 20-30 mg%. His most recent 4-h oral glucose tolerance test (OGTT), performed after three months of treatment with SSA, showed fasting glucose level 3.22 mmol/l with insulin level 3.82 uU/ml and c-peptide 1.1 ng/ml. The lowest glucose level (1.58 mmol/l) was observed in 180 min in OGTT. Glucose levels increased by 20-30 mg% with complete remission of hypoglycemia. However, hypoglycemia during OGTT and after meals might correlate with increased self-reported hunger and weight gain as well as no side effects of SSA. The SSA treatment of HH with activating GCK mutation, c.295T>C improved both fasting and after meal glucose levels by 20-30 mg% with complete remission of hypoglycemia. However, hypoglycemia during OGTT and after meals might correlate with increased self-reported hunger and weight gain as well as no side effects of SSA. Therefore efficient treatment with SSA analogues should be combined with the low glycemic diet.

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P596
Transient Refractory Hyperinsulinemic Hypoglycemia
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Fasting hypoglycemia in the setting of hyperinsulinemia typically is persistent and often progressive. We present a case where fasting hypoglycemia with hyperinsulinemia was transient in nature over a fortnight. This occurred in the setting of recurrent seizure-like activity. Seizures are a well known sequela of hypoglycemia; however, the reverse is not nearly as well documented. A 20 year old male with a history of developmental delay, chronic PEG tube, and nonverbal age presented for breakthrough seizures after a 17 year seizure-free period. On day 3 of admission, his fasting glucose levels fell to less than 65 mg/dL. He required D10 infusion, and experienced return of hypoglycemia when D10 was stopped. Labs obtained during a hypoglycemic episode showed blood glucose 47 mg/dL, insulin 12 uU/mL, beta-hydroxybutyrate 0.07 mmol/L, C-peptide 7.9 mmol/L. Sulfonylurea screen negative, and negative insulin antibodies. Octreotide was started in addition to D10 for persistent hypoglycemia. MRI abdomen did not reveal pancreatic lesions and 68 Gallium-DOTATAE PET scan showed normal pancreatic structure. Over a two-week period, octreotide and D10 infusion were slowly weaned off without return of hypoglycemia. During his admission, he underwent EEG assessment, which showed a moderate degree of diffuse or possibly multifocal cerebral dysfunction warranting clinical correlation. True hypoglycemia needs to fulfill Whipple’s Triad. Documented venous hypoglycemia, symptoms consistent with hypoglycemia, and resolution of symptoms with correction of hypoglycemia. In this case, the triad was presumed to be positive based on laboratory evaluation and a report of behavioral changes with hypoglycemia from patient’s parents. Laboratory assessment met criteria for endogenous hyperinsulinemia. Imaging did not reveal a source for excess insulin. He went from requiring D10 and octreotide to being euglycemic off both medications. Critical illness is also implicated in fasting hypoglycemia, particularly in end-organ failure or sepsis. The patient did not have any organ damage to this degree, but there was recurrent seizure-like activity. Status epilepticus causes a massive release of catecholamines, which increases serum glucose. The latter then leads to a large insulin release from the pancreas, which can lead to a period of hypoglycemia. Although clear epileptiform activity was not noted on EEG, the patient’s clinical presentation with seizures raises the possibility that the hypoglycemia was related to recurrent seizures. This case highlights the need to consider epileptiform activity as a cause of hyperinsulinemic hypoglycemia.

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P597
The Impact of Changes to Joint British Diabetes Societies’ Diabetes-Related Ketoacidosis Management Guidelines on Trends of Complications and Outcome
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Background
Serious complications of diabetes-related ketoacidosis (DKA) and its management with fixed rate insulin infusion (FRIII) include hypoglycaemia, hyperkalaemia and hypokalaemia. Revised Joint British Diabetes Societies for Inpatient Care (JBDS) guidelines in July 2021 recommended a reduced rate FRIII of 0.05 units/kg/hour from 0.1 units/kg/hour once blood glucose levels fall to ≤14.0 mmol/l to alleviate the risk of these complications.

Aim
To study the impact on trends of hypoglycaemia, hyperkalaemia, and hypokalaemia in DKA patients prior to and following the JBDS guideline update.

Method
We performed a retrospective analysis of all DKA admissions between February and November 2021 across six hospitals in the UK. Three out of the six hospitals have updated their management guidelines to reflect the new national recommendations. The trends in hypoglycaemia, hyperkalaemia, and hypokalaemia episodes pre- (February to June) and post-guideline update (July to November) was compared.

Results
220 (February-June) and 188 (July-November) DKA admissions were identified. 23 (10.5%) patients experienced hypoglycaemic episodes prior to the guideline update compared to 29 (15.4%) patients post-guideline update (P = 0.116). 55 and 58 episodes of hypoglycaemia were identified pre- and post-guideline update, respectively. 82 (37.3%) admissions pre-guideline update experienced episodes of hyperkalaemia compared to 51 (27.1%) admissions post-guideline update (P = 0.033). Overall, 141 and 142 episodes of hypo- and hyperkalaemia were identified pre-guideline update in comparison to 189 and 72 hypo- and hyperkalaemic episodes post-guideline update. The median DKA duration was 13.5(IQR: 9.0-20.6) hours in February-June vs 14.1(IQR: 9.6-19.7) hours in July-November (P = 0.424). Median length of stay was 4.4(IQR: 2.3-8.2) days in February-June vs 3.4(IQR: 2.0-6.7) days in July-November (P = 0.58) respectively. Lack of awareness and understanding was listed as the reason for minimal changes in complications and outcome post-guideline update.

Conclusion
With an exception a higher number of hypokalaemic episodes was observed after the guideline revision, there was no significant changes in the complications or outcomes of DKA. These findings suggest more work needs to be done in implementing and educating the end-user to improve the anticipated outcomes from the revised guidelines.

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P598
Impact of Bariatric Surgery on the Liver - An Adolescent cohort
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Introduction
Obese patients are at an increased risk of develop nonalcoholic fatty liver disease. Evidence supports that bariatric surgery might have an important impact on hepatic profile in obese adults. Literature suggests that bariatric surgery in adolescents might decrease the prevalence of some comorbidities, but information about its impact on liver profile and steatosis and fibrosis risk remains scarce.

Aim
To evaluate the impact of bariatric surgery on liver parameters and on Hepatic Steatosis Index (HSI, predictor of hepatic steatosis) and AST to Platelet Ratio Index (APRI, predictor of hepatic fibrosis) in adolescents.

Material and methods
We conducted an observational retrospective cohort study in obese adolescents who underwent sleeve gastrectomy in our center between 2013 and 2021. Clinical and laboratory parameters were evaluated before surgery, and at 6 months, 12 months, and 24 months after surgery. The variation after surgery of anthropometric parameters, lipid profile, liver parameters, HIS and APRI were evaluated with paired t-tests.

Results
The population included (n=24) had an average age of 18.0 [17.0; 18.0] years at the time of the surgery, a body mass index of 47.0±5.4 Kg/m² and 70.4% were female. In the pre-operative study, 44.4% used metformin, 37.0% had hypertension, and 48.1% dyslipidemia. Six months after the surgery, there was a clinically significant decrease in weight (127.8±17.5 vs 96.6±16.3 Kg, P<0.01), body mass index (46.9±5.3 vs 34.9±5.2 Kg/m², P<0.01), and percentage of fat mass (47.7±7.6 vs 38.0±12.1 %, P<0.001). There was also a decrease in AST (34.0±22.5 vs 20.0±12.0, P<0.001). HSI score, which predicts hepatic steatosis, was also markedly decreased (60.0±6.7 vs 45.5±7.6, P<0.001). One year after surgery, there was still a noticeable decrease in weight, body mass index, percentage of fat mass and HSI score. There was also an increase of HDL (P=0.03) and a decrease of triglycerides (116.4±57.6 vs 81.7±36.8 mg/dl, P<0.01). After a two-year follow-up period years after the surgery, the reduction of HIS, weight, body mass index, and percentage of fat mass remained significant (P<0.01). There were no statistically significant differences in the hepatic fibrosis score (APRI), AST, ALT, FA, total bilirubin, direct bilirubin, total cholesterol, and LDL levels during follow-up.

Conclusions
Among severely obese adolescents, sleeve gastrectomy is associated with an improvement of steatosis and triglycerides levels, and this might have a long-term impact on the progression of nonalcoholic fatty liver disease.

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P599
Effect of bariatric surgery on metabolic profile – a pediatric cohort
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Introduction
Obesity is a complex multifactorial disease and its prevalence in pediatric age has increased. Obesity prejudices the individual metabolic profile due to the adipotoxicity involved in this condition. Bariatric surgery improves the weight of obese patients along with metabolic comorbidities, being today one of the most effective treatments for obesity. Time of exposure to adipotoxicity appears to be an important risk factor for the development of metabolic complications.

Objective
To assess the impact of bariatric surgery in the metabolic profile of adolescents.

Methods
Observational cohort study in obese adolescents selected to the criteria for sleeve surgery between 2013 and 2021. Clinical and laboratory parameters were evaluated before retro surgery and at 6 and 12 months after surgery. The effects of surgery were used to test the functioning test and the McNemmar test.

Results
The population included (n=24) had a mean age of 17.5 [17.0; 18.0] years at the time of surgery and 70.8% were female. The mean body mass index (BMI) at the time of surgery was 46.0±9.7 kg/m², 45.9% arterial hypertension, 50.0% dyslipidemia and 54.2% used metformin. After 6 months of follow-up, there was a significant reduction in weight (127±20.5 vs 96±17.3 kg, P<0.001), BMI (46.7±5.7 vs 35.6±5.4 Kg/m², P<0.001) and percentage of fat mass (47.6±8.3 vs 39.0±12.0%, P<0.001). At the end of one year, the decrease in weight gain, BMI and percentage of fat mass remained statistically significant. Glycated hemoglobin levels significantly decreased compared to baseline (5.4±0.2%, at 6 (5.2±0.3%, P=0.001) and 12 months (5.2±0.3%, P=0.01). Also, a significant reduction in HOMA-IR was observed, compared to the initial value (5.7±2.6 mg/dl), at 6 (2.3±0.9 mg/dl, P<0.0001) and at 12 months (2.1±1.2, P=0.002) after surgery. These changes culminated in a reduction in metformin use, from 54% to 6% (P=0.05), 6 months after surgery.

Conclusion
These results evidence that bariatric surgery has a beneficial effect on the metabolic profile. Knowing the cumulative effects of obesity, performing this surgery earlier will reduce the time exposed to adiposity and glucotoxicity, and may mitigate the long-term consequences of obesity. Longer follow-up is needed to assess these benefits.

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P600
Estrogen receptors have different functions in Glut4 expression of 3T3-L1 cells
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Diabetes mellitus (DM) is an important cause of morbidity and mortality on a global scale. The pathophysiology of DM involves insulin resistance, even in insulin-treated type 1 DM, which in turn is related to the amount of glucose transporter GLUT4 (Slc2a4 gene). Estrogen activity can be mediated by two distinct receptors (ESR1 and ESR2) and may involve genomic and non-genomic mechanisms. Estrogen has been described as involved in glycemic homeostasis, but the related mechanisms are only now beginning to be investigated. Previous studies conducted by our group have demonstrated that estradiol (E2) can modulate the Slc2a4/SLC2A4 expression in muscle and adipose cells and have suggested that the ESR1- or ESR-mediated effects may be different. The present study seeks to demonstrate the ESR1- and ESR2-induced effects upon the Slc2a4/SLC2A4 expression in adipose cells. Differentiated 3T3-L1 adipocytes were treated with 10 nM E2, 10 nM PPT (ESR1 agonist), 1μM MPP (ESR1 antagonist) and 100 nM DPN (ESR2 agonist) alone, or E2+PPT, E2+MPP and E2+DPN (in the same concentrations), for 24h. Oil Red (OR) staining for analysis of cell differentiation, RT-qPCR for Slc2a4 mRNA quantification and Western blotting for GLUT4 protein quantification were used. Differentiation of 3T3-L1 cells was successfully achieved and similarly preserved after the treatments. E2 and PPT promoted a similar increase (2 to 3 folds, P<0.005) in Slc2a4/SLC2A4 expression; and their association did not induce any additional effect. The presence of MPP or DPN in E2-treated cells abrogates the E2 enhancer effect upon the Slc2a4/SLC2A4 expression (P<0.05). Curiously, MPP alone was capable of reducing (P<0.01) the Slc2a4/SLC2A4 expression as compared to that of control cells (cultivated without E2), suggesting some enhancer effect of ESR1 even in the absence of the ligand. Therefore, E2 increases the Slc2a4/SLC2A4 expression in adipocytes by an ESR1-mediated mechanism; an effect that can be counterbalanced by the hyperactivation of ESR2. These data indicate that the E2-induced and ESR1-mediated effects increase the GLUT4 expression, contributing to the improvement of cellular glucose uptake, which can explain a beneficial effect of estrogen upon glycemic homeostasis. On the other hand, the hyperactivity of ESR2, by repressing the GLUT4 expression, may play a diabetogenic effect.
Results

At metaproteomic, we identified more than 250000 peptides, and 70000 proteins. We were able to identify common features between patients from the same time group. We detected changes associated with an improvement of the gut inflammatory state directly dependent on the diet. Bacterial phylogenetic and functional changes were observed in relation to the dietary intervention, BMI reduction, and adherence to the Mediterranean diet. Both after 6 and 12 months, patients lost weight and contemporarily showed a reduction of fecal SCFA (acetic, butyric, propionic, and lactate) and an increase of the Bacteroidetes/Firmicutes ratio. Acetic acid and butyric acid were also decreased in serum after 6 and 12 months. Functionally, we observed an increase in pectin catabolism. We also identified fecal sugars and amino acid changes associated to the dietary intervention.

Conclusions

This preliminary data confirm that also pediatric obese individuals losing weight reverse their microbiota, increasing their Bacteroidetes/Firmicutes ratio. At the same time, most SCFA were found to be reduced both after 6 and 12 months after the intervention. Observing this, individuals could have an impaired utilization of SCFA that translates into a higher lipogenic effect compared to lean individuals who might better take advantage of the anti-inflammatory role. More intervention studies should be performed in this promising area by utilizing similar innovative techniques.

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P602

Mediterranean Diet and 12 months weight loss result in complex serum metabolic and fecal metaproteomic changes in paediatric obesity

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Background

The relationship between composition and function of microbiota, obesity and nutrition has been increasingly studied and is still a challenge.

Aims

To test whether in a group of 12 pediatric patients with obesity the treatment with a structured hospital and in-home Mediterranean Diet intervention had an impact on gut microbiota composition, function, and metabolitie production, including Short chain fatty acids (SCFAs).

Methods

An untargeted metaproteomics analysis through nano-LC chromatography coupled to high-resolution mass spectrometer (Triple TOF 5600+, Sciex), for the identification of phyla, and GC-MS for the analysis of SCFA and small molecules in serum and stools were carried out. All identified peptides were annotated (UniProtKB database, KEGG) and their functions were identified by UniPep software. Phylogenetic analysis was also performed. Subjects were evaluated at baseline, and after 6 and 12 months.

Binge-eating disorder is the most prevalent eating disorder diagnosed, affecting three times more women than men. It is characterised by binge-eating episodes: the rapid consumption of a large amount of food, without needing the calories. The gut hormone ghrelin stimulates appetite and reward signalling, and loss of its receptor reduces binge-eating behaviour in male mice. We aimed to examine the influence of ghrelin itself on binge-eating behaviour in mice of both sexes. 5-week-old wild-type (WT) and ghrelin-deficient (GKO) mice were housed individually in an indirect calorimetry system for 9 weeks. Binge-like eating in mice given ad libitum chow was induced by time-restricted access to Western-style diet (WD; 2h access, 3 days/week) in the light phase (BE); control groups received ad libitum chow (CO), or ad libitum access to both diets (CW). Food intake, locomotor activity, body composition, and white adipose tissue (WAT) gene expression were assessed. All groups of BE mice showed binge-eating behaviour, eating up to 60% of their 24h intake during the WD access period. Subsequent dark phase chow intake was decreased by 12.4% in GKO mice (P=0.029) and remained similarly decreased, especially in GKO females, on non-binge days (P=0.015). As a result, on binge days, chow comprised a smaller proportion of the 24h caloric intake of GKO BE (48±4%) compared with WT mice (60±2%; P=0.02). This reduction in chow preference was also observed in CW mice (GKO: 3±1%; WT: 8±2%; P=0.029). Compared to males on the same diet, dark phase locomotor activity was increased by 97.6% in CO females (P<0.0001), 107.0% in CW females (P<0.0001), and, on binge days, by 46.0% in BE females (P=0.003). Interestingly, on non-binge days, locomotor activity remained increased in WT females but was reduced to the level of the males in GKO females (interaction P=0.03). Upon sacrifice, GKO BE mice weighed 7.8% less (P=0.001) and had a 2.2% lower lean body mass percentage than WT BE mice (P=0.014). In inguinal white adipose tissue of BE and CW groups, ghrelin deficiency and female sex were associated with suppression of macrophage polarization-regulatory genes, and increased expression of genes that modulate thermogenesis. We conclude that, in contrast to ghrelin receptor deficiency, ghrelin deficiency does not hamper the development of binge-like eating. Moreover, ghrelin deficiency sex-dependently alters food intake timing, locomotor activity, and inguinal white adipose tissue function. These results add to the growing body of evidence that ghrelin signalling is sexually dimorphic.

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**P604**

**Glucocorticoids enhance browning and thermogenic functions of mouse and human adipocytes**

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White adipose tissue (WAT) stores excess energy as triglycerides, while brown adipose tissue (BAT) dissipates energy through heat, acting as a defence against cold and obesity and as a positive regulator of metabolic functions. BAT thermogenic functions are mainly induced by mitochondrion uncoupling protein 1 (UCP-1), which induces uptake of lipids and glucose to sustain oxidation and thermogenesis in both brown and beige adipocytes. Beige/brite adipocytes arise in WAT depots and morphologically and functionally resemble to brown adipocytes. The glucocorticoid receptor (GR) agonist dexamethasone plays an important role in energy homeostasis, regulation of insulin sensitivity, lipid metabolism and adipose tissue distribution. Indeed, in vivo studies suggest that Dex increases the effects on UCP-1 mRNA expression in BAT. However, the role of Dex in adipose browning and BAT function is yet not fully known. Thus, we aimed to assess the role of Dex on browning of white adipocytes and brown adipocyte thermogenic functions. 3T3-L1 murine preadipocytes and human mesenchymal stem cells (hMSCs), isolated from bariatric surgery of lean subcutaneous and visceral adipose tissues, were differentiated into white adipocytes for 9 and 21 days respectively. Browning was induced for 72 h with rosiglitazone (Rosi) and insulin, in the presence or absence of Dex. Our results showed that in 3T3-L1 adipocytes Dex increased both mRNA and protein expression of BAT markers UCP-1, PRDM16, and PGC-1α. Moreover, the GR antagonist RU486 completely blocked Dex-induced mRNA expression of Ucp-1, indicating the involvement of GR on these effects. Dex also strongly enhanced the mRNA expression of the beige markers transmembrane protein 26 (TMEM26) and sirtuin 1(SIRT1), while inhibited the WAT marker Cebpa. Interestingly, oil red O staining revealed that Dex increased the number of small lipid droplets and enhanced iso-induced lipolysis, promoting the expression levels of adipose triglyceride lipase (ATGL) and hormone sensitive lipase (HSL). Furthermore, Dex enhanced mitochondrial biogenesis, determined by staining with MitoTracker, and showed that in 3T3-L1 adipocytes Dex increased both mRNA and protein expression of CPT1α. Our results also showed that Dex enhances the differentiation of 3T3-L1 and human white adipocytes into beige adipocytes, by regulating the expression of genes characteristics of browning and increasing beige thermogenic functions.

**Table 1**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Beginning</th>
<th>3 yr</th>
<th>5 yr</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IG (FBG) &gt; 5.6 mmol/l</td>
<td>15.93%</td>
<td>24.14%</td>
<td>35.71%</td>
<td>0.1</td>
</tr>
<tr>
<td>LDL &gt; 2.7</td>
<td>88.89%</td>
<td>88.89%</td>
<td>80.00%</td>
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</tr>
<tr>
<td>HDL &lt; 1.03</td>
<td>10.53%</td>
<td>10.00%</td>
<td>0.00%</td>
<td>0.07</td>
</tr>
<tr>
<td>TG &gt; 1.7</td>
<td>77.27%</td>
<td>33.33%</td>
<td>60.00%</td>
<td>0.23</td>
</tr>
<tr>
<td>Cholesterol &gt; 4.5 mmol/l</td>
<td>100.00%</td>
<td>85.71%</td>
<td>100.00%</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension BP &gt; 95th centile for age</td>
<td>23.30%</td>
<td>12.50%</td>
<td>23.00%</td>
<td>0.9</td>
</tr>
</tbody>
</table>

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**P605**

The effects of Long-term (five years) prednisone therapy in frequently relapsing nephrotic syndrome of childhood: impact on glycemia and the different components of the metabolic syndrome (MetS)

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Although widely prescribed for their anti-inflammatory and immunosuppressive properties, glucocorticoids have various common metabolic side effects including hypertension, dysglycemia and diabetes.

**Aim**

This study was carried out to investigate the prevalence of different metabolic components and dysglycemia in children with steroid sensitive nephrotic syndrome (SSNS) with multiple relapses for 5 years in relation to the cumulative dose of steroids.

**Methods**

Data of 30 children with SSNS was analysed retrospectively. They received prednisone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. The cumulative dose of steroids over the period of 5 years was calculated for each child. The growth data was recorded along the treatment period. The different metabolic criteria including impaired fasting glucose (IFG), high LDL and cholesterol, lower HD and high blood pressure for age and sex were studied over this period of time.

**Results**

The mean cumulative prednisone = 125 +/- 28 mg/kg/year given over an average duration of 5 years. Obesity (OB) and overweight (OW) increased from 25% pre-treatment to 59.2% after 5 years of treatment. After 3 and 5 years of treatment IFG was found in 24 and 36 % respectively, high LDL in 89% and 80% respectively, high cholesterol in 85% and 100% respectively. Hypertension was detected in 12.5% and 23% of patients after 3 and 5 years of treatment. The mean serum cholesterol and LDL levels were significantly higher than normal in treated children after 3 and 5 years of treatment.

**Conclusion**

Long term prednisone therapy (for 5 years) with a mean cumulative dose of prednisone = 125 +/- 28 mg/kg yr, was associated with increased prevalence of OW and obesity as well as with higher risk of developing hypertension and dyslipidemia.

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**P606**

The ecology of the microbiome in children with congenital generalized lipodystrophy type 4 (CGL4) is quickly modified after metreleptin treatment

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**Introduction**

Lipodystrophy syndromes are characterized by a progressive metabolic impairment secondary to adipose tissue dysfunction and genetic background. The role of microbiota is still uninvestigated.

**Objective**

Evaluate the gut microbiome ecology in relation to dietary and clinical parameters in two infant siblings with congenital generalized lipodystrophy type 4 (CGL4) before and after treatment with recombinant leptin.
The incidence of non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of the metabolic syndrome, continues to rise. NAFLD is associated with significant liver-specific and cardiovascular morbidity and mortality, including hepatocellular carcinoma (HCC). Currently, there are no licensed therapies, highlighting the importance of understanding the pathogenic mechanisms that drive the condition. Cytochrome p450 oxidoreductase (POR) plays an essential role in activation of all microsomal cytochrome p450s (CYPs) by electron transfer. Rodent models of POR deletion develop hepatic steatosis, but the underpinning mechanisms remain poorly understood. The role of POR in human models to modulate hepatic metabolic phenotype has not been explored in detail. We have tested the hypothesis that POR contributes to NAFLD progression through dysregulation of major metabolic pathways using clinical samples from patients with NAFLD and HCC, in vivo rodent models (American Lifestyle-Induced Obesity Syndrome, ALIOS) and human hepatoma cells. In liver biopsies of NAFLD patients, relative POR mRNA expression was significantly lower compared to non-NAFLD controls (P < 0.01). In addition, POR activity as measured by the analysis of urine steroid metabolites, decreased with advancing NAFLD severity (control vs F0-F2, P < 0.01; control vs F3- F4, P < 0.0001). In patients with cirrhosis or HCC, POR activity was also decreased when compared to healthy controls (P < 0.0001). Mice fed the ALIOS diet (12-months) developed significant hepatic steatosis and fibrosis. In both male and female ALIOS mice, POR mRNA expression was significantly decreased in comparison with normal chow-fed animals (P = 0.01, FDR = 0.04). In human hepatoma cells (HepG2), lipid loading was associated with decreased POR expression. To determine the cellular impact of decreased POR expression, siRNA knockdown experiments were performed. RNA-sequencing analysis combined with real-time PCR identified multiple metabolic pathways that were dysregulated. Changes in fatty acid metabolism were indicative of futile cycling with increased expression of fatty acid synthesis (AMPK, ACC, FASN) and oxidation (CPT1A) markers. These findings were endorsed with biochemical analysis demonstrating increased triacylglycerol (P < 0.01) and 3-hydroxybutyrate (P = 0.03) levels in cell culture media, and increased rates of de novo lipogenesis in cellular triacylglycerol (P < 0.01). Moreover, there were significant changes in glucose metabolism suggesting increased gluconeogenesis and reduced glucose uptake. Finally, bile acid synthesis was impacted with increased expression of rate limiting synthetic enzymes and altered cellular bile acid production. Altered POR expression and activity has the potential to contribute to the complex metabolic phenotypes associated with NAFLD. Further studies are needed to determine whether this represents a putative cause or consequence of disease.

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P608

Dysregulation of cytochrome P450 oxidoreductase (POR) in NAFLD and hepatocellular carcinoma; evidence from clinical, rodent and cellular models

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Methods
Two siblings (male, 5.5 years; female 2.5 years) with CGL4 caused by a new homozygous PTRF mutation (NM_012232 exon1:c.T21A;p.Y7X) were identified and followed after the starting of leptin treatment. We collected aaxiological, metabolic, nutritional parameters, and stool samples at baseline and every 3 months. Two baseline stool samples were pooled. DNA was extracted directly from 0.25 g of stool using the QIAamp PowerFecal Pro DNA Kit. DNA was amplified with primers for V3 and V6 regions of 16S rDNA, tagged with Multiplex Identifier sequences using Microbiota Solution II Kit optimized for Illumina MiSeq sequencing. Raw FastQ sequences were analyzed using MicrobiAT Software. Statistical analyses were performed using MicrobiomeAnalyst and R software.

Results
At baseline, reduced subcutaneous fat, muscular hypertrophy, distinct facial features, myopathy, atlantoaxial instability were observed. Stature and BMI were normal. Blood tests showed elevated CK, mildly elevated levels of liver enzymes and triglycerides, low leptin and adiponectin levels. Fasting glucose and HbA1c were normal; HOMA-IR was mildly elevated in the female, and continuous glucose monitoring often detected glucose higher than 180 mg/dl after meals in male. They were hyperphagic, mainly for foods in fats and sugars. The 2 subjects showed a Bacteroides enterotype (F/M): 46%/44% Bacteroidetes, 49%/42% Firmicutes, 0.02%/0.04% other Bacteria, 3.2%/1.9% Archaea, 0.0001%/0.00002% Actinobacteria, 0.7%/0.4% Proteobacteria; 0%/11% Verrucomicrobia. Treatment with metformin was started at standard dose according to age and weight. All the metabolic parameters and hyperphagia improved, and they were more adherent to dietary indications. The male subject lost 0.8 kg after 3 months, female weight was stable. We present microbiome ecology after 3 months of treatment demonstrating increased alpha-diversity in both children. Ecology was modified (P < 0.006) with a reproducible signature with decreased and increased relative abundance of species linked to metabolic homeostasis.

Discussion
These preliminary results highlight as dietary adherence and leptin treatment were followed up with Endocrine. 18.3% of these patients were classified as increased cardiovascular risk, with 9% of patients having to have plasmapheresis. With regards to continued on insulin therapy (11% were on IV insulin only for management of diabetes secondary to alcohol use (it was unclear whether these patients were referred to alcohol liaison services). Only 4% of these patients were referred to endocrine after screening for diabetes highlighting a significant gap in secondary screening. 34.7% of these patients underwent screening for familial hypercholesterolaemia and were referred to a specialised lipid clinic. Our audit highlighted the gap in management of patients getting followed up in primary care vs being admitted in the hospital. The authors felt that dual guidelines emphasizing on discharge based planning from hospital and a more secure safety net for patients with significant cardiovascular risk is needed. A GP guided approach with early referrals to lipid clinic/endocrine may achieve positive outcomes in such cases.

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P609
Modern method of diagnosing of cerebral microangiopathy in patients with diabetes mellitus type 2 by doppler ultrasound
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Background
To identify opportunities for Doppler ultrasound in the diagnosis of cerebral microangiopathy in patients with diabetes mellitus type 2 and hypertension.

Methods
The study included the diagnosis of 72 patients with type 2 diabetes and hypertension who were hospitalized in the 2 and 3 clinics TMA. The control group consisted of 25 patients aged 61.9 ± 2.6 years, suffering from type 2 diabetes. The study group included 47 patients (19 men and 28 women), older age groups with diagnosed type 2 diabetes and hypertension history, besides the patients of the second group were divided into two groups - those with diabetes complications flow - 23 patients without microvascular complications - 24 patients. Time monitoring of patients ranged from 3 to 8 years. All patients underwent Doppler ultrasound of the main arteries of the head and neck - the internal carotid artery. Evaluated the speed of blood flow indices, the PI index (which determines the stiffness and elasticity of the arteries), the RI index (reflecting peripheral resistance), systolic and diastolic index (the ISD), assessed cerebrovascular reactivity (according to tests with breath-holding and hyperventilation).

Results
Changes dopplerographic index in the BCA were observed in 19 patients in the subgroup with diabetes complications compared with 2 patients of the subgroup without complications. In the subgroup with diabetes complications 21 patients had signs of nephropathy and in 18 of them were identified changes in dopplerographic indicators BCA, which may indicate vascular remodeling processes in the body of patients with type 2 diabetes. Significant moderate and strong correlation LED current duration of type 2 and the presence of diabetic retinopathy and nephropathy, altered dopplerographic indices PI and RI. So a critical increase in the ICA RI index was observed after 6.8 years after the diagnosis of type 2 diabetes. It was revealed that the predictors of microcirculatory disorders in patients with type 2 diabetes mellitus were the duration of 8 years. It is shown that microcirculatory disorders, diagnosed by means of ultrasound diagnostics, develop an average of 7 years after the onset of diabetes. Changes in dopplerographic indices were observed mainly in patients with type 2 diabetes complications. At the same time in all patients with a diabetes study group for the duration of 2 years, more than 7 marked changes in cerebrovascular reactivity by reducing vasodilatation reserve.

Conclusions
These results suggest that Doppler ultrasound diagnoses cerebral microangiopathy in patients with type 2 diabetes.

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P610
Impact of the COVID-19 pandemic on diabetic foot
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Introduction
The COVID-19 pandemic has presented many challenges in the management of diabetics around the world. While many people can be managed using new methods such as tele-consulting, the diabetic foot presents unique challenges due to the frequent need for “face-to-face” consultation and treatment. The pandemic has thus made the management of diabetic feet, already complex, even more difficult. This study aims to assess the impact of the COVID-19 pandemic on the diabetic foot.

Methods and results
It’s a retrospective study conducted at the endocrinology and diabetology department of the Ibn Rochd University Hospital, including patients who consulted in the emergency room for diabetic foot ulcer starting from the announcement of confinement in March 2020 until September 2021. Our study included 340 patients. The average age was 59 years, 62.35% were male and type 2 diabetics accounted for 93.23% with an average duration of diabetes of 12.3 years. Among the patients, 64.7% were on insulin, 22.6% on ADO and 7.3% on mixed treatment. Patients at very high cardiovascular risk represented 46.7% of which 6.9% were followed for ischemic cardiomyopathies and 40.8% for peripheral arterial disease. About microangiopathy, 27.3% had diabetic retinopathy and 25.3% diabetic kidney disease. Compared to the years 2018-2019, the number of patients who consulted was 1.9 times higher, the number of ulcers and cellulitis was 32.9% each, i.e. 6.8% more ulceration and 4% more cellulitis. The percentage of necrotizing fasciitis also increased by 18.4% as well as dry gangrene (22.6% vs 17%). 39.7% had to be referred for immediate surgical management due to the advanced stage of the lesions, which was 5.7% higher than in previous years. This increase in the number of emergencies was contrasting with a decrease in the number of outpatient consultations because of confinement.

Conclusion
The severity and increasing of the diabetic foot ulcers observed during the period of COVID-19 confirms the need for appropriate and rapid management to avoid dramatic results. Telemedicine and the use of new technologies are needed to provide optimal wound care while minimizing the exposure risk.

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P611
Influence of dopamine receptor d2 and dopamine transporter polymorphisms in angiopathy in patients with type 2 diabetes mellitus
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Introduction and Aim
Dopamine receptor D2 (DRD2) polymorphism (rs1800497) appears to be associated with increased susceptibility to the development of type 2 diabetes mellitus (T2DM). The dopamine transporter (DAT) determines dopamine signalling, responsible for the reuptake of its active form from the synapse. Polymorphism in the DAT gene (rs2836317) can increase dopamine reuptake in the synaptic cleft. However, its association with T2DM is still controversial. This study aimed to evaluate the relationship between genetic polymorphisms of DAT and DRD2 and the susceptibility to the development of angiopathy in T2DM and its influence on the biochemical parameters.

Design and Methods
150 patients with T2DM were divided into: G1: 75 patients with angiopathy and G2: 75 patients without angiopathy. The DRD2 and DAT polymorphism were determined by endpoind analysis method and PCR, respectively. Blood levels of malondialdehyde (MDA), ascorbic acid, homocysteine and cysteine, vitamins B6 (vit.B6), B12 (vit.B12) were measured by HPLC methods, and standardized methods determined the other biochemical parameters. Statistical analysis was performed using SPSS with statistical significance for P<0.05.

Results
There were differences only in the DRD2 polymorphism between G1 to G2 (P=0.016). Carriers of allele A of DRD2 had a 3.18-fold increased risk as compared with non-carriers (OR=3.18 [1.40-7.21], P=0.006). Analyzing the relationship of biochemical parameters between groups was found an increase in systolic blood pressure (SBP) (P=0.023), M AD (P=0.010) and retinol (P=0.011) in G1. Regarding DRD2 polymorphism, there was an increase in HDL cholesterol (HDL-C) (P=0.035) for genotype GG and of vit.B12 in carriers of the allele G (P=0.013). For DAT polymorphism, it was found an increase in weight (P=0.042) and waist circumference (P=0.050) and a decrease in ascorbic acid (P=0.039) for genotype 10/10 and an increase in LDL cholesterol (LDL-C) (P=0.027) in genotype 9/10. Biochemical parameters were compared between groups, but dividing the population by the studies polymorphisms, for DAT it was found higher values of SBP (P=0.014), triglycerides (P=0.019) and retinol (P=0.031) and lower HDL-C values (P=0.050) for carriers of allele 10 in G1; for DRD2 it was found in carriers of the allele A, higher values of homocysteine (P=0.038), cysteine (P=0.035) and retinol (P=0.007) and in the genotype GG higher values of SBP (P=0.020) and triglycerides (P=0.011) in G1.

Conclusions
DRD2 polymorphism appears to influence susceptibility to angiopathy in T2DM patients directly. DAT and DRD2 polymorphism may modulate disease-associated biochemical parameters.

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An Experience of Insulin Basal Titration in Lombardy (Italy) during the Pandemic

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Introduction
Correct titration of basal insulin is one of the most important conditions allowing Type 2 Diabetes Mellitus patients to reach correct and personalised fasting plasma glucose. The persistence of the pandemic, together with the persistence of the SARS-CoV2 virus made titration process more complex, and pushed the Lombardy diabetologists to develop solutions which could be handled by the patient independently, or with the remote online assistance of diabetes team.

Patients, materials and methods
The Lombardy diabetologists participating in a training program shared their titration experiences of degludec insulin and its association with liraglutide (DegLira). These physicians collected aggregated data of 387 subjects with T2DM (W:60%; M: 40%); homogeneous distribution in age groups 50 and 65 (31%); 65 and 75 (32%), and over 75 (28%), with 9% of the patients below 50, duration of illness <5 years (13%), 5 and 10 years (17%), 10 and 20 years (39%), over 20 years (29%). The patients had not adequate glycemic control (90% with HbA1c >7.0%) with overweight or obesity (84.5% with BMI ≥25 kg/m2). Degludec was introduced for 129 patients, DegLira for 258, titration was set up through modifications recommended by the diabetes team (244 patients); through the program “Titolando” (www.titolando.it) (132 patients); with no education to titration (11 patients).

Results and discussion
Thanks to the diabetes centres support, the patients reached an adequate FPG (average 174.7 mg/dl at baseline; 122 mg/dl after 6.1 weeks of controlled titration, increase of basal insulin dose by 4.7 U/die); the self-titration with the program “Titolando” obtained overlapping results (average FPG 178.5 mg/dl at baseline; 127 mg/dl after 7 weeks of self-managed titration, increase of basal insulin dose equal to 7U/die). Less satisfactory the evolution of FPG in those who have independently modified the dosages of basal insulins (average FPG 199 mg/dl vs 140 mg/dl at six months follow-up, with increase of 5.9 U of daily doses). The main limit and drawback of this retrospective observation consists in the fact of not having collected hypoglycaemia episodes.

Conclusions
During the pandemic, the remote support by Lombardy diabetes centres allowed to obtain satisfactory FPG after introduction of Degludec or DegLira. Similarly, the purpose of self-titration led by the “Titolando” program proved adequate, easy to understand and manage, and such as to offer a valid alternative in all the situations where it is not possible to provide clinical regular feedback to patients who are in therapy with basal insulins.

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Use of continuous glucose monitoring for treatment adjustment in type 2 diabetes patients

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Continuous Glucose Monitoring (CGM) is proved to be useful for dose adjustment in patients treated with multiple insulin injection regimens or with continuous subcutaneous insulin infusion. CGM give precise information about glucose variability in type 1 diabetes but are rarely used in type 2 patients. We assessed continuous glucose monitoring systems (CGMs) as control assessment tool in patients with type 2 diabetes receiving different treatment regimens. We studied 85 patients (50 men, 35 women; mean age 43.93 ± 10.87 years, mean disease duration 21.91 ± 6.07 years) with type 2 diabetes (31 receiving non-insulin preprandial GLP-1, treated with pre-mixed insulin; 21 with multiple insulin injections. Continuous glucose monitoring by using ProTM was performed for seven days and HbA1c was measured at the end of this period. High positive correlation was found between HbA1c (7.46 ± 1.19%) and average glucose level during CGM period (7.47 ± 1.57 mmol/l) (r=0.73), and percentage of time spent with glucose above 7 mmol/l (38.26 ± 26.38%, Z <0.05, r=0.69). There was similar but negative correlation between HbA1c and percentage of time within the limit 3.9-7.8 mmol/l for all groups (56.07 ± 24.28%, Z <0.05, r=−0.63). Comparing CGM results in different treatment groups we found similar correlations of HbA1c and percentage of time spent within limit (non-insulin treated group 55.65 ± 25.99%, phi2 = 0.48; pre-mixed insulin treated group 54.33 ± 24.85%, phi2 = 0.67; intensified insulin treatment group 59.62 ± 21.36%, phi2 = 0.58). No correlations were found between HbA1c and number of all, positive and negative excursions. These results do not differ for age and gender. We conclude that performing CGM in patients with type 2 diabetes could give more precise information about the overall control nevertheless short time reflected and could present details about glucose deviations and hypoglycemic episodes and thus be useful for current treatment adjustment.

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Dopaminergic system and adipose tissue: in vitro effect of cabergoline on white, brown and beige adipogenesis and lipogenesis in human subcutaneous adipose tissue

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Adipose tissue is an endocrine organ releasing adipokines and expressing specific markers and intracellular mediators, which regulate whole-body energy by balancing lipid accumulation and utilization through adipogenesis, the differentiation of preadipocytes into mature adipocytes associated with gradual lipid storage, and lipogenesis, the additional lipid accumulation in mature adipocytes. Adipogenesis and lipogenesis, strongly induced by insulin, occurs in white adipocytes, specialized in excess energy storage as fat depots, and in brown and beige adipocytes, specialized in energy storage dissipation. Decreasing white and increasing brown and beige adipogenesis and lipogenesis, may represent therapeutic tools for obesity. This study aims at investigating the effects of the dopamine agonist cabergoline (CAB) on white, brown and beige adipogenesis as well as on basal and insulin-induced lipogenesis. At this purpose, CAB (10^-7 to 10^-6 M) was administered in 3T3L1 preadipocytes induced to differentiate, in order to evaluate its effect on white, brown and beige adipogenesis, and in white, brown and beige mature 3T3L1, in order to evaluate its effect on lipogenesis. Adipogenesis and lipogenesis were investigated measuring lipid accumulation using Oil red O staining. Messenger and protein levels of leptin, adiponectin and PPARy, as white adipogenesis markers and mediators, and of UCPI, PPARy and PKA, as brown lipogenesis markers and mediators, were analyzed by RT-qPCR and/or WB. During white adipogenesis, CAB10^-4 M and 10^-6 M significantly inhibited lipid accumulation (27-37%; P <0.05) and lipogenesis in absence (63-64%; P<0.001) and presence (85-51%; P<0.0001) of insulin administration, compared to controls, with significant decrease of leptin protein and messenger levels (P<0.01), slight increase of adiponectin protein and slight decrease of PPARy protein. During brown adipogenesis, CAB10^-4 M-10^-6 M slightly stimulated lipid accumulation (18-24%) and lipogenesis in presence of insulin (15-30%), compared to controls, with slight increase of UCPI and PPARy messenger and PPARy and PKA protein levels. Finally, during beige adipogenesis, CAB10^-4 M-10^-6 M slightly inhibited lipid accumulation (34-38%) and lipogenesis (38-43%), with slight increase of UCPI and PPARy messenger levels. In conclusion, the current study demonstrated a novel CAB effect on adipose tissue modulation, defining a pivotal role of dopaminergic system in the obesity pathophysiology.

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Is age-related hepatic elevation of endogenous SERM 27-hydroxycholesterol associated with hepatocellular degeneration female-specific? — Results from Rat study

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The cholesterol oxidation product 27-hydroxycholesterol (27OHC) is enzymatically produced from cholesterol by CYP27A1 in an alternative pathway of cholesterol degradation to bile acids. This oxysterol also acts as an endogenous selective estrogen receptor modulator (SERM). In healthy humans its concentration in circulation increases in hypercholesterolemia and with age, and is associated with increased risk of atherosclerosis, cardiovascular diseases and breast cancer. Several drugs with SERM activity used for treatments of breast cancer or osteoporosis have been reported to have sporadic hepatotoxic effects. Women suffer from liver diseases more prominently (acute liver failure, autoimmune hepatitis, benign liver lesions, or primary biliary cirrhosis). For all of these the incidence increases with advancing age. To the best of our knowledge, there is no information in the literature, clinical or experimental, relating changes in hepatic 27OHC with incidence of liver disease in the context of aging and sex. To address this problem, we examined the effect of age and sex on liver and serum concentrations of 27OHC, as well as the immunostaining pattern of CYP27A1 in the liver of four-month and 24-month-old Wistar rats (experiments were repeated twice with similar results, n=5-6 animals/group) using LC MS/MS and immunohistochemistry, respectively. Furthermore, we examined changes in total cholesterol and concentration in liver and serum, liver histopathology, as well as serum concentration of hepatic enzymes, alanine (ALT) and aspartate aminotransferase (AST). The effect of age (P<0.05) on increase of serum and hepatic 27OHC was obtained both in males and females (P<0.05) and followed the same pattern of age-related total cholesterol increase (P<0.05). However, the intrahepatic increase of 27OHC was dramatically more pronounced only in old-aged females (P<0.0001). CYP27A1 immunostaining intensity was similar in all experimental groups, being the strongest in the cytoplasm of centrilobular hepatocytes, but the immunopositivity was diffusely spread throughout the liver lobule. Histopathological analysis revealed age-related hepatocellular degeneration (swelling and hydropic degeneration, increased fraction of binuclear hepatocytes and focal fatty changes) only in females. Moreover, age-related elevation of alanine transaminase (ALT) was observed only in female rats (P<0.01). In conclusion, the obtained results confirmed age-related female-specific increase of hepatic 27OHC as well as hepatocyte degeneration observed only in the liver of rat females. These age-related adaptive changes in cholesterol metabolism may attenuate hepatoprotective estrogen-like effects in the liver.

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Ketogenic diet is protective against atherosclerosis development in ApoE−/− mice (ApoE KO). Ketogenic diet (KD) positively impacts several cardiovascular risk factors, yet its effect on atherosclerosis, is elusive. We hypothesize that, KD protects from development of atherosclerotic plaques in ApoE KO mice, a murine model of atherosclerosis.

Methods

Eight-week-old male ApoE KO mice were fed an ad libitum KD (90.5-fat, 0.4-carbohydrate, 9.1-protein; n=12) or a moderate high fat diet (HFD) (42-fat, 42.7-carbohydrate, 15.2-protein; n=12) and treated with aldo-(6 μg/mouse per day) or vehicle through osmotic mini-pumps. Cholesterol content was comparable in KD and HFD. After 4 weeks of treatment, intraperitoneal glucose tolerance test was performed, and peripheral blood samples were collected and used to quantify beta-hydroxybutyrate (OH-But). At the endpoint, mice were euthanized and their cryosections of embedded aortic root were used to quantify the atherosclerotic plaque size, lipid and collagen content in all experimental groups. Vascular inflammation was assessed in specimens of thoracic aorta through mRNA analysis of pro-inflammatory (ICAM-1, VCAM-1, IL-6, TNF-α and MCP-1) and anti-inflammatory (Arg-1, RETNLA, CCL5) genes.

Results

In ApoE KO mice treated with aldo, KD determined a significant improvement in glucose tolerance compared to mice fed a HFD without any significant effect on body weight. OH-But levels were always significantly higher in KD-mice than in AD-mice, confirming nutritional ketosis in KD-mice. Histological sections of aortic root showed that aldo treatment determined a significant increase in atherosclerotic plaque size and lipid content in HFD-mice. Such effects were significantly reduced in KD mice, suggesting a positive impact of ketosis in the prevention of atherosclerosis development. Plaque fibrosis, as measured by collagen content, did not differ among treatment groups. Finally, we observed a significant reduction in vascular inflammatory markers in KD-mice, when compared to AD mice. In particular, KD determined a significant reduction of gene expression of pro-inflammatory markers (ICAM-1, VCAM-1, IL-6, TNF-α and MCP-1) with the concomitant up-regulation of anti-inflammatory markers (Arg-1, RETNLA, CCL5), compared to AD.

Conclusion

The present study identifies KD as a potential non-pharmacological approach to prevent the development of atherosclerotic disease in subjects with high cardiovascular risk. Indeed, we demonstrated that KD decreases vascular inflammation and reduced atherosclerotic lesions in ApoE KO mice.

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place of plasma injections rich in autologous platelet in the management of diabetic foot ulcer (preliminary results)

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Introduction

Diabetic foot ulcer (DFU) is one of the leading causes of non-traumatic lower extremity amputations worldwide. Conventional treatment is expensive and often requires a long hospital stay, placing a heavy burden on any healthcare system. Using autologous platelet-rich plasma (PRP), which is rich in various growth factors, can approximate the natural healing process.

Objective

Evaluate the place of PRP injections and its interest in the management of DFU.

Material and methodology

Prospective descriptive study including 21 patients hospitalized in the endocrinology department of the Ibn Rochd UTH in Casablanca for DFU, having received PRP injections, from September 2016 to September 2019. We excluded those with positive hepatic or HIV serologies and hemostasis disorders.

Results

The mean age was 56 years (34-75 years). A male predominance with an M/F sex ratio of 1.5. The average duration of diabetes was 13 years (3 to 30 years). The mean HbA1c was 10.9% (8.6-14.9%). The majority (86%) had grade 2 feet according to the TEXAS classification. The patients benefited from 4 to 7 sessions of PRP injections at the rate of one per week. The evolution was marked by good

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healing in 92% of patients with budding and epidermization. No incident of blood or infection were noted.

Conclusion
PRP injections offer a promising alternative in the management of DFU. It is less expensive, less invasive, promotes safe and natural healing by reducing healing time. This is a method of the future taking place in the therapeutic arsenal of DFUs.

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Impact of teaching communication techniques to family member on quality of life score in patients with T2DM
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Introduction
Impact of teaching communication techniques to family member on quality of life score in people with T2DM.

Communication holds an important place in Diabetes management. People with diabetes usually have low self esteem. Proper communication with them can help in improving quality of life of people with diabetes. Family plays an integral part in Diabetes management. Benefits of proper communication has long been seen in various studies.

Aim
To see the Impact of teaching communication techniques to family member on quality of life score in people with T2DM.

Method
234 patient with diabetes were selected from Central India. They were divided in two groups of 117 each. Family members of one group were taught about communication techniques (called communication group) along with standard treatment while the second group was treated as such. The patients were surveyed for Quality of life and Depression at 30 days and 90 days. Results were analysed using MS excel.

Results
The Communication Group showed a decrease in Depression and improved quality of life score as compared with routine group. (P<0.0001), the communication group also showed better disease control (Target HBA1C <7 % in 72 % vs 43 % in routine group)

Conclusion
Communication is an integral aspect in Diabetes Care and most of the times it’s with family members. The family members should be taught proper Communication techniques for better outcomes in terms of quality of life in patients with Diabetes. A guideline should be set in place to make communication a core part of overall Diabetes Management. The family members should be motivated to be a part of communication technique programs to improve their communication.

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Injection of epidermal growth factors in the treatment of diabetic foot ulcers
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Introduction
Diabetic foot ulcer (DFU) is one of the major complications of diabetes mellitus. It can be a cause of amputation. A multidisciplinary approach is essential to promote wound healing and decrease amputation rates. Epidermal growth factor (EGF) is used as an adjuvant to close the wound in addition to standard care in diabetic foot ulcers.

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Phase angle, a raw bioelectrical impedance analysis (bia) variable, as a prognostic factor for mortality at 90 days in patients with covid-19
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Introduction
COVID-19 has taken on pandemic proportions. Phase angle (PhA) and Standardized phase angle (SPhA) have been related to mortality and severity in several diseases.
Disturbances in melatonin, leptin and ghrelin rhythms in women with metabolic syndrome with and without polycystic ovary syndrome

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Background
Polycystic ovary syndrome (PCOS) is a highly prevalent heterogeneous disease associated with ovulatory dysfunction and hyperandrogenemia. Recent data support a critical role of neuroendocrine dysfunction and metabolic disturbances in the pathophysiology of the syndrome, including hyperleptinaemia. Accumulating evidence suggests that circadian desynchrony is linked to obesity and metabolic syndrome (MetS). Both prevalence and incidence of the metabolic syndrome is very high in women with PCOS.

Objective
To examine daily fluctuations in serum levels of melatonin, leptin and ghrelin in women with PCOS and MetS

Patients and methods
The study included 12 women with PCOS and MetS and age-and BMI-matched 12 women with MetS without PCOS. The diagnosis PCOS was made according to the Rotterdam criteria. MetS was verified against IDF criteria (2009). Anthropometric measurements and circulating levels of melatonin, leptin and ghrelin at 3AM and 8AM, fasting insulin, fasting blood glucose, cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels were evaluated. Statistical analyses were performed using SPSS Ver. 26.0. A P-value less than 0.05 was considered statistically significant.

Results
Women with PCOS and MetS had significantly higher levels of 8AM leptin (P<0.02), fasting insulin (P=0.05) and HOMA-IR (P=0.05) compared to the patients with MetS only. In both groups we did not find significant difference between day and night melatonin and ghrelin levels. In women with PCOS and MetS we found significant difference between day and night leptin levels (P=0.37) while such difference was missing in women with MetS only. In both groups there was preserved cortisol rhythm.

Conclusions
Our results indicate that leptin is increased, but with preserved circadian rhythm in women with PCOS. Circadian misalignment of melatonin and ghrelin rhythms might be associated with metabolic dysregulation in women with PCOS and metabolic syndrome.

Key Words
PCOS, Metabolic syndrome, Leptin, Ghrelin, Melatonin Rhythm

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Table

Steroid-associated adverse events (SAAE) include hypertension, hyperglycemia, and diabetes, overweight and obesity and short stature.

Aim
The goal of this study was to assess the occurrence of steroid-associated metabolic and clinical adverse events (SAAE) in patients with NS and frequent relapses treated with long-term prednisone compared to another high-risk group (obese children BMISDS > 2)

Methods
Data of 30 children with SSNS was analysed retrospectively. They received prednisolone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. The cumulative dose of steroids over the period of 5 years was calculated for each child.

Conclusion
In children with SSNS and frequent relapses, long-term steroid therapy was associated with higher rate of obesity, short stature as well as the occurrence of
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The action of WAY163909, central selective serotonin receptor, in obese and diabetic Wistar rats

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Background and aims

Obesity can be cause because of reduction in energy expenditure and/or increased caloric intake. Total caloric intake has increased in recent decades and studies on eating behavior have reported increased intake of foods rich in fats and sugars. Many regulatory pathways for food intake, including those that use serotonin as a neurotransmitter, are affected by obesity or by hypercaloric diets. Summarizing the data known so far, it can be said that reduced serotonergic signaling and low availability of SERT are associated with hyperphagia and obesity. In addition, obesity has increased eating motivation and decreased D2/3 receptor binding, and lower DAT binding can be detected as well. Because of these facts, it is important to know brain serotonin mediation.

Materials and methods

WAY-163909 is a novel 5-hydroxytryptamine (5-HT)2C (serotonin) receptor-selective agonist that we used in our study. We used forty Wistar rats separate in 2 groups-rats with obesity and diabetes and healthy rats (control group). Each of this groups was separated in other 2 - one with daily intraperitoneal injection (i.p.) of WAY-163909 (for 1 mg/kg increasing till 32 mg/kg, 1 mg/kg per day) and one without. In 4 weeks period we were tracking blood glucose level, insulin secretion and rats weight. The differences in the mean values among the groups are greater than would be expected by chance; there is a statistically significant difference (P<0.001) using SPSS program.

Results

It was shown that after application of WAY-163909, the weight of the rats in diabetic and obese group rats decreased by 55.2% (P<0.05), and by 25.3% (P<0.05) in the control group using and no significant dynamic in the groups without WAY-163909. In the diabetic and obese rats group in which WAY-163909 was applied we had registered reduction of hyperglycemia (blood glucose over 7.0 mmol/l) by 35.4% (P<0.05) comparing the results before the start of using WAY-163909, which is greater in the rats which reduce more body weight. The research also shows decreasing of insulin resistance by 42.3% (P<0.05) in diabetic and obese rats group using WAY-163909.

Conclusion

Using WAY-163909 for treatment of obesity and obesity-induced diabetes in male Wistar rats, WAY-163909 significantly reduces body weight hyperglycemia and peripheral insulin resistance. In the study was registered reduction of body weight not only in the obese and diabetic rats group, but also in the control group.

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The role of endocrine disruptors, obesity, and cytokines in PCOS

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As genetic and environmental components contribute to the PCOS expression, we compared levels of endocrine disruptors, steroid hormones, cytokines, and metabolic parameters in twenty healthy, nine normal-weight PCOS women, and ten obese PCOS women. Steroid hormones, bisphenols (BPA, BPS, BPF, BPAF) and parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-parabens) were measured by liquid chromatography-tandem mass spectrometry. Differences between the groups were assessed using the Mann-Whitney U test. Spearman correlation coefficients were calculated for the individual parameters relationship. Significantly higher levels of BPA, Anti-Mullerain hormone, lutropine, lutropine/folitropine ratio, testosterone, androstenedione, 17β-OH-epiandrosterone, and cytokines (IL-6, VEGF, PDGF-bb), were found in normal-weight PCOS women compared to controls. In PCOS women concerning the weight, there were no differences in hormonal, but in metabolic levels. Obese PCOS women had significantly higher insulin resistance, fatty-liver index, triglycerides, cytokines (IL-2, IL-13, IFN-γ). In healthy, but not in PCOS, women, there was a positive correlation of BPA with testosterone, SHBG with lutropine, and follitropine, while testosterone negatively correlated with SHBG. In obese women with PCOS, insulin resistance negatively correlated with SHBG and estriol. No differences were observed in the paraben exposure. Levels of BPA were higher in PCOS women, indicating its role in the etiology. Obesity significantly worsens the symptoms.

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P626

MODY 6: To be, or not to be, that is the question

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Introduction

Maturity-Onset Diabetes of the Young (MODY) is a rare cause of Diabetes Mellitus (<5%), resulting from autosomal dominant monogenic defects.

NEUROD1 gene is expressed in pancreatic and neuronal cells, being associated with MODY type 6. Mutations in NEUROD1 gene are reported in 20 families worldwide to date. Heterozygous variant c.616C>A p.(His206Asn) has never been described.

Case Report

The authors report a case of a 38-year-old woman, with normal BMI, medical history of Hashimoto’s thyroiditis and family history of presumed Type 2 Diabetes (mother and maternal uncles), as well as pancreatic cancer (maternal grandmother). Patient presented with de novo Diabetes: A1C 7.2%, fasting glucose of 146 mg/dl and serum C-peptide 1.8 mg/l. She did not complain about polydipsia, polyuria, or weight loss. Being a young adult, without classical clinical features of type 1 or type 2 diabetes, and with a strong family history, MODY gene panel was evaluated. An extremely rare mutation on NEUROD1 gene was documented — Heterozygous c.616C>A p.(His206Asn) variant.

Patient’s mothers was also a carrier of the same mutation. Medical Genetics found the mutation pathogenicity doubtful and considered its clinical influence uncertain. The peculiarity of the case led to further analytical investigation: antibodies to GAD65 were positive (113,0 U/ml). Glycaemic control was achieved with a low dose of long-acting insulin (12 units glargine). It has been 4 years since the initial diagnosis and patient is metabolically stable (A1c 6.7%). The peculiarity of the case led to further analytical investigation: antibodies to GAD65 were positive (113,0 U/ml). Glycaemic control was achieved with a low dose of long-acting insulin (12 units glargine). It has been 4 years since the initial diagnosis and patient is metabolically stable (A1c 6.7%). Serum C-peptide was revaluated: 0.4 ng/ml (with fasting glucose of 98 mg/dl).

The family is being genetically studied at the time of this report.

Conclusion

Current International guidelines consider the presence of antibodies GAD65 an exclusion factor for MODY’s diagnosis. We present a case of a 38-year-old woman with heterozygous mutation (c616C>A p.(His206Asn)) of the NEUROD1 gene and concomitant antibodies GAD65. Patient had detectable C-peptide at the diagnosis but after 4 years C-peptide is below the normal range. However, glycaemic control was achieved with a single daily dose of long-acting insulin. The most probable diagnosis is a type 1 diabetes with long “honey-moon period” being the genetic mutation in NEUROD1 gene an analytical incidentaloma.

Further genetic evaluation is necessary to define de main cause of metabolic disorder in this patient.

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P627

Anxiety-depressive disorders in diabetic pregnant women on the circumstances of the COVID 19 pandemic

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Introduction

The COVID 19 pandemic is causing a considerable degree of fear and concern among the general population. In diabetic pregnant women, this risk is even higher given the physiological and psychological changes that occur during pregnancy.

Goal of the study

To assess the frequency of autoimmune diseases in type 1 diabetics and study the particularities of this association.

Patients and Method

This is a retrospective study including 120 type 1 diabetic patients hospitalized in department C of the National Institute of Nutrition of Tunis.

Results

The mean age of our patients was 30 ± 12 years with a sex ratio M/F = 0.7. The average duration of diabetes was 12 ± 8 years. The mean glycated hemoglobin (HbA1c) was 10.3%. The frequency of autoimmune diseases was 20% with a frequency of 13.3%. The frequency of hyperthyroidism, celiac disease and diabetic nephropathy (HbA1c) was 10.3%. The frequency of autoimmune diseases was 20% with a frequency of 13.3%. The frequency of hyperthyroidism, celiac disease and diabetic nephropathy was 10.3%.

Conclusion

Our study demonstrated a significant increase in the prevalence of anxiety-depressive disorders in diabetic pregnant women during the COVID 19 pandemic compared to the control group. This is mainly due to the beliefs of the patients vis-à-vis the virus. This justifies the need for screening and management of these disorders in this population during this period.

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P629

Deep soft tissue masses as a manifestation of type 2 diabetes

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Introduction

Xanthomas are defined as aggregates of lipid-laden histiocytes. They are generally present in superficial soft tissues such as skin and subcutis but can occasionally involve deep soft tissues. Xanthomas are classically associated with hyperlipidemia, that can be primary or secondary to numerous disorders such as diabetes. This case highlights an atypical manifestation of T2D.

Case report

A 61-year-old woman was referred to our endocrinology outpatient clinic in July, 2020, due to new-onset diabetes. The patient mentioned weight loss, polyuria, polydipsia and blurred vision for 1 months before diagnosis. Importantly, she mentioned the appearance of several subcutaneous nodules on the buttocks, thighs and forearms 2 months before diagnosis. Her past medical history revealed hypertension controlled with metoprolol. There was no history of alcohol or tobacco use. Laboratory findings showed an elevated fasting blood glucose 444 mg/dl and HbA1c 15.2%, and an altered lipid profile (total cholesterol 249 mg/dl, HDL cholesterol 50 mg/dl, triglycerides 252 mg/dl). Other laboratory findings were unrevealing. On physical examination we outline the presence of multiple firm deep soft tissue masses, with irregular margins and no pain on palpation on the patient’s gluteal region, thighs and forearm. She also had thin yellow to orange plaques on the left lower eyelid compatible with xanthelasma. Subsequent ultrasonography of these lesions revealed multiple hypoechogenic and heterogeneous expansive lesions, with undefined borders, they were in touch with aponeurosis but did not infiltrate it, the biggest with the diameter of 56 mm in the gluteal region. The x-ray excluded bone involvement. She started glargine 100U/day with self-adjustment of dosage and metformin 500 mg tid. Three months after introduction of anti-diabetic therapy the masses started to reduce in size and after four months, they had totally disappeared. Biopsy was not performed due to the complete involution of masses. Furthermore, HbA1c decreased to 6% and the lipid profile had improved (total cholesterol 190 mg/dl, HDL cholesterol 58 mg/dl, triglycerides 96 mg/dl).

Discussion

Poor glycemic control has a negative impact on lipid profile. We report a unique case where deep soft tissue masses developed in association with newly diagnosed diabetes with spontaneous resolution after institution of anti-diabetic therapy. The fact that the patient had already a xanthelasma and the complete resolution of the nodules with glycemic and lipid profile improvement favours the diagnosis of deep soft tissue xanthomas.

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P628

Type 1 diabetes and autoimmune diseases

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Introduction

Type 1 diabetes (T1DM) is an autoimmune disease in 90% of cases and is frequently accompanied by other autoimmune diseases.

Objective

To assess the frequency of autoimmune diseases in type 1 diabetics and study the particularities of this association.

Patients and Method

This is a retrospective study including 120 type 1 diabetic patients hospitalized in department C of the National Institute of Nutrition in Tunis.

Results

The mean age of our patients was 30 ± 12 years with a sex ratio M/F = 0.7. The average duration of diabetes was 12 ± 8 years. The mean glycated hemoglobin (HbA1c) was 10.3%. The frequency of autoimmune diseases was 20% with a frequency of 13.3%. The frequency of hyperthyroidism, celiac disease and diabetic nephropathy (HbA1c) was 10.3%. The frequency of autoimmune diseases was 20% with a frequency of 13.3%. The frequency of hyperthyroidism, celiac disease and diabetic nephropathy was 10.3%.

Conclusion

The coexistence of autoimmune diseases in the type 1 diabetic patient is not rare, the practitioner is encouraged to screen them at least, as soon as diabetes is discovered and in front of evocative signs.

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P630

Dyplidemia in type 1 diabetic patients

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Introduction

Dyplidemia in type 1 diabetic patients is a frequent situation and seems to be a risk factor for the occurrence of degenerative complications. The aim of this study is to evaluate the lipid profile of type 1 diabetic patients and to study the relationship between dyplidemia and the occurrence of degenerative complications.

Method

This is a retrospective study conducted at the National Nutrition Institute of Tunis including 110 diabetic patients during the year 2021.

Results

The population consists of 45 men and 65 women, with mean age of 30 ± 12 years. The average duration of diabetes was 12 ± 8 years. The majority of patients had poorly controlled diabetes with a mean HB1AC of 10.3 ± 2%. Hypertriglyceridemia was present in 25.5% of patients. Moreover, hyper-LDL cholesterol and hypo-HDL cholesterol were noted in 42.7% and 32.4% of patients respectively. A significant association was noted between hyper-HDL cholesterol and diabetic nephropathy (P = 0.035), diabetic retinopathy (P = 0.025) and diabetic neuropathy (P = 0.017). In addition, hyper-LDL cholesterol was associated with diabetic nephropathy (P = 0.003). However, no association was found between hypertriglyceridemia and microangiopathic complications.
P631

Predictive factors of glycaemic control in type 2 diabetic patients during the COVID-19 crisis
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Introduction
Glycaemic control is still difficult to achieve despite advances in the pharmacotherapy of type 2 diabetes. Moreover, the COVID-19 crisis led to a disruption in medical consultations and in the access to medications. The aim of our study was to identify factors associated with poor glycaemic control in Tunisian type 2 diabetic patients during the COVID-19 crisis.

Methods
This is a cross-sectional study, carried out in December 2021, on type 2 diabetic patients followed up at the outpatient clinic of the department of endocrinology in Rabta University hospital. Three hundred patients with type 2 diabetes mellitus followed up for at least two years were included. Each patient underwent a clinical examination. Data on glycaemic control during 2019 and 2021 were collected from the medical file.

Results
Patients were 117 men (39%) and 183 women (61%), with a mean age of 61.6 ± 9.7 years (22-91). One or more micro or macrovascular complications were present in 47.5%. Twenty-nine percent were previously infected with COVID-19 and 87% were vaccinated. More than half (52%) had poor socio-economic conditions and 46.7% were unable to buy their medications if unavailable in the public structures. The mean annual HbA1c in 2021 was 8.2 ± 1.8 % in 2021 (P=0.12). The mean annual fasting blood glucose was 1.71 ± 0.56 g/l in 2019 and 1.79 ± 0.72 g/l in 2021 (P=0.22). Compared to 2019, glycaemic control in 2021 was stable in 36.4%, worsened in 33.6% with an increase in HbA1c of 0.11%, and improved in 30% of the patients.

Conclusion
Glycaemic control was not worsened during the COVID crisis despite the difficulties in the availability of the drugs.

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P632

Assessment of glycaemic control in type 2 diabetic patients before and during the COVID-19 crisis
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Introduction
Chronic hyperglycemia in type 2 diabetic patients is associated with an increased risk of micro and macrovascular complications. Therefore, glycaemic control is the cornerstone of its management. The aim of this study was to evaluate glycaemic control in patients with type 2 diabetes before and during COVID-19 crisis.

Methods
A cross-sectional study was conducted during December 2021, in the outpatient clinic of the department of endocrinology in Rabta University hospital. The study included 300 patients with type 2 diabetes mellitus followed up for at least two years. Each patient underwent clinical examination and data on glycaemic control during 2019 and 2021 were collected from medical files.

Results
Patients were 117 men (39%) and 183 women (61%), with a mean age of 61.6 ± 9.8 years (22-91). The mean duration of the disease was 9.6 ± 6.1 years (2-35). The main cardiovascular risk factors were smoking (21%), hypertension (56.7%) and dyslipidaemia (57.3%). Eighty-eight percent of the patients were treated with metformin as a monotherapy in one quarter of the cases and in combination with other oral antidiabetic agents, mainly sulfonylurea in 41% or insulin therapy in 35%. The mean number of medical visits per patient was 1.78 ± 0.67 in 2019 and 1.9 ± 0.74 in 2021 (P=0.005). A poor compliance with medication during the past three months was noted in 27% of the patients and was explained by a lack of availability of the drugs in 46.7%. Hypoglycemia was reported by 18% of the patients. It occurred more than once a week in one quarter of the cases and it was severe in 9.8% of them. The mean annual HbA1c was 8.1 ± 1.7 % in 2019 and 8.2 ± 1.8 % in 2021 (P=0.0015).

Conclusion
Metabolic emergencies during the month of Ramadan
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Introduction
Fasting during the month of Ramadan, if authorized in balanced patients, must be a cornerstone of its management. The aim of this study was to evaluate glycaemic control in patients with type 2 diabetes before and during COVID-19 crisis.

Methods
A cross-sectional study was conducted during December 2021, in the outpatient clinic of the department of endocrinology in Rabta University hospital. The study included 300 patients with type 2 diabetes mellitus followed up for at least two years. Each patient underwent clinical examination and data on glycaemic control during 2019 and 2021 were collected from medical files.

Results
Patients were 117 men (39%) and 183 women (61%), with a mean age of 61.6 ± 9.8 years (22-91). The mean duration of the disease was 9.6 ± 6.1 years (2-35). The main cardiovascular risk factors were smoking (21%), hypertension (56.7%) and dyslipidaemia (57.3%). Eighty-eight percent of the patients were treated with metformin as a monotherapy in one quarter of the cases and in combination with other oral antidiabetic agents, mainly sulfonylurea in 41% or insulin therapy in 35%. The mean number of medical visits per patient was 1.78 ± 0.67 in 2019 and 1.9 ± 0.74 in 2021 (P=0.005). A poor compliance with medication during the past three months was noted in 27% of the patients and was explained by a lack of availability of the drugs in 46.7%. Hypoglycemia was reported by 18% of the patients. It occurred more than once a week in one quarter of the cases and it was severe in 9.8% of them. The mean annual HbA1c was 8.1 ± 1.7 % in 2019 and 8.2 ± 1.8 % in 2021 (P=0.0015).

Conclusion
Glycaemic control was not worsened during the COVID crisis despite the difficulties in the availability of the drugs.

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Determinants and consequences of nonadherence among patients with type-2 diabetes

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Objective
To determine the cumulative incidence of nonadherent patients with type-2 diabetes from an outpatient clinic, and to examine determinants and consequences of premature discharge.

Research design and methods
A cohort comprising patients with type-2 diabetes referred to a Diabetes Clinic from 2009-2012 was assessed. Patients were categorized as nonadherent if discharged within two years of referral due to nonattendance and/or nonadherence to medication and control. Medication and biochemical values at baseline and two years later were assessed. Data regarding co-morbidity, mortality and socioeconomic data were extracted from national registers, and determinants and consequences of nonadherence were assessed.

Results
1072 patients were identified, and of these 1008 met the inclusion criteria. The cumulative incidence of patients classified as nonadherent was 20.3%. Nonadherent patients were younger at time of type-2 diabetes diagnosis and had poorer glycaemic control at referral and two years later. Both non-western ethnicity and low education were determinants of nonadherence, but the effect of ethnicity became insignificant when adjusting for education, whereas the effect of education was less influenced by ethnicity. Cohabitation had no influence on adherence. Nonadherence was significantly associated with increased mortality also after adjusting for ethnicity and education, whereas the significance disappeared when adjusting for education.

Conclusions
Significant differences in glycaemic control, socioeconomic, and mortality were found between an adherent and a nonadherent group of type-2 diabetes patients. Low education seemed to be the principal determinant of nonadherence, while living alone was a mediator of increased mortality. To reach nonadherent patients and to reduce their risk of complications and reduced life expectancy, differentiated efforts should be considered.

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The importance of hepatocyte STAT5b, glucokinase and ChREBP in GH receptor-mediated regulation of steatosis and de novo lipogenesis is dependent on the nutritional state

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Fatty liver (steatosis) can progress to non-alcoholic fatty liver disease, increasing the risk of diabetes and cardiovascular disease. Growth hormone (GH) deficiency is associated with steatosis, while raising GH reduces steatosis. To date it remains to be determined how GH mediates this hepato-protective effect. To investigate the hepatocyte-specific actions of GH, a mouse model of adult-onset hepatocyte-specific GH receptor knockdown (aHepGHRkd) was generated by treating adult mice, homozygous for the GHR-flox allele, with an adeno-associated viral vector expressing a thyroxin-binding globulin promoter driven Cre recombinase (AAV8-TBGp-Cre). Ties treated with an AAV8-TBGpNull serve as GHR-intact controls. We reported that 7d-post aHepGHRkd, steatosis develops associated with enhanced expression of glucokinase (GCK), ketohexokinase (KHK) and de novo lipogenesis (DNL) genes, and increased rate of DNL, which was measured by deuterated water labeling. New data demonstrate the aHepGHRkd-mediated alterations in liver phenotype persist under thermoneutral conditions (mice housed at 30°C). Also, the increase in cytoplasmic GCK protein (active), but not KHK, occurs just 3d-post aHepGHRkd, suggesting enhanced glycolysis may be an initiating event to drive enhanced DNL, since the expression of KHK is upregulated by carbohydrate response element binding protein (ChREBP), a transcription factor activated by glycolytic metabolism. In fact, in preliminary studies we found that knockdown of hepatocyte ChREBP, in aHepGHRkd mice, prevented the rise in KHK, but did not prevent the rise in GCK or steatosis. Since GHR signals through JAK2/STAT5b to regulate many genes in hepatocytes, we sought to determine if restoration of STAT5b activity in aHepGHRkd would normalize the liver phenotype. To this end, we co-treated a subset of aHepGHRkd mice with an AAV expressing a constitutive active form of STAT5b (AAV8-TBGp-STAT5bC). Since regulation of hepatic lipid accumulation is dynamically mediated by multiple hormones and substrate availability, we compared the impact of aHepGHRkd, without or with STAT5bC, under multiple nutritional conditions: natural fasting (10h after food withdrawal at 0600h), overnight fasting (16h), or overnight fasting with 6h refeeding. Data collected thus far show hepatocyte STAT5b, in the absence of GHR, can suppress GCK expression/activity, but this is not always associated with a reduction in steatosis or DNL, depending on the nutritional state. These findings imply that the GHR may signal independent of STAT5b to suppress DNL.

Endocrine-Related Cancer

Novel panels of tissue microRNAs to diagnose adrenocortical malignancy based on artificial intelligence tools

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Adrenocortical tumors are common, occurring in 5-7% of the population. Adrenocortical carcinoma (ACC) is rare (0.7-2/million/year) and it has a poor prognosis with a five-year survival of less than 30% in advanced stages. The histological differentiation of benign and malignant adrenocortical tumors is challenging.

Objectives
To explore the diagnostic utility of multiple microRNAs in various combinations as markers of adrenocortical malignancy by using artificial intelligence methods, based on machine learning and neural networks.

Materials and Methods
63 formalin-fixed, paraffin-embedded (FFPE) adrenocortical tissues were studied. The discovery cohort included 10 adrenocortical adenoma (ACA) and 10 ACC samples. An independent validation cohort encompassed another 21 ACC and 22 ACA samples. 16 microRNAs shown to be differentially expressed based on literature data were included. MicroRNA expression was studied by a 2-step TaqMan RT-qPCR. RNU48 was used as an internal, alongside with cel-miR-39 as an external control. Normalization of microRNAs was performed with the ΔCt method using R package NormpCt. The order of microRNAs for the grouping of ACA and ACC samples was determined by the random forest classification method. The possibility of automatic classification of samples into ACA or ACC groups was tested by machine learning methods (R packages caret and mlr). Only models with more than 90% classification capability were selected for RT-qPCR validation and subsequent artificial intelligence-based classification. The best performing microRNA combinations (statistical models) were selected by network-based, 90-10% random learner-tester cross validation. 24 microRNA models were included in the validation performed in a blind manner.

Results
Hsa-miR-195, hsa-miR-375, hsa-miR-483-3p, hsa-miR-483-5p and hsa-miR-503 were the best 5 microRNAs revealed by random forest algorithm to correctly classify the previously unknown samples. The following three, best performing statistical models were selected out of the former microRNAs: hsa-miR-195 + hsa-miR-210 + hsa-miR-503; hsa-miR-210 + hsa-miR-375 + hsa-miR-503; and hsa-miR-210 + hsa-miR-483-3p + hsa-miR-503 with sensitivity and specificity of 90.91-90.48; 90.91-90.48 and 90.91-95.24 %, respectively. The diagnostic performance of these three models was clearly superior over that of individual microRNAs.
Conclusion
We have established three microRNA combinations with outstanding diagnostic performance using artificial intelligence-based methods. These biomarker combinations can help histological analysis, and their use in small amount preoperative biopsy samples might also be envisaged.

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P121

Abstract withdrawn
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P122

Diagnostic evaluation of selected granin family proteins and INS-1 (Insulinoma-associated protein 1) in patients with medullary thyroid carcinoma
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Introduction
Medullary thyroid carcinoma (MTC) accounts for 3.5-5% of thyroid cancers. The biochemical diagnosis of MTC is based on the determination of concentration of a sensitive and specific biomarker - calcitonin (CT) as well as CEA and procalcitonin (PCT). Neuroendocrine cells have the ability to produce various proteins and neuropeptides (e.g. granin proteins and INS-1), which are secreted into the circulation with calcitonin and can be measured in the blood as so-called circulating tumor markers.

Purpose
The aim of the study was to assess the usefulness of determining levels of selected granin family proteins and INS-1 in the diagnosis of patients with medullary thyroid cancer.

Material and methods
34 patients with medullary thyroid carcinoma (MTC) were enrolled in the study. Patients were divided into 2 groups:
1. MTC - active form (7 patients with newly diagnosed MTC and 8 patients with distant metastases (4-15 years after thyroidectomy),
2. MTC – stable form, with no recurrence nor metastases (n = 19).

Forty healthy individuals were the control group. The following levels were determined in all patients: calcitonin, procalcitonin, CEA, INS-1, pro-SAAS, chromogranin B (CgB), chromogranin A (CgA) and derivates peptides: Pancreastatin/chromogranin A (250-301), Serpinin/prepro-chromogranin A (429-454), WE-14/prepro-chromogranin A (342-355) and Catestatin.

Results
In MTC-active patients levels of: CT, CEA, PCT, INS-1, WE-14, Catestatin and Serpinin were significantly different vs. control group, with higher level in MTC patients. No significant difference was confirmed for CgA, CgB, pro-SAAS and Pancreastatin between MTC-active and the control group. For MTC-stable patients, only CEA, INS-1 and Serpinin levels were significantly higher compared to the control group. In the group of patients with the active form of MTC, the following indicators of the diagnostic evaluation of the analyzed biomarkers were obtained: CT: 93% sensitivity and 100% specificity (AUC 0.968), PCT: 100% sensitivity and specificity, INS-1: 100% sensitivity and 95% specificity (AUC 0.997), WE-14: 86.7% sensitivity and 87.5% specificity (AUC 0.922), Catestatin: 80% sensitivity and 85% specificity (AUC 0.899), Serpinin: 53% sensitivity and 95% specificity (AUC 0.764). In the group of MTC-stable form patients, the highest diagnostic usefulness was the determination of INS-1 level: 57.9% sensitivity and 82.5% specificity (AUC 0.720) and Serpinin: 47.4% sensitivity and 90% specificity (AUC 0.737).

Conclusion
In patients with active MTC, the greatest diagnostic usefulness was found for the determination of CT, PCT and CEA levels as well as of new biomarkers: INS-1 and selected peptides from the granin family: WE-14, Catestatin and Serpinin.

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P123

The transcriptomic and methylation landscape of POU1F1 pituitary tumors
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Pituitary adenomas (PA) are primarily benign lesions with monoclonal origins from the adenohypophyseal cells and represent 10-15% of all intracranial tumors. Tumors derived from POUIF1 cell lineage are GH-, TSH-, and PRL-secreting tumors that cause important syndromes such as acromegaly, hyperthyroidism, and sexual dysfunction, respectively. Surgical resection is the first line of treatment; the secondary treatment is pharmacological, despite having targets pharmacological in tumors derived of POUIF1 cell lineage, a high percentage of patient’s present resistance to pharmacotherapy over time. The molecular alterations continue unclearly understood. We performed global transcriptome and methylome profiling in six non-tumoral pituitary glands and sixteen POUIF1 tumors distributed as follows ten GH-, four TSH- and two PRL-tumors identifying differentially expressed genes regulated by methylation, miRNA-mRNA regulation, and pathway alterations. Our results showed distinctive transcriptome and methylome profiles segregating control glands from tumor samples. The transcriptomic analysis further revealed better segregation clusters according to the hormone-secreting tumor. We identified up-regulated coding genes such as DGKG, GRM5, and GPR173 common to the three tumors derived from the POUIF1 lineage. Interestingly, in each tumor identified up-regulated coding and non-coding genes such as CDKAS1R1, MET, GRIN3A and miR4771-1 in PRL-; CHKA, THEMEM23, miR95, LINC01347 and LINC01524 in GH-; NTRK3; GRIK4, miR4510, miR95923 and LINC0662 in TSH-secreting tumors, that could serve for future specific targets for molecular therapy. In addition, inside up-regulated genes we also identified hypomethylated status genes such as DGKG, miR590, miR4510, LINC0662, LINC0100, LINC01347, LINC01524; DNA hypomethylation in CPG islands in these genes potentially participate in up-regulated gene expression. miRNA-target gene found an interaction between miR590 with ANXA1, S100A10, YAP1, STA53, ATP15A3, PTTP14, PCDG11X that also were identified down-regulated in our transcriptomic analysis. Pathway analysis revealed alterations in glycerophospholipids, phospholipase, and calcium signaling pathways. Overall, these results indicate potential molecular markers that could become specific targets for developing novel therapies.

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Hirsutism as the first manifestation of a mesonephric-like adenocarcinoma of the ovary

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Mesonephric adenocarcinoma (MA) is an uncommon gynecologic tumor that are thought to arise from embryonal remnants of the mesonephric ducts, also known as Wolffian ducts. Mesonephric-like adenocarcinoma (MLA), despite absence of Wolffian origin, have similar morphology and immunophenotype and exhibit molecular aberrations like MA. These tumors are generally negative for estrogen and progesterone receptor.

Case Report
An 83-year-old Spanish female was referred to our outpatient clinic of endocrinology to study hirsutism. She had a history of 4 uncomplicated pregnancies and experienced menopause at age 42 years. She had not taken hormone replacement therapy and she didn’t experience uterine bleeding. A drug history excluded anabolic steroid use or exposure to exogenous androgens. In the amanessia she referred a recent-onset hirsutism, less than 3 months, without signs of virilization and constitutional syndrome with anthesia and anorexia. Ferriman-Gallwey score was not calculable by depilation of facial and body hair; it was only visible the presence of excess terminal hair growth in the abdomen. She had no stries. Laboratory testing revealed the following levels: total testosterone 4.46 ng/ml (normal range, <0.25), androstenedione >10 ng/ml (normal range, 0.3-3.3), 17-hydroxyprogesterone 0.3 ng/ml, dehydroepiandrosterone sulfate (DHEA-S) 183 mg/dl. Abdominopelvic CT revealed two tumors in the pelvis of 11.5x9 cm and 8.5x5.5 cm. The largest one had necrotic degeneration. No significant adenopathies were found and adrenal glands were normal. A laparoscopic bilateral salpingo-oophorectomy was performed. Histopathology revealed two tumors of 13x11x17 cm, of 851 gr of weight, and another one of 9x8x2. The first one was solid with gray-white solid areas associated with areas of necrosis with admixture of growth patterns (ductal and tubular), as well as intraluminal eosinophilic colloid-like material resembling mesonephric remnants, and atypical nuclear cells. No evidence of mesonephric remnants or endometriosis were observed. The other one was a fibrous fragment which included the other ovary and fallopian tube. There was no neoplastic infiltration of other tissues, and the peritoneal fluid was positive for malignancy. By immunohistochemistry, tumor cells were positive for GATA3, CD10 and androgen receptor and negative for calretinin, PAX8, estrogen and progesterone receptors, TTF1 and CDX2. The final diagnosis was MLA of the ovary pT2aNx (TNM, 8 edic), FIGO IIA. After the surgery, testosterone level was 4.46 ng/ml (normal range, 0.3-3.3), androstenedione >10 ng/ml, 17-hydroxyprogesterone 0.3 ng/ml and DHEAS 34.3 mg/dl.

Conclusion
Here we describe the first case of mesonephric-like adenocarcinoma of the ovary with positive androgen receptors

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P124

Elevated SGPL1 expression is associated with increased metabolic rate in cells and reduced survival in individuals with adrenocortical carcinoma

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Introduction
Sphingosine-1-phosphate lyase (SGPL1) catalyses the final step in sphingolipid metabolism, irreversibly degrading the lipid signalling molecule sphingosine-1-phosphate (SIP). The relative abundance of SIP compared to its precursors sphingosine and ceramide finely tunes signal transduction for a wide range of cellular pathways including proliferation, apoptosis, migration and calcium handling. Loss-of-function mutations in SGPL1 cause a spectrum of disorders, including primary adrenal insufficiency (PAI). Adrenocortical carcinomas (ACCs) are invasive tumours arising in the adrenal cortex, and steroidogenic tumours are associated with worse prognostic outcomes. Given that loss of SGPL1 expression causes PAI, we hypothesised increased SGPL1 expression might increase steroidogenesis and therefore be linked to increased disease severity in ACC.

Conclusions
Here we describe the first case of mesonephric-like adenocarcinoma of the ovary with positive androgen receptors

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P126

Ultrasound and cytolological features of thyroid nodules with aggressive behavior: from histology to clinic

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Fine-Needle Aspiration Biopsy (FNAB) is the recommended diagnostic tool for differentiating malignant from benign thyroid nodules and provides indication for surgical decisions. According to the Italian system, thyroid nodules are classified as TIR 1/1C, TIR 2, TIR 3A, TIR3B, TIR4 or TIR5, which correspond to Thy I, Thy II, Thy III, Thy IV, Thy V and Thy VI categories of the Bethesda system. TIR 3 identifies the indeterminate nodules. Surgery is usually recommended for TIR 3B, TIR 4 and TIR 5 nodules. Among papillary thyroid carcinomas (PTC), the classic and follicular (CV-PTC and PV-PTC) are characterized by a good prognosis and require a less aggressive treatment, while the tall cell (TC-PTC) and the solid variants (SV-PTC) and others rarer (cromoblast, hombnal and diffuse sclerosing variants) have a worse prognosis. In addition, thyroid ultrasound often identifies thyroid nodules <1 cm, which are usually characterized by an indolent behavior and active surveillance may be advised. We aimed at identifying which ultrasound and cytolological features enable to recognize, among TIR4-5 nodules, the aggressive variants and, among TIR3B nodules, the malignant ones. To this purpose we retrospectively analyzed the histopathological records of 1117 patients (for a total of 1668 nodules, 650 malignant) who underwent surgery in 2017 and who had previously undergone FNAB and thyroid ultrasound (available for 390 nodules). Of the 566 PTC, 18.7% were TIR 3A, 20.7% TIR 3B and 51.6% TIR 4-5, while of 50 FTC 42.0% were TIR3A, 42.0% TIR3B and 6.0% TIR 4-5. Of
the 11 PTC 54.5% had been diagnosed as TIR 3B. Of the 249 classic variant of PTC, 0.8% had resulted TIR3A, 14.1% TIR3B and 79.9% TIR4-5. Among 49 TC- PTC, none had resulted TIR3A, 2% had been diagnosed as TIR3B and 95.9% as TIR4-5. Of the 219 FTC-PTC 42.9% had resulted TIR3A, 39.7% TIR3B, and 12.3% TIR4-5. Among 34 SV-PTC, 32.4% had been diagnosed as TIR3A, 41.2% TIR3B and 0.6% TIR-4-5. At ultrasound, blurred margins were the only feature associated with malignancy (P = 0.034) in TIR3B category. The coexistence of hypocho- genicity and blurred margins in absence of microcalcifications were more common in the TC (7/28) compared to the CV (10/120) of PTC (P = 0.021). In conclusion ultrasound helps to identify, among TIR4 and TIR5 nodules, the aggressive variants, and among TIR3B, the malignant ones, and therefore to choose the extent of surgical treatment and, when < 1 cm, to confidently advise active surveillance.

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P127 Role of DKK1 in growth and migration of prostate cancer cells Letizia Rinella1,2, Mara Compagno3, Gloria Fiorentino1, Nicoletta Fortunati1, Trinidad Moreno Montilla1,2,3, Ricardo Blázquez Encinas Rey1,2,3,

Androgen deprivation therapy is the choice treatment of metastatic prostate tumors. Unfortunately, very often, resistance occurs and chemotherapy is needed. Results are however disappointing with frequent side effects. Therefore, new therapeutic approaches for metastatic and advanced prostate cancer are necessary. DKK1, an inhibitor of the Wnt signaling pathway, is expressed in high levels in other cancers. In prostate cancer patients with bone metastases, an increase of DKK1 is observed both in the serum and in the prostate tissue, suggesting that DKK1 might be considered as a new molecular target in the metastatic prostate cancer therapy. The aim of this study was to evaluate the role of DKK1 in growth and migration of prostate cancer cell lines (PC3 and DU145), expressing high levels of DKK1. To this end, we carried out DKK1 gene silencing and knockout in PC3 and DU145 cells. Silencing was obtained by specific siRNA to DKK1; permanent knockdown was performed using a CRISPR/CAS9 system. Real-Time PCR, Western Blotting analysis, and secretion levels by ELISA confirmed DKK1 silencing and knockout, respectively. The effects of silencing (PC3-siRNA and DU145-siRNA) and knockdown (PC3-KO and DU145-KO) were evaluated in terms of cell growth by colorimetric WST-1 test and cell migration by transwell migration assay. A significant reduction of mRNA, protein levels and secretion of DKK1 was observed in both cell lines where DKK1 was silenced or knocked- down. Functionally, DKK1 inhibition resulted in a reduction of cell growth and migration. In conclusion, our data support a key role of DKK1 in the growth and migration of prostate cancer cells. Based on our study, DKK1 may represent a specific target for a new therapy intended to specifically block its function in metastatic and advanced prostate cancer.

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P128 Splicing machinery dysregulation in rare neuroendocrine tumors: pheochromocytomas and paragangliomas

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Pheochromocytomas and paragangliomas (PPGL) are commonly benign catecholamine-producing neuroendocrine tumors (NETs); however, up to 25 % of patients develop distant metastases or aggressive behavior. The current classification of PPGL comprises pseudohypoxia-profile, MAPK-pathway alteration, and Wnt-pathway dysregulation clusters according to their genomic characterization. However, to date, there are no biomarkers to help stratify patients based on their prognosis. Alternative splicing is an emerging cancer feature that has been linked to a more aggressive phenotype in a variety of neoplasms, including NETs. In this context, we have recently discovered alterations in the splicing machinery in other NETs, such as pancreatic and lung NETs. The splicing process has not been studied in detail before in PPGL, but there are reasons to expect that it could be altered. Thus, the aim of this study was to assess the profile of the splicing machinery in PPGL and study its potential relationship with clinical-molecular features. To this end, we studied the expression of 313 splicing-related genes in the data available in the TCGA dataset, which includes 151 patients (29 paragangliomas, PGL, and 122 pheochromocytomas, PCC). Most splicing-related genes were found to be similar in PCC and PGL, but 16 genes, including RBM22, CELF4, and PABPC1, exhibited significant differences. Interestingly, a detailed analysis among the three genomic clusters revealed considerable differences, standing out 143 of 313 splicing-related genes, which were found over- or under-expressed. It is also worth noting that just the expression of CELF4 and API5 was sufficient to clearly distinguish the three clusters: low expression of both genes in pseudohypoxia cluster, high in kinase signaling, and CELF4 high and API5 low expression in Wnt-altered cluster. Furthermore, 27 genes were shown to be associated with aggressive PCC; in particular, categorizing PCC samples based on high or low expression of specific genes, such as LSSM or SMCI1, allowed us to predict aggressive/metastatic behavior. In addition, aggressive PGLs had differential expression of 25 genes. Altogether, our findings show that the splicing machinery is disrupted in PPGL, which encourage us to explore the splicing process in a larger cohort of PPGL samples and investigate the functional importance of these splicing-related genes in vitro.

Keywords: pheochromocytoma, paraganglioma, metastasis, splicing dysregulation, splicing machinery. This work was supported by MICINN (PII2019-105201RB-I00), Beca GETNE 2019, Fundación Eugenio Rodríguez Pascual, ISCIII (CDI19/00255).

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P129 The impact of pregnancy on disease outcome in patients with persistent differentiated thyroid carcinoma

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Background Pregnancy does not cause differentiated thyroid cancer (DTC) recurrence in patients without structural or biochemical evidence of disease at the time of conception. However, data regarding pregnancy’s impact in patients with persistent DTC before conception are still controversial.

Aim The aim of the study was to determine whether pregnancy could significantly influence the outcome in DTC patients in persistence before pregnancy, but with a biochemical and structural stable disease.

Methods This was a retrospective evaluation of all women followed for DTC at a tertiary Italian thyroid cancer center who had a pregnancy after initial treatments between 2003 and 2020. Subjects included were required to have biochemical and/or structural persistence within 12 months before pregnancy. Results We enrolled 8 patients with papillary thyroid carcinoma (PTC) with a mean age at diagnosis of 27.6 years and a mean time between PTC diagnosis and pregnancy of 60 months. Among the 7 patients with structural disease, five patients had lung metastases, two lymph node metastases and one patient biochemical persistence. Patients were treated with total thyroidectomy, lymphadenectomy and radioactive iodine ablation (RAI). According to 8th edition of the American Joint Commission on Cancer (AJCC) and 2015 American Thyroid Association (ATA) 2015 guidelines, 75% of women had AJCC stage I and intermediate
risk of recurrence and 25% had AJCC stage II and high risk of recurrence. Evaluation of Dynamic Risk Stratification (DRS) during the 24 months of follow-up showed 88% patients with structural incomplete response and 12% with a biochemical incomplete response. During a mean follow-up of 153 months, none of the patients showed biochemical and radiological progression of disease during pregnancy or within 6 months of delivery and no further treatments were required. One patient with lung metastases had an increase of thyroglobulin during pregnancy, which returned to the pre-pregnancy levels after delivery.

**Conclusions**

Our data demonstrate that pregnancy is not associated with significant progression in patients with stable persistent DTC before conception. However, further studies are needed to verify the effect of pregnancy on the outcome of patients with persistent and progressive disease.

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**P130**

**Origins of progesterone in male mice**

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The role of progesterone in male physiology is mainly unknown. We recently observed that progesterone was the most abundant sex hormone in orchietomized (ORX) mice with most of it stored in white adipose tissue (WAT) (1). The aim of the present study was to use a sensitive and validated gas chromatography/tandem mass spectrometry method to determine the origins of progesterone in male mice. Tissue levels of progesterone were high in adrenals of male mice, indicating that male progesterone may be predominantly adrenal-derived. To determine if progesterone only originates from the adrenals in males, we compared WAT levels of progesterone in ORX + adrenalectomized (ADX) and intact mice. Surprisingly, combined orchietomy and adrenalectomy did not reduce progesterone levels in WAT (mean ± SEM, 1.638 ± 239 pg/g vs. 1.871 ± 124 pg/g, non-significant). In both groups, we also observed high levels of progesterone along the gastrointestinal tract including the gastric contents. To evaluate food as a potential progesterone source, we analyzed progesterone levels in 20 types of mouse chow and found varying but substantial levels in all tested types (2.319-17.702 pg/g). To identify main sources of food-derived progesterone, we analyzed progesterone levels in several food items, reveling no/low levels in non-animal-derived food items, medium levels in meat and very high levels in dairy products such as cream (123.162 ± 1.282 pg/g). To functionally test if orally ingested progesterone could contribute to tissue levels, we administered isotope-labeled progesterone or vehicle by oral gavage for 10 days to adult ORX + ADX male mice, and data indicated some uptake of labeled progesterone into the WAT. Interestingly, a recent metagenomic study showed an association between gut microbiota (GM) functional traits and circulating progesterone levels in humans (2). Accordingly, we determined the impact of the GM on progesterone levels in WAT and found that germ-free male mice, completely lacking GM, had substantially increased progesterone levels in WAT compared with conventionally raised mice (+132% vs. +6%; P<0.001). In conclusion, in the absence of adrenal-derived progesterone in male mice progesterone levels are maintained by an alternative progesterone source. We propose that food-derived progesterone may be taken up and maintain close to normal progesterone levels in ORX + ADX male mice. Furthermore, GM composition may regulate this uptake of progesterone.

**References**

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**P131**

**Neuropeptide Y (NPY) and Human cocaine- and amphetamine-regulated transcript (CART) in patients with adrenal pheochromocytoma**

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**Introduction**

Pheochromocytoma is a rare tumor that develops from chromaffin cells of the adrenal medulla. In about 5% of cases, it is a benign tumor. Along with catecholamines, neuropeptide cys of the adrenal medulla have the ability to produce various proteins and neuropeptides and secrete them into the blood. Among the known biologically active substances are: neuropeptide Y and human cocaine- and amphetamine-regulated transcript (CART).

**Purpose**

The aim of the study was to assess the usefulness of the determination of levels of neuropeptides: neuropeptide Y and CART in the diagnosis of patients with adrenal pheochromocytoma.

**Material and methods**

Patients were divided into 4 groups:
1. Patients with pheochromocytoma (n=51),
2. Patients with adrenal incidentaloma (n=23),
3. Patients with primary arterial hypertension (n=20),
4. Control group – healthy volunteers (n=52).

The following biochemical determinations were performed in all patients: plasma levels of metanephrine and normetanephrine, concentration of chromatogam A (CgA), neuropeptide Y (NPY) and human cocaine- and amphetamine-regulated transcript (CART). Biochemical determinations were made using the LC-MS/MS technique and immunochemical techniques (IRMA, ELISA) were used.

**Results**

Concentrations of the analyzed biomarkers: CgA, NPY and CART were significantly higher (P<0.001) compared to control groups (adrenoma, primary hypertension and healthy subjects). Sensitivity, specificity and AUC indices of the analyzed biomarkers: CgA, NPY and CART were compared in the group of patients with pheochromocytoma vs. control groups: adenoma, primary hypertension and healthy subjects. Pheochromocytoma vs. adenoma: CgA: 84% sensitivity and 96% specificity (AUC 0.932); NPY: 80% sensitivity and 78% specificity (AUC 0.808) and CART: 43% sensitivity and 100% specificity (AUC 0.768), Pheochromocytoma vs. primary hypertension: CgA: 78% sensitivity and 100% specificity (AUC 0.945); NPY: 47% sensitivity and 100 specificity (AUC 0.615) and CART: 72% sensitivity and 85% specificity (AUC 0.797). Pheochromocytoma vs. healthy subjects (blood donors): CgA: 84% sensitivity and 98% specificity (AUC 0.923); NPY: 90% sensitivity and 86% specificity (AUC 0.897) and CART: 60% sensitivity and 49% specificity (AUC 0.403).

**Conclusion**

Among the analyzed biomarkers, CgA concentration determination presented the highest discriminant value between patients with pheochromocytoma and other study groups. Neuropeptide Y showed a high specificity between the analyzed groups, especially in the differential diagnosis of patients with adenoma and patients with essential hypertension.

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**P132**

**Somatostatin receptor splicing variant SSTR5TM4D overexpression in glioblastoma is associated to poor survival, increased aggressiveness features and somatostatin analogs resistance**

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Glioblastoma (GBM; grade IV astrocytoma) is the one of the most malignant and lethal endocrine-related cancers worldwide. Current standard treatment consists of surgery followed by radiotherapy and/or chemotherapy; however, this is only a palliative approach with a mean post-operative survival of scarcely ~12-15 months. Therefore, the identification of novel therapeutic targets to treat this devastating pathology is urgently needed. In this context, the truncated splicing-variant of the somatostatin receptor subtype 5 (SSTR5TM4D), which is produced...
by aberrant alternative splicing, has been demonstrated to be overexpressed and associated with increased aggressiveness features in several endocrine-related cancers/tumors. However, the presence, functional role, and associated molecular mechanisms of SST5TMD4 in GBM have not been yet explored. Therefore, we performed herein a comprehensive analysis to characterize the expression and pathophysiological role of SST5TMD4 in human GBM. We demonstrated that SST5TMD4 was significantly overexpressed (at mRNA and protein levels) in human GBM tissues (n = 47) compared to non-tumor brain tissues (control, n = 15) and grade III-astrocytoma patients (n = 9). Remarkably, SST5TMD4 expression was significantly associated with poor overall survival and recurrent tumors in GBM patients. Moreover, in-vitro SST5TMD4 overexpression (by specific siRNA) decreased, key malignant features (i.e., proliferation and migration capacity) of GBM cells (U-87 MG/U-118 MG models). Furthermore, SST5TMD4 overexpression in GBM cells altered the activity of multiple key signaling-pathways associated with tumor aggressiveness and progression (AKT, JAK-STAT, NF-κB and TGFβ routes), and its silencing sensitized GBM cells to the antitumor effect of pasireotide (a somatostatin analog). Altogether, these results demonstrated that SST5TMD4 is overexpressed and associated with enhanced malignancy features in human GBMs and revealed its potential utility as a novel and useful diagnostic and prognostic biomarker and as a potential target in the future development of therapeutic approaches in patients with this devastating endocrine-related cancer, offering a clinically relevant opportunity that should be tested for use in humans.

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P133
Rapidly progressive cases of ectopic adrenocorticotropic hormone syndrome
Lucia González Gracia, Gema López Gallardo, Bothayna Oulad Ahmed, Elena Dios Fuentes, Luis Beltrán Romero & Alfonso Soto-Moreno
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Introduction
Adrenocorticotropic hormone (ACTH)-dependent Cushing’s syndrome (CS) secondary to an ectopic source is an uncommon condition, accounting for 4-5% of all cases of CS and between 9-18% of cases of ACTH-dependent CS. Although numerous malignancies have been associated with ectopic ACTH syndrome (EAS), lung neuroendocrine tumours (NETs) are the most common. Refractory hypokalemia can be the presenting feature in EAS and is seen in up to 80% of cases. We present two cases which first presented with hypokalemia, refractory to treatment with potassium supplementation and spironolactone.

Cases reports

Table 1

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>Age: (years)</td>
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<td>56</td>
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<tr>
<td>Clinical presentation</td>
<td>- Hypertension</td>
<td>- Constitutional syndrome</td>
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<tr>
<td></td>
<td>- Newly diagnosed hyperglycaemia</td>
<td>- Newly diagnosed hypertension and hyperglycaemia</td>
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<tr>
<td></td>
<td>- Hyperpigmentation</td>
<td>- Peripheral edema</td>
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<tr>
<td>Biochemical parameters</td>
<td>Glucose 187 mg/dl</td>
<td>Glucose 150 mg/dl</td>
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<tr>
<td></td>
<td>K⁺ 2.5 mEq/l (3.5 – 5)</td>
<td>K⁺ 2.2 mEq/l (3.5 – 5)</td>
</tr>
<tr>
<td>Hormone parameters</td>
<td>UFC 14219.7 mg/24 h (35 – 135)</td>
<td>UFC 1268 mg/24 h (35 – 135)</td>
</tr>
<tr>
<td>Tumor localization</td>
<td>ACTH &gt; 1500 pg/ml (3.6 – 60.5)</td>
<td>ACTH 276.9 pg/ml (3.6 – 60.5)</td>
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<tr>
<td>Tumor size</td>
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<td>Lung</td>
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<tr>
<td>Histopathology</td>
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<td>17 mm</td>
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<tr>
<td>Immunohistochemistry</td>
<td>Large-cell neuroendocrine carcinoma</td>
<td>Small-cell neuroendocrine carcinoma</td>
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<tr>
<td>Ki-67 metastasis</td>
<td>70-80%</td>
<td>&gt;90%</td>
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<tr>
<td>Treatment of hypercortisolism</td>
<td>Ketoconazole + somatostatin analogs</td>
<td>Ketoconazole</td>
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<tr>
<td>Outcome</td>
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<td>Deceased</td>
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<tr>
<td>Survival from time of diagnosis</td>
<td>19 days</td>
<td>12 days</td>
</tr>
</tbody>
</table>

UFC: 24 h-urinary free cortisol; Chromogranin, synaptophysin and CD56: markers of neuroendocrine differentiation. TTF1: primary site marker (lung and thyroid)

Conclusions
We present two cases of ectopic ACTH syndrome similar in their clinical presentation (newly diagnosed hyperglycaemia and hypertension and severe hypokalemia), tumour aggressiveness and rapidly fatal outcome. Furthermore, we present a case of EAS produced by a NET from the ileum tract. To our knowledge this is extremely rare and only described in isolated case reports.

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P378
Serial liquid biopsies - the NETest - in gastroenteropancreatic NET surveillance
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Introduction
The variable tumor behavior in patients with gastro-entero-pancreatic neuroendocrine tumors (GEP-NETs) is challenging. Current general biomarkers are insufficient to predict the disease course. An emerging biomarker is the NETest, a blood-borne gene signature that can predict disease status based on the expression of genes involved in tumor biology. While promising, the accuracy and reproducibility of results in daily practice during years of follow up has never been assessed. Evaluation of serial NETest measurements in an individual is needed to determine its place in the clinical armamentarium.

Aims
To evaluate if serial NETest measurements can predict treatment response and reflect disease evolution during years of follow up.

Methods
Serial NETest scores were compared with RECIST1.1 defined disease status in 132 GEP-NET patients over 46 (6-71) months of follow-up. A median of 4 samples was collected in patients on a watch-and-wait strategy or undergoing systemic treatment. Pre- and post-treatment scores (<6 months) were compared with progression-free survival (PFS).

Results
Fluctuating scores [0-100%] were seen in patients with no evidence of disease (NED) and stable disease (SD). None of the 30 patients with NED and 1 of the 28 (4%) patients with SD had all outcomes within the low range. In patients with progressive disease (PD) and not receiving any treatment (n = 16), ongoing tumor progression was confirmed in consecutive samples in 82%. Patients responding to treatment (PFS > 12 months) had higher pre-treatment NETest scores (76.5; n = 22) compared to non-responders (33; n = 12; p = 0.001). Patients with low pre-treatment scores had a 21 months shorter PFS after treatment (10 vs 31 months).
P379
First case report of a natural killer T (NK/T) extranodal nasal lymphoma presenting as a diabetes insipidus
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A 52-year-old male patient with no past medical history of interest was admitted to our Endocrinology Unit with a clinical course developed in the last month of sudden polyuria, nocturia and polydipsia (8 liters/day) associated with bilateral low back and leg pain, a right-side nasal congestion with eye swelling and paresthesia. Physical examination revealed a doubtful thickening of the nasal mucosa and several two-cm- scattered erythematous disseminated skin lesions. Blood samples showed basal sodium levels between 146-148 mEq/l. A Miller test confirmed the diagnosis of Central Diabetes Insipidus (CDI) with a urine osmolality of 444 mOsm/kg that raised to 720 mOsm/kg after desmopressin. Anterior pituitary hormone levels were within normal range. A pituitary MRI showed a focal 10x7x10 mm posterior lesion with extension towards the pituitary stalk, along with bilateral nasocaudal thickening in ethmoid cells and occupation of nostrils, especially in the right side. During admission, the patient presented worsening of nasal symptoms, solid and liquid dysphagia and advance of skin lesions, which were biopsied. Oral desmopressin was started at a dose of 90 mg/day and subsequently moved on to 240 mg/day due to persistent polyuria. Infectious processes, germinoma, autoimmune and associated granulomatous disease were ruled out. Due to symptomatology and imaging tests, a diagnostic lumbar puncture was performed, showing infiltration of 66% NK cells by flow cytometry in CSF. Similar findings were observed in skin biopsy with cutaneous and central nervous involvement was stated. The patient started a chemotherapy treatment (SMILE protocol) that included dexamethasone, with cutaneous and central nervous involvement was stated. The patient started a chemotherapy treatment (SMILE protocol) that included dexamethasone, ifosfamide, L-asparaginase and etoposide with clinical improvement and radiological resolution of brain lesions three months after the diagnosis.

Conclusion
The diagnosis of central DI always makes it necessary to rule out infectious, autoimmune, infiltrative and hematological diseases. Extranodal NK/T lymphoma (nasal type) is a rare neoplasm with an aggressive behavior, first reported here in presenting with CDI, in which early diagnosis and treatment is essential.

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P381
A metastatic ACC mouse model: Combined inactivation of Znrf3 & Tp53 results in consistent adrenocortical carcinoma formation
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Adrenocortical carcinoma (ACC) is an infrequent and aggressive cancer that originates from steroidogenic cells within the adrenal cortex. Half of patients present with metastatic spread at initial diagnosis, and to date, there is no curative therapy for advanced disease. Recent genomic analysis has established that the most aggressive subgroup of ACC patients have overlapping alterations in the WNT/β-catenin pathway and the p53/RB pathway. We therefore set out to develop a metastatic ACC mouse model based on patient genomic alterations. Using Cre IoxP technology, we inactivated both Znrf3, a negative regulator of the WNT/β-catenin pathway, and p53, a potent tumor suppressor, in steroidogenic cells. By 6 months of age, mice with individual inactivation of p53 (PKO) or Znrf3 (ZKO) did not show tumor formation, while the combined inactivation of p53 & Znrf3 (DKO) resulted in aggressive carcinomas that metastasized at a rate of 36.8%. Using the ROSA26/LacZ reporter, we identified metastatic deposits in the lymph nodes, peritoneal cavity, lungs and liver of DKO mice. Importantly, metastatic DKO mice showed a significant increase in adrenal weight and Ki67 index, while having a significant decrease in overall survival. Furthermore, these tumors

P380
Hormonal therapy in breast cancer patients and malignancy risk of thyroid nodules
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Introduction
The bidirectional relationship of risk between breast cancer (BC) and thyroid cancer (TC) has been debated. Estrogens are proposed as agents implicated in the risk of developing TC promoting thyroid tumorigenesis. Therapies that reduce the effect of estrogens on their receptors in cancer cells are widely used.

Objective
To correlate the use of hormonal therapy in BC with the prevalence of TC.

Material and Methods
We performed a retrospective analysis of female patients with nodular thyroid pathology and BC followed in our consultation from January 2016 to January 2021. The variables were analyzed using the SPSS software; they are expressed as mean and standard deviation (with a 95% confidence interval).

Results
A total of 3253 patients with nodular thyroid disease were identified. In 4.1% of patients (n = 132) BC was described in the medical records. Twenty-eight patients were excluded due to lack of data. Regarding the patients included (n = 104), the mean age at diagnosis of BC was 56 ± 12 years. Patients underwent radiotherapy in 75.9% of cases (n = 79), hormonal therapy in 72.1% (n = 75) and chemotherapy in 52.9% (n = 55). Considering the largest thyroid nodule, the mean diameter in thyroid ultrasound was 22.8 ± 8.5 mm. Fine needle aspiration cytology (FNAC) was performed in 88.5% of patients (n = 92) and was repeated in 23.9% (n = 22), mostly due to an initial non-diagnostic result. Considering both procedures, the result was benign in 82.6% (n = 76), non-diagnostic in 9.8% (n = 9), follicular lesion of undetermined significance in 2.2% (n = 2), suspected of malignancy in 2.2% (n = 2), Hurthle cell tumor in 1.1% (n = 1) and follicular tumor in 2.2% (n = 2). Thyroid surgery was performed in 18.3% of patients (n = 19) with a prevalence of thyroid malignancy of 8.7% (n = 9). Papillary thyroid carcinoma was diagnosed in eight patients and follicular thyroid carcinoma in one patient. Compared with patients who did not undergo hormonal therapy, patients undergoing hormonal therapy did not show a decrease in cytological (OR = 0.88 [0.16-4.88]; P = 0.88) or histological (OR = 0.28 [0.07-1.15]; P = 0.08) risk of TC.

Conclusion
An increased risk of thyroid cancer has been reported in breast cancer survivors. Despite the published evidence on the role of estrogens in the association of BC and TC, in our studied sample there was no relationship between the use of hormonal therapy and the prevalence of TC. Further studies with a larger sample size should be encouraged.

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P383
The bidirectional relationship of risk between breast cancer (BC) and thyroid cancer (TC) has been debated. Estrogens are proposed as agents implicated in the risk of developing TC promoting thyroid tumorigenesis. Therapies that reduce the effect of estrogens on their receptors in cancer cells are widely used. Objectives:

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Conclusion:
An increased risk of thyroid cancer has been reported in breast cancer survivors. Despite the published evidence on the role of estrogens in the association of BC and TC, in our studied sample there was no relationship between the use of hormonal therapy and the prevalence of TC. Further studies with a larger sample size should be encouraged.

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are hormonally inactive, representing a subtype of ACC that has not been previously established in available mouse models. Taken together, these results establish that combined inactivation of Znrf3 & p53 in steroidogenic cells provides a habitable environment for the development of metastatic ACC. The timeline and consistent rate of metastasis in this mouse model highlights its importance for the study of metastatic ACC dissemination, immune-tumor interactions, and potential anti-cancer therapies.

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P382
Effect of metformin on the activity of the mTORC1 complex in patients with type 2 diabetes
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Introduction
The increased risk of cancer in patients with diabetes mellitus (DM) creates an interest in finding mechanisms of the possible association of antidiabetic drugs and carcinogenesis. Metformin has the most documented evidence of pleiotropic oncoprotective effects, including increased stabilization of tumour suppressor p53, inhibition of NF-κB activation, slowing of the cell cycle and inhibition of mitosis due to decreased expression of cyclin D and cyclin E, as well as the positive effect on intestinal microbiota. The study of the drug’s ability to affect the activation of insulin signalling PI3K/Akt/mTOR, which is involved in the regulation of carcinogenesis and metabolism, continues. The aim of the study was to compare the activity of PI3K/Akt/mTOR in patients with type 2 diabetes on metformin monotherapy and other antidiabetic regimens.

Methods
To assess the activation of the PI3K/Akt/mTOR pathway in patients with type 2 diabetes by enzyme-linked immunosorbent assay in peripheral blood mononuclear cells, the content of natural inhibitor of mTORC1 - phosphorylated PRAS40 and the content of phosphorylated protein kinase p70S6K1 were determined. The amounts of phospho-PRAS40 (P-Thr244) and phospho-p70S6K1 (P-Thr389) were determined using a microplate reader of “Bio-tek Instruments” company (USA) at a wavelength of 450 nm with the diagnostic ELISA kits (KHO0421, 85-86053 respectively (Invitrogen, USA)).

Results
Significantly lower phospho-PRAS40 levels in patients with type 2 DM on metformin monotherapy compared with patients on combination therapy with sulfonylurea derivatives (SUD) and metformin (t = 2.34, P < 0.05); lower levels of phospho-p70S6K in patients on monotherapy with metformin in comparison to patients on combination therapy with SUD and metformin (t = 4.13, P < 0.05), combination therapy with SUD and insulin (t = 3.76, P < 0.05), combined therapy with SUD, metformin and DPP-4 inhibitors (t = 4.0, P < 0.05), on insulin monotherapy (t = 3.85, P < 0.05). The decrease in the content of phospho-PRAS40 on metformin monotherapy can be explained by the ability of the drug to increase the interaction of PRAS40 with Raptor in the mTORC1 complex, which influences the phosphorylation activity of PRAS40. Decrease in the content of phospho-p70S6K (depending on the activity of the mTORC1 complex) may be explained by the ability of metformin to increase the level of AMPK, the negative regulator of mTORC1.

Conclusion
The obtained results confirm the property of metformin to inhibit the activity of the mTORC1 complex.

Key words
metformin, type 2 diabetes mellitus, PI3K/Akt/mTOR, phospho-PRAS40, phospho-p70S6K.

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P383
Circulating cell-free tumour DNA (ctDNA) utilisation in diagnosis and monitoring of thyroid cancer response to - systematic review
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Thyroid cancer is the most common endocrine malignancy accounting for 1% of new cancer cases each year. Even after treatment, one in five patients develop recurrence eventually. Current tumour biomarkers are not perfect, and there is a need for a more sensitive and specific way of detecting early recurrence. Liquid biopsies have emerged as a novel marker in tumour surveillance and monitoring response to treatment. In particular, circulating cell-free Tumour DNA (ctDNA) have been investigated. Here, we review the available evidence regarding the use of ctDNA as a liquid biopsy in the diagnosis and monitoring of thyroid cancer response to treatment.

Methodology
Online database search of PubMed (Medline) was performed using keywords:

Circulating Tum* DNA, ctDNA, liquid biopsy, thyroid cancer, thyroid neoplasms, thyroid carcinoma, papillary, medullary, follicular, anaplastic.

Reference lists were reviewed for relevant literature. Modified PRISMA model was adopted for article extraction. Due to significant heterogeneity in trial population characteristics, methodology and outcomes, meta-analysis was not feasible.

Results
After filtering our search to human only trials, some articles were excluded after title reading and screening the text. 11 relevant articles were identified from the online database. 8 more articles were identified from reference lists of relevant reviews raising the total number of articles to 19. Trials included a total of 1163 patients. Of the different tumour types, papillary thyroid cancer (PTC) was the most common type in 71% of patients followed by medullary (MTC) then anaplastic thyroid cancer (ATC) in 14.4% and 10.3% of patients respectively.

BRAFV600E was the most commonly sought after ctDNA variant amongst others which included RET and TP53. Tissue mutant DNA detection was performed using digital droplet PCR (ddPCR) and real-time PCR (qPCR) in most trials. Few trials used targeted Next Generation Sequencing technique limited to previously reported mutational hotspot. Concordance rate of tissue-to-peripheral blood mutant DNA detection rate varied from 0% to 86% in trials of diagnosis and surveillance for disease recurrence. The main pitfall was that seeking mutations commonly reported in the literature in both tissue and blood risks missing ctDNA containing less common/unique mutations thereby reducing ctDNA analysis sensitivity.

Conclusion
ct-DNA offers a novel and minimally invasive tool for surveillance and monitoring of thyroid cancer. Research utilizing wider or individualised gene mutation panels is warranted to improve test sensitivity.

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P384
Appendiceal neuroendocrine neoplasms diagnosed during pregnancy-case series and review of the literature
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Introduction
Although appendicitis occurs in approximately 1:1000 pregnancies, appendiceal neuroendocrine neoplasm (ANEN) diagnosis during pregnancy is very rare. Data on presentation, treatment and prognosis is scarce.

Aim
To describe ANEN cases diagnosed during pregnancy.

Materials and Methods
A retrospective appraisal of 7 consecutive ANEN patients diagnosed during pregnancy from four Israeli tertiary medical centers and comparison with 17 cases described in the literature from 1965-2021.

Results
Age at ANEN diagnosis was 26.4±5.5 years (range 21-33). Patients were diagnosed between gestational weeks 6-40, most frequently in the third trimester (53%). The most common presenting symptom was abdominal pain. Tumor size

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was 14.3 ± 8.9 mm (range 3-45 mm). In patients from our series appendiceal base involvement was reported in 2/7; mesoappendiceal invasion in 5/7; lympho-vascular invasion in 2/7; KI-67 staining was reported in 6/7 cases and ranged from 1-10%. Pathway details were lacking in most of the previously published cases. All 7 pregnancies in our series resulted in term delivery with no complications, whereas in historical cases there were one first trimester abortion, one ectopic pregnancy, and one stillbirth. Right hemicolectomy was performed in 5/7 patients in our series and reported in 2/7 historical cases. All hemicolectomies were performed after delivery, 3-16 months after appendectomy. Local metastases were reported in two cases. Follow-up duration was 7-98 months in our patients and 3-48 months in 5 previous cases. No disease recurrence, distant metastases or mortality were noted.

Conclusions

ANEN diagnosis during pregnancy is extremely rare. Pregnancy outcomes were usually favorable and long-term prognosis was excellent.

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P385

PD-1 and PD-L1 immune checkpoint expression - the prognostic impact on adrenocortical carcinoma

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Adrenocortical carcinoma (ACC) is a very severe endocrine malignancy with poor prognosis. While cancer immunotherapies have revolutionized the treatment of several cancer entities, the results of initial studies of different immune checkpoint inhibitors in ACC were heterogeneous and clinically substantial responses were observed only in a subset of patients. Expression of immune checkpoint molecules - programmed cell death 1 (PD-1) and its ligand PD-L1 - has been shown to predict response in different, but not all cancer entities. Using immunohistochemistry, a cohort of 129 ACCs was examined for PD-1 and PD-L1 expression. PD-1 and PD-L1 were present (threshold of ≥1% of cells) in 17.4% and 24.4% of samples, respectively, but expression was heterogeneous and in general rather low (median 3.9% (range 1-15) and 19.7% (range 1-90)). Interestingly, PD-1 expression was significantly associated with beneficial progression-free (HR: 0.30, 95% CI 0.13-0.72) and overall survival (HR: 0.21, 95% CI 0.53-0.84) independently of established prognostic factors, including ENSAT tumor stage, resection status, Ki67 proliferation index and glucocorticoid effects. In contrast, its ligand PD-L1 was not associated with clinical outcome in this ACC cohort. In addition, we analyzed the correlation of PD-1 and PD-L1 with tumor-infiltrating lymphocytes. Whereas PD-L1 correlated significantly with the number of CD3+ , CD8+ , and FoxP3+ T cells (P<0.0003, < 0.0001 and < 0.0001, respectively), PD-1 correlated only with FoxP3+ T cells (P=0.020). When including both PD-1 and different T cell subtypes in the above-mentioned multivariate Cox regression, the presence of PD1+ cells was the strongest predictor of favorable clinical outcome. In conclusion, this study provides several potential explanations for the heterogeneous results of the immune checkpoint therapy in advanced ACC. In addition, PD-1 expression serves as a strong prognostic biomarker that can easily be applied in routine clinical care as part of histo-pathological assessment.

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P386

Urinary steroid metabolomics for adrenocortical carcinoma diagnosis. Comparison of gas chromatography mass spectrometry to liquid chromatography mass spectrometry

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Introduction

Gas chromatography mass spectrometry (GC-MS) is the gold standard method for urinary steroid profiling. However, GC-MS requires chemical derivatisation, long run times, is labour intensive, expensive, and unsuitable for rapid multi-sample analysis, limiting its use in routine clinical practice. GC-MS urinary steroid metabolomics, the combination of steroid profiling and machine learning (Generalized Matrix Learning Vector Quantization) was shown to have superior specificity and sensitivity for adrenocortical carcinoma (ACC) diagnosis compared to imaging technologies (1). The method has subsequently been transferred to liquid chromatography tandem mass spectrometry (LC-MS/MS), selecting 15 diagnostically relevant steroids, decreasing the complexity and the cost of the assay. This method was applied to the EURINE-ACT cohort, 2017 prospectively recruited adrenocortical tumours patients through an ENSAT/T collaboration (2). Here we compare GC-MS to LC-MS/MS to evaluate the differences in quantitation and ACC diagnostic ability.

Experimental and Results

After deconjugation the steroid extract was either derivatised for GC-MS analysis (Agilent MSD 5975 with a DB1 column) or run directly via LC-MS/MS (Waters-Xevo with Acquity uPLC, HSS T3 column). Correlation between the two technologies was investigated by comparing steroid quantitation in 481 urines from a range of endocrine conditions, including a healthy control cohort 129 urines (75/54 female/male, 20-81 years). Correlation plots and Bland-Altman plots were used to assess method agreement. To compare diagnostic ability urines from 40 patients with adrenal carcinoma (17/23 female/male, 22-79 years, tumour size 50-230 mm) and 99 patients with non-cancerous adrenal tumours (61/38 female/male, 29-83 years, tumour size 9-55 mm) were assessed. Diagnostic ability was determined via calculation of the area under receiver operated characteristic curve (AUROC). There were statistically significant correlations between the methods for all steroids. The diagnostic ability, AUROC for 31 steroids by GC-MS was 0.969, (SD = 0.044), and for 15 steroids by LC-MS/MS, was 0.954 (0.067). The highest estimated specificity = sensitivity = LC-MS/MS for 15 steroids (0.901), followed by GC-MS 31 steroids (0.890).

Conclusions

Despite differences in sample preparation and mass spectrometer design GC-MS and LC-MS/MS showed significantly similar quantitation for all steroids. Reduction of the number of analytes from 31 by GC-MS to 15 by LC-MS/MS does not impact the diagnostic ability for ACC diagnosis. LC-MS/MS should now be introduced into clinical biochemistry laboratories as a routine test for the diagnostic work up for patients with adrenal tumours.


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P387

Prognostic role of targeted methylation analysis in formalin-fixed paraffin-embedded samples of adrenocortical carcinoma

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Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine neoplasia with heterogeneous molecular background and clinical outcome. Previous studies identified hypermethylation in specific genes to be associated with poor
prognosis. Here, we aimed to investigate the role of methylation pattern for prognostic stratification of patients with ACC as compared to clinical parameters, using methods easily applicable in clinical routine. We investigated a total of 237 ACC data were obtained from previously published retrospective cohort (n=107, Lippert et al 2018) with updated follow up data (median overall survival (OS)=65 months) and a novel independent cohort (n=130, median OS=53 months). Tumour-DNA was isolated from formalin-fixed paraffin-embedded specimens. Leukocyte-DNA was used as reference. Targeted pyrosequencing or Deep Bisulfite Sequencing was used to detect methylation in the promoter region of 5 selected genes (G0S2, GSTP1, PAX5, PAX6, and PYCARD). Genes were considered “hypermethylated” if percentage values were >25%. Clinical and histological parameters were collected for S-GRAS score calculation as previously published (Elhassan et al 2021). Survival analysis was performed for progression-free survival (PFS) and OS. A Cox survival model was applied to test the prognostic impact of hypermethylation in each gene and S-GRAS score, separately and combined. Analyses were also adjusted for cohorts. A total of 25%, 14%, 29%, 40% and 49% cases showed hypermethylation in G0S2, GSTP1, PAX5, PAX6, and PYCARD, respectively. Hypermethylation in all individual genes – except GSTP1 – was significantly associated with worst PFS and OS in ACC. However, only were 4.5 and 6.8, respectively, when compared to an S-GRAS score group 0. In conclusion, this study confirms that hypermethylation in preselected genes is significantly associated with worst PFS and OS in ACC. However, only hypermethylation in PAX5 was related to OS when accounting for S-GRAS score. Assessing targeted methylation is straightforward and feasible in the clinical setting. Therefore, the addition of methylation status of PAX5 in the baseline evaluation of ACC patients could help to improve accuracy of prognostic classification and enable the direction of personalized management.

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Endocrine-metabolic disorders in patients with gastroenteropancreatic and lung neuroendocrine tumors

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Background

Neuroendocrine tumors (NET) are characterized by long survival and slow progression. In the clinical practice adfifferent types of endocrine-metabolic disorders can occur. Such disorders are either comorbidities related to the neoplasm or side effects of specific oncological treatments. The aim of this study is to evaluate type and prevalence of the endocrine-metabolic disorders in patients with gastroenteropancreatic (GEP) and lung NETs.

Materials and Methods

This single-center study evaluated 58 consecutive patients with sporadic NETs referring to the ENEST Center in Rome (Sant’Andrea Hospital) from November 2020 to December 2021. Of them 53(53.4%) were affected by GEP NET and 27 (46.6%) by bronchial carcinoma. Twenty patients underwent surgical resection, 12 medical therapy and 26 combined therapies. All patients underwent clinical and biochemical screening for endocrine-metabolic disorders at the baseline and during the follow-up.

Results

Fifty-six over 58 patients (96.6%) were affected by at least one metabolic endocrine disorder. Thyroid dysfunctions were detected in 19 patients (33.9%), including primary hypothyroidism in 16 patients and central hypothyroidism in 1 patient. Six of them occurred after NET diagnosis: 1 after somatostatin analogues (SSA); 2 after targeted therapy and 3 after surgery. Subclinical hypothyroidism occurred in 2 patients after SSA therapy. Impaired fasting glucose occurred in 23 subjects (41%) and was detected after NET diagnosis in 20 patients (5 after SSA, 4 after surgery, 1 after targeted therapy and 10 after combined therapy). Diabetes occurred in 12 subjects (21.4%) and was detected after NET diagnosis in 8 patients (3 after surgery, 1 after targeted therapy and 3 after combined therapy). Dyslipidemia occurred in 23 subjects (41%) and was detected after NET diagnosis in 9 patients (2 after surgery, 1 after targeted therapy and 5 after combined therapy). Hypovitaminosis D occurred in 36 subjects (64.3%) and was detected after NET diagnosis in 19 patients (5 after surgery, 5 after SSA and 9 after combined therapy). Primary hypogonadism occurred in 2 patients and central hypogonadism in 1 patient. Primary adrenal insufficiency occurred in 2 patients after surgery and after SSA, respectively, 1 patient was affected by Cushing Syndrome detected after combined therapy.

Conclusions

NET patients represent a high-risk population for the development of endocrine-metabolic disorders. The most frequent alterations are hypovitaminosis D, dyslipidemia and glucose impairment, mainly occurring after medical therapy and/or surgery. In all patients with NET a screening of endocrine-metabolic disorders at diagnosis and during the follow-up is strongly recommended.

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Uncovering the immune profile in well-differentiated gastroenteropancreatic neuroendocrine tumors

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Introduction

Immune tumor microenvironment plays a key role in tumors’ growth and metastatic spread, while its role in the heterogeneous field of neuroendocrine
antimicrobial peptides (AMPs) remains unclear. There is evidence that tumor progression in NETs is promoted by an immunosuppressed microenvironment created by a plethora of infiltrating immune cells. Changes in circulating leukocyte and peripheral blood mononuclear cell (PBMC) subpopulations can mirror the local alteration of the microenvironment, as demonstrated in different kinds of tumors but data in NETs are lacking.

Methods
A prospective controlled observational study was performed recruiting 15 consecutive patients naive to treatment with histologically proven gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) and 15 healthy controls (Ctrl), matched for age and sex. The primary aim was the quantification of PBMC subpopulations (profiled via flow cytometry).

Results
The mean age of the patients was 60.3 ± 9.7 years (73.3% males). G1 NETs were 46.7%, G2 were 53.3%. Locally advanced or metastatic disease represented the 80%. Immune cell profiling revealed a lower CD3-CD56+ natural killer (NK) cell count in patients with NET than in Ctrl (median [interquartile range], 124 [90-572] vs 402 [265-530] cells/μl; p = 0.04). NK subset analysis showed a reduced percentage of CD56+CD16+ NK cells (81.8% [76.8-89.7%] vs 91.7% [88.9-97.6%]; p = 0.06), a reduced absolute count of CD56+CD16+ NK cells (114 [73-468] vs 340 [247-480] cells/μl; p = 0.026), and a reduced absolute count of CD56dim NK cells (105 [66-544] vs 362 [237-461] cells/μl; p = 0.04) in patients than in Ctrl. Total monocyte count was not significantly different between the study groups. However, patients with NET had a higher percentage of CD4+CD16+ CD68+ classical monocytes (1.8% [1.1-2.5%] vs 1.7% [1.1-2.5%]; p = 0.01), a higher absolute count of CD14+CD68+ classical monocytes (14 [6-23] vs 6 [3-10] cells/μl; p = 0.04), and a lower percentage of CD14+CD16+ intermediate monocytes (5% [2.6-9.2%] vs 8.8% [6.1-11.6%]; p = 0.04). Total CD3+ T lymphocyte count was not significantly different between the study groups. However, a decrease in percentage (mean ± standard deviation, 55.4 ± 8.1% vs 63.9 ± 6.6%; p = 0.004) and in absolute count (554 ± 307 cells/μl vs 820 ± 285 cells/μl; p = 0.02) of CD4+ T helper lymphocytes was found in NETs patients.

Conclusions
The study shows that patients with GEP-NETs have an immune alteration characterized by a low count of cytotoxic NK cells and a high count of anti-inflammatory non-classical monocytes, suggesting a deregulation of CD14 expressing cells. Moreover, a low count of T helper lymphocytes was found. This unfavorable and immunosuppressed immune profile could contribute to tumor growth and progression.

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P391
Effect of mitotane on male gonadal function
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Mitotane (MTT) currently represents the treatment of choice for adrenocortical carcinoma (ACC). Clinical evidence shows the occurrence of hypergonadism following treatment with this drug, observed more frequently in male patients. The aim of the study, therefore, was to evaluate the impact of MTT treatment on male gonadal function on adult CD1 mice. At the end of the 45 days of treatment, tests were collected for morphological examination, and a blood sample of each animal was retrieved to evaluate serum hormone levels. Serum testosterone was significantly lower in MTT-treated animals than the control siblings. The testis of animal was retrieved to evaluate serum hormone levels. Serum testosterone was significantly lower in MTT-treated animals than the control siblings. The testis of animal was retrieved to evaluate serum hormone levels. Serum testosterone was significantly lower in MTT-treated animals than the control siblings. Therefore, we can conclude that MTT treatment adversely affects male gonadal function, as measured by serum testosterone levels.

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P636
Struma ovarii with NIFTP tumor; case report
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Struma ovarii is a form of mature teratoma, a rare germ cell tumor, containing more than 50% thyroid tissue. Malignancy is uncommon. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) inside struma ovarii was never described. A 32 y.o. female with previous history of ovarian cysts was admitted in the emergency room with painful acute abdominal distention. The MRT revealed a right adnexal mass, predominantly cystic with 82x66x80 mm and surrounding oedema. Suspecting of right ovarian torsion, exploratory laparotomy was performed. The torsion was confirmed and the adnexal mass removed. Histopathological examination showed mature thyroid follicles with abundant colloid in more than 50% of the tissue - consistent with struma ovarii - and a 1 cm area of NIFTP tumor. Thyroid ultrasound was normal and laboratory exams (thyroid function and thyroglobulin levels) within reference range. Malignant struma ovarii is a rare clinical entity that poses a therapeutic challenge, as there is no "gold standard" of care. NIFTP is an encapsulated or clearly delimited, noninvasive neoplasm with follicular growth pattern and nuclear features of papillary thyroid carcinoma, that has an excellent prognosis in thyroid gland, but with yet unknown/uncharacterized behavior as struma ovarii. Of our knowledge, this is the first reported NIFTP in a struma ovarii. The patient is being kept under surveillance by the multidisciplinary team.

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Aim
In the current study we wished to compare the characteristics of VHL-related and sporadic PNET. We also tested the hypothesis that diagnosis of VHL according to the International and Danish criteria may comprise two distinct patient populations.

Methods
Patients with a diagnosis of PNET were identified using the MD Clones platform and data including demographic and tumor specific characteristics were gathered. In addition, the presence of any clinical feature of VHL and presence of a family or genetic diagnosis was noted for each patient. Patients were grouped according to a diagnosis of VHL (following either International or Danish criteria) or sporadic PNET.

Results
Twenty-nine patients with VHL, 17 (58%) with PNET and 65 patients with sporadic PNET were identified. Patients with VHL were younger at PNET diagnosis compared with sporadic PNET (50.1 ± 4.7 vs. 62.8 ± 1.5 years, P < 0.001). There was no significant difference between VHL-related or sporadic PNET in stage and grade, nor in progression or survival. Sporadic PNET were more often located in the body and tail of pancreas. In the subgroup comparison of International vs Danish criteria –based VHL diagnosis, age at diagnosis of PNET, RCC and VHL was younger in the International group. Hemangioblastomas were diagnosed in 90% of patients in the International compared with none in the Danish group. First manifestation of VHL was hemangioblastomas (47%) followed by phaeochromocytomas (31%) in the International group compared with RCC (62%) and PNET (37%) in the Danish group. Finally, 50% in the International and none in the Danish group had a family or genetic VHL background.

Conclusions
Patients with PNET diagnosed with VHL according to the International and Danish criteria seem to form two distinct clinical groups, with a greater similarity of the Danish group to patients with sporadic PNET. Further comparisons in other cohorts are warranted, as this may call for different clinical management.

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P639
Does the length of a polyalanine tract in the FOXE1 gene impact the course of familial non-medullary thyroid cancer?
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Familial non-medullary thyroid cancer (FNMTC) constitutes about 3–9% of all thyroid cancers. One of the genes believed to predispose to non-syndromic FNMTC is FOXE1. It contains a polyalanine tract (polyAla) with a variable number (11 – 22) of alanine residues. This length polymorphism could lead to changes in the FOXE1-encoded protein (FOXE1 transcription factor) structure and predispose to papillary thyroid cancer (PTC). The aim of the study was to investigate the relationship between the length of the polyAla tract and the stage of PTC at diagnosis (according to AJCC 8th edition) in patients with FNMTC. The study included 27 patients with familial PTC (at least two family members were diagnosed with the disease). The length of the polyAla tract of the FOXE1 gene was analyzed. The following numbers of polyAla variants were detected: 11-Ala – 2, 12-Ala – 1, 14-Ala – 23, 16-Ala – 28 alleles. The staging at diagnosis was compared in two groups: less than 16-Ala and at least 16-Ala. The stages of pt1a and pt1a (m) were found in 20 alleles in the less than 16-Ala group, whereas in 16 alleles of the at least 16-Ala group, pt1b (pt2) (m) was the most common (P = 0.039). Lynny hormone metastases were found more frequently in the less than 16-Ala group than in the at least 16-Ala group but this difference was not statistically significant (10 vs. 3 respectively; P = 0.680).

Conclusions
The analysis of the length of the polyAla tract may be a useful diagnostic tool in predicting the course of PTC in patients with a positive family history.

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P640
Short fasting test as reliable and effective tool to diagnose insulinoma
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Introduction
Insulinomas are rare pancreatic NETs presenting with chronic hypoglycaemia. Current guidelines for diagnosis require a prolonged fasting test (72 h), which implies hospitalization and is difficult to perform, delaying prompt diagnosis and treatment. It has been reported that 65 to 85% of insulinomas could be diagnosed after less of a 24 h fasting period and 94 to 95.7% within 48h, although a shorter test for diagnosis has not yet been standardized.

Objective
To predict weather a shorter outpatient fasting test initiated overnight and portrayed up until 24h could be a sensitive method for diagnosing insulinoma.

Materials & Methods
we conducted a retrospective monocentric study to evaluate the diagnostic performance of the short fasting test to achieve the diagnosis of insulinoma. All subjects admitted from 2019 to 2021 at the Unit of Endocrinology of the Sant'Andrea Hospital with clinical suspicion for insulinoma (documented
hypoglycaemia in absence of other known causes or intake of hypoglycaemic drugs) underwent the short fasting test (n = 9). A comparison study was performed with subjects who underwent the standard prolonged fasting test from 2003 to 2018 (n = 22). The short fasting test is initiated by the patient overnight at home and proceeds the following day in outpatient setting (Day Hospital). As in the standard protocol, symptoms and capillary blood glucose (CBG) are strictly monitored. Venous blood is drawn for glycaemia, insulin and C-Peptide at admission, in case of symptoms of hypoglycaemia or if CBG ≤ 45 mg/dl. Diagnostic values for insulinoma consist of glucose < 55 mg/dl with insulin ≥ 3 μU/ml and C-Peptide ≥ 0.6 ng/ml. In case of a negative result and a remaining high suspicion for insulinoma, the prolonged test would be performed subsequently.

Results

The final sample consisted of 31 patients, with mean age ± Standard Deviation (SD) of 44.5 ± 12.6 years (17-74). Diagnostic values for insulinoma were found in a total of 10 patients: in 6/22 who underwent the prolonged test and in 4/9 who underwent the short fasting test. Time counting from the last meal until diagnosis ranged from 4h to 30h, with average ± SD of 11 ± 7.3 h; however, only one patient showed diagnostic values at > 24h (30h).

Conclusion

In our series, 9/10 (90%) patients with insulinoma were diagnosed within 14 h from the beginning of the fast. A short fasting test could be a valid, sensitive and reliable first-line workup in diagnosing insulinoma, without hospitalization.

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P641

Management and long term follow up of hyperparathyroidism in multiple endocrine neoplasia type 1: single center experience

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Background and objective

Multiple Endocrine Neoplasia type 1 (MEN 1) is an autosomal dominant disease characterized by a broad clinical spectrum. Previous multi-center studies, that analyzed large groups of patients with MEN 1 have been reported before but long term follow up data of these patients focusing exclusively on primary hyperparathyroidism (PHPT) are scarce.

Patients and Methods

In this retrospective cohort study we include all patients with PHPT in the context of MEN1 that were under regular follow up in our institution.

Results

Our cohort consisted of 68 patients (39 males and 29 females), with a mean age at MEN1 diagnosis of 39 ± 13.06 years. Obvious family history of MEN1 was present in 76.7% of the patients. Besides PHPT, pancreatic neuroendocrine tumors were the most commonly neoplasm encountered in 80% of patients (62% non-functioning), followed by pituitary adenomas in 66% (micro 73%, non-functioning 49%). The mean age at PHPT diagnosis was 35.2 ± 14.0 years. Fifteen patients developed osteoporosis (22%), 22 (64.7%) nephrocalcinosis and one nephrocalcinosis. Parathyroidectomy was performed in 57 patients (82.3%). At the initial parathyroid surgery the majority of patients had subtotal parathyroidectomy (61.4%, n = 35). Long term remission of PHPT was reported in 32 patients (56%), persistence in 7 (12.2%), and recurrent disease in 18 patients (31.5%) at a median follow-up of 4 years (1 to 21 years). Reoperation for recurrent disease was performed in 11 of the 18 patients (61%), and permanent hypoparathyroidism occurred in 11 patients (19.2%). A total of 23 patients (33.8%) were treated with a calcimimetic agent with favorable results on serum calcium levels, including both first-line and second-line treatment in unoperated patients and persistent or recurrent disease, respectively. Gene analysis was performed in 44 patients (65%) and a variant known to cause MEN1 was identified in 34 patients (77.2%) while 5 (11.3%) had a variant of uncertain significance. No genotype – phenotype associations were reported, albeit the number of patients was small (n = 34).

Conclusions

PHPT in the context of MEN1 involves a multiglandular disease and remains a therapeutic challenge over long term for treating physicians, as recurrent disease can develop even after 20 years of follow up. Collection of clinical, biochemical, and genetic characteristics of MEN1 in referral centers at a national level is critical for the optimal management of these patients.

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P642

 Thyroid cancer and thalassemia major: new hypotheses from an old clinical scenario

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Thyroid cancer (TC) is one of the most frequent neoplasia diagnosed in general population with an estimated incidence of 6.6 cases per 100.000 and mortality of 0.43 cases per 100.000. Differentiated thyroid cancer (DTC), which includes papillary (PTC) and follicular cancer (FTC), comprises the large majority (up to 90%) of all thyroid cancer cases. At the moment etiology of TC is not completely understood, with multiple genetic and epigenetic factor that are thought to be important. We report our recent experience, as a dedicated tertiary care unit in the cure of thalassemia major (TM), that could be useful in the knowledge about induction and progression of carcinogenic process. TM is a clinical disorder characterized by abnormalities in hemoglobin’s synthesis with main treatment that is characterized by regularly blood transfusion. This therapy usually estivate in iron overload and tissue damage and could be cause of serological viruses transmission (like hepatitis B and C virus or human immunodeficiency virus). In a group of 126 patients affected by TM and studied by neck ultrasound we found thyroid nodules in 36 out of 126 with a prevalence of about 28.5%. Regarding patients affected by thyroid nodules we found 10 cases of TC with a prevalence of nearly 27% of neoplastic lesion that is higher than one reported in general population. Most of TC patients were female, with median age at diagnosis of 37 years and with an histological picture of papillary in 9 out of 10. Interestingly most of all were affected by relevant endocrine tissue damage (more than 3 endocrinopathy in nearly 80% of cases) giving us the chance to consider iron overload as a main actor in pathogenesis. Moreover 80% of patients affected by TC showed Hepatitis C virus (HCV) positivity raising the suspicion that HCV infection could perform a relevant role in induction and progression of disease, as previously reported. In conclusion our work would give a key to consider newer pathogenetic aspects in TC induction and progression. These considerations could be relevant especially in some clinical scenario and could be useful in innovative strategy in prevention, diagnosis and treatment.

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P644

Sublethal hyperthermia decreases cellular proliferation and transiently disrupts steroidogenesis in adrenal cells

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Sublethal hyperthermia decreases cellular proliferation and transiently disrupts steroidogenesis in adrenal cells

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Introduction

Primary Aldosteronism is the most common cause of secondary hypertension. First-line treatment; adrenalectomy resets adrenal nodules and adjacent normal tissue, limiting suitability to those who present with unilateral disease. Use of thermal ablation represents an emerging approach as a possible minimally invasive therapy for unilateral and bilateral disease, to target and disrupt hypersecreting aldosterone producing adenomas, while preserving adjacent normal adrenal cortex. Ablation involves heating tissue >30°C to induce cellular necrosis. Outside the core ablation zone, the transitional zone is an area exposed to variable temperatures between 37°C – 50°C. To understand the feasibility of precision ablation in the adrenal gland, we examined the effect of applying these temperatures to adrenocortical cells to identify i) the required temperature to effectively ablate adrenal cells ii) the extent of damage that may occur to surrounding healthy adrenal cells with exposure to transitional zone temperatures.

Methods

Steroidogenic adrenocortical cell lines, HE95R and HAC15, were treated with hyperthermia (high precision water bath) at temperatures of 37, 42, 45, 48 and 50°C. Steroidogenesis was subsequently stimulated using forskolin (10µM) and angiotensin II (10 nM), or cells were treated with Thapsigargin (10µM). Cell death (Propidium iodide staining by flow cytometry), proliferation (xCELLigence real-time cell analysis), protein expression (Western blot/RT-PCR), steriod secretion (HPLC-Mass spectrometry) and intracellular calcium release (Fluo-4 AM flow cytometry/confocal live imaging) were analysed immediately and 7-days post-treatment. Results

Cell death occurred at 48°C and 50°C (P<0.05 vs 37°C control), but not 45°C, or 42°C. Sublethal hyperthermia (45°C for 30 minutes) induced a heat shock response (upregulated HSP70 and HSP90), alongside a decrease in aldosterone and cortisol secretion (P<0.05), reduced expression of steroidogenic enzymes (CYP11B1, CYP11A1, P<0.05), and decreased intracellular calcium release 18-h post treatment. At 7-days post sublethal hyperthermia, steroid secretion and steroidogenic enzymatic expression returned to baseline levels.

Conclusion

Hyperthermia at 48°C and 50°C for 15 minutes is required for sustained cell death at 7-days post treatment. Sublethal hyperthermia, equivalent to that produced in the transitional zone during thermal ablation, produces a short-lived unsustained inhibition of steroidogenesis that recovers 7-days post treatment. Therefore, segmental adrenal sparing ablation is possible with recovery of transitional zone following ablation. This underlines the potential for precision technology development for bilateral adrenal ablation as definitive measure to treat PA caused by APA or Micronodular disease.

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Methodology of the SORENTO clinical trial: assessing the efficacy and safety of high exposure oCREtide subcutaneous depot in patients with GEP-NETs

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Background

Somatostatin receptor ligands (SRLs) are first-line standard-of-care therapies for gastroenteropancreatic neuroendocrine tumours (GEP-NETs), showing efficacy in tumour and symptom control with an established safety profile. However, disease progression may occur despite standard-dose SRL treatment, requiring more aggressive and toxic treatments. Retrospective/non-randomized data suggest higher-dose SRLs may benefit patients with GEP-NETs who do not respond to standard-dose treatment and provide improved disease control. Ocreotide depot (CAML2029) is a novel high-exposure, subcutaneous (SC) formulation. Clinical trials showed ~500% higher CAM2029 bioavailability vs ocreotide long-acting release (LAR) (Tiberg et al. 2015), and maintenance/reduction of NET symptoms (Pavel et al. 2019). Prospective, randomised trial data are needed to confirm the efficacy/safety of higher-dose SRLs such as CAM2029, vs standard-dose SRLs (including octreotide LAR and lanreotide Autogel [ATG]).

Methods

SORENTO is a randomised, multi-centre, open-label, active-controlled Phase 3 trial, aiming to enrol 302 adults with GEP-NETs. Key eligibility criteria: advanced, well-differentiated NET of GEP presumed GEP origin, ≥ 1 measurable and somatostatin receptor-positive (by nuclear imaging) lesion according to RECIST 1.1; no or <6 months consecutive treatment with long-acting SRLs. Notably, patients with well-differentiated Grade 3 GEP-NETs (excluded by CLARINET and PROMID trials) are eligible. Patients will be randomised 1:1 to CAM2029 20 mg every two weeks (Q2W), or active comparator (octreotide LAR 30 mg intramuscular or lanreotide ATG 120 mg SC, every four weeks). CAM2029 self-/care-administration is permitted after 30 mg intramuscular or lanreotide ATG 120 mg SC, every four weeks). Patients (in either treatment group) who experience progressive disease in the primary analysis, the comparator group may switch to CAM2029 20 mg every two weeks (Q2W), or active comparator (octreotide LAR 30 mg intramuscular or lanreotide ATG 120 mg SC, every four weeks). CAM2029 self-/care-administration is permitted after 30 mg intramuscular or lanreotide ATG 120 mg SC, every four weeks). Patients (in either treatment group) who experience progressive disease in the randomised part of the study may proceed to an open-label extension with intensified CAM2029 treatment, to investigate effects of higher frequency dosing. First patient randomised in Nov-2021; read-out (achieved after 194 events) expected by end of 2024. This novel head-to-head superiority trial is anticipated to demonstrate the potential benefits of CAM2029 as first-line therapy in patients with well-differentiated GEP-NETs. ClinicalTrials.gov identifier: NCT05050942.

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Ectopic Cushing’s syndrome due to thymic neuroendocrine tumour - a case report

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Introduction

Ectopic Cushing’s syndrome (ECS) is a rare endocrine condition caused by corticotrophin (ACTH) hypersecretion of nonpituitary neoplasms. Thymic neuroendocrine tumours (NETs) account for about 5-10% of ECS cases, typically with aggressive clinical course.

Case Report

A 31-year-old previously healthy female presented to the emergency department with a 3-week history of fatigue, muscle weakness, headaches and generalized swelling. Physical examination revealed peripheral oedema, high blood pressure (170/100 mmHg) and tachycardia (170 beats/min). Laboratory tests showed...
leukocytosis (13.95 x10^9/L), hyperglycemia (478 mg/dl) and metabolic alkalosis with profound hypokalaemia (2.5 mmol/l). She was started on insulin therapy along with aggressive hypokalaemia repletion and antihypertensive treatment. Given the overall clinical presentation and resistance to initiated treatment, aggressive CS was suspected. Hormonal tests were as follows: midnight serum cortisol 69.17 mg/dl, urinary free cortisol 11587.5 μg/24h, ACTH 963.7 pg/ml. Chromogranin A (CgA) level was notably elevated (1385.0 ng/ml). Negative HDDST and CRH tests, negative pituitary imaging with short duration and rapid progression of symptoms were highly suggestive of ECS. To control hypercortisolism, continuous etomidate infusion was started with significant improvement in the patient’s general condition, oedema reduction and normalization of blood pressure, glycaemia and potassium level. Computed tomography (CT) revealed a left adrenal mass measuring 80x56x39 mm infiltrating the diaphragm. Whole-body 18F-FDG-PE/TCT showed a metabolically active lesion of the left adrenal gland and multiple active bone lesions suggestive of metastatic malignancy. The patient underwent laparoscopic left adrenalectomy with a postoperative significant decline in cortisol level (4.08 mg/dl) and required hydrocortisone replacement. However, histopathology showed adrenal adenoma with extensive necrosis. A follow-up (8 weeks) body PE/TCT finally revealed 18F-FDG-avid (SUVmax 9.3) 42x33 mm lesion in the anterior mediastinum. Due to the local invasion, only a partial resection was performed. Histopathology revealed a thymic large cell neuroendocrine carcinoma with atypical thymic carcinoid component [ACTH (+), CgA (+), synaptophysin (+), CD56 (+), MGMT:70%, Ki-67:30%, p53: <15%]. Thymectomy was followed by mediastinal radiotherapy and chemotherapy with the ADOC regimen. The patient has been under endocrine and oncological follow-up for almost 3 years, however, due to the progression of the disease, the prognosis is poor.

Conclusions
The diagnosis and management of ECS remain challenging. ACTH-secreting thymic NETs often behave aggressively and lead to the rapid development of severe hypercortisolism causing uncontrolled hypertension and hyperglycemia with hypokalaemic alkalosis requiring prompt intervention. Due to the rarity and complexity of the disease, management of ECS caused by malignant thymic NETs needs a personalized and multidisciplinary approach.

Environmental Endocrinology
P134
Autoimmune polyglandular syndromes in childhood: casuistic of a pediatric unit
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Introduction
Polyglandular Autoimmune Syndromes (PAS) are a group of diseases characterized by the association of different endocrine and non-endocrine autoimmune pathologies. Although the diagnosis of PAS is more frequent in adulthood, it can occur in pediatric age, with PAS type 3 being the most frequent. Objective To study the prevalence and characteristics of PAS in the pediatric population of a tertiary center.

Methods
Retrospective analysis of the clinical files of patients with type 1 diabetes mellitus, autoimmune thyroid disease (ATD), Celiac Disease and Addison’s disease (AD) followed in a Pediatric Endocrinology consultation from 1 January 2010 to 31st December 2020.

Results and Conclusions
Of the 879 cases consulted, 35 patients with PAS were identified, 27 female, with a mean age at diagnosis of 7.8 ± 4.9 years, time mean elapsed between the 1st and 2nd manifestation of 50.2 ± 4.3 months and 37.1% had a family history of autoimmune disease. Regarding classification, 3 patients had PAS type 2, 9 patients PAD type 3A, 14 patients PAS type 3C and 9 patients PAS type 4. In the group of PAS type 2 patients (2 males), all had ATD (2 Hashimoto’s thyroiditis and 1 Graves’ disease). Among patients with PAS type 3 (22 females), 24 had ATD, 9 DM1, 9 CD, 3 Vitiligo, 1 Autoimmune Hepatitis and 1 Systemic Lupus Erythematosus. CD was the first manifestation in 9 patients, DM1 in 6, DAT in 5, Vitiligo in 2 and Autoimmune Hepatitis in 1. Regarding PAS type 4 (5 females), all patients had DM1 and CD, the former representing the first diagnosis in 88.9% of cases.

Conclusion
PAS are rare among the pediatric population. In this sample, all patients were diagnosed with PAS type 2, type 3 or type 4, with the majority being female. The variable clinical presentation is consistent with what is described in the literature, as well as the high prevalence of a family history of autoimmune diseases. Frequently, the time interval until the diagnosis of a second endocrinopathy can be long (decades), which demonstrates the importance of active surveillance of patients with autoimmune diseases.

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P135
Effects of decamethylcyclopentasiloxane by maternal exposure on the offspring mice behaviors
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Decamethylcyclopentasiloxane (D5) is one of the most common chemical ingredients for daily necessities that can be absorbed through the skin, aerosol, or even orally. People are exposed to D5 daily, but the risk of prenatal exposure to D5 is not completely understood. In this study, the effects of prenatal exposure to D5 on neural development were assessed through behavioral tests on offspring mice. First, the developmental neurotoxicity test (DNT) was performed to determine if D5 is a neurotoxicant. From the DNT, D5 was classified as a developmental neurotoxicant because their score of the discriminant function (SDF) was -1.55603, which is less than the standard score 0 of DNT. The estimated daily exposure of D5 to humans has been reported to be around 0.6 mg/kg. In this study, the pregnant mice were treated with 3, 6, and 12 mg/kg of D5 with corn oil per day from embryonic day 10 (E10) through postnatal day 7 through oral administration. All behavior tests were performed after the pups reached six weeks of age. As a result, the administration of 12 mg/kg of D5 (high dose group) increased the repetitive activity in both the grooming and marble burying tests and even a depression in tail suspension and forced swimming test compared to the vehicle group. In addition, high dose group showed a decrease in social behavior and cognitive ability in the three-chamber test. In the novel object recognition test, impairment of memory and exploring ability was found on the high dose group. The expression level of the four genes, brain-derived neurotrophic factor (BDNF), tyrosine hydroxylase (TH), acetylcholinesterase (AChE), and GABA type A receptor associated protein like 1 (GABARAPL1) related to neural development, were measured in the whole brain. The administration of high dose of D5 decreased the transcription level of BDNF and increased AChE and TH compared to the vehicle. On the other hand, there is no meaningful difference in GABARAPL1. These results show that the maternal exposure to D5 impairs the social and memory ability of mouse offspring and alters gene expression in the brain. In conclusion, maternal exposure to D5 can cause behavioral disorders in their offspring. Therefore, it is necessary to discuss the excessive usage of D5.

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P136

Orbital inflammatory disease following mRNA SARS-CoV-2 vaccine: a case report

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SARS-CoV-2 vaccination campaigns document a satisfactory high profile of protection against Covid-19 infection, but auto-immune/inflammatory diseases have been reported following Covid-19 vaccines. A 65-year-old woman reported two days following her first dose of the BNT162b2 mRNA vaccine tearing, eye irritation, conjunctival redness, peri-orbital swelling, spontaneous haemorrhage of the right lower eyelid, right greater than left proptosis, with a spontaneous improvement of symptoms during the following two weeks. She received the second dose of BNT162b2 vaccine after 6 weeks and noted an aggravation of the right proptosis. An ophthalmic examination noted high intraocular pressure on the right eye (30 mmHg) and brinzolamide, timolol and latanoprost eye drops were progressively introduced. After 3 months, Hertel values were 25 and 19 mm and palpable tissues 12 and 11 mm for right and left eyes, respectively. The clinical activity score (CAS) was 4/7, but visual acuity, ocular motility and color vision test were normal. TSH concentration was 0.83 µIU/mL and anti-thyroid antibodies were negative. CT and MRI scans confirm an asymmetric proptosis with a diffuse infiltration of the orbit fat and hypertrophy of extra-ocular muscles in the right orbit. At 4th month, she reported a visual acuity loss of the right eye (20/30) but fundus examination and optical coherence tomography were normal. She had intravenous 500 mg methylprednisolone infusion every two days and she reported transitory improvement of symptoms. Then she received iv 500 mg methylprednisolone once weekly for 4 weeks. She noted a transient improvement of pain and eyelid edema after each infusion, without reduction of proptosis and CAS after the first 6 intravenous infusions. Then the patient had intravenous 250 mg methylprednisolone once weekly for 4 weeks. She noted a transient improvement of symptoms that returned, and visual acuity and orbit extra-conjunctival evaluation reported Hertel value (23 mm), intraocular pressure (17 mmHg) and CAS (2/7) for right eye. To our best knowledge, there is the first report of an orbital inflammatory disease following mRNA SARS-CoV-2 vaccination. The temporal relationship between Covid-19 vaccination and onset of orbital symptoms suggest that SARS-CoV-2 mRNA vaccine can probably be associated with this orbital inflammatory disease. The mechanisms of occurrence of this orbital inflammatory disease side effect are a manner of debate (molecular mimicry, bystander activation, autoimmune/inflammatory syndrome induced by adjuvants). There is no treatment consensus when patients do not respond to first-line glucocorticoids (immunomodulatory therapy, orbital radiation, decompressive surgery).

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P137

Di-butyl phthalate exposure in a human adrenocortical cell line impairs steroid hormone synthesis

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Phthalates are man-made chemicals that are used in many different types of products. The main use is as plasticizers, but they can also be added to, for example, cosmetics, drug coatings, and perfumes. One of the most commonly used phthalates is di-butyl phthalate (DBP), which has been detected in both food and drinking water globally. Once ingested, DBP is rapidly metabolized to its main metabolite, mono-butyl phthalate (MBP), which is frequently detected in human plasma and urine. Studies suggest that DBP has anti-androgenic potential and that it can induce reproductive and developmental effects. However, the molecular mechanisms behind these effects are unknown. We used the human adrenocortical cell line H295R to investigate how DBP and MBP may affect steroid hormone synthesis. After 48-h exposure, samples were collected and the supernatant analyzed by mass spectrometry and cell pellet by western blot to measure the levels of several steroid hormones and key steroidogenic enzymes, respectively. The results demonstrated that DBP induced a dose-dependent decrease in testosterone levels, and a similar decrease was detected for the precursor androstenedione. The corticosterone level also decreased after DBP-exposure, while cortisol increased. MBP induced similar effects as DBP, but with a lower effect size. However, MBP-exposure caused a decrease in cortisol, thereby indicating that there are differences in the mechanism of action between the two compounds. In addition, it was discovered that the decreases in steroid hormone levels are potentiated when the cells are co-treated with dibutyl-cyclicAMP, which mimics endogenous stimulation of adrenal cells by adrenocorticotropic hormone to increase production of steroid hormones. The results also revealed that the levels of several steroidogenic enzymes were altered, with similar differences between MBP and DBP exposure as for the hormone concentrations. To conclude, these findings suggest that MBP is less potent than its parent compound, that the effects of phthalate exposure on the steroidogenesis are more profound during stimulation, and that both compounds affect steroid hormone production by alterations to the steroidogenic enzymes.

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P392

A cell-based platform to screen chemical mixtures for endocrine disruptive effects

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Chemical contaminants from human activity are omnipresent in the environment. A great number of common industrial compounds are detected in human blood and urine. Common chemicals such as phthalates, phthalates and parabens that can interfere with endocrine signaling are classified as endocrine disruptive compounds (EDCs). The sex steroid hormonal signaling pathway is complex and sensitive to interference, as circulating concentrations of these hormones are low. Even miniscule amounts of an active chemical could therefore result in endocrine effects as DBP, but with a lower effect size. However, MBP-exposure caused a decrease in cortisol, thereby indicating that there are differences in the mechanism of action between the two compounds. In addition, it was discovered that the increases in steroid hormone levels are potentiated when the cells are co-treated with dibutyl-cyclicAMP, which mimics endogenous stimulation of adrenal cells by adrenocorticotropic hormone to increase production of steroid hormones. The results also revealed that the levels of several steroidogenic enzymes were altered, with similar differences between MBP and DBP exposure as for the hormone concentrations. To conclude, these findings suggest that MBP is less potent than its parent compound, that the effects of phthalate exposure on the steroidogenesis are more profound during stimulation, and that both compounds affect steroid hormone production by alterations to the steroidogenic enzymes.

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disruption and cause adverse effects on development, brain function, and the reproductive- and immune systems. Industrial chemical production require risk assessments that balance societal benefits to potential negative effects on human- and environmental health. These risk assessments are based on observations in short term single-chemical exposure studies, which is not reflective of real-life scenarios where exposure to different chemicals and classes from many sources occur simultaneously. Additive or synergistic effects are a concern, since the toxicity of different compounds in the biological system could interact and produce an unexpected and exaggerated toxicological response. The single compound approach therefore runs the risk to potentially underestimate the biological impact of mixture effects. We have set up a small chemical library of environmental contaminants and employ liquid handling dispensing to reproduce real-world mixtures for screening of toxic effects. The endocrine disruptive potential of these mixtures is investigated by using OECD-validated in vitro cell-based methods that assess effects on steroidogenesis and androgen- and estrogen receptor interactions. Our aim is to establish medium or high throughput (MTS/HTS) micro plate-based screening methods for toxicological investigation of the complex chemical mixtures. This set-up will later be applied to investigate the effects of reconstructed individual exposures based on chemical profiles detected by advanced mass spectrometry analysis of serum collected from a Swedish cohort. This will aid in the development of highly relevant risk assessments for chemical mixtures, in order to protect the general population from endocrine disruptive mixture toxicity.

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P393

Dioxin-like polychlorinated biphenyl (PCBs) congeners induce inflammatory responses and reduce thyroid-specific genes expression in human thyrocytes via ahr pathways

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Background
PCBs are persistent organic pollutants, able to affect thyroid function (endocrine disruptors) and promote inflammation through multiple mechanisms. The aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor able to bind dioxins and dioxin-like pollutants including PCBs, play a key role in xenobiotic response, by up-regulating specific responsive genes, the so-called “AhR gene battery”, including cytokrome P450 1A1 (CYP1A1) and Nuclear-factor 2 dioxin-related factor-2 (Nrf2), a master regulator of the redox homeostasis with simultaneous anti-inflammatory activity. Aim of the present study was to investigate the influences of the AhR agonist PCB congeners on thyrocytes in vitro.

Methods
Cultured primary thyrocytes were exposed for 24 h to increasing concentrations (5 and 10 μM) of 2,3,4,4’,5-Pentachlorobiphenyl (PCB 118) and 3,3’,4,4’,5-Pentachlorobiphenyl (PCB 126). mRNA and proteins expression for IL-1β (IL-1β), IL-6, TGF-β (TGF-β), TSH, FT3, FT4, TPO, AHR, CYP1A1 and Nrf2 were evaluated by real-time PCR and Western Blot and ELISA, respectively. Protein quantification was assessed by densitometry analysis.

Results
In cultured thyrocytes, exposure to PCB 126 and PCB 118 at 5 and 10 μM concentrations significantly induced the increase of both mRNA and protein levels of the inflammatory cytokines IL-1β and IL-6 (P < 0.05 and P < 0.001, at 5 and 10 μM respectively for mRNA expression; P < 0.05 and P < 0.01 at 5 and 10 μM for protein levels). Additionally, both mRNA and protein levels of the AhR and the downstream molecules CYP1A1 and Nrf2 were increased in PCB-treated thyrocytes (for AhR and Nrf2 P < 0.05 at highest concentration; for CYP1A1 P < 0.05 and P < 0.01 at 5 and 10 μM respectively), suggesting activation of AhR pathways and oxidative stress sensitive markers (CYP1A1 and Nrf2) induction in response to PCBs exposure. On the contrary, the levels of Tg and NIS mRNA and related protein decreased after PCBs treatments at 5 and 10 μM concentrations (P < 0.05 and P < 0.01, for mRNA expression at 5 and 10 μM respectively; P < 0.05 at 10 μM for protein levels), indicating down-regulation of these thyroid-specific genes in PCBs-induced inflammation.

Conclusion
PCBs 118 and PCB 126 may promote inflammatory responses, leading to alteration in Tg and NIS genes expression in thyrocytes. Such effects can be partially attributed to the activation of the AhR that, in turn, induces CYP1A1 and Nrf2, causing changes in the cellular redox status. These data may contribute to explain the mechanisms underlying thyroid toxicity of dioxin-like PCBs and highlight the potential role of these environmental pollutants in contributing to autoimmune thyroid inflammation and damage.

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P394

Synergism between bisphenol a exposure and overweight/obesity in increasing the malignancy risk in a cohort of patients with thyroid nodules

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Introduction
The plasticizer Bisphenol A (BPA) is an endocrine disruptor with thyroid interfering activity. Obesity is a recognized risk factor for thyroid cancer. A recent study showed that subjects with BMI ≥ 25 are more prone to BPA-related thyroid disruption. To date, few and controversial experimental and epidemiological data provide weak evidence about a correlation between BPA exposure and thyroid cancer development. Aim of the present study was to assess a possible link between BPA, body fat excess, and thyroid cancer risk.

Patients and Methods
Multicentre, cross-sectional study including consecutive patients subjected to cytology for diagnostic definition of thyroid nodules. Blood samples were obtained for all enrolled patients. Serum BPA determination was performed by means of high performance liquid chromatography coupled in tandem with fluorescence and ultraviolet detection. Inclusion criteria: a) age ≥ 18 years; b) clinical management performed in one of the involved centres. Exclusion criteria: a) inconclusive cytology (TIR -3A, -3B, -1 categories); b) clinical and/or cytological and/or histological features of medullary thyroid cancer; d) modifications in lifestyle and anthropometric variables occurred within the previous 5 years. BPA exposure was assessed by means of a qualitative approach, categorizing the subjects in exposed (detectable serum BPA levels) and not-exposed (undetectable BPA levels). Statistical analysis included 94 patients: 30 males and 64 females (median age 52 years); 54 benign nodules, 40 thyroid cancers; 28 normal weight patients (BMI < 25), 66 overweight/obese patients (BMI ≥ 25 in 30 in 30 cases; BMI ≥ 30 in 36 cases). Detectable BPA was found in 78 cases. In the overall study group and in the BMI ≥ 25 group exposure to BPA was not significantly related to the risk of malignancy (P = 0.119; OR 1.84 with 95% CI 0.76-4.45 and P = 0.755; OR 0.83 with 95% CI 0.28-2.47, respectively). By contrast, in the BMI ≥ 25 group, BPA-exposed subjects showed significantly higher risk of malignancy (P = 0.048; OR 2.88 with 95% CI 0.79-10.54).

Conclusions
In our series, BPA exposure conferred higher risk of thyroid cancer only in case of concomitant overweight/obesity, therefore suggesting a synergistic action between BPA and the excess of adipose tissue in promoting thyroid carcinogenesis.

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The endocrine disruptor cadmium affects both ER\textsuperscript{a}+ and ER\textsuperscript{a}- breast cancer cell lines

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The highly toxic heavy metal Cadmium (Cd) is widely spread in the environment and could exert estrogen-like activity in tissues including breast. Previous studies demonstrated that Cd binds to estrogen receptor \(\alpha\) positive (ER\textsuperscript{a}+) breast cancer (BC) cells. In this new study, we evaluated effects of Cd on both ER\textsuperscript{a}+ and ER\textsuperscript{a}- BC models with the aim to further characterize the mechanisms involved in Cd-related BC carcinogenesis. Specifically, the effect of Cd exposure was evaluated on BC cell lines MCF7 (ER\textsuperscript{a}+), T47D (ER\textsuperscript{a}+), MDA-MB-231 (ER\textsuperscript{a}-) cell models. We evaluated the ratio of AR/ER\textsuperscript{a} and we found that Cd induced a significant increase in the two ratios in both ER\textsuperscript{a}+ and ER\textsuperscript{a}- cell models. Furthermore, activation of cellular signaling pathways were evaluated. Cd induced activation of p38 MAPK in all cell lines, activation of PhAKTser473 in T47D and activation of ERK1/2 in MDA-MB-231 cells. Finally, Cd exposure induced a significant increase in the cell viability in both ER\textsuperscript{a}+ cell models, activation of PhAKTser473 in T47D and activation of ERK1/2 in MDA-MB-231 cells. In conclusion, our study demonstrates that Cd has a role in regulating cell viability, steroid receptors phenotype, cellular signaling pathways and pro-inflammatory cytokines in both ER\textsuperscript{a}+ and ER\textsuperscript{a}- cell models.

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Potential synergetic and antagonistic effects of EDC mixtures on human prostate cells

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Endocrine Disrupting Chemicals (EDCs) are a heterogeneous class of compounds so called for their ability to interfere with the endocrine system. These environmental pollutants are detected in different environmental matrices; they can bioaccumulate in adipose tissue and biomagnify in food chain due to their high hydrophobicity and low water solubility\textsuperscript{1}. Two EDCs usually used in the manufacture of domestic, industrial, and agricultural products are Dibutylphthalate (DBP) and Nonylphenol (NP). They are found in personal-care products, children’s toys, and food products, so human population appears to be predominantly exposed to them, through ingestion or skin contact. It has been demonstrated that both are able to damage male reproductive system\textsuperscript{2,3}. Due to the important role of prostate gland in male reproduction and fertility, in the present work, we evaluated the effects of DBP and NP, used alone or in different mixtures with or without endogenous sexual hormones as \(17\alpha\)-estradiol and testosterone on human prostate cell line PNT1A. The first data showed that all EDCs, alone or in mixtures affected cell proliferation. Specifically, we observed a hyperproliferative estrogen-like behaviour of NP that in mixtures seemed to hide the antiproliferative effect of DBP. We have also shown that DBP and NP activated estrogen receptor pathways, mainly interacting with ER\textsuperscript{a}. Moreover, we investigated EDC ability to induce inflammation that is a first step to prostate gland hyperplasia. We observed that cytokines and chemokines levels, such as IL-9, PDGF, TNF\textsubscript{a}, MIP-1\textalpha, MIP-1\textbeta, IL-1\textbeta were altered after all the treatments, suggesting NP and DBP involvement in the onset of inflammation processes. In conclusion, we have pointed attention on dangerousness of the mixtures able to induce a strong imbalance of prostate cell physiology.

References


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Di-(2-ethylhexyl) phthalate decreases forskolin-stimulated progesterone synthesis in human granulosa cells

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Di-(2-ethylhexyl) phthalate (DEHP) is an endocrine disruptor that belongs to the group of phthalates. Human exposure to DEHP is ubiquitous, considering its use in plastics and other common consumer products. In vivo and in vitro studies demonstrate its harmful effects on female reproductive system. The aim of this study was to investigate the effects of short term exposure to DEHP on progesterone synthesis in human granulosa cells. The human nonluteinized granulosa cells (HGRC1) were exposed for 48 h to 25 µM DEHP alone or in the presence of 25 µM forskolin (FOR), stimulator of progesterone synthesis. The results showed that exposure to DEHP did not affect the viability of HGRC1 cells. DEHP did not affect basal but decreased FOR-stimulated progesterone production in HGRC1 after 48 h. To clarify the potential mechanism of DEHP-induced decrease in progesterone production in FOR-stimulated HGRC1, we have analyzed the expression of key genes involved in progesterone synthesis. The results showed that DEHP decreased FOR-stimulated mRNA and protein expression of steroidogenic acute regulatory protein, which regulates rate limiting step in progesterone synthesis. Furthermore, the mRNA expression of 3-beta-hydroxysteroid dehydrogenase, an enzyme that converts pregnenolone to progesterone, was downregulated in FOR-stimulated cells after DEHP exposure.

These results indicate that short-term exposure to DEHP decreases progesterone production in human granulosa cells, which could have negative impact on ovarian function and fertility.

P651

Introduction
The aim of this study was to investigate the effects of short term exposure to DEHP on progesterone synthesis in human granulosa cells.

Materials and Methods
Human nonluteinized granulosa cells (HGRC1) were exposed for 48 h to 25 µM DEHP alone or in the presence of 25 µM forskolin (FOR), stimulator of progesterone synthesis. The results showed that exposure to DEHP did not affect the viability of HGRC1 cells. DEHP did not affect basal but decreased FOR-stimulated progesterone production in HGRC1 after 48 h. To clarify the potential mechanism of DEHP-induced decrease in progesterone production in FOR-stimulated HGRC1, we have analyzed the expression of key genes involved in progesterone synthesis. The results showed that DEHP decreased FOR-stimulated mRNA and protein expression of steroidogenic acute regulatory protein, which regulates rate limiting step in progesterone synthesis. Furthermore, the mRNA expression of 3-beta-hydroxysteroid dehydrogenase, an enzyme that converts pregnenolone to progesterone, was downregulated in FOR-stimulated cells after DEHP exposure.

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P651

Di-(2-ethylhexyl) phthalate decreases forskolin-stimulated progesterone synthesis in human granulosa cells

Dragana Samardzija1, Nenadov, Biljana Tesic, Nebojsa Andric & Galazzi1, Noemi Giancola1, Valeria Citterio1, Mirella Moro1, Milano, Italy; 2Istituto Auxologico Italiano, Division of Neurology and 1Istituto Auxologico Italiano, Endocrine and Metabolic Diseases Unit, Milano, Italy; 6Istituto Auxologico Italiano, Allergology, Clinical Immunology and 1Istituto Auxologico Italiano, Department of Neurology.

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The endocrine system is responsible for the production of hormones that regulate various physiological functions in the body. Phthalates, a class of compounds commonly found in plastics and personal care products, have been linked to endocrine disruption due to their ability to interfere with hormone synthesis and function. In this study, the effects of Di-(2-ethylhexyl) phthalate (DEHP) on progesterone synthesis in human granulosa cells were investigated.

Human non-luteinized granulosa cells (HGRC1) were exposed to DEHP at concentrations of 25 µM for 48 hours. The study found that DEHP decreased the forskolin-stimulated production of progesterone in HGRC1 cells, indicating a potential disruption in progesterone synthesis. This is significant as progesterone is a critical hormone involved in fertility and ovarian function.

The mechanism behind these effects is further explored by analyzing the expression of key genes involved in progesterone synthesis. The results showed that DEHP decreased the expression of steroidogenic acute regulatory protein (StAR), an essential enzyme in progesterone production, as well as the expression of 3-beta-hydroxysteroid dehydrogenase (3β-HSD), which converts pregnenolone to progesterone. These findings suggest that DEHP may interfere with the production of progesterone by downregulating the expression of these key genes.

Additionally, the study assessed the potential impact on ovarian function and fertility. The results suggest that exposure to DEHP may have negative implications for ovarian function and fertility, highlighting the importance of further investigation into the endocrine-disrupting effects of phthalates.

In conclusion, the findings of this study provide evidence for the disruption of progesterone synthesis by DEHP, potentially impacting ovarian function and fertility. Further research is needed to fully understand the mechanisms involved and to assess the broader implications for human health. This study underscores the importance of continued surveillance and regulation of phthalates to mitigate potential endocrine disruption effects.
Efficacy of lanreotide 120 mg primary therapy on tumor shrinkage and ophthalmologic symptoms in acromegaly after one month

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Introduction
Few studies to date have attempted to evaluate the early efficacy of first-generation somatostatin analogs in somatotroph macroadenomas.

Objective
To investigate the short-term efficacy of primary therapy with lanreotide 120 mg on tumor shrinkage and ophthalmologic symptoms in newly diagnosed patients with acromegaly.

Design and patients
This single-center retrospective study included 21 patients who were newly diagnosed with acromegaly resulting from pituitary macroadenoma and were receiving a primary monthly treatment with lanreotide 120 mg. Clinical, hormonal, ophthalmologic and MRI scan evaluations were conducted after the first and the third months of treatment.

Results
Tumor volume reduction was more pronounced at one month [mean volume change -31.4 ± 19.5%, P < 0.0001] than between the first and third month of treatment [mean volume reduction -20.6 ± 13.4%, P = 0.0009]. The mean volume change between baseline and the third month was -86.4 ± 21.6, (P < 0.0001). A significant volume reduction (≥ 25%) was observed in 61.9% of individuals (13/21) at the first month and in 82.3% (14/17) after three months of treatment. Among 14 individuals with optic chiasm compression and visual field defects, visual field normalization was observed in 3 cases (21.4%) and improvement in 7 cases (50%) at one month. The decrease in GH and IGF-1 serum levels was significant at one month.

Conclusions
Primary treatment with lanreotide 120 mg in patients with somatotroph macroadenomas provides early significant tumor shrinkage with rapid improvement of visual symptoms at the end of the first month.

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Case report
We present the case of a 3 and 7 months-old boy, admitted to our Pediatric Endocrinology Department for short stature (H = 87 cm, -3.2 SD), weight (W = 9.5 kg) and massive polyuria-polydipsia syndrome (ingestion volume = 5000-7000 ml/day and urine volume = 4000-5000 ml/day) with normal blood pressure. He is the first child of non-consanguineous parents, born prematurely by cesarian section at 32 weeks gestation, appropriate for gestational age, with perinatal asphyxia requiring intensive care. Severe unexplained polyhydramnios was diagnosed in the second trimester and required 3 amnioreductions. During his first 3 years of life, he had multiple hospitalizations in the Pediatric Gastroenterology department where celiac disease, mucoviscidosis and intestinal parasitosis were excluded. In our department, the laboratory tests revealed metabolic alkalosis, hypokalemia, hypoponatremia, a high urinary calcium/creatinine ratio and a high urinary potassium/creatinine ratio. Hormonal evaluation identified normal for age thyroid, adrenal and gonadal function, with a possible growth hormone (GH) deficiency (low baseline GH and IGF-1), as well as an elevated copeptin value. The abdominal ultrasound showed bilateral medullary nephrocalcinosis and the brain MRI was normal. As the clinical diagnosis of BS was established, we noted a reduction of polyuria (≈ 3500 ml/day) and polydipsia (≈ 4000 ml/day), with improved weight gain, while plasma potassium and bicarbonate levels normalized.

Despite being rare in clinical practice, the diagnosis of BS should be considered in any premature neonate with unexplained polyhydramnios and in any child with growth failure, hypokalemia, polydipsia and polyuria. Correct diagnosis and early treatment improve the quality of life of these children, allowing them to reach their full growth potential. Genetic testing helps to establish a specific diagnosis and provides the basis of genetic counseling for family members.

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Chondrosarcoma of the cavernous sinus treated with postoperative proton radiation therapy: case report and endocrinologic follow up after 36 months

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1Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy; 2Sapienza University of Rome, Department of Molecular Medicine, Roma, Italy

Case Summary
In May 2018, a 22-year-old man was admitted to the Emergency Room of Polyclinic Umberto I Hospital of Rome, because of progressive headaches and binocular diplopia. Brain MRI revealed a heterogeneous T1WI-hypointense and T2WI-hyperintense mass of 40x28x25 mm (CC, LL, AP) arising from the left cavernous sinus, expanding into the left sphenoid wing and impinging the pituitary gland, located proximally to the lesion. This case confirms that IMPT can prevent tumour enlargement while preserving normal pituitary function.
Purpose
The aim of this study was to identify any predictive factors for need of high doses of cabergoline (CAB) in prolactinomas and to study any relationship between adverse events onset and CAB cumulative dose.

Methods
Forty-two patients harboring resistant prolactinomas (High Dose group-HD; cabergoline dose > 600 µg/day) were compared with 42 patients treated with CAB dose ≤ 600 µg/day (Standard Dose group-SD). Biochemical and clinical parameters were evaluated every 3 months and at diagnosis, before and at nadir (respectively p = 0.016, P = 0.0001, P = 0.0001, P = 0.0001). Five patients (5.9%) developed impulse control disorder, equally distributed among the two groups (P = 0.67), without significant difference (P = 0.40) in CAB cumulative dose.

Conclusion
A PRL value higher than 58 ng/ml after 6 months resulted as the best predictive factor for high doses necessity. No additional risk of impulse control disorder was detected in HD, but a higher prevalence of heart valvular fibrosis was recorded. A PRL value higher than 1081 ng/ml at diagnosis (sensitivity 62% and specificity 71%, AUC 0.80; P = 0.003) was predictive for high doses necessity, of 75 ng/ml after 3 months of therapy (sensitivity 81% and specificity 60%, AUC 0.74; P = 0.0001), of 58 ng/ml after 6 months (sensitivity 76% and specificity 81%; AUC 0.80; P < 0.0001) and of 10 ng/ml after 12 months (sensitivity 97% and specificity 48%; AUC 0.77; P < 0.0001). All ten patients (over 45 studied, 22.2%) who developed valvular fibrosis were in HD (P = 0.019) and underwent a higher cumulative dose of CAB (P = 0.003). The patients clustered over (n = 23), serum proteins were measured by immunoassay. Correlations between GH, insulin like growth factor-I (IGF-I), and visceral AT (VAT), SAT, total AT and serum proteins were analyzed. The in vitro effects of GH and IGF-I stimulation on the gene expression of HTRA1, METRNL, S100A8 and S100A9 and PDGFD in human subcutaneous adipocytes, endothelial cells (HUVEC) and monocytes (THP-1) were investigated.

Results
743 genes were significantly differentially expressed (470 genes downregulated, 273 upregulated after disease control, p-adjusted < 0.05). The patients clustered according to disease activity. Pathways related to growth hormone activity, extracellular matrix deposition/adhesion/collagen, and inflammation/vascularization were among the differentially expressed signaling pathways. Of notice, several collagen genes were upregulated in active disease. Serum levels of HTRA1, METRNL, S100A8, S100A9, PDGFβ, PTX3, MMP9, TNK, ANGPT1, GRN and FLT1 and corresponding proteins were selected for further analyses. In a large patient cohort (n = 23), serum proteins were measured by immunosassay. Correlations between GH, insulin like growth factor-I (IGF-I), and visceral AT (VAT), SAT, total AT and serum proteins were analyzed. The in vitro effects of GH and IGF-I stimulation on the gene expression of HTRA1, METRNL, S100A8, S100A9 and PDGFD in human subcutaneous adipocytes, endothelial cells (HUVEC) and monocytes (THP-1) were investigated.

Objective
Patients with acromegaly present increased insulin resistance despite reduced adipose tissue (AT) mass. Growth hormone (GH) stimulates lipolysis, but the role of AT as a better biomarker of disease activity in acromegaly.

Methods
RNA-sequencing was performed on paired subcutaneous AT (SAT) biopsies from patients (n = 6) with active acromegaly and after disease control obtained by surgery. Clustering and pathway analyses were investigated. HTRA1, METRNL, S100A8, S100A9, PDGFD, PTX3, MMP9, TNK, ANGPT1, GRN and FLT1 and corresponding proteins were selected for further analyses. In a large patient cohort (n = 23), serum proteins were measured by immunosassay. Correlations between GH, insulin like growth factor-I (IGF-I), and visceral AT (VAT), SAT, total AT and serum proteins were analyzed. The in vitro effects of GH and IGF-I stimulation on the gene expression of HTRA1, METRNL, S100A8, S100A9 and PDGFD in human subcutaneous adipocytes, endothelial cells (HUVEC) and monocytes (THP-1) were investigated.

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P145

The role of advanced glycation end products on vertebral fractures in patients with acromegaly
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Introduction
Acromegalic osteopathy is an emerging complication characterized by high risk for vertebral fractures (VFs), whereas bone mineral density (BMD) may not be useful to predict the risk. Recent studies have reported that increased advanced glycation end products (AGEs) are associated with bone fragility. We aimed to evaluate the relationship between AGES and VFs in patients with acromegaly.

Study design
Cross-sectional Patients & Methods
We enrolled 70 subjects from the Department of Endocrinology and Metabolism Disease, Marmara University Medical School in acromegaly group (AG) and compared with 70 healthy controls (HC) without any risk factors for secondary osteoporosis and pituitary disorder. We performed vertebral morphometric evaluation of the lateral thoracic and lumbar spine X-ray images, and collected demographic, biochemical, clinical data. AGES were measured by the auto-fluorescence (AF) reader.

Results
The prevalence of VFs was significantly higher despite elevated BMD in AG than HC (32.9% vs. 8.6%; P < 0.001). Controlled/cured acromegaly had higher VFs prevalence than active acromegaly (12.5% vs. 38.9%, P = 0.06). AG had significantly higher levels of AGES, HbA1c and CTx than HC (P = 0.01, respectively). There was a negative correlation between AGES and CTx in AG (r = -0.371, P = 0.001). In multivariable logistic regression analysis (Table-1), disease duration, IGF-1 levels were negatively correlated with VFs, whereas AF was positively related to the VFs (R² = 0.192, P = 0.02) in the AG.

Conclusion
VFs might occur independently from the disease activity and duration and be an early complication of the acromegaly. AGES may be useful for assessing the risk of prevalent VFs in this clinical setting.

References

Table 1

<table>
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<th>Age</th>
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<th>P value</th>
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<tr>
<td>Disease duration</td>
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<td>Insulin-Like</td>
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DOI: 10.1530/endoabs.81.P145

P147

Are pre-operative intratumoral haemorrhages and post-operative bleeds sentinel indicators of "silent" corticotroph adenomas?
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Introduction
Silent corticotroph adenomas (SCAs) are considered to be clinically silent and non-secreting but exhibit positive adrenocorticotropin hormone (ACTH) immunostaining. Whether, SCAs behave more aggressively than other non-functioning adenomas, remains controversial. We characterized our tertiary centre cohort of SCA patients, compared them to gonadotroph adenomas (GAs) and assessed for features predictive of recurrence.

Objective
To compare characteristics and outcomes of SCAs with GAs at a major tertiary centre.

Table 1

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P146

Central Diabetes Insipidus, family report, molecular study, and its importance
Luis Filipe Silva1, Rafaela Sousa2, Darine Villela2, Thereza Cavalcanti2, Michele Migliavacca2, Rosita Fontes1, Marilia Guimarães2
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Introduction
Central diabetes insipidus (CDI) occurs due to deficient secretion of arginine vasopressin (AVP) or antidiuretic hormone (ADH) by the posterior pituitary. It is a rare disease with an estimated prevalence of 1:25000. CDI can be acquired or congenital, secondary to malformation or genetics. Familial CDI (genetic inheritance) is mainly autosomal dominant. More than 80 mutations in the AVP gene have been described. In hereditary CDI, the age of onset is variable. Symptoms arise mostly in childhood but, very often, later. Clinical features include polyuria and polydipsia of variable severity, dehydration, in the absence of volume replacement, and hypotension. Partial deficit of oxytocin and carrier protein, estrogen-stimulated neurophysin (ESN), and anterior pituitary hormone deficiency may coexist. The aim of this study is to describe the clinical cases and genetic study of a father and his male firstborn with familial CDI diagnosed with a rare variant c.329G>A;p.(Cys110Tyr), in heterozygosity in the AVP gene.

Case Reports
Patient 1 presented polydipsia and low body weight at two years of age. Diagnosis of CDI was confirmed with a water deprivation test. Magnetic resonance imaging (MRI) of skull and sella showed only absence of the neurohypophyseal signal. Treatment was instituted with intramuscular synthetic vasopressin, and posteriorly modified to nasal desmopressin acetate (DDAVP) spray. He remains without signs and symptoms to date, at 41 years of age, on regular use of DDAVP. Patient 2 is the firstborn of patient 1 and first presented polydipsia and nocturia at age of four. Diagnosis was established at 11 years of age with a water deprivation test. MRI of skull and sella showed only absence of the neurohypophyseal signal. Treatment was instituted with DDAVP nasal spray and maintained until the present time; at 17 years of age, he remains asymptomatic. Genetic study was performed by exome sequencing, which described the c.329G>A;p.(Cys110Tyr) variant, identified in heterozygosity in the AVP gene. This very rare variant results in the substitution of amino acid in the protein encoded and is classified as likely pathogenic. The absence of any other manifestation, unlike other genetic causes of CDI, is highlighted.

Conclusion
We emphasize the possibility that rare diseases, such as CDI may be familial, and the need for a clinical investigation of family members with similar manifestations and molecular testing and genetic counseling if possible.

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P148
AZP-3813, a bicyclic 16-amino acid peptide antagonist of the human growth hormone receptor as a new potential treatment for acromegaly

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Medical treatment of acromegaly is based on either suppressing pituitary GH secretion or inhibiting GH action by preventing interaction with its receptor in order to suppress the elevated levels of IGF1. AZP-3813 is a 16-amino acid, bicyclic peptide antagonist of the GH receptor (GHR) derived from peptide sequences discovered using a unique, cell-free in vitro transcription-translation system screened against the human GHR, and that was optimized by rational design to increase binding affinity, solubility and half-life. The Ki of AZP-3813 for the human GHR is 1.9 nM, and 18.5 nM for the rat GHR. The circulating half-life of AZP-3813 in the rat is 11.2 h. To examine the ability of AZP-3813 to antagonize the interaction between GH and its receptor in vivo and thereby reduce IGF1 levels, we injected normal, 5-week old (~150g), male Sprague Dawley rats subcutaneously either with vehicle or with AZP-3813 at doses of 0.3, 1, 3, 10 or 30 mg/kg BID or with 10 or 30 mg/kg QD (n=8/group). Blood samples were collected immediately prior to AZP-3813 injection and at 24, 48 and 72 h after injection, and were assayed for total IGF1 content by radioimmunoassay. Twenty-four hours after injection, IGF1 levels were suppressed in a dose-related manner, with maximal and similar degrees of suppression achieved with 30 mg/kg AZP-3813 administered either QD or BID (38.4 ± 3.8% and 39.2 ± 3.7% decrease from vehicle-treated controls, respectively). By 48 h post-injection, IGF1 levels had returned to the level observed in vehicle-treated control rats. In a follow-up experiment, AZP-3813 was administered subcutaneously daily for 4 days at a dose of 30 mg/kg, either QD or BID. As a comparator, the commercially available GH antagonist, pegvisomant, was also administered subcutaneously for 4 days at a dose of 100 mg/kg QD. Blood samples to be assayed for IGF1 were collected immediately prior to compound injection on all days, and at 24, 48 and 72 h after the last injection. IGF1 was maximally suppressed by AZP-3813 within 24 h after the first injection (47.2 ± 2.6% decrease vs vehicle-treated controls), and, with continued treatment, the suppression was maintained through 24 h after the last injection. In contrast, pegvisomant treatment gradually lowered IGF1, reaching a maximal suppression of 32.5 ± 3.6% 24 h after the third injection. These results demonstrate that the potent GHR antagonist activity exhibited by AZP-3813 translates to in vivo suppression of IGF1 levels, and support its development as a potential therapy for acromegaly.

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P149
Clinical aspects of pituitary tumours in patients with Multiple Endocrine Neoplasia Type 1: results from the preliminary study

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1Medical University of Warsaw, Department of Internal Medicine and Endocrinology, Warsaw, Poland; 2Medical University of Warsaw, Doctoral School of the Medical University of Warsaw, Warsaw, Poland; 3Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Warsaw, Poland; 4Medical University of Warsaw, Department of Internal Medicine and Endocrinology, Warsaw, Poland

Introduction
Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare disease inherited in an autosomal dominant pattern, caused by mutations in the MEN1 gene. The cardinal components of this syndrome are: primary hyperparathyroidism (PHPT), gastroenteropancreatic neuroendocrine tumors (NETs) and pituitary tumors. The aim of the study was to evaluate clinical features of MEN1 patients under care of two tertiary centers in Warsaw, Poland with special focus on pituitary lesions.

Material and methods
We have used an authorial pre-prepared form in order to gain detailed data on the clinical course of the disease. Until the submission of this abstract (January 2022), study group consisted of 73 participants with diagnosed MEN1 syndrome, aged from 18 to 76 years old (mean 43 ± 14 years) and followed-up from 2014 to 2022. As many as 47 of patients were women, 26 were men.

Results
In our group nearly 42% of subjects suffered from all three main components of MEN1 syndrome. Among them: 93% developed PHPT, 78% NETs, 60% pituitary tumors. In 77% of patients we have found other benign neoplasms of which the most common were adrenal adenomas (38%). What is more, 12% of subjects developed other malignant tumors. Out of 44 patients with pituitary tumors, in 26 imaging tests showed pituitary microadenomas, yet macroadenomas were present in next 18 cases. Most common type of tumor was prolactinoma (52%), with a predominance of microadenomas (32% of all pituitary tumors). Moreover, acromegaly was diagnosed in 6 patients what accounted for 14% of pituitary gland lesions cases. At least one pituitary surgery was performed in 11 subjects, 9 of them had hormonally active adenomas (4 prolactinomas, 3 cases of acromegaly, 2 non-functioning pituitary adenomas, 1 thyrotropinoma and 1 corticotropinoma). In two cases more than one operation was required. Dopamine agonists were administered to 18 patients. After PHPT, pituitary tumor was second most frequent first diagnosed component of MEN1 (26% of the group). In nearly 10% of all patients it manifested itself as menstrual disorders or decreased libido. Only in 9% patients NETs were diagnosed as the first component.

Conclusions
Despite the fact that pituitary tumors are the third most frequent tumors in MEN1, they are more likely to cause clinical manifestations than NETs. In our group there was relatively high prevalence of acromegaly. What is more, we observed frequent occurrence of other malignant tumors and noted a large number of adrenal gland adenomas.

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P150
Glucagon-stimulated copeptin measurements in the differential diagnosis of diabetes insipidus: a double-blind randomized placebo-controlled study

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In conclusion, glucagon stimulates the neurohypophysis, and glucagon-stimulated plasma copeptin has the potential to be used for a safe, novel, and increase of 0.55 pmol/l (0.21; 1.65), whereas copeptin was stimulated in patients with central diabetes insipidus, copeptin showed no relevant increase after glucagon injection, with an increase of 9.67 pmol/l (4.99; 39.60) pmol/l. Plasma copeptin levels were measured at baseline and 30, 60, 90, 120, 150, 180 minutes after injection. The primary objective was to determine whether glucagon stimulates copeptin and to explore whether the copeptin response differentiates between central diabetes insipidus and primary polydipsia.

Results
All 42 participants underwent both tests. The median (IQR) age of all participants was 27 years (23; 32). Female participants, glucagon injection stimulated copeptin with a median (IQR) increase of 7.56 (2.38; 28.03) pmol/l, while placebo had no effect (0.10 pmol/l; 0.00; 0.25; treatment difference: 7.67 (1.98, 27.09) pmol/l; P < 0.001). In patients with central diabetes insipidus, copeptin showed no relevant increase after glucagon injection, with an increase of 0.55 pmol/l (0.21; 1.65), whereas copeptin was stimulated in patients with primary polydipsia with an increase of 15.70 (5.99; 24.39) pmol/l. Using a copeptin cutoff level of > 4.6 pmol/l had a 100% sensitivity (95% CI: 100-100) and 96% specificity (95% CI: 70-100) to discriminate between diabetes insipidus and primary polydipsia. The test was safe and well tolerated with a median (IQR) test burden according to VAS of 1.5 (1; 4) in healthy participants, 3 (1.5; 4.5) in central diabetes insipidus, and 3 (2; 4.5) in primary polydipsia.

Conclusion
In conclusion, glucagon stimulates the neurohypophysis, and glucagon-stimulated plasma copeptin has the potential to be used for a safe, novel, and precise test in the differential diagnosis of polyuria-polydipsia syndrome.

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P151
Sexual brain processing is enhanced by melanocortin-4 receptor agonism
Layla Thurston1, Tia Hunjan1, Edouard Mills1, Matt B Wall1,2, Natalie Ertl1,2, Maria Phylactou1, Beatrice Muzi1, Bijal Patel1, Emma Alexander1, Sofiya Suladze1, Manish Modi1, Pei Eng1, Paul Bassett3, Herve Caci1 & Philippe Caron1
1Hopital Pediatric de Nice, CHU Lenval, Nice, France; 2CHU Larrey, Endocrinology, Toulouse, France

Introduction
Hypothalamic sexual desire disorder (HSDD) is characterized by a persistent deficiency of sexual fantasies and desire for sexual activity, causing marked distress or interpersonal difficulty. It is the most prevalent female sexual health problem worldwide, affecting approximately 1 in 10 women, but has limited treatment options despite its substantial health, social, and economic burden. Melanocortin-4 receptor (MC4R) agonists have emerged as a promising therapy for women with HSDD, although, to date, their mechanism of action is unknown. This study aims to use functional MRI to uncover the reproductive neuroendocrine pathways involved and elucidate how MC4R agonists treat HSDD in women.

Methods
We conducted a randomized, double-blinded, placebo-controlled, crossover clinical study in 31 premenopausal women with HSDD. A combination of psychometric, functional neuroimaging and hormonal analyses were used to investigate the effect of MC4R agonism on sexual brain processing. Participants attended twice, receiving either a subcutaneous injection of an MC4R agonist (Bremelanotide 1.75 mg) or placebo at each study visit, thereby acting as their own controls.

Results
MC4R agonism significantly increased self-reported sexual desire for up to 24 h post administration, compared to placebo (P = 0.007). During functional MRI, MC4R agonism enhanced cerebellar and supplementary motor area activity, as well as deactivating the secondary somatosensory cortex, specifically in response to visual erotic videos, compared to placebo (Z = 2.3, P < 0.05). In addition, MC4R agonism enhanced functional connectivity between the amygdala-insula and amygdala-thalamus during pro-longed visual erotic stimuli, compared to placebo (P = 0.025). MC4R agonism resulted in a mean increase in LH of 1.1 IU/l (13.38, P = 0.0005), and FSH of 0.35 IU/l (10.97, P = 0.0016) across the 300-minute duration of the study, with no effect observed on circulating estradiol or progesterone levels.

Discussion
We demonstrate that MC4R agonism deactivates the secondary somatosensory cortex which can reduce the detrimental self-monitoring process often observed in HSDD, thereby increasing sexual desire. Furthermore, cerebellar and supplementary motor area activation by MC4R agonism are associated with increased sexual arousal and sexual motor imagery respectively. Finally, MC4R agonism enhanced functional connectivity between key limbic structures which can be disrupted in HSDD. In conclusion, these data identify the previously undescibed neural substrates and connections through which MC4R agonism modulates sexual brain processing to increase sexual desire. These findings provide mechanistic insight for the action of MC4R agonism in sexual behaviour and are relevant to ongoing therapeutic development for HSDD and for MC4R agonist development more widely.

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P152
Up to one third of the children with attention deficit with hyperactivity disorder (ADHD) may have an isolated and increased free-T3 level
Hervé Caci1 & Philippe Caron1
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Introduction
Thyroid hormones are involved in the development of the fetus and the child, and abnormal thyroid function is expected to play a role in neurodevelopmental disorders such as Attention Deficit Hyperactivity Disorder (ADHD). The high prevalence of ADHD in patients with resistance to thyroid hormone syndrome is well documented but, surprisingly, the reported literature showed ambiguous results mostly suggesting that the thyroid function tests are normal in the majority of patients with ADHD. However, it is possible to pinpoint a number of methodological and analytical limits in the thyroid evaluation of patients in the studies. Here we report on the prevalence of isolated and increased free-T3 level in the presence of normal free-T4 and TSH levels in children with ADHD.

Methods
Serum free-T3, free-T4 and TSH levels were measured in children referred to the first author (HC) in the last two decades and diagnosed with ADHD. No control was possible on the analytic methods as thyroid function tests were performed in town laboratories.

Results
Out of 1,967 patients, 701 children with ADHD (boys n = 562, girls n = 139) between 6 and 18 years old had complete thyroid function tests (free-T3, free-T4 and TSH levels). According to the reference intervals not reported in laboratory reports, a TSH level was abnormal in 16 patients (2.28%): 2 decreased TSH level with normal free-T3 and free-T4 level, 14 increased TSH level with either normal or elevated free-T3 and/or free-T4. Out of the 685 normal-TSH remaining patients, 435 (63.50%) had a normal thyroid profile, and 217 (31.68%): 180 boys (32.67%) and 37 girls (26.71%) showed an isolated and increased free-T3 level. There was no effect of gender: χ² (1) = 0.677 (P > 0.4).

Discussion
In children with ADHD, an isolated and increased free-T3 level is frequent and unrelated with gender. This result should be further confirmed and documented. If so, this abnormal thyroid profile may constitute an endophenotype for a significant proportion of children with ADHD, and yield to new pathophysiological hypotheses in the neurodevelopmental disorders.

Conclusion
Abnormal thyroid function tests are not rare in children with ADHD, more specifically we highlighted an isolated and increased free-T3 level with normal free-T4 and TSH levels in up to one third of children with ADHD. These results warrant confirmation; this is the main objective of the on-going prospective “ThyrADHD” study (NCT05080491).

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P153

Subtype-specific pattern of white blood cell differential in endogenous Cushings’s syndrome
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Objective
Gluocorticoid excess impairs immune function, thereby predisposing patients with endogenous Cushings’s syndrome (CS) to infections. However, it is still not clear whether there is a CS subtype specific pattern in white blood cell (WBC) and WBC differential (WBCD) count. Hence, we analyzed Total leukocytes and neutrophils correlated positively with serum cortisol after 1-mg dexamethasone (1 mg-DST) (r=0.346 and r=0.471, respectively, P<0.0001), while a negative correlation was observed for lymphocytes and eosinophils (r=-0.399 and r=-0.519, each P<0.0001). Correlations were confirmed with the 24-h-urinary cortisol (24h-UFC), CD and ECS differed in numbers of neutrophils and lymphocytes (P<0.0001). A cut-off of 6.1 for the neutrophil/lymphocyte ratio (NLR) allowed reliable differentiation between CS and ECS (sensitivity 90.0%, specificity 89.4%, AUC 0.918). NLR allowed a better differentiation between CD and ECS than 1 mg-DST and 24h-UFC (AUC respectively 0.83 and 0.74). Regarding CPA and ACC, a difference in platelet/lymphocyte ratio (PLR) was observed (sensitivity 59.6%, specificity 80.6%, and AUC 0.713 with a cut-off of 187.9). Already 3 months after biochemical remission, neutrophils decreased (delta change -47.0%, -29.7%, and -26.2%) and lymphocytes increased (delta change 40% was used to identify volume-depleted TAH patients. Descriptive analysis was carried out to find differences between volume-depleted and SIAD-like TAH patients, and patients with SIAD without thiazide use. Logistic regression and ROC curves were computed to investigate the role of aSID >40 for differential diagnosis of hyponatremia in TAH patients, in addition to known factors for identifying SIAD patients as body mass index (BMI) and fractioned uric acid excretion (FUA) with the previous described cut-off of 12%

Results
Out of 303 hyponatremia patients, 131 (43.2%) had a TAH and 75 (24.8%) SIAD without thiazide use. Among TAH patients, 81 (61.8%) were successfully treated with fluid substitution and 31 (23.7%) with fluid restriction. 19 patients (14.5%) were excluded as they received no treatment, or needed to switch treatment during hospitalization. No differences in baseline characteristics were seen between patients with SIAD and SIAD-like TAH patients, except for BMI, lower in SIAD patients (mean(SD) 23.5(5.1) vs 27.0(5.7) kg/m2, P=0.003). A higher BMI and a FUA <12% had a sensitivity of 84% with a specificity of 60% in identifying volume-depleted TAH patients. Adding aSID >40 improved the specificity to 74% maintaining a sensitivity to 82%.

Conclusion
In hospitalized patients with TAH, calculation of aSID may help differentiating patients with volume depletion in need of fluid substitution from SIAD-like manifestation requiring fluid restriction.

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P154

Role of apparent strong ion difference in the differential diagnosis of thiazide associated hyponatremia
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Background
Differential diagnosis of hyponatremia is challenging, particularly for thiazide associated hyponatremia (TAH), patients might have either volume depletion in need for fluid substitution or syndrome of inappropriate antidiuresis (SIAD)-like presentation requiring fluid restriction. Urine indices are of little utility, because they are influenced by thiazide therapy. Apparent strong ion difference (aSID) describes the relation between sodium, potassium and chloride in serum and is used in evaluation of acid-base disorders according to Stewart model. aSID could help in the differential diagnosis of TAH because a value >40 identifies patients with contraction alkalosis due to relative hypocloremia, and hypocloremic alkalosis is a well-known possible adverse effect of thiazide diuretics.

Material and Methods
This was a post-hoc analysis of prospectively collected data of hospitalized patients with hypotonic hyponatremia <125 mmol/l. TAH patients were divided according to treatment response in patients needing intravenous fluid substitution or fluid restriction. Treatment response was defined as a sodium increase of at least 4 mmol/l/day or > 130 mmol/l based on chart review. aSID at baseline was calculated with the formula serum sodium plus potassium minus chloride and a value >40 was used to identify volume-depleted TAH patients. Descriptive analysis was carried out to find differences between volume-depleted and SIAD-like TAH patients, and patients with SIAD without thiazide use. Logistic regression and ROC curves were computed to investigate the role of aSID >40 for differential diagnosis of hyponatremia in TAH patients, in addition to known factors for identifying SIAD patients as body mass index (BMI) and fractioned uric acid excretion (FUA) with the previous described cut-off of 12%

Results
24th European Congress of Endocrinology
Prevalence of comorbidities in a US adult population with growth hormone deficiency

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Background
Adults with growth hormone deficiency (GHD) have increased central fat deposits, hypertriglyceridemia, and hyperglycemia, with an increased risk of developing metabolic syndrome and cardiovascular disease, conditions that can lead to a diminished quality of life. This study analyzed comorbidities among adults with GHD in the US who had Medicaid or commercial health insurance.

Methods
In this retrospective cohort study using IBM MarketScan Medicaid and Commercial Research Database data, adults (aged ≥18 years) diagnosed with GHD between Jan. 1, 2008, and Dec. 31, 2017, were matched (1:3) to controls without GHD (or other short stature-related disorders) on age, gender, plan type (commercial vs Medicaid), region, and race (Medicaid only). Baseline comorbidities and medications were measured during the 12 months pre-index. All-cause and GHD-related healthcare utilization and somatropin use were measured during the variable follow-up period.

Results
A total of 24,373 commercial and 2,579 Medicaid patients with GHD met the study inclusion criteria and were matched to 73,119 commercial and 7,728 Medicaid controls, respectively. Demographic makeup of patients with and without GHD was similar, demonstrating effective matching. About half the patients were male. Median age at index was 48 years for commercial patients and 37 years for Medicaid patients. Mean follow-up time was 35 and 37 months for commercial patients and controls, and 41 and 31 months for Medicaid patients and controls, respectively. GHD patients were disproportionally affected by comorbidities compared to controls: endocrine conditions (>68% in GHD cases vs. ≤10% in controls), metabolic conditions (>93% in GHD cases vs. ≤35% in controls), hepatic and renal function conditions (18-23% in GHD cases vs. ≤10% in controls), and cardiovascular disease (41-53% in GHD cases vs. <29% in controls), and were disproportionately treated with concomitant medications.

Conclusions
Adults with GHD experience a substantial comorbidity burden compared to non-GHD controls.

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Effect of growth hormone deficiency on serum high-sensitivity C-reactive protein levels in adult patients with non-functioning pituitary tumors

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Background
Growth hormone (GH) deficiency causes visceral obesity and fatty liver and increases cardiovascular event risks. Because serum high-sensitivity C-reactive protein (hs-CRP) levels, which has been used to estimate those risks, was reported to be decreased by GH supplementation therapy in GH deficient patients, it has been suggested that inflammatory processes might be activated in GH deficient state. However, the clinical factors associated with increased hs-CRP levels in patients with GH deficiency have been still unknown.

Patients and Methods
We retrospectively reviewed charts of 134 patients with non-functioning pituitary adenoma (NFPAs) and Rathke’s clefts who underwent preoperative GH-releasing peptide-2 (GHRP-2) tests and investigated the association between GH secretion and background characteristics. Patients who had a history of pituitary surgery, severe renal insufficiency or active inflammatory diseases or received GH supplementation therapy were excluded. GH secretion was determined by GHRP-2 tests.

Results
Among 134 patients (94 NFPAs and 40 Rathke’s clefts), 46 (34%) presented severe GH deficiency, as diagnosed using GHRP-2 tests. Serum hs-CRP levels were significantly higher in the patients with severe GH deficiency than in those without severe GH deficiency (723 [299-1285] vs 278 [124-561] μg/ml, P < 0.001). Serum hs-CRP levels were significantly higher in men (P = 0.003) and in patients with diabetes mellitus (P = 0.040) and were significantly correlated with age (r = 0.19, P = 0.039), body mass index (r = 0.37, P < 0.001), serum levels of gamma-glu-tamyl transpeptidase (r = 0.28, P = 0.001), creatinine (r = 0.30, P < 0.001), low-density lipoprotein cholesterol (r = 0.21, P = 0.013), triglyceride (r = 0.38, P < 0.001) and free thyroxine (r = -0.30, P = 0.001), blood hemoglobin A1c levels (r = 0.41, P = 0.018), peak GH response to GHRP-2 (r = 0.47, P < 0.001) and IGF-1 SD score (r = -0.18, P = 0.040). In the multiple regression analysis, peak GH response to GHRP-2 was a significant variable for determining serum hs-CRP levels (P = 0.18). The patients with severe GH deficiency had significantly higher hs-CRP levels in patients with GH deficiency have been still unknown.

Conclusions
GH deficiency is significantly associated with increased serum hs-CRP levels independent to obesity and liver dysfunction in adult patients with non-functioning pituitary tumors. GH deficient state might cause inflammation independent to development of visceral obesity and fatty liver.

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P159
What is the relevance of he systematic use of gadolinium (Gd) during the MRI follow-up of non-functioning pituitary adenomas (NFPAs)?
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Objective
To compare the performances of the coronal contrast-enhanced T1-weighted (ceT1-w) and T2-weighted (T2-w) sequences, for the diagnosis of progression during the MRI follow-up of NFPAs.

Materials and methods
106 patients who had at least two MRIs for the follow-up of NFPAs were retrospectively included. The largest diameter of the adenomas was measured on the corT1-w and separately on T2-w sequences for all the MRIs of the follow-up, and by 2 independent neuroradiologists on a sample of 100 examinations to assess interobserver variability. Progression was defined by an increase ≥ 2 mm of this diameter between 2 MRIs. Progress thresholds of 3 and 4 mm were also tested. The concordance was analyzed between the results of ceT1-w and T2-w sequences.

Results
On 580 follow-up MRIs, there was 93.1% concordance between ceT1-w and T2-w coronal sequences. In case of a possible progression, there was 64.4% concordance for a threshold of 2 mm, 87.7% for 3 mm and 97.1% for 4 mm. The discordance was mainly observed on the first postoperative MRI and in case of multiple recurrences. Kappa was better for the diagnosis of progression on T2-w than on ceT1-w sequences (0.67 vs 0.54). Of note, an agreement of 100% was noted between the 2 sequences on the 82 follow-up MRIs of patients with complete surgical resection.

Conclusion
The coronal ceT1-w and T2-w sequences were concordant in 93.1% during the MRI follow-up of NFPAs, meaning that the systematic injection of Gadolinium should be questioned. If first-line examination without gadolinium injection could be proposed, our results indicate that ceT1-w sequences should be kept for the first postoperative MRI and for the follow-up of aggressive and recurrent NFPAs.

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P160
Differences in pituitary apoplexy
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Objective
Pituitary apoplexy (PA) is a rare, sometimes life-threatening clinical syndrome. However, some cases are subclinical (SPA), just revealed by MR performed during the follow-up of known pituitary adenomas or due to other conditions. Our aims were to describe the clinical characteristics and evolution of the patients with SPA compared with patients with acute PA (APA). We also compare the results of surgery vs conservative management in the APA group.

Design
Retrospective longitudinal study.

Methods
We retrospectively analysed a database of a tertiary reference centre searching for patients diagnosed with pituitary apoplexy between January 2010 and August 2020. We analysed the risk factors that differentiate SPA to APA and compared the clinical course between patients who received conservative vs surgical treatment. Statistical analysis was done using Fisher’s exact, Mann-Whitney test or Kruskal-Wallis with Bonferroni correction if required.

Results
Thirty-seven patients were identified (17 men, 20 women; age range 18.3–80.8 years, median age 47.7 years). Out of 37 patients, 29 (78.4%) had APA [of which 17 underwent surgery and 12 were conservatively managed] and 8 (21.6%) had SPA. T2DM (11 vs 0; P < 0.05), dyslipidemia (10 vs 0; P = 0.05) and bigger tumours (558 ± 8562 mm vs 650 ± 879 mm; P < 0.05) with chiasmat Masson and sinus invasion were more frequent in APA vs SPA and in patients requiring surgery. During follow-up (23.0 ± 42.0 months), 13/37 (35.1%) patients developed hypopituitarism without differences between groups. Pituitary adenomas’ volumes shrank spontaneously in 13/30 (65%) of non-surgical patients with a median of volume reduction at 1 year MRI of (40.0% vs 23.7%) in conservatively APA vs SPA group respectively. 2 patients had a new apoplectic episode and 4 patients died; 1 related to PA.

Conclusions
These data suggest that bigger tumours in T2DM patients have higher risk of APA and could require surgery. In non-surgical group, the pituitary tumor shrinkage is clinically relevant after 1 year of PA. Hypopituitarism is quite frequent independently of PA type even in patients with SPA.

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P161
The prevalence of metabolic syndrome in patients with hyperprolactinemia
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Objective
Hyperprolactinemia might be related to weight gain, metabolic syndrome, and insulin resistance. The aim of this study was to evaluate that patients with hyperprolactinemia were higher prevalence of metabolic syndrome than civilian population.

Methods
From 1st Jan. 1998 to 17th Nov. 2017, 950 patients newly diagnosed hyperprolactinemia in Fusan National University Hospital, Pusan, South Korea, were selected to enroll in a study conducted on hyperprolactinemia and metabolic syndrome. We analyzed the metabolic components measured value within 3 months of the highest plasma prolactin value recorded. Information of waist circumference, serum triglyceride, serum HDL cholesterol, blood pressure, fasting plasma glucose, and medication for dyslipidemia or hypertension or diabetes mellitus were collected. Moreover, we also collected the measured value of BMI, LDL cholesterol, total cholesterol. We compare the metabolic component value of our hyperprolactinemia patients with KNHANES 2010-2015 data.

Results
In 20s~50s fasting blood glucose and in 20s and 30s LDL cholesterol of hyperprolactinemia patients were higher prevalence of metabolic syndrome than civilian population.

Conclusion
This study suggests the necessity of evaluation of metabolic syndrome for patients with hyperprolactinemia. In the future, larger epidemiological studies on prevalence of metabolic syndrome in patients with hyperprolactinemia should be performed.

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P162
Pituitary apoplexy: a retrospective study in a pituitary reference unit
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Objective
To describe the clinical characteristics and evolution of the patients with SPA compared with patients with acute PA (APA). We also compare the results of surgery vs conservative management in the APA group.
Pituitary apoplexy (PA) is a rare syndrome that requires urgent assistance. It is due to ischemia or hemorrhage of pituitary tissue, almost always inside a pituitary tumor. PA may be the first manifestation of a neuroendocrine tumor or occur during follow up.

Objective
To describe the characteristics of patients with PA treated in the Department of Endocrinology and Nutrition in the last 10 years and study the presence of possible risk factors for it. Patients and methods
Descriptive, single-center, retrospective study. We selected from electronic records 48 patients with the diagnosis of PA treated in the Endocrinology and Nutrition Department from 2010 to 2020. Demographic, clinical, biochemical, radiological and anatomopathological data were collected. The results are expressed as mean and standard deviation (SD) in the case of quantitative variables or percentage in the case of qualitative variables (SPSS 25.0).

Results
67% of the patients were men with a median age at diagnosis of 58.5 years (SD 13.9). As vascular risk factors they presented: hypertension (50%), diabetes (9.5%), and dyslipidemia (42.9%). Other coexisting clinical situations were: pregnancy (1), rheumatoid arthritis (1), Wègener’s disease (1) and postoperative coronary bypass (1). The diagnosis was established with an average of 3 days from the onset of symptoms. The most frequent symptoms were: headache (79.1%), visual alterations (69.8%), nausea/vomiting (51.2%) and fluid and electrolyte disorders (20.9%), especially hyponatremia (50%). 40.5% of the patients had a known pituitary neuroendocrine tumor; pituitary macroadenomas (82%), pituitary macroadenomas with invasion of the cavernous sinus (45.2%), non-functioning tumors (52.9%) and prolactinoma treated with cabergoline (17.9%). Most patients (90.4%) presented some hormonal deficit: LH/FSH (76.3%), TSH (50%), GH (44.7%), ACTH (42.8%), ADH (2.3%). Panhypopituitarism was present in 26.2%. No patient passed away in the acute moment. 71.4% of the cases were treated with endoscopic transphenoidal surgery for persistent headache and/or visual alterations. 76.2% of the patients continued with hormonal replacement treatment after surgery, of which 7 patients (21.9%) recovered total pituitary function, with an average of 4.6 months (SD 2.6) after the event.

Conclusions
- Pituitary apoplexy is more frequent in males and in pituitary neuroendocrine tumors bigger than 1 cm especially in cases with cavernous sinus invasion.
- Hypertension and dyslipidemia are very prevalent in patients with pituitary apoplexy.
- Despite being a condition that requires urgent assistance, the diagnosis is delayed for days from the onset of symptoms even with patients with known pituitary tumors.

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P164
Links between posterior pituitary activity, other endocrine abnormalities and psychometric profile in anorexia nervosa: a multimodal evaluation
Bogdan Galusca1,2, Dous Singoh Sandra Emmanuelle1,2, Natacha Germann1,2, Merabeth Manuel 3, and A and all AcroQol subscales. The presence of swelling at baseline had a significant effect on the global AcroQol score (P = 0.035). At follow up, the significant elements that correlated with the global AcroQol score were joint symptoms (P = 0.002), head pain (P < 0.001), sleep apnea (P = 0.006) and hypertension (P = 0.002).

Conclusions
Our results emphasise the complementary nature of Patient- and Clinician-reported outcome tools in assessing acromegaly control status. The data identifies the critical role of signs, symptoms, and associated comorbidities as important patient-oriented treatment targets, beyond SAGIT sub-scores G, I, and T, by which clinicians could further increase the impaired QoL in this population.

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P163
Clinical applicability of using SAGIT instrument and AcroQol in the management of patients with acromegaly
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Objective
We aimed to evaluate the ability of SAGIT Instrument and AcroQol questionnaire to discriminate acromegaly control status and to correlate SAGIT scores to AcroQol results in a cohort of the national referral centre.

Methods
Cross-sectional study included 72 patients followed between 2000 and 2020. We retrospectively determined SAGIT score at the diagnosis. Based on the data from the most recent follow up and additional telephone interviews, we determined the patients’ current SAGIT score and assess quality of life by AcroQol.

Results
At follow up (median duration of 8.5 (5-12) years), 55 (76.4%) patients were classified as cured or controlled on pharmacotherapy based on biochemical criteria (median IGF-1 0.97 times ULN), while 17 patients (23.6%) had uncontrolled disease (median IGF-1 2.65 times ULN). All 5 SAGIT categories significantly lowered from baseline to follow up, with the global score decreasing from 14 (12-15) to 4 (3-6) (P < 0.001). The duration of diagnostic delay significantly correlated with subscores S, A, G and global score at diagnosis. SAGIT at baseline did not discriminate the current disease status, whereas the follow up global score and its G and I components discriminated between the current disease activity status, with the global score 4 (3-5) in cured/controlled group vs 6 (4.5-8) in uncontrolled group (P = 0.007). At follow up, the median global AcroQol score for our cohort was 69.3% (50-84.1), with the highest median score in the Personal relationship subscale and the most affected Physical Performance subscale. AcroQol, was not able to discriminate disease activity status. From the examined variables (BMI, IGF-1 levels, time to remission, disease duration, diagnostic delay, age, gender, adenoma size, and the presence of diabetes mellitus and hypopituitarism), only BMI had significant negative correlations with the global AcroQol score. At baseline and follow up, there were statistically significant negative correlations between SAGIT G and A and all AcroQol subscales. The presence of swelling at baseline had a significant effect on the global AcroQol score (P = 0.035). At follow up, the significant elements that correlated with the global AcroQol score were joint symptoms (P = 0.002), head pain (P < 0.001), sleep apnea (P = 0.006) and hypertension (P = 0.002).

Conclusions
Our results emphasise the complementary nature of Patient- and Clinician-reported outcome tools in assessing acromegaly control status. The data identifies the critical role of signs, symptoms, and associated comorbidities as important patient-oriented treatment targets, beyond SAGIT sub-scores G, I, and T, by which clinicians could further increase the impaired QoL in this population.

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correlations with the psychological characteristics of anorexia nervosa still suggest a pathophysiological involvement.

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P165
Effects of the SGLT2-inhibitor empagliflozin in patients with chronic syndrome of inadequate antidiuresis (SIAD) - results of a double-blind, randomized, placebo-controlled, crossover trial
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Introduction
Hyponatremia is the most common electrolyte disorder and the syndrome of inappropriate antidiuresis (SIAD) is one of its main causes. However, treatment options for chronic SIAD-induced hyponatremia are inadequate. This is probably because hyponatremia has been associated with neurocognitive deficits, although there is little data on its reversibility. We previously showed that the sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin is a promising short-term treatment option for hospitalized patients with SIAD-induced hyponatremia, promoting osmotic diuresis via urinary glucose excretion. However, there are no data on long-term treatment in outpatients nor its effect on neurocognitive function.

Material and Methods
In this double-blind, randomized, placebo-controlled, crossover trial we compared 4-week treatment with empagliflozin 25 mg/day to placebo in addition to fluid restriction of ≤ 1.5 L/24h in outpatients with chronic SIAD-induced hyponatremia (serum sodium < 135 mmol/L). At baseline and after both treatment cycles, patients underwent neurocognitive testing (Montreal Cognitive Assessment (MoCA) test). There was a 2-week wash-out period between the two treatment cycles, and a follow-up visit was scheduled 30 days after completion of the treatment phase. The primary endpoint was the difference in serum sodium levels (mmol/L) after 4 weeks of treatment with empagliflozin or placebo, calculated using a linear mixed-effects model.

Results
14 patients, 50% female, with a median (IQR) age of 72 years (65-77) completed the trial. Median (IQR) serum sodium level at baseline was 131 mmol/L (130-132). Under treatment with empagliflozin, median (IQR) serum sodium level increased to 134 mmol/L (132-136), while no notable change was seen under placebo (130 mmol/L (128-132)). This resulted in a 4.1 mmol/L (95% CI 1.7-6.5) higher serum sodium level after 4 weeks of empagliflozin treatment compared to placebo (P = 0.004). This effect was independent of severity of SIAD. In addition, treatment with empagliflozin led to improved neurocognitive function, as shown by an increase of 1.2 points (SE 0.5) in the MoCA test (P = 0.042). Treatment with empagliflozin was generally well tolerated, no serious adverse events occurred during the observation period.

Conclusion
This trial shows that the SGLT-2 inhibitor empagliflozin is a promising new treatment option for outpatients with chronic SIAD-induced hyponatremia. Furthermore, hyponatremia treatment led to an improvement of neurocognitive function.

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P166
Pasireotide imaging study: magnetic resonance imaging as a predictor of therapeutic response in acromegaly
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Background
T2-weighted magnetic resonance imaging (MRI) signal has been recently linked with a better tumor response to pasireotide treatment in patients with acromegaly (ACRO). Our aim was to evaluate the prevalence of this radiological feature and its association to therapeutic outcomes in a large cohort of ACRO patients treated with pasireotide.

Methods
A retrospective multicentre study was performed in 15 Spanish tertiary university hospitals including patients with active ACRO who have been taking pasireotide as a second-line treatment according to current clinical guidelines. Pituitary tumor T2-weighted MRI signal was classified as “iso-hyperintense” or “hypointense” by local neuro-radiologists. Insulin-like growth factor 1 (IGF-1) levels and tumor volume reduction (≥ 25% from baseline) were assessed after 6 and 12 months of pasireotide treatment and results analysed according to MRI pre-treatment signal. Response to pasireotide was defined as “complete” when normalization of IGF-I levels and tumor volume reduction (≥ 25% from baseline) was achieved or “partial” when a decrease of ≥ 50% in IGF-I was obtained. “No response” was defined as < 50% decrease in IGF-I from baseline. Results
Sixty-nine patients were included (50.7% females, age 48.3 ± 13.3), of whom 55 (79.7%) had previously undergone surgery and 63 (92.6%) were treated with first-generation somatostatin analogues, remaining with active disease before initiation of pasireotide. MRI signal was hypointense in 20 (29%) and hyperintense in 49 (71%) of the patients. Hyperintense group showed larger initial tumor compared to hypointense (7900 ± 2000 mm3 vs 679 ± 1500 mm3 P = 0.001). Complete response to pasireotide treatment at 6 months was observed in 40 (58.8%), partial response in 1 (1.5%), and no response in 27 (39.7%) patients, while at 12 months, 40 (69%), 1 (1.7%) and 17 (29.3%) were under the follow-up. Initial tumor shrinkage response over time. Compared to hypointense patients, while at 12 months, 40 (58.8%), partial response in 1 (1.5%), and no response in 27 (39.7%) were under the follow-up. Compared to hypointense patients, while at 12 months, 40 (58.8%), partial response in 1 (1.5%), and no response in 27 (39.7%) were under the follow-up.

Conclusion
Almost 70% of acromegaly patients who had not responded to first-generation somatostatin analogues showed a complete hormonal response to pasireotide, regardless of the T2-weighted MRI signal, at one year of follow-up. Compared to hypointense, hyperintense T2-weighted MRI signal is associated to a better tumor shrinkage response over time.

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P167
Patient-reported outcomes (PRO) in adult growth hormone deficiency (AGHD) for an improved patients’ management: results from the management of AGHD(MAGHD) study
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Background
AGHD is a recognized clinical entity, but symptoms are quite nonspecific; the lack of objective tools able to measure patients’ health status remains the main barrier in clinical monitoring and treatment.

Aim
The MAGHD Study aims improving AGHD patients’ management through a Smartphone app (MAGHDApp) and a fit-watch integrated with a software...
framework able to merge daily data of patients’ well-being and physical activity with clinical data collected in institutional databases, giving feedbacks to both patients and clinicians.

Methods
Eighty-three AGHD patients (31 Females, 52 Males, mean age 56.27 ± 14.68 years) referring to a single endocrinological center entered the 24-months study. During the first year, AGHD patients performed biannual clinical visits with clinical, biochemical and multidimensional assessment through validated questionnaires (QoL-AGHD, QLS-II, IIEF-15, FSFI, WEMWBS, IPAQ, PSQI). In parallel, MAGHDApp was developed to daily collect patient reported outcomes (PRO) derived from answers to questionnaires; moreover, a web-platform was exploit to collect data from fit-watch (number of steps, calories burned and hours of sleep). During the second year, patients were invited to use MAGHD technologies recording data, independently from patients’ biannual visits. Up-to-now, only data from MAGHDApp have been analyzed.

Results
Fifty-eight patients (70%, mean age 59.9 ± 13.3) entered the second phase using MAGHD technology (MAGHDGroup), the other 25 (30%, mean age 64.4 ± 14.8) were monitored in the second phase as well as in the first. Patients of MAGHDGroup were younger than the others (P < 0.05), with no differences in gender distribution between the two groups (P = 0.09). During the second year, each questionnaire was sent to patients 6 times and MAGHD platform collected about 12,000 PRO. Globally, the mean response rate was 60%, no differences were registered according to the type of questionnaire addressed (QoL-AGHD = 62%, QLS-II = 62%, IIEF-15 = 58%, FSFI = 69%, WEMWBS = 61%, IPAQ = 58% and PSQI = 57%), 66% of questions were answered within 3 h from sending.

Conclusions
This real-life study suggests innovative and technological solutions for management of AGHD patients. These preliminary data document the feasibility of this kind of monitoring, especially in young AGHD patients, and a fair patients’ adherence. PRO from MAGHDApp seems to guarantee a reliable, daily monitoring of patients’ well-being. This information, coupled with physical activity data, could make patients directly involved in the healthcare process and help clinicians in AGHD management and follow-up.

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vivo engagement of SSTR3 and a predominantly SSTR3-driven antitumor activity of ITF2984 and provide an in vivo proof-of-concept for the potential clinical use of ITF2984 in NFPAs and other SSTR3-driven diseases.

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**P170**

**Safety comparison of 40- vs 60- mg/day doses of oral octreotide capsules for treatment of acromegaly in the chiasma optimal trial**

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**Background**

Oral octreotide capsules (OOC) are a treatment option for patients with acromegaly in the United States who have previously responded to injectable somatostatin receptor ligands (iSRLs, octreotide or lanreotide). In previous phase 3 studies, the safety of OOC was shown to be consistent with iSRLs, without dose-dependent adverse reactions. In a double-blind, placebo-controlled period (DPC) of the CHIASMA OPTIMAL trial (NCT03252353), patients were randomized to twice-daily OOC at 40- mg/day, with the option for up-titration to 80- mg/day. In contrast, patients entered the open-label extension (OLE) at a 60- mg/day dose.

**Objective**

Examine the safety of 40- mg/day vs 60- mg/day OOC doses.

**Methods**

Eligible patients had the option to enroll in the OLE following the core trial. All patients received OOC 60- mg/day upon entering the OLE regardless of prior treatment in the DPC, including patients who received placebo in the DPC. OOC doses were up- or down-titrated based on insulin-like growth factor I (IGF-I) level and/or acromegaly signs or symptoms. The current analysis compared the incidence of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), TEAE-related study drug discontinuation, and acromegaly-related TEAEs (defined as new or worsening signs or symptoms of acromegaly).

**Results**

Twenty-eight patients randomized to OOC in the DPC (40- mg/day dose) and 19 who were originally randomized to placebo and continued into the OLE (60- mg/day dose) were included in the analysis. Biochemical control was similar in both groups as demonstrated by mean IGF-I levels over the respective periods. Ninety-six percent of patients on 40- mg/day and 57.9% on 60- mg/day experienced ≥ 1 TEAEs. Two patients on 60- mg/day reported a total of 2 SAEs, both deemed unrelated to study drug. Two patients on 40- mg/day experienced TEAEs leading to study drug discontinuation (headache and gastrointestinal symptoms). The incidence of acromegaly-related TEAEs was generally lower in those on 60- mg/day vs 40- mg/day.

**Conclusions**

This is the first analysis exploring differences in OOC doses. The nature and incidence of TEAEs occurring with a starting OOC dose of 60- mg/day vs 40- mg/day were similar, though this analysis was limited by differences in TEAE reporting across sequential phases of a lengthy trial. A trend was observed for decreased incidence of acromegaly-related TEAEs with the 60- mg/day dose. This finding is in line with previous analyses showing no dose-related TEAEs with OOC.

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**P171**

**Efficacy of pasireotide LAR for acromegaly: a long-term real-world monocentric study**

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**Patients**

Nineteen acromegalic patients (8 females, 21-69 years-old, with macroadenoma, microadenoma or no evidence of pituitary tumor in 15, 2, 2, respectively) resistant to first generation somatostatin analogs (FG-SA) at high doses and/or intolerant to pegvisomant were switched to pasireotide LAR (PasLAR). Eleven had persistent disease after neurosurgery and two had also undergone radiosurgery (12 and 24 months before starting PasLAR). Six complained of acromegalic headache (symptomatic score was 3/3 in 2 and 2/3 in the other). On FG-SA IGF-I, GH and HbA1c were (mean, range) 193% upper limit normal age-matched range (ULNR) (120-303), 5.2 ng/ml (0.6-25), and 40.6 mmol/mol (29-54), respectively. No patient was taking antidiabetics drugs.

**Protocol**

PasLAR was injected every 28 days, starting with 40 mg for 3 months, uptitrated to 60 mg if IGF-I persisted pathologic or downtitrated to 20 mg if IGF-I was < 50% ULNR. GH, IGF-I, HbA1c were assessed at 28, 84 and 168 days after starting protocol. Treatment was withdrawn if IGF-I remained pathologic after 3 months on 60 mg q 28 days.

**Results**

PasLAR normalized IGF-I in 10/19 patients after the first injection and was withdrawn in 5 unresponsive patients at 6 months. After 12 months, IGF-I was 74% ULNR (29-133, normal in 9/14) and GH 1.2 ng/ml (0.2-3.9). At the last follow-up (mean 26 months, range 6-60, ongoing dose 20 mg in 3, 40 mg in 7 patients, and 60 mg in 4) IGF-I was 74% ULNR (22-195, normal in 11/14) and GH 0.7 ng/ml (0.1-2.5). **Headache** quite disappeared in all patients (in 5/6 after the first injection) and reappeared with pathologic IGF levels after PasLAR withdrawal in one irradiated patient. **Tumor shrinkage** (20-35% of basal volume) was observed in 6/7 evaluated patients without previous irradiation at 6-36 months after the start of PasLAR. HbA1c was 43.9 mmol/mol (32-66) at 12 months and 43.3 mmol/mol (29-66) at the last follow-up. Glucose metabolism derangement was observed in 6 patients (until DKA in one). Metformin was started in 4 patients and GLP-1 RA in two (in one coupled with insulin). In two patients PasLAR was withdrawn at 36 and 60 months due to poor compliance in the first and QTc lengthening in the second, who had started amiodarone treatment.

**Conclusion**

Pas-LAR should be considered a second option in patients resistant to FG-SA for its high efficacy and safety. Its quick action allows early identification of responsive patients. Efficacy on severe headache is outstanding.

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**P172**

**Towards a pituitary apoplexy classification based on clinical presentation and patient journey**

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**Purpose**

The condition of pituitary apoplexy contains the clinical specere from life-threatening emergency to a condition with chronic symptoms and self-limiting course, which partly determines diagnostic delay and management. Outcome evaluation of course and management of pituitary apoplexy is hampered by the diverse presentation of this condition and requires appraisal. This study aimed to describe the patient journey, clinical presentation and management of various types of pituitary apoplexy in a new classification to facilitate future outcome evaluation and identify unmet needs in the current care process.
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The positive feedback exerted by mtor inhibitor everolimus in pituitary neuroendocrine tumoral cells is reverted by cabergoline co-treatment

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The mTOR inhibitor everolimus has been shown to display antimitotic effects on diverse neoplasms, including pituitary neuroendocrine tumors (PitNETs); however, its effect is reduced by an escape mechanism that increases AKT phosphorylation (P-AKT) leading to survival pathway activation. Dopamine receptor type 2 (DRD2) reduces P-AKT in some non-functioning PitNETs (NF-PitNETs) and in lactotrophs MMQ cells, through a-2-agonist 2-dependent mechanism. This study aims to analyze the efficacy of everolimus combined with DRD2 agonist cabergoline in reducing proliferation in primary cultured NF-PitNETs and MMQ cells, to analyze AKT phosphorylation and a-2-agonist 2 activity. We found that 9 out of 14 NF-PitNETs were resistant to everolimus 1 nM, but the combined treatment with cabergoline inhibited cell proliferation in 7 out of 9 tumors (31.4 ± 9.9%, P < 0.001 vs basal), accordingly increased p27 and reduced cyclin D3 expression. In everolimus unresponsive NF-PitNETs group, 3 h everolimus treatment determined a significant increase of p-AKT/total-AKT ratio (2.1-fold, P < 0.01, vs basal), and this effect was significantly reverted by cabergoline cotreatment. To investigate the molecular mechanism involved, we used MMQ cells as a model of everolimus escape mechanism. Indeed, 1 nM everolimus did not affect MMQ cells proliferation and increased p-AKT/total-AKT ratio (+1.53 ± 0.24-fold, P < 0.001 vs basal), whereas cabergoline significantly reduced cell proliferation (-22.8 ± 6.8%, P < 0.001 vs basal) and AKT activity. The combined treatment of everolimus and cabergoline induced a significant reduction of both cell proliferation (-34.8 ± 18%, P < 0.001 vs basal and P < 0.05 vs cabergoline alone) and AKT/total-AKT ratio (-34.5 ± 14%, P < 0.001 vs basal and P < 0.05 vs cabergoline alone). Moreover, to test a possible involvement of a-2-agonist 2 activity, we performed p27 and cyclin D3 expression in everolimus unresponsive NF-PitNETs group. Our data showed that the lack of a-2-agonist 2 prevented everolimus and cabergoline co-treatment inhibitory effects on both AKT activation and cells proliferation. These results unveiled that cabergoline overcomes the everolimus escape mechanism in primary NF-PitNETs cultured and MMQ cells inhibiting AKT phosphorylation, paving the way for a potential role of a-2-agonist 2 as a biomarker predicting PitNETs responsiveness to combined therapy with dopamine agonists.

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The immune microenvironment landscape in pituitary tumors, genes and cells

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The tumor immune microenvironment is essential, it could influence a favorable or negative response against the tumor cells, and it has been related to therapy response and prognostic factors. Tumor infiltrating lymphocytes (TILs) plays an important role in the development, progression, and tumor control, thus presence of TILs could be related to disease-specific traits. The aim of the present work is to evaluate the expression of immune-related genes in forty-two pituitary adenomas (PA) distributed in the three major lineages, NR5A1- (Clinically non-functioning PA), TSHB-19- (ACTH adenoma) and POU1F1- (GH, TSH, PRL adenoma) through whole transcriptome analysis and RT-qPCR, and to identify the microenvironment immune cells infiltrating the tumor through transcriptome deconvolution and immunofluorescence. We found characteristic expression profiles of immune-related genes including interleukins and chemokines for each tumor lineage. Genes such as IL11, IL36A, TLR4, IL17REI and CCL5 were upregulated in all PA whereas IL-34, IL20RA and IL2R1 characterize the NR5A1-, TBX19- and POU1F1-derived tumors, respectively. Transcriptome deconvolution showed that macrophages, CD4+ T cells, CD8+ T cells, NK cells, and neutrophils could be infiltrating the PA. CD4+ and CD8+ T cells and NK cells infiltration predicted was corroborated by immunofluorescence in pituitary adenomas. In conclusion, we found characteristic immune response gene expression profiles for each pituitary tumor lineage, that explain partially, the immune response CD8+ , CD4+ T cells, NK cells and macrophages infiltration. Our results suggest a crosstalk between the tumor cells and its microenvironment.

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remission post-operatively, 23% relapsed and all had a further intervention (2nd
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cytokines like interleukin-1 beta (IL-1
ARDS), commonly observed in severe COVID-19 patients. In these cells, SARS-
has been implicated in epithelial damage in acute respiratory distress syndrome
P176
TSS
n
those with immediate post-op cortisol
re-exploration. 12/52 (23%) relapsed during follow-up. Using a Kaplan Meier
and 71% of microadenoma) after TSS including 5/9 patients who had immediate
was 9 years (range 1-16). 52/86 (60%) patients were in remission (39% of macro-
We wished to determine the rate of late recurrence and need for consequent intervention in patients who had initial biochemical remission after TSS for pituitary dependent Cushing’s.
Methods
We performed a retrospective analysis of our patients who underwent TSS for pituitary Cushing’s between 2004 and 2019. Remission was defined as post-
operative 0900 cortisol of <50 nmol/l within 3 months following TSS including patients who had surgical re-exploration during the initial admission due to a high day 2 post-operative cortisol. Those with post-operative basal cortisol greater than or equal to 50 nmol/l were considered to have ‘persistent disease’. Late recurrence was defined as the emergence of biochemical cortisol excess during the follow-up period (non-suppressible cortisol, and/or elevated urine free cortisol). Kaplan-Meier curves were plotted to determine the rates of recurrence and need for second intervention in patients initially in remission and re-intervention rates were compared to those with persistent disease.
Results
86 patients (mean age 47years; 65 females, 21 males) underwent TSS for pituitary Cushing’s; 28/86 had macro- and 58/86 micro-adenomas. Median follow-up time was 9 years (range 1-16). 52/86 (60%) patients were in remission (39% of macro-
Our data demonstrate a significant recurrence rate (32% at 5yrs) in patients considered by the most stringent criteria to be in remission following TSS leading to further intervention. Our data also demonstrate that those with persistent disease are likely to require a second intervention shortly after initial surgery. A post-operative cortisol of <50 nmol/l is a predictor of short-term remission but is not necessarily a confident long-term predictor of remission.

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P176
Antagonist of growth hormone-releasing hormone (GHRH) inhibits SARS-CoV-2 Spike protein-induced inflammation in macrophages and PBMCs
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Macrophages play essential roles in the immune defence and their hyperactivation has been implicated in epithelial damage in acute respiratory distress syndrome (ARDS), commonly observed in severe COVID-19 patients. In these cells, SARS-

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P177
Use of corrected SU Vmax as a prognostic indicator of response to PRRT
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Background
PRRT is an effective treatment option (especially for controlling disease progression) for disseminated neuroendocrine tumors (NETs), with good expression of the somatostatin receptors. Despite significant progress in NET personalized management, searching for novel predictive and prognostic factors of response to PRRT is crucial for more effective follow-up, better treatment choices leading to more favorable final outcome. Some recent studies indicate that the response to PRRT assessed on the basis of imaging of somatostatin receptors may be a potentially useful tool for prediction of overall PRRT effect.

Methods
10 patients with disseminated NET lesions who underwent [68Ga]Ga-DOTA-TATE-PET/CTs before and after PRRT were eligible to the analysis. 5 patients received 177Lu-DOTA-TATE whereas 5 tandem (mix 1:1 of 177Lu- and 90Y-DOTA-TATE)therapy. PET/CTs examinations were performed on average 3.2 months before and 4.6 months after treatment. For all measurable metastatic lesions in both PET/CTs (before and after PRRT) the corrected SUVmax was calculated as the ratio of SUVmax of lesion to SUVmax of normal liver tissue. The next step was to evaluate the change of corrected SUVmax between PET/CTs done before and after PRRT, compared to the first PET/CT. Finally, those results were complied with the result of PRRT assessed after mean follow-up time 20.3 months as: 1. Partial response (PR) 2. Stabilization(SD) 3. Progression(PD) of the disease.

Aim
Assessment if corrected SUVs change in 68Ga-somatostatin analogue PET/CT in response to PRRT may have a predictive value in patients with NET and if it differ in between PRRT with 177Lu-DOTA-TATE alone or tandem therapy.

Results
During follow-up the PR was confirmed in 1 patient, 4 had stabilization and 5 progression of the disease. Among the whole group of lesions there was a mean 27.3% reduction in corrected SUVmax in comparison between PET/CTs done before and after PRRT, and 27.4% and 27.2% reduction in Lu-177 group and tandem group, respectively. The decrease of lesion’s corrected SUVmax for patient with PR was 56.4% for tandem therapy, in none of patients treated with 177Lu-DOTA-TATE regression was observed. In the SD group the average decrease of SUVmax was 42.9% for Lu-177 and 8.7% for a tandem PRRT. In patients with PD the increase in corrected SUVmax was observed, 3.6% for Lu-177 and 14.6% for tandem therapy.

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Conclusion
A decrease of the mean value of corrected SUv/Max in metastatic NET lesions after PRRT may have a predictive value in estimation of progression risk. There were no statistically significant differences in SUVmax changes between 177Lu-DOTA-TATE and tandem therapy.

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P178
Metastatic pheochromocytoma and paragangliomas: clinical and follow-up characteristics in a reference unit
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Introduction
Pheochromocytomas (PCC) and paragangliomas (PGGLs) are rare neuroendocrine tumors. Management is very complex, this is why physicians involved in the management of these patients need to take into account not only clinical aspects but also genetics of these tumors. We present a group of patients diagnosed of metastatic PCC or PGCC, their characteristics and long term follow-up.

Methods and design
Descriptive and unincentric study that includes 23 patients diagnosed with metastatic PCC/PGGLs, assessed at Hospital Universitari i Politècnic La Fe in Valencia, Spain between 2011 and 2022. Demographic, surgical, anatomopathological, clinical, imaging tests and treatments variables are included. Results are expressed as mean and standard deviation (SD) in the case of quantitative variables or percentage in the case of qualitative variables (SPSS 25.0).

Results
55% of the patients were women. Mean age at diagnosis of the primary tumor was 39 years, and at diagnosis of the first metastasis was 45 years (SD 19.46%). Patient's median age at diagnosis of the primary tumors was 43 years (IQR, 32-53) with a prevalence of 74.1% in patients with tumors located in the adrenal gland. All patients were managed in our endocrine and medical oncology units.

Conclusions
We present a group of patients diagnosed of metastatic PCC/PGGLs, assessed at Hospital Universitari i Politècnic La Fe in Valencia, Spain between 2011 and 2022. Demographic, surgical, anatomopathological, clinical, imaging tests and treatments variables are included. Results are expressed as mean and standard deviation (SD) in the case of quantitative variables or percentage in the case of qualitative variables (SPSS 25.0).

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P396
Precision medicine: new perspectives for the treatment of GH-secreting tumours - the miss study
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Dopamine receptor type 2 (DRD2) agonists (DA) are the first-choice treatment for prolactin (PRL)-secreting pituitary tumors, but poorly effective in non-functioning (NF)-PitNETs. Along with G protein-dependent signaling, DRD2 also mediates non-canonical beta-arrestin-dependent pathways, where reduction of AKT phosphorylation plays a leading role for the antiproliferative effect of DRD2 in pituitary tumors. Through UNC9994 and ML5147, a beta-arrestin 2-biased and a G protein-biased agonist, respectively, the present study aimed to clarify the role of G proteins and beta-arrestin 2 in mediating DRD2 signaling in rat tumoral lactotroph cells MMQ and in human primary cultured NF-PitNET cells. In MMQ cells, treatment with UNC9994 reduced cell proliferation (-4.1% vs 0.0% at 100 nM, P < 0.01 vs basal) with a greater efficacy compared to cabergoline (22.2% at 100 nM vs 10.9%, P < 0.01 vs basal), while ML5147 treatment resulted into a slight lowering of cell proliferation (-10.8% vs 7.3% at 100 nM, P < 0.05 vs basal). Accordingly, UNC9994 was more efficient in reducing AKT phosphorylation (-45.5% vs -27.4% at 100 nM, P < 0.05 vs basal), whereas an increased AKT phosphorylation was detected after ML5147 treatment. Consistently, cabergoline and UNC9994 treatments determined a significant reduction of cyclin D3 (-14.7% vs 5.8% at 100 nM, P < 0.05 vs basal) and -18.8% vs 9.6% at 100 nM, P < 0.05 vs basal, respectively) together with an up-regulation of p27Kip1 (+35.2% vs +1.1% at 100 nM, P < 0.05 vs basal, respectively). Beta-arrestin 2 silencing reverted either UNC9994 and cabergoline anti-proliferative effects, as well as their effects on AKT phosphorylation. Pretreatment with pertussis toxin (PTX) maintained the antiproliferative effect of cabergoline (-16.0% vs 3.6%, P < 0.001 vs basal) and UNC9994 (-31.1% vs 19.9%, P < 0.001 vs basal), while it abolished the ability of ML5147 in reducing cell proliferation. After 6 h treatment with ML5147, cell migration showed a considerable reduction (-42.1% at 100 nM, P < 0.001 vs basal), to a greater extent than cells treated with UNC9994 (-31.1% at 100 nM, P < 0.001 vs basal). 5 out of 8 human primary cultured NF-PitNET cells in vitro responsive to cabergoline antiproliferative effects (P < 0.001 vs basal) showed a significant reduction of cell proliferation after UNC9994 and ML5147 treatments (-27.4% vs 7.1%, P < 0.001 vs basal, and -21.7% vs 9.3%, P < 0.01 vs basal, respectively). On the other hand, 3 out of 8 NF-PitNETs that did not respond to cabergoline appeared to be unresponsive also to UNC9994 and ML5147. In conclusion, our data demonstrated a relevant role for the beta-arrestin 2 dependent pathway in regulating DRD2 inhibitory effects on tumoral growth, whereas the canonical G protein-mediated signaling seemed to be key in controlling cell migration.

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Role of beta arrestins and G proteins in mediating DRD2 signaling in pituitary tumors
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Dopamine receptor type 2 (DRD2) agonists (DA) are the first-choice treatment for prolactin (PRL)-secreting pituitary tumors, but poorly effective in non-functioning (NF)-PitNETs. Along with G protein-dependent signaling, DRD2 also mediates non-canonical beta-arrestin-dependent pathways, where reduction of AKT phosphorylation plays a leading role for the antiproliferative effect of DRD2 in pituitary tumors. Through UNC9994 and ML5147, a beta-arrestin 2-biased and a G protein-biased agonist, respectively, the present study aimed to clarify the role of G proteins and beta-arrestin 2 in mediating DRD2 signaling in rat tumoral lactotroph cells MMQ and in human primary cultured NF-PitNET cells. In MMQ cells, treatment with UNC9994 reduced cell proliferation (-4.1% vs 0.0% at 100 nM, P < 0.01 vs basal) with a greater efficacy compared to cabergoline (22.2% at 100 nM vs 10.9%, P < 0.01 vs basal), while ML5147 treatment resulted into a slight lowering of cell proliferation (-10.8% vs 7.3% at 100 nM, P < 0.05 vs basal). Accordingly, UNC9994 was more efficient in reducing AKT phosphorylation (-45.5% vs -27.4% at 100 nM, P < 0.05 vs basal), whereas an increased AKT phosphorylation was detected after ML5147 treatment. Consistently, cabergoline and UNC9994 treatments determined a significant reduction of cyclin D3 (-14.7% vs 5.8% at 100 nM, P < 0.05 vs basal) and -18.8% vs 9.6% at 100 nM, P < 0.05 vs basal, respectively) together with an up-regulation of p27Kip1 (+35.2% vs +1.1% at 100 nM, P < 0.05 vs basal, respectively). Beta-arrestin 2 silencing reverted either UNC9994 and cabergoline anti-proliferative effects, as well as their effects on AKT phosphorylation. Pretreatment with pertussis toxin (PTX) maintained the antiproliferative effect of cabergoline (-16.0% vs 3.6%, P < 0.001 vs basal) and UNC9994 (-31.1% vs 19.9%, P < 0.001 vs basal), while it abolished the ability of ML5147 in reducing cell proliferation. After 6 h treatment with ML5147, cell migration showed a considerable reduction (-42.1% at 100 nM, P < 0.001 vs basal), to a greater extent than cells treated with UNC9994 (-31.1% at 100 nM, P < 0.001 vs basal). 5 out of 8 human primary cultured NF-PitNET cells in vitro responsive to cabergoline antiproliferative effects (P < 0.001 vs basal) showed a significant reduction of cell proliferation after UNC9994 and ML5147 treatments (-27.4% vs 7.1%, P < 0.001 vs basal, and -21.7% vs 9.3%, P < 0.01 vs basal, respectively). On the other hand, 3 out of 8 NF-PitNETs that did not respond to cabergoline appeared to be unresponsive also to UNC9994 and ML5147. In conclusion, our data demonstrated a relevant role for the beta-arrestin 2 dependent pathway in regulating DRD2 inhibitory effects on tumoral growth, whereas the canonical G protein-mediated signaling seemed to be key in controlling cell migration.

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Introduction

First-generation SRL (fg-SRL) represent the treatment of choice in acromegaly patients with post-neurosurgical adenomatous remnant and GH-hypersecretion. Anyway, approximately 60% of patients do not achieve adequate disease control. The main predictors of resistance include male sex, young age, invasiveness of the lesion and its hyperintensity on T2-weighted MRI scans; but also, SSTR2 expression, the cytokeratin pattern, Ki-67 and the presence of AIF gene mutation.

Aim

To identify the most relevant predictors of fg-SRL resistance among the most used clinical and histological parameters, specific to the Italian acromegaly population.

Methods

The MISS was an Italian multicenter, retrospective, case-control study, involving the Centers of Turin, Rome, Milan, Messina, Treviso and Ferrara (study duration 5/2018-12/2020). Non-response was defined after six months of full-dose fg-SRL treatment by the presence of both uncontrolled age-adjusted IGF-I random GH levels and a tumor shrinkage <20%. Controls were collected in a ratio of 1 to 2 compared to resistant cases.

Results

Ninety-six patients were enrolled (63 resistant cases and 33 controls). Age at diagnosis was associated with the condition of fg-SRL resistance, even when corrected for IGF-I values (coefficient -0.04, OR 0.96, AUC 0.62, P=0.035). An iso/hyperintense signal in T2-weighted MRI scans resulted the strongest radiological predictor (coefficient 1.19, OR 3.3, AUC 0.6, P=0.027), even if corrected for the maximal tumor diameter at diagnosis. Both a low grade SSTR2 expression and a sparsely granulated (SG)/intermediate cytokeratin pattern proved to be predictors of the resistant condition (coefficient 1.52, OR 4.58, AUC 0.7, P=0.013; coefficient 0.97, OR 2.65, P=0.047, respectively); the latter resulting also to be superior to the T2-weighted intensity on MRI (coefficient 1.71, OR 5.56, AUC 0.76, P=0.003). Among those patients undergone neurosurgery without any neoadjuvant treatment, the absence of an appreciable tumor remnant led to a negligible probability of non-response to medical treatment, even considering random GH at three months after surgery for the inclusion in the model (coefficient -3.09, OR 0.04, AUC 0.82, P=0.003).

Conclusions

A T2-iso/hyperintense MRI pattern was associated with a 3.3-fold greater probability of resistance to fg-SRL. Moreover, both a SG/intermediate granulation pattern and a low grade SSTR2 expression led to a 5 times greater probability of being resistant. Finally, the absence of an appreciable post-surgical remnant suggested a better response to fg-SRL. These factors deserve to be evaluated before setting up medical treatment with fg-SRL. Future guidelines should take this emerging evidence into account when making recommendations on therapeutic choice.

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The cut-off limits of GH response to GHRH + arginine test related to body mass index for the diagnosis of adult GH deficiency: do we need to review our diagnostic criteria?

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Introduction

The diagnosis of GH deficiency (GHD) in adults is based on a reduced GH response to provocative tests. The proportion of patients with low GH response to provocative tests increases with the number of other pituitary hormone deficiencies and several studies involving panhypopituitary patients have shown that under certain circumstances GH stimulation tests may be unnecessary to diagnose GHD.

Objective

Aim of this study was to re-evaluate the diagnostic cut-offs of GH response to GHRH + arginine (ARG) test in function of BMI. To this aim the patients’ pituitary function was considered as the gold standard for the diagnosis or exclusion of GHD; in particular GHD was defined by the presence of at least 3 others pituitary deficits, while a preserved somatotropic function was defined by the lack of others pituitary deficits.

Methods

The GH responses to GHRH + ARG were studied in 349 patients with history of hypopitathalamic-pituitary disease [age (mean ± SD): 43.8 ± 16.5 years; BMI: 27.4 ± 9.2 kg/m²]. Patients were divided into lean (143), overweight (107) and obese (99) subjects according to BMI. The best GH cut-off to GHRH + ARG, defined as the one with the best sensitivity (SE) and specificity (SP), was identified using the receiver-operating characteristic curve (ROC) analysis.

Results

The best GH cut-off to GHRH + ARG was 5.5 µg/l in lean subjects (SE 89.2%, SP 79.7%), 4.2 µg/l in overweight subjects (SE 94.0%, SP 62.5%) and 2.8 µg/l in obese subjects (SE 85.7%, SP 83.3%). The diagnostic accuracy was 85.3, 82.2 and 84.8% respectively.

Conclusions

To our knowledge this is the first study that evaluate the diagnostic cut-offs of GH response to GHRH + ARG in function of BMI using a clinical definition of GHD as gold standard. Our results suggest that with this new approach, the GHRH + ARG cut-offs should be revised.

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SARS-CoV-2 infection in acromegaly patients: case series

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Introduction

SARS-CoV-2 infection challenged the appropriate management of acromegaly, because of delayed or limited admissions and treatment. Despite lack of data regarding SARS-CoV-2 infection in acromegaly patients (only one case reported to date), increased susceptibility to infection and poor prognosis might be triggered by the associated metabolic, cardiovascular and respiratory comorbidities. We report a series of acromegaly patients with a positive PCR test at their admission in our Endocrinology Department and their COVID-19 disease evolution.

Methods

All inpatient admissions in our unit undergo RT-PCT testing for SARS-CoV-2 infection from the debut of the pandemic according to the local protocol. Inpatient admissions for acromegaly diagnosis and monitoring during the first 4 waves of the COVID-19 pandemic (March 1st 2020 to November 30th 2021 – 21 months) were reviewed and compared to the acromegaly inpatient admissions during the same period of time before the pandemic (June 1st 2018 to February 29th 2020).

Results

The number of inpatient admission for acromegaly dropped by approximately 50% during the first 4 waves of the pandemic compared to the same length of time prior to the pandemic (155 vs 359 inpatient admissions for acromegaly). Among the 86 patients admitted for acromegaly diagnosis or monitoring during the first 4 waves of the COVID-19 pandemic (March 1st 2020 to November 30th 2021 – 21 months) were reviewed and compared to the acromegaly inpatient admissions during the same period of time before the pandemic (June 1st 2018 to February 29th 2020).

Conclusions

Although SARS-CoV-2 infection occurs is thought to have a worse prognosis in acromegaly patients due to the coexistence of cardiometabolic complications and...
Familial neurohypophyseal diabetes insipidus: an extremely rare report of a family with a nonsense mutation in the arginine vasopressin gene

Introduction
Familial neurohypophyseal diabetes insipidus (FNDI) is a rare form of central diabetes insipidus (CDI) characterized by childhood-onset progressive polydipsia and polyuria due to mutations in the arginine vasopressin-neurophysin II (AVP-NPII) gene. Case description
Two male siblings were referred at 1 month of age to exclude CDI owing to a family history of CDI in the father and paternal grandfather. The proband was the father diagnosed at 3 months old. The grandparent was diagnosed later, in his early twenties, when diabetes was observed in both. Physical examination and past medical history were unremarkable. Random urine specific gravity was lower than 1.005. Glycemia, uric acid, creatinin, sodium, potassium and calcium were within normal range. The sibling 1 was admitted for elective water deprivation test that confirmed CDI (basal serum and urinary osmolality: 278 mOsm/Kg and 292 mOsm/kg; serum and urinary osmolality at the end: 289 mOsm/kg and 281 mOsm/kg; urinary osmolality after 10 mg of desmopressin [DDAVP]: urinary osmolality of 574 mOsm/kg [increased by 102%]).

Discussion and conclusions
To our knowledge, there is only another family with this autosomal dominant mutation described worldwide. Genetic counselling should be offered to ensure an early and adequate diagnosis and treatment. It should also provide the family with accurate information on preimplantation genetic testing (PGT) in order to obtain genetically healthy descendants. In Portugal, FND1 requires prior authorization from the “National Council for Medically Assisted Procreation” for couples who intend to perform a PGT cycle.
Prevalence, type and evolution of autoimmune diseases with respect to hormone control in patients with cortisol, GH and prolactin hyperscretion

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Background
In vitro and animal experiments have clearly demonstrated that excessive cortisol, GH and prolactin secretion, as well as dopamine agonists (D2As) and somatostatin analogs (SSAs), often prescribed for their treatment, affect the immune response and the onset/evolution of autoimmune diseases (AIDs) through direct and indirect complex mechanisms. Data from clinical studies are very scanty.

Methods
To assess the 1) distribution of AIDs according to patient age and gender, adenoma and AID type; and 2) evolution of AID(s) with respect to hormonal activity and eventual DA/SSA treatment, in patients with Cushing’s disease (CD), acromegaly and prolactinoma with respect to patients with non-functioning adenoma (NFPAs; controls).

Results
Clinical data of interest were collected retrospectively and prospectively from patient records and a purposely designed questionnaire.

Conclusions
In patients with CD, GH and prolactin hyperscretion, AIDs occurred from some weeks to years after CD diagnosis, as well as AIDs occurring before and after prolactinoma diagnosis. AIDs mainly occurred during active disease (P < 0.01) for both groups AID evolution was independent from hormone control and SSA/D2A treatment.

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GH/IGF-I impact hepatic lipid accumulation in non-acromegalic individuals with and without non-alcoholic fatty liver disease

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Background
Central pontine myelinolysis: Case report
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Introduction
Central pontine myelinolysis (CPM) is a rare and potentially life-threatening complication of a sudden rise in serum osmolality. Along with extrapontine myelinolysis, it is part of the osmotic demyelination syndrome (ODS).

Case report
We report the case of a 31-year-old male with history of alcohol and cannabis dependence, who had attended a private clinic two weeks earlier for gastric balloon placement, he was admitted to the emergency-department reporting nausea and vomiting with oral intolerance, nervousness, and agitation. He was initially detected to have hypothyroid myxedema with BMI: 25.7 ± 4.3 kg/m², IGF1-ULN: 65.7 ± 17.2% (IGF-I: 53.6-102 kg/m²) the median HCL was 2.7% (IGF-1: 1.35-3.5%) with 27 patients presenting with a HCL higher than 5.5% indicating NAFLD. Liver parameters, like HCL and ATP synthesis rate (AATP), as well as high energy phosphorous metabolites were analysed using 1H as well as 31P-magnetic resonance spectroscopy (MRS) at 7 Tesla. NAFLD was defined as HCL > 5.5%.

Results
In the whole cohort (age: 43.4 ± 15.3y; BMI: 25.7 ± 4.3 kg/m²; IGF-I:ULN: 65.7 ± 17.2% (IGF-I: 53.6-102 kg/m²) the median HCL was 2.7% (IGF-1: 1.35-3.5%) with 27 patients presenting with a HCL higher than 5.5% indicating NAFLD. Fasting GH (0.21 [0.1; 0.6] ng/ml vs 0.67 [0.2; 2.5] ng/ml; P = 0.0055), as well as dynamic GH levels during OGTT (AUCGH: 15.30 [7.2; 25.6] ng/ml/min vs 48.8 [25.7; 143.2] ng/ml/min;P = 0.0002). IGF-1:ULN correlated significantly with risk factors include severe hyponatraemia, alcoholism, thiazide use, hypokalaemia, and malnourishment.

Discussion
In patients with multiple risk factors, CPM might be prevented by frequent control of electrolytes and osmolality in combination with volume status and urinary output.

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high-energy phosphorous metabolites but did not correlate with ATP in the whole cohort. In the multiple logistic regression analysis IGFI-ULN as well as fasting glucose were next to BMI and OGIS a significant, independent predictor for NAFLD. Conclusion
In summary, here we show that increased HCL is associated with lower fasting and post-glucose-load GH concentrations in otherwise healthy individuals with or without NAFLD, while both GH and IGFI independently relate to the presence of NAFLD. The relationship between GH/IGFI-1 metabolism and HCL could be further investigated as a potential therapeutic target in patients with NAFLD.

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P404
Impact of urinary and late-night salivary cortisol levels on clinical signs of hypercortisolism and quality of life in patients with Cushing’s disease treated with osilodrostat
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Introduction Osilodrostat decreases cortisol production by inhibiting 11b-hydroxylase, increasing adrenal hormones above the blockade. Here, we describe these effects of osilodrostat and associated adverse events (AEs). The efficacy and safety of osilodrostat in patients with Cushing’s disease (CD) were confirmed in the published Phase III, prospective LINC 3 study (NCT02180217).

Methods
137 patients with CD (mUFC > 1.5x upper limit of normal) were enrolled in a 48-week (W) core phase including an 8W double-blind, randomised-withdrawal period for eligible patients. 106/113 patients who completed W48 entered an optional extension, ending when all ongoing patients completed ≥72W of treatment or discontinued. Testosterone, 11-deoxycortisol, 11-deoxycorticosterone, and aldosterone were assessed centrally at baseline and regular intervals by liquid chromatography-tandem mass spectrometry, and dehydroepiandrosterone sulfate (DHEAS) by chemiluminescence immunoassay. Hirsutism (females; rated on a semi-quantitative scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe), blood pressure, oedema and serum potassium were assessed regularly.

Results
Median osilodrostat exposure was 130W (range 1–245); median osilodrostat dose was 7.4 mg/day (range 0.8–46.6). Following an increase during the core phase, mean testosterone levels stabilised in males and decreased towards baseline in females during long-term treatment. Of females with baseline, W48 (n = 76) and W72 (n = 64) assessments, hirsutism score improved from baseline in 26 and 22 patients at W48 and W72, respectively, and remained unchanged in 37 and 33 patients. Mean (SD) DHEAS levels decreased during the core phase to within the normal range, then stabilised during the extension (W48 and W72: females: 1.6 [1.6] and 1.0 [0.9] μmol/l; males: 3.4 [3.3] and 3.0 [3.1] μmol/l). Aldosterone levels also decreased and then stabilised during long-term treatment. Overall, mean potassium levels remained stable throughout the study. AEs related to accumulation of adrenal hormone precursors were reported in 58.4% (n = 80/137) of patients, regardless of study drug relationship, and managed with additional therapy in 36.5% (n = 50/137) of patients. The most common AEs were hypertriglyceridaemia (n = 24), peripheral oedema (n = 22) and hypokalaemia (n = 18), managed with concomitant medication in 17, 6 and 4 patients, respectively. They mostly occurred during the first 26W of treatment (females: 35.5%; males: 49.1%) at different osilodrostat doses (1–60 mg), with no discernable dose-related effect. Few patients discontinued treatment because of these AEs (1.5%; n = 2/137).

Conclusions
Adrenal hormone levels frequently change when initiating osilodrostat but stabilise during long-term treatment. AEs associated with these changes are manageable without osilodrostat discontinuation; they should be closely monitored and treatment initiated as needed to achieve optimal patient outcomes.

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P407
Endoscopic surgery for acromegaly: results and predictors of outcome
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1IRCCS Istituto delle Scienze Neurologiche di Bologna, Pituitary Unit, Bologna, Italy; 2Alma Mater Studiorum - Universita` di Bologna, range 12-240.8), 197 patients (67.7%) were cured; 94 (32.3%) had residual adenoma. At last follow-up (mean duration 67.8 months), 217 (74.6%) patients presented disease remission, 74 (25.4%) had persistent disease, 41 GH-PRL-secreting adenomas. At 3-month follow-up, 217 (74.6%) patients presented disease remission, 74 (25.4%) still had residual adenoma. At last follow-up, 217 (74.6%) patients presented disease remission, 74 (25.4%) still had residual adenoma. 134 were at least 1 month apart and received randomly oral semaglutide (7 mg) or placebo. Participants were asked to avoid strenuous physical activity the day before testing. Basal fasting (≥ 8 h) blood samples were taken in the morning (8-9 am) after at least 15 minutes of rest. Study medication was taken with up to 40 ml of water. Post-treatment blood samples were drawn 60, 90, 120, 150, 180, and 240 minutes thereafter. The intensity of nausea according to the visual analog scale (0 - no nausea, 10 – vomiting) was also registered. The primary endpoint of the study was the change in growth hormone concentration. The effect of oral semaglutide on GH was variable but did induce a clinically significant GH increase in some study subjects. We conclude that GLP-1 RA holds a promise for a GH stimulation test and further studies are warranted.

Background
Endoscopic surgery (ES) performed in Pituitary Centers of Excellence (PCOE) represents the gold standard treatment for GH-secreting adenomas. However, rate of cure greatly varies according to definition criteria, follow-up duration, various patient and adenoma features, and surgeon ability.

Study aim
To assess short- (3 month) and long-term (≥ 1 year) outcome and identify predictors of ES, in a large and homogeneous cohort of acromegaly patients.

Subjects and methods
Clinical, radiological, and histological data at enrollment and follow-up of consecutive patients with GH-secreting adenoma, treated by ES at an Italian PCOE, from 1998 to 2020, were retrospectively analyzed.

Results
291 patients (167 females; mean age at surgery 46.2 ± 12.4 years) were included. 195 (67%) had a macroadenoma with invasion of surrounding structures (Hardy-Wilson-Knosp classification) in 92.3% of the cases. According to Trouillas grading, 183 (62.9%) were grade 1a, 35 (12%) 1b, 48 (16.5%) 2a, and 25 (8.5%) 2b. 269 patients were treated by ES and 22 by combined ES-craniotomy. 134 were naïve for treatment; 35 had been treated with surgery; 107 with medical therapy and 21 with radiation therapy. Histological examination revealed 250 GH- (150 sparsely and 99 densely granulated) and 41 GH-PRL-secreting adenomas. At a pilot single-group, open-label clinical trial the effect of a single subcutaneous injection of 10 µg exenatide was tested on healthy volunteers (n = 10). Exenatide elicited a robust increase of GH levels compared to pre-treatment values (P < 0.05) with the peak occurring around 60-90 minutes in most subjects. Oral semaglutide is the first oral GLP-1 RA available. We next conducted a randomized, placebo-controlled, crossover clinical trial to test the effect of oral semaglutide on GH release. The study included 10 adult healthy volunteers (age 26-47; 5 females, and 5 males). All participants were tested on two occasions that were at least 1 month apart and received randomly oral semaglutide (7 mg) or placebo. Participants were asked to avoid strenuous physical activity the day before testing. Basal fasting (≥ 8 h) blood samples were taken in the morning (8-9 am) after at least 15 minutes of rest. Study medication was taken with up to 40 ml of water. Post-treatment blood samples were drawn 60, 90, 120, 150, 180, and 240 minutes thereafter. The intensity of nausea according to the visual analog scale (0 - no nausea, 10 – vomiting) was also registered. The primary endpoint of the study was the change in growth hormone concentration. The effect of oral semaglutide on GH was variable but did induce a clinically significant GH increase in some study subjects. We conclude that GLP-1 RA holds a promise for a GH stimulation test and further studies are warranted.

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P408
Pituitary adenomas in the elderly may be hiding behind age-related comorbidity
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Background
Extended life expectancy and increase in neuroimaging availability, lead to increase in incidence of pituitary adenomas (PA) diagnosed after the age of 70. Recognition of PA in the elderly may be challenging and delayed due to symptoms overlapping with aging and comorbidities.

Objective
To investigate character and presenting symptoms of PA in patients diagnosed after the age of 70.

Methods
105 patients (7.9%) with PA diagnosed after the age of 70 (58 males, 55.2%) were identified from the PA database (n = 1332) of the Department of Neuroendocrinology for the past 17 years. Gender, age at diagnosis, tumor size, presenting signs and symptoms, presence of comorbidities and hypopituitarism, functional type of PA and treatment modality were analyzed.

Results
Mean age at diagnosis was 74.5 ± 0.4 years (range: 70-85). Thirteen patients (12.4%) were older than 80 years at diagnosis. Eighty-three patients (79%) had two or more comorbidities. Non-functioning PA (NFPA) were significantly more prevalent (58% vs. 81%) than functional PA (19%; P < 0.01). Eleven patients (10.5%) had acromegaly, six (5.7%) had prolactinoma, and three patients had corticotropinoma (2.9%). NFPA patients were older than those with functional PA (75.0 ± 5.2 vs. 72.7 ± 6.8; P < 0.05). Macroadenomas (75%; 92.4%) were significantly more prevalent than microadenomas (n = 8; 7.6%; P < 0.001). Six patients with microadenoma had acromegaly. PA were significantly larger in males (28.6 ± 2.7 vs. 21.8 ± 1.8 mm; P = 0.01). Thirteen patients (12.4%) had gigantican adenomas (> 4 cm), nine with NFPA. Pituitary adenomas (55.6 ± 3.8 mm) were significantly larger than NFPA (25.8 ± 1.4 mm) and acromegaly (11.1 ± 2.9 mm; P < 0.01). Presenting symptoms included: headache (n = 52, 49.5%), visual impairment (often misinterpreted as cataract) (n = 46, 43.8%), and cranial nerve palsies (n = 11, 10.5%). Twelve patients (11.4%) had hypopituitarism due to secondary hypocorticism. Dyslipidemia was diagnosed in 58 patients (55.2%). In 60 (57.1%) PA was detected fortuitously by imaging for reasons unrelated to pituitary disease, during investigation for non-specific neurological symptoms (gait, speech impairment, dizziness, falls, memory impairment, dementia, depression, loss of consciousness, deafness), headache, head trauma, cerebrovascular insults or subarachnoid hemorrhage. Hypopituitarism was confirmed as complete in 45 patients (42.9%), and partial in 15 patients (14.3%). Fifty-two patients (49.5%) underwent transphenoidal surgery, with no

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severe complications. Six patients (5.7%) with prolactinomas and six patients (5.7%) with acromegaly were medically treated.

Conclusion
The age-incidence for pituitary tumors shows a typical high risk in the elderly. Nonfunctioning macroadenomas are the most prevalent. Age-related comorbidities led to the late diagnosis of pituitary tumors in most elderly patients which accounted for the pituitary tumor size (macroadenomas in most).

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P409

Effects of clinical characteristics and treatment of sporadic and MEN-1 related insulinomas
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Background
Although in most cases insulinomas are small and benign tumors, in about 4% they are malignant, mainly in course of inherited syndromes like MEN1, tubular sclerosis or neurofibromatosis type 1. While in case of benign tumors surgery is usually curative, the metastatic form brings difficulties in managing due to dissemination and the risk of recurring, life-threatening, severe hypoglycemia. To elucidate the clinical differences between sporadic and MEN-1 linked insulinoma we review clinical characteristics and treatment in cohort of patients treated in our centre since implementation of electronic database.

Material
Data was reviewed from patients diagnosed with insulinoma managed at our centre from 2015 to 2021 year.

Results
There were 19 cases of insulinomas (9 women and 10 men). In 6 (32%) cases the mutation in menin gene were confirmed. The median age at diagnosis in the whole group was 58 years, (range 16-87 years) in case of sporadic and MEN-1 related insulinoma 69 years (range 29-87 years) and 40 years (range 6-79 years) respectively. In case of MEN-1 related insulinoma at diagnosis 5/6 patients had primary hyperparathyroidism (PHP) in one case it was confirmed 11 years after insulinoma diagnosis. None of patients with negative MEN-1 gene mutations had PHP. 2 out of 13 (13%) had dissemination of insulinoma at diagnosis. Median of Kd67 in case of sporadic insulinoma was 2% range (1-12%) and in case of MEN-1 related insulinoma 2% range (1-5%). In 3 cases (50%) of MEN-1 related insulinoma there was more than one lesion of neuroendocrine characteristic in pancreas. In 6 out of 19 cases (32%) insulinoma was disseminated at diagnosis, in 23% cases (3 out of 13) of sporadic and in 50% (3 out of 6) cases of MEN-1 related insulinoma. All patients with insulinomas limited to pancreas were treated radically by surgery (in 3 cases by tumor enucleation, in 8 cases with partial or total pancreaticoduodenectomy). One of MEN-1 patient had recurrence of hypoglycemia after surgery due to appearance of new insulinoma lesion. The patients with dissemination were treated, due to symptoms of hypoglycemia, with combination of diazoxide, somatostatin analogues and PRRT. 5 out of 6 patients with insulinoma in course of MEN-1 mutation are still alive, one died because of coexisting pancreatic cancer.

Conclusion
There are clinical differences between the course of sporadic and MEN-1 associated insulinoma. In the case of disseminated disease, there is often a need for multi-drug treatment to delay progression and prevent episodes of severe hypoglycemia.

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P411

Independent injection vs healthcare-setting administration of somatostatin analogues: A systematic literature review
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Background
A systematic literature review (SLR) was conducted to assess the use of independent injections (self/partner/home-administered) as an alternative to healthcare-setting injections for chronic diseases. The primary objective was to identify studies reporting on independent injection of somatostatin analogues (SSAs). Comparative evidence on independent injection of other medications was examined as a secondary objective.

Methods
MEDLINE/Embase/the Cochrane Library were searched for records published between January 2001–September 2021, using terms for independent injection. Congresses (2019–2021) and SLR bibliographies were also hand-searched. Abstracts/full-text publications were reviewed by two independent reviewers. Studies were eligible if they reported on efficacy/effectiveness, adherence, safety, economic or patient-reported outcomes in populations receiving independent injections of SSAs (primary objective) or other monthly subcutaneous treatments (secondary objective). Studies investigated under the secondary objective were required to include a comparator in the healthcare setting.

Results
3,430 unique records were screened, of which 12 studies, comprising 18–3,921 patients, were included, all reporting on SSAs (lanreotide or octreotide).

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No studies were identified to support the secondary objective. In four studies reporting comparative efficacy/effectiveness, independent injection was associated with equal/greater disease control in patients with acromegaly and neuroendocrine tumors (NETs) compared with healthcare-setting administration. Treatment adherence, defined as successful injection administration, was shown in 74%–93% of patients with acromegaly receiving independent injections in two studies, both assessing lanreotide. A higher proportion of injection-site reactions was observed in patients self-injecting lanreotide compared with partner injections (19% vs 2%, P < 0.05). Two studies reported no serious adverse events, which were rare in both the independent and healthcare-administration settings. Preference for independent injection varied between studies/disease indications, ranging from 4%–100% across five studies, with patients citing increased autonomy and convenience for preference over healthcare-set setting administration. Lower anxiety, perceived safety, and the ability to communicate with a healthcare provider (HCP) were factors underlying a preference for healthcare-setting administration. Self- or partner-injection was associated with economic savings compared with the healthcare setting across five studies, including nurse, travel, and administration time.

Conclusions
Independent injection is similar to the healthcare setting regarding efficacy/effectiveness, adherence, and safety outcomes. Patient preferences for administration setting varied and may reflect the need for improved patient education/training, or home care program support for those where independent injection is a preferred/suitable option. Self- or partner-injection also provided cost savings. Our findings provide a basis to understand outcomes related to independent injection and empower patients to discuss optimal treatment choices with their HCP.

P413
Osilodrostat provides sustained clinical benefits and improves health-related quality of life in patients with cushing’s disease: results from the Phase III LINC 4 study
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Background
Cushing’s disease (CD) is associated with hypercortisolism-induced cardiovascular morbidity and mortality and impaired patient quality of life (QoL). We report long-term effects of osilodrostat (potent 11β-hydroxysteroid) inhibitor on cardiovascular/metabolic-related risk factors, physical features of hypercortisolism and QoL in CD patients following the core and extension phases of the LINC 4 study (NCT02697734).

Methods
LINC 4 comprised a 12-week (W), randomised, double-blind, placebo-controlled period, 36W of open-label osilodrostat, and an optional extension in adults with CD and (m)UCF > 1.3x upper normal limit. Dose adjustments were permitted based on efficacy/tolerability (open-label range, 1–30 mg bid). Cardiovascular/metabolic-related parameters, physical features of hypercortisolism (rating: 0 = absent; 1 = mild; 2 = moderate; 3 = severe), and CushingQoL scores were evaluated at core baseline, every 2, 4, 12 or 24W (depending on study phase/parameter) and at extension end-of-treatment (EOT). Change from baseline is provided for patients with assessments at core baseline, W48 and EOT. Results
Of 65 patients completing W48, 60 entered the extension. Median (range) osilodrostat exposure from core baseline to study end: 87.1 (2–127) W; median (IQR) average dose: 4.6 (3.7–9.2) mg/day. Mean changes (95%CI) in cardiovascular/metabolic-related parameters from core baseline to W48 and EOT, respectively, included decreases in systolic (− 9.7 [− 14.9, − 4.6]) and − 12.4 [− 17.4, − 7.4] mmHg; baseline: 131.5 mmHg and diastolic (− 4.2 [− 7.3, − 1.2]) and − 5.6 [− 8.9, − 2.4] mmHg; baseline 87.5 mmHg) blood pressure, fasting plasma glucose (− 3.1 [− 8.6, 0.06] and − 3.5 [− 8.5, 1.4] mg/dl; baseline: 95.3 mg/dl) and cholesterol (− 0.5 [− 0.8, − 0.2] and − 0.6 [− 0.9, − 0.3] mmol/l; baseline: 5.5 mmol/l).

Improvements (mean change [95%CI]) from core baseline to W48 and EOT occurred for weight ([4.3 [− 5.9, 2.6] and [6.8 [− 8.8, 2.4] kg; baseline: 78.3 kg) and waist circumference ([4.5 [− 6.0, 1.3] and [7.6 [− 9.6, 5.6] cm; baseline: 102.8 cm). Physical features of hypercortisolism improved (severity reduced) or remained stable from core baseline to most patients (respectively): eumetabolic (21% [n = 10/48], 79% [n = 38/48]); strie (26% [n = 12/46], 72% [n = 33/46]); hirsutism

Conclusions
Similarly to what happens in other acute medical conditions, COVID-19-related sodium alterations are frequently associated with hospital readmissions and long-term mortality. The worst outcomes involve patients whose sodium alterations recur after discharge, particularly hyponatremia at the time of hospital readmission and mixed dysnatremia occurring during hospital stay.

References

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Alongside cortisol control, most cardiovascular/metabolic-related parameters continued to improve during long-term oslodrotast treatment. Additionally, most physical features of hypercortisolism, including hirsutism, improved or remained stable, and CushingQol score improved. Oslodrotast is an effective treatment that may alleviate disease burden for many CD patients.

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P414
Predictive factors of somatostatin receptor ligand response in acromegaly – a prospective study
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Objective
To prospectively confirm that SST2A and adenoma granularity are good predictors of response to SST2A ligands in acromegaly.

Methods
Multicentric, prospective, observational cohort study, conducted in France.

Results
In Group 1 (IGF-I decrease from baseline to month 6 positively correlated with SST2A immunoreactive score (IRS), P < 0.01. Densely granulated/intermediate adenomas had greater IGF-I and GH decrease under octreotide than sparsely granulated adenomas (P = 0.02 and P = 0.006, respectively), and expressed ghrelin levels of SST2A (P < 0.001) and SST5 (P < 0.004). T2WSI changed between the preoperative MRI and month 6-MRI in half of the patients. SST5 IRS was higher in hypertensive adenomas (P = 0.04. Most sparsely granulated and most hypertensive adenomas expressed high SST5 levels.

Conclusion
We prospectively confirm that SST2A and adenoma granularity are good predictors of response to octreotide, and that SST5 is not. We propose the IRS for scoring system harmonization. The MRI sequences must be optimized in order to improve from core baseline to W48 and EOT (mean change [95% CI]: 12.0 [8.2; 15.9] and 17.1 [12.5; 21.7]; baseline: 51.8).

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P416
Cabergerone monotherapy in acromegaly – a multicenter, retrospective, cohort study of non-irradiated patients using current criteria for disease control
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Objective
To evaluate the effects of somapacitan on glucose metabolism compared with daily GH or placebo in patients with AGHD using data from three previously published phase 3 trials: REAL 1 (NCT02229851), REAL 2 (NCT02382939) and REAL Japan (NCT03075644). REAL 1 was a randomised, placebo-controlled (double-blind) and active-controlled (open-label) trial in GH-naïve patients, who received somapacitan (n = 120), daily GH (n = 119) or placebo (n = 61) for 34 weeks (main phase). In a subsequent 52-week extension (86 weeks of treatment in total), patients receiving somapacitan continued with somapacitan (n = 114), patients receiving daily GH were re-randomised to receive either somapacitan (n = 51) or daily GH (n = 52), and patients receiving placebo were switched to somapacitan (n = 55; not included in this analysis). REAL 2 and REAL Japan were randomised, open-label, active-controlled trials in patients previously treated with daily GH. In REAL 2, patients received somapacitan (n = 61) or daily GH (n = 31) for 26 weeks. In REAL Japan, patients received somapacitan (n = 46) or daily GH (n = 16) for 52 weeks. In these post hoc analyses, the absolute or relative change from baseline between treatments for HbA1c, fasting plasma glucose (FPG), fasting serum insulin and index of insulin resistance (HOMA-IR) were explored. In treatment-naïve patients (REAL 1), there were no statistically significant (P < 0.05) differences between somapacitan and placebo for any glucose-related endpoints at week 34 (main phase). No statistically significant differences in HbA1c were observed between somapacitan and daily GH at week 34 or week 86 (main phase plus extension). Transient differences were seen at week 34 between somapacitan and daily GH (with higher values reported for daily GH) for FPG (estimated treatment difference [95% CI]: −0.16 mmol/l [−0.30; −0.03]), fasting serum insulin (estimated treatment ratio [ETR] [95% CI]: 0.85 [0.73; 0.99]) and HOMA-IR (ETR [95% CI]: 0.80 [0.69; 0.94]); these differences were not observed at any other timepoint. In previously treated patients (REAL 2, REAL Japan and REAL 1 patients who received daily GH in the main phase and were re-randomised for the extension), no statistically significant differences were seen between treatments for any glucose-related endpoints. No new cases of diabetes were reported in somapacitan-treated patients in these trials. In conclusion, somapacitan was similar to daily GH and had no clinically relevant adverse effects on glucose metabolism in treatment-naïve or previously treated patients with AGHD in these phase 3 trials.

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between 0% and 100% of the patients during treatment periods ranging between 2.6 and 24 months. However, in many of these studies, previous radiotherapy is a confounding factor. Furthermore, real world data applying the current disease control criteria (normal IGF-1 and GH <1 mU/l) are not available. The aim of this study was to investigate the efficacy and safety profile of cabergoline monotherapy in non-irradiated patients with uncontrolled acromegaly.

Patients and methods
In this multicenter, retrospective cohort study, non-irradiated patients offered cabergoline monotherapy for uncontrolled acromegaly were identified from the registries of four UK Pituitary centers (Birmingham, Bristol, Leicester and Oxford). Clinical, laboratory and imaging data were collected and analyzed.

Results
Sixty-nine patients were included. Median age at diagnosis of acromegaly was 50.5 years (range 28-78), 34.7% of the patients were females and 21.7% of the tumours were prolactin co-secreting. Prior to starting cabergoline, IGF-1 levels were 2.13 (median) times the upper limit of normal (ULN) (range 1.02-8.54). Median duration of cabergoline treatment was 23 months (3-252). Normal IGF-1 was achieved in 31.8% (22/67) of the patients within a reported median interval of 12.5 months (2.84). Median weekly cabergoline dose at most recent review was 2.5 mg (0.25-4) in the responders, and 3 mg (0.25-7) in the non-responders (P = 0.39). On univariate regression analysis, IGF-1 normalisation was significantly related with the presence of a prolactin co-secreting adenoma (B 1.38, P = 0.030) and lower pre-cabergoline IGF-1 ULN levels (B -0.73, P = 0.015). ROC analysis showed that IGF-1 < 1.55 ULN had sensitivity 50% and specificity 85% in predicting achievement of normal IGF-1; sensitivity and specificity for IGF-1 < 1.97 ULN were 75% and 67.5%, respectively (AUC 0.760). GH <1 mg/l was found in 25% (14/56) of the patients, whereas 16.1% (9/56) had achieved both GH and IGF-1 criteria. Side effects were recorded in 5 patients (nausea n = 2, nasal congestion n = 1, dizziness/blurred vision/ abdominal pain/weakness n = 1, hair loss n = 1).

Conclusions
In this large cohort of non-irradiated patients with acromegaly, cabergoline normalised IGF-1 in 32% of the cases and dose did not differ between responders and non-responders; efficacy of treatment was associated with the presence of prolactin co-secreting adenoma and pre-cabergoline IGF-1 ULN levels. Achievement of both optimal GH and IGF-1 levels was seen in only 16% of the patients.

P417
Terlipressin induced acute severe hyponatremia
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Introduction
Terlipressin is a non-selective vasopressin analogue used in patients with decompensated cirrhosis, gastrointestinal haemorrhage or hepatorenal syndrome. It directly binds to V1 receptors improving circulatory volume by causing splanchic vasoconstriction and portal hypertension inhibition, and has a full V2 receptor agonism in the collecting duct. In consequence, it increases reabsorption of water and can lead to a decrease in plasma osmolality and hyponatremia. Hyponatraemia induced by Terlipressin is uncommon (1/1,000 to < 1/100, Summary of Product Characteristics). Maximal plasma levels are reached after 1-2h following iv administration and metabolic elimination takes place within a 4-6 h period.

Case Presentation
We present the case of a 46-year-old man admitted to hospital with cirrhosis needing liver resection for liver metastases from colorectal cancer. Patient was treated with 1 mg of terlipressin intravenously every 6 h and isotonic intravenous maintenance fluids (0.9% NaCl) 1000 ml every 24 h. 36 h later he presented with lethargy, confusion, nausea and vomiting. Laboratory findings showed severe hyponatremia (108 mmol/l[134-145]) with low osmolality (231 mOsm/kg [280-305]) and normal blood glucose levels (100 mg/dl). He was euvolemic at physical examination. Natriemia levels 36 h before the start of terlipressin treatment were 132 mmol/l. Urinary osmolality and urinary sodium were not available at this moment, given the priority of correcting the symptomatic severe hyponatremia. Treatment with intravenous infusion of hypertonic saline was started and terlipressin was discontinued, sodium levels returning to normal over 48 h (132 mmol/l[134-145]).

Conclusion
Hyponatremia induced by Terlipressin is uncommon and can develop rapidly. It is reversible with cessation of therapy and requires careful consideration. This case is an illustration of this undesirable effect. As endocrinologists, we must be familiar with terlipressin pharmacokinetic properties. Sodium levels and fluid balance should be monitored intensively and immediately after first terlipressin dose.

P418
Is there a difference in clinical skills gained between healthcare professionals of high- and low and middle-income countries with online simulation-based learning?
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Background
There is a differential clinical learning opportunity for healthcare professionals in low- and middle-income countries (LMICs) compared to high-income countries (HICs). Barriers to learning include cost, time and accessibility. Simulation via Instant Messaging - Birmingham Advance (SIMBA) is a free virtual simulation-based model aimed at improving clinicians’ professional development, without compromising patient safety. The study compared the impact of SIMBA in LMICs and HICs on participants’ professional development and learning. Methods
Between May 2020 and October 2021, 16 SIMBA sessions were conducted. Participants interacted with moderators over WhatsApp to solve anonymised real-life clinical scenarios. Following simulation, interactive Zoom sessions were led by experts in relevant fields, allowing participants to ask any questions regarding the cases. Participants completed pre- and post-SIMBA surveys as part of their activity on the day of simulation. They were grouped based on their country of residence as HICs and LMICs based on the 2022 World Bank Report to compare their performance, perceptions and improvements in core competences as defined by the Accreditation Council of Graduate Medical Schools using the Chi-square test. Thematic analysis of open-ended questions was also performed.

Results
In total, 462 participants completed both the pre- and post-SIMBA surveys, of which 29.7% (n = 137) were from LMICs. While participants from HICs reported better knowledge on patient management (LMIC: 77.4% vs HIC: 86.5%; P = 0.01), those from LMIC reported higher improvement in professionalism (LMIC: 41.6% vs HIC: 31.1%; P = 0.02). Both groups reported similar gains in patient care (LMIC: 51.8% vs HIC: 57.2%; P = 0.28), systems-based practice (LMIC: 56.9% vs HIC: 47.1%; P = 0.052), practice-based learning (LMIC: 72.3% vs HIC: 65.5%; P = 0.15), communication skills (LMIC: 31.4% vs HIC: 23.8%; P = 0.22), applying simulated topics to their practice (Engagement: P = 0.197), and overall quality of the teaching session (P = 0.101) . In thematic analysis, the major strengths of SIMBA over traditional methods were providing individualised, structured, and engaging sessions. Conclusion
SIMBA improves healthcare professionals’ clinical competencies from both LMICs and HICs demonstrating that SIMBA can provide equivalent teaching experiences irrespective of country of residence. Furthermore, international accessibility due to the virtual nature of SIMBA shows potential for global scalability, especially in LMICs where it can help to provide standardised medical training and steer future global health education policy development.

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Obstructive sleep apnea syndrome (OSAS) in acromegaly: does the gender matter?
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Obstructive sleep apnea syndrome (OSAS) is a frequent cardiovascular risk factor in acromegaly. We aimed to retrospectively evaluate sex-related differences in OSAS characteristics and indicators of non-invasive ventilation.

Patients and Methods
Thirty-nine adult patients (16 F, 23 M) from two European centers were studied by home sleep apnea test (HSAT) or polysonomography (PSG). OSAS was defined by an apnea-hypopnea index (AHI) ≥ 5/h and analyzed according to age, gender, disease activity, obesity, diabetes mellitus, hypertension and nocturnal continuous positive airway therapy (CPAP). Categorical variables were considered in all cases, whereas, except for post/pre-ventilation AHI, sleep parameters were used in cases defined according to the last International Classification of Sleep Disorders (ICSD-3, 2014) (n = 33). Data are expressed as median (range) and statistical analysis based on non-parametric tests.

Results
The median age at diagnosis of acromegaly and at PSG were 48.5 and 52.0 yrs respectively, 25/39 patients (64.1%) had an active disease. OSAS was diagnosed in 36/39 patients (92%) and classified as mild/moderate (≥ 5 AHI <30) in 12/39 (30.8%) and severe (AHI ≥30) in 24/39 patients (61.3%). Severe OSAS tended to be more frequent in M (17/23 vs 7/16 F, P = 0.057), who were more frequently advised to start CPAP therapy (21/23 vs 9/15 F, P = 0.037). Males had a significantly higher BMI (32.6 vs 28.4 kg/m² P = 0.017) and higher prevalence of hypertension (21/23 vs 8/16, P = 0.004) despite similar age, GH and IGF1 ULN at the time of diagnostic HSAT/PSG. Overall, AHI was significantly correlated with patients age (ρ = 0.36, P = 0.023) but not with BMI and similar in diabetic and non-diabetic patients. By univariate logistic regression, hypertension was the only independent predictor of severe OSAS (P = 0.018). Nocturnal cardiorenal monitoring. Sleep evaluation was also obtained on CPAP therapy in 17 patients (6 F, 11 M), out of which 10 (58.8%) had controlled acromegaly (3 F, 7 M). A significant decrease in AHI (median – 90.4%, P< 0.001) was observed in all but one patient. OSAS was controlled in 11/17 patients (64.7%; 5/6 F, 6/11 M), including 8/12 with severe OSAS (66.7%), and regardless of hypertension.

Conclusion
OSAS is extremely common in acromegaly, especially using the ICSD-3 criteria, and HSAT may be recommended for routine screening. We found hypertension as a major predictor of severe OSAS, which tended to be more frequent in men. CPAP was found to be effective regardless of OSAS severity and should be encouraged in such patients.

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Isolated sarcoidosis of the hypothalamic-pituitary system is a very rare form of neurosarcoidosis. It usually leads to secondary damage to endocrine function, resulting in hypopituitarism and diabetes insipidus. A 32-year-old male patient with progressive deterioration of his general condition, weakness, polyuria, dizziness and visual field disturbances was admitted to the Department of Endocrinology for the diagnosis of a tumor in the hypothalamic-pituitary region.

MRI showed a tumor (19x16x15 mm) with suprasellar extension, and hormonal examinations performed 3, 12 and 24 months after the initiation of methotrexate therapy MRI showed a progression of the infiltrative process: the tumor was enlarged (20x19x17 mm) and two satellite foci appeared. Due to the clinically and radiologically identified steroid resistance of the lesions, immunosuppressive treatment with methotrexate was introduced in the 15 mg sc regimen for 7 days for 4 weeks, and then 25 mg sc every 7 days chronically. Subsequent MRI examinations performed 3, 12 and 24 months after the initiation of methotrexate therapy showed a regression of the infiltrative process in the CNS and decompression of the optic chiasm together with clinical improvement and no signs of sarcoid lesions in other locations. At the same time, no complications of the applied treatment were observed. In the control hormonal tests, the features of multi-hormonal anterior pituitary insufficiency were maintained, which required continuation of substitution treatment. In conclusion, an optimal treatment of isolated neurosarcoidosis of the hypothalamic-pituitary system has not been clearly established. Steroid therapy with high doses of methylprednisolone should be considered first, but the possibility of steroid resistance should also be considered. The use of immunosuppressants, such as methotrexate as a second line therapy, may have a positive effect on reducing the extent of the sarcoid

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process. Such a treatment is effective and safe, although the time frame and the dosing schedule of methotrexate are still unknown.

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P422

Aberrant expression of clock genes in human gastric neuroendocrine tumors type 1
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Introduction
Gastric neuroendocrine tumors (GNETs) are rare gastric neoplasms which are developed due to hypergastrinemia and enterochromaffin-like (ECL) cell hyperplasia. Although the effect of the circadian clock system disruption on tumorigenesis has been already studied in various malignancies and autoimmune diseases, the role of the peripheral clock system in the transition from ECL-cell hyperplasia to GNE1 (Type 1 Gastric Neuroendocrine Neoplasms) remains unexplored.

Aim
We aimed to investigate the expression of clock-related genes in peripheral blood mononuclear cells (PBMCs) and gastric tissues of the same patients with ECL-cell hyperplasia and patients with GNE1.

Methods
Fresh frozen gastric tissues were collected between (9:00-11:00 am) from 9 patients diagnosed with GNE1. The histological reports confirmed the presence of ECL and GNE1 lesions (in each separate specimen) collected from the same patient. PBMCs were also isolated from the whole blood (8:00-9:00am) of the same patients and 10 patients with confirmed ECL-cell hyperplasia. CLOCK, BMAL1, CRY1, PER2, REV-ERβ, ROR-α, GR-α gene expression was evaluated by qPCR in PBMCs, ECL-cell hyperplasia and their paired GNE1 lesions. Clinical, histological and epidemiological data of patients were also collected.

Results
The mean age of patients was 57.8 ± 12.8 years old. Paired analysis revealed that the expression of BMAL-1 and CLOCK was significantly (P < 0.01) increased while the expression of REV-ERβ and GR-α was reduced (P < 0.05) in GNE1 tissue as compared to adjacent ECL tissue. There was no significant difference in the expression of PER-2 and CRY-1 in GNE1 tissues as compared to adjacent ECL tissues. Interestingly, the expression of CLOCK, PER2 and REV-ERβ was significantly increased in PBMCs of GNE1 as compared to patients with ECL-cell hyperplasia.

Conclusion
Our data indicate for the first time that there is aberrant circadian clock gene expression in human gastric neuroendocrine tumors in both gastric lesions and PBMCs. Since CLOK gene was overexpressed, apart from GNE1 lesions, in PBMCs of patients with GNE1 as compared to PBMCs isolated from subject diagnosed with ECL-cell hyperplasia, its potential role as an non-invasive biomarker of transition of ECL-cell hyperplasia to non-invasive GNE1 could be explored. However, a larger sample size of patients is necessary to evaluate the role of dysregulation of the local circadian clock system in the development and/or evolution of these neoplasms.

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P424

Assessment of quality of life in women with Sheehan syndrome
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Introduction
Sheehan syndrome represents a rare cause of hypopituitarism. It results from postpartum ischemic necrosis of the pituitary gland. Data evaluating the quality of life in women with Sheehan syndrome are scarce. The aim of this study was to assess the quality of life in patients with Sheehan syndrome and to determine its associated factors.

Methods
A cross-sectional study including women with Sheehan syndrome was conducted in the department of endocrinology, La Rabta hospital. Clinical and paraclinical data were collected. Quality of life was assessed using the Short Form Survey-36 (SF-36). Predefined thresholds were used to categorize patients’ quality of life: SF-36 overall score < 30: poor quality of life, 30-60: average quality of life, and > 60: good quality of life.

Results
Forty-two women with Sheehan syndrome were enrolled in this study. Their mean age was 61.9 ± 9.6 years. The mean duration and the mean delay in diagnosis of Sheehan syndrome were 31.5 ± 10.2 and 11.8 ± 9.3 years, respectively. All participants had corticosteroid, thryrotropin, gonadotropin, and prolactin deficiencies. The overall quality of life score was 50.9 ± 15.2. The averages of role limitation due to physical health, vitality, emotional well-being, bodily pain, and general health scores were below 50. The quality of life was good in 11 patients (26%), average in 27 patients (64%), and poor in 4 patients (10%). Role limitation due to physical health score was negatively correlated with age (r = -0.326, P = 0.04) and the disease duration (r = -0.423, P = 0.006).

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P423

The diagnosis of vertebral fractures on routine chest radiography of acromegaly patients: a real-life study
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Objectives
The primary objective was to study the prevalence and the risk factors of vertebral fractures (VFs) in acromegaly patients either at diagnosis of acromegaly or during the follow-up. The role of routine chest radiography for detecting VFs in acromegaly was also evaluated.

Design and methods
A retrospective cohort study was performed on 60 consecutive acromegaly patients, in a tertiary referral center. The presence of VFs was firstly evaluated in each patient on lateral radiograph of the thoracolumbar spine (X-spine) performed at the last clinical visit during the follow-up. Secondly, routine chest X-rays (X-chest) performed at the time of diagnosis of acromegaly because part of the general evaluation at admission, were retrospectively reviewed for detecting VFs and compared to X-spine. Data were evaluated using binary logistic regression.

Results
Overall, 27 (45%) out of 60 patients had VFs at X-spine. Among those patients 37% had fractured vertebrae at the time of the diagnosis of acromegaly, although undiagnosed. Patients with VFs at baseline had higher IGF-1 index compared to those who had fractures after the diagnosis of acromegaly (P = 0.043). The comparison between the X-spine and the X-chest revealed an incidence of new VFs in 40% of patients, after diagnosis of acromegaly. The determinants of VFs were age (HR 1.05, P = 0.038), and hypogonadism (HR 6.14, P = 0.025). Conversely, therapy for acromegaly or bone mineral density values did not influence the outcome.

Conclusion
Nearly 40% of patients, who suffer from VFs, had fractured vertebrae undiagnosed on chest radiography at time of diagnosis of acromegaly. At baseline, VFs might correlate to the severity of acromegaly. After diagnosis of acromegaly, patients are at high risk of developing new fractures especially when hypogonadism is associated. Routine chest radiography, acromegaly patients should be also evaluated for the presence of VFs.

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score ($r=0.354, P=0.027$) and vitality score ($r=0.365, P=0.022$) were correlated with the daily dose of hydrocortisone.

Conclusion
The majority of women with Sheehan syndrome had average to poor quality of life. The most affected dimensions were role limitation due to physical health, vitality, emotional well-being, bodily pain, and general health. Age, disease duration, and the daily dose of hydrocortisone may affect the quality of life in women with Sheehan syndrome.

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P425
In-hospital hyponatremia is associated with loss of independence at discharge among older patients
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Context
Hyponatremia is a hormonal disorder of water metabolism encountered in 2% of community dwelling adults in America and in over 15-20% of hospitalized adults.¹,² Hyponatremia leads to increase in risk of falls, cognitive deficits, gait disturbances, loss of independence, prolongation of hospital stay and mortality among older patients admitted to hospitals.¹,²

Objective
To determine in-hospital mortality among older patients admitted to the hospital with concomitant hyponatremia and to assess length of hospital stay and degree of independence at discharge from hospital

Methods
This was an observational cohort recruited from the medical and allied wards of a tertiary care teaching hospital in India. Older patients (≥60 years) with documented hyponatremia (Serum Sodium < 135 mEq/l) who provided informed consent were included. Patients with suspected pseudohyponatremia and those with functional impairments prior to hospitalization were excluded. A similar number of age and gender matched older patients without hyponatremia during hospital stay were recruited as a control group. Demographic and clinical data was noted from the patients’ records. Primary outcome measured was in-hospital mortality. Other outcomes included length of hospital stay (LOHS) and loss of independence recorded on the day of discharge by assessment of Katz index of independence (KII) in daily living.³ A lower score indicates loss of independence.

Results
Hundred and twenty-five patients with hyponatremia and an equal number of controls were consented. Mean age (68.8±7.7 vs.68.2±6.5 years, $P=0.8$) and male gender (57.6% vs.56.8%, $P=0.8$) were comparable and mean serum sodium were 127.1±5.5 vs 137.9±2.5 mEq/l respectively among cases vs. controls ($P=0.0001$). In-hospital mortality was higher among patients with hyponatremia (20%(16) vs. 11.8%(8), $P=0.08$) but not statistically significant. LOHS was longer (8.4±5.7 vs. 5.0±2.8 days, $P=0.0001$) and KII scores were lower (3.9±1.9 vs. 4.8±1.5, $P=0.0003$) among cases. Severe functional impairment at discharge (KII <2) was significantly higher among cases (29.5% vs. 13.1%, $P=0.006$). Significant positive correlation was seen between serum sodium and KII scores (correlation coefficient 0.39, $P=0.003$) suggesting increasing loss of independence at discharge with lower sodium values.

Conclusions
Older patients with hyponatremia during hospitalization were less likely to survive the hospital stay and spend longer time in hospital. Loss of independence was significantly associated with both presence of hyponatremia and co-related with the severity of hyponatremia.

References
4. JAGS, 31(12), 721-726

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P427
Long-term Tolvaptan therapy in the treatment of SIAD in Elderly- A case report with challenging cytochrome P 450 drug interactions
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Background
Chronic SIAD with its disabling impact is challenging to manage in elderly patients as fluid restriction or demeclocycline often has a limited success. Tolvaptan is a novel selective antagonist of vasopressin receptor (V2R) which is safely used in patients with SIAD and other conditions with hypervolemia. We report a case of longest Tolvaptan use with significant challenges amongst our case series which we had previously published

Method
A Case Report of SIAD managed with long term Tolvaptan therapy with significant cytochrome P450 drug interactions. A 78-year-old male presented with recurrent falls and reduced mobility in April 2017. He had multiple falls prior and was being investigated for cavitating lung lesion in Right Upper lobe. He was found to have severe euvoletic hyponatremia (serum sodium of 104 mmol/l) with a paired serum (228 mOsm/kg) and Urine Osmolalities (419 mOsm/kg), a normal Cortisol of 666 mmol/l and a normal Thyroid function test. His prior baseline sodium was around 130 mmol/l. SIAD was confirmed which failed to respond to fluid restriction (19 days) and demeclocycline (10days). A clinical diagnosis of Aspergillus was made and oral Itraconazole was started. We commenced Tolvaptan 7.5 mg once daily dose (smaller dose) given drug interaction between Itraconazole (CYP3A4 Inhibitor) and Tolvaptan. Hyponatraemia improved back to baseline within 48 h and patient was discharged on Tolvaptan (7.5 mg OD).

Trials of stopping Tolvaptan therapy were unsuccessful (2017, 2019). Patient presented with increased fatigue and low basal cortisol (9 mmol/l) in 2018 despite normal serum electrolytes. Diagnosis of Secondary adrenal Insufficiency was made (250 microgram Short Synacthen test - Cortisol 0 Minutes- 73 mmol/l, 30-minutes- 131 mmol/l, Serum ACTH < 3 ng/l). This is due to known interaction of potent CYP3A4 inhibitor (Itraconazole) with Sertide Inhaler therapy (Fluticasone dipropionate) in our patient. Steroid replacement therapy with Hydrocortisone was commenced. Tolvaptan dose frequency was gradually reduced to 7.5 mg twice weekly (since 2020). There were only 15 endocrine clinic

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Neuroendocrine tumours, especially pheochromocytomas, paragangliomas and pituitary adenomas, are more common in younger patients in 3rd-5th decade of life. PiNETs are the most common intracranial tumours, while PHEO and PGL are rare. The hormonal activity, signs and symptoms of NET are variable. PGL, PHEO and PiNET in one patient remains an exceptional association. 72 cases of concomitant pituitary adenoma and PGL have been reported to date. The first record of a patient with acromegaly and PHEO dates back to 1952. We present a case of a 39-year-old man with non-specific symptoms including high blood pressure, headache, sweating and specific apparent acromegalic features on the face and hands. Screening CT scan found vascularized expansion (up to 6.5 cm) with cystic necrosis in the area of both adrenal glands. Initial measurement showed high plasma levels of catecholamines and their metabolites, prolactin, growth hormone and IGF-I. Then MRI examination of the brain was indicated and found intrasellar expansion (2 cm x 2.3 cm x 2 cm) prominent into the sphenoid cavity. Genetic analysis was performed due to endocrine syndrome comorbidities in a young patient which revealed a germline mutation in the MAX gene. Treatment included bilateral adrenalectomy of PHEO and neurosurgical intervention. Because acromegaly was not adequately controlled after surgery, somatostatin analogue was introduced. In up to 25 % of cases, especially in younger people, pheochromocytomas may be caused by an increased production of various genes (SDHBI, SDHID, SDHIC, VHL, MAX, RET). Mutation frequencies in the MAX gene are uncommon. They lead to incorrect regulation of the MYC-MAX-MXD1 path, which is coupled to the mTOR path. So far, the most effective treatment is the surgical removal of the neuroendocrine tumours. Performing genetic analysis is not a routine, but for related individuals, it’s a possibility to detect a malignant form of the disease earlier.
appointments over 246 weeks with no adverse effects and no further admissions since 2017.

Conclusion

We present our experience of longest use of Tolvaptan in an elderly patient with no adverse events. Clinicians must be aware of potential Cytochrome P450 drug interactions to avoid complications. Long term Tolvaptan use in chronic refractory SIAD appears to be safe, feasible and cost effective. More prospective studies are needed for guidance in using vasopressin receptor antagonists in chronic disabling SIAD.

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P428

RNA profiling of human growth hormone-secreting and non-functioning pituitary adenomas reveals novel and differentially expressed immune related genes

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Pituitary neuroendocrine tumours (PitNETs) are broadly classified as non-functioning pituitary adenomas (NFPA) and functional pituitary adenomas (FPAs) which include growth hormone secreting adenomas (GHPA). Since the role of the immune system in PitNET pathogenesis is still poorly understood, we employed RNA-sequencing technology to unravel differentially expressed genes in NFPA and FPAs. Here we present an RNA-sequencing workflow of GHPA (n=3) and NFPA (n=7) which revealed a total of 7945 differentially expressed genes. Reactome, Gene Ontology and KEGG pathway analysis further revealed the most pronounced in immune regulation. These genes fell into functional categories of chemokines, cytokines, interleukins, signal transduction and adhesion molecules. 6 immune genes including GATA3, CCL3, and CXCL9 were selected for further validation by qRT-PCR in 14 additional PitNET samples. A number of possible pathways implicated in PitNET functioning were also highlighted. The most significant were TLR1 and TLR2 cell differentiation, cytokine-chemokine receptor pathway, and chemokine receptors bind chemokines. Through our findings, we highlight distinct gene expression profiles in PitNETs and suggest that some of these genes could be considered as novel PitNET diagnostic markers for these two subtypes. We are currently validating these novel markers by immunohistochemistry in an array of PitNET subtypes.

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P429

Time from first symptoms to diagnosis in patients with pituitary adenomas

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Pituitary neuroendocrine tumours (PitNETs) are broadly classified as non-functioning pituitary adenomas (NFPA) and functional pituitary adenomas (FPAs) which include growth hormone secreting adenomas (GHPA). Since the role of the immune system in PitNET pathogenesis is still poorly understood, we employed RNA-sequencing technology to unravel differentially expressed genes in NFPA and FPAs. Here we present an RNA-sequencing workflow of GHPA (n=3) and NFPA (n=7) which revealed a total of 7945 differentially expressed genes. Reactome, Gene Ontology and KEGG pathway analysis further revealed the most pronounced in immune regulation. These genes fell into functional categories of chemokines, cytokines, interleukins, signal transduction and adhesion molecules. 6 immune genes including GATA3, CCL3, and CXCL9 were selected for further validation by qRT-PCR in 14 additional PitNET samples. A number of possible pathways implicated in PitNET functioning were also highlighted. The most significant were TLR1 and TLR2 cell differentiation, cytokine-chemokine receptor pathway, and chemokine receptors bind chemokines. Through our findings, we highlight distinct gene expression profiles in PitNETs and suggest that some of these genes could be considered as novel PitNET diagnostic markers for these two subtypes. We are currently validating these novel markers by immunohistochemistry in an array of PitNET subtypes.

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P430

Psychological impact of Covid-19 national lockdown on patients with Cushing’s syndrome in Italy: a case-control study

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Background

Subtle symptoms such as fatigue, weight gain and depression are commonly present for years in patients with pituitary adenoma (PA) before the diagnosis is made. A delayed diagnosis with risk of increased morbidity and mortality may be due to differences between patient-reported symptoms and symptoms reported in the patient’s medical record.

Aim

To estimate diagnostic delay and investigate the concordance between patient-reported symptoms and the medical record documentation in patients with PA.

Method

Patients with PA attending seven University Hospitals in Sweden participated. Age at first symptoms, age at diagnosis, experience of first symptoms, symptoms at diagnosis, and first healthcare contact were collected from the medical records, the Swedish Pituitary Register and patient questionnaires. The concordance between patient reports and medical record documentation was assessed using kappa statistics.

Results

657 patients (322 women) were included (non-functioning PA (NFPA) n=314, prolactinoma n=118, acromegaly n=164, Cushing’s Disease (CD) n=58. Median age at inclusion was 61 yrs (19-92) for men and 52 yrs (18-91) for women. A significant difference in duration of onset of symptoms to final diagnosis between men and woman was reported; median 1 yr (0-31) for men and 2 yrs (0-44) for women (P<0.001). Patients with acromegaly had the longest diagnostic delay; median 4 yrs (0-32), significantly longer than for NFPA; median 1 yr (0-20), (P<0.001). Among NFPA the most frequent patient-reported symptoms were headache, visual deficit and tiredness; for prolactinomas menstrual irregularities, headache, tiredness; for acromegaly change in appearance, snoring, headache and for CD weight gain, tiredness and weakness. Substantial agreement between patient report and medical record was found in visual deficit in NFPA and prolactinomas (Cohen’s kappa >0.6) and in menstrual irregularities in prolactinomas (Cohen’s kappa >0.7). In prolactinomas we found poor agreement for galactorrhea, and in acromegaly for weakness and tiredness. In CD we found no agreement at all in weakness and dizziness. The first healthcare contact was endocrinologists for NFPA and general practitioners for prolactinomas, acromegaly and CD.

Conclusion

We report a substantial and highly variable diagnostic delay in patients with PA, most pronounced in women. Visual deficit and menstrual irregularities showed substantial agreement between the endocrinologists’ documentation and patient reported data, whereas weakness, tiredness and dizziness showed poor agreement. The most frequent entry to diagnosis was general practitioners. An increased awareness of symptoms from pituitary adenomas through increased information to the general population and directed education of health professionals may contribute to earlier diagnosis.
During the spring of 2020, a national lockdown was adopted in Italy to prevent COVID-19 pandemic spread. Restrictive measures have been associated with impaired psychological outcome in the general population. As patients with Acromegaly and aging: a double hit against quality of life?

P431
A systematic literature review to evaluate extended dosing intervals in the pharmacological management of acromegaly

P432
Acromegaly and aging: a double hit against quality of life? Irene Gagliardi1, Sabrina Chiloiro2, Maria Vallillo2, Marta Bondanelli1, Federico II University, Naples, Italy;1University of Turin, San Luigi Hospital, Division of Internal Medicine, Turin, Italy;1Università Politecnica delle Marche, Ospedali Riuniti di Ancona, Clinica di Endocrinologia e Malattie del Metabolismo, Dipartimento di Scienze Cliniche e Molecolari (DISCLIMO), Ancona, Italy;1Università degli studi di Palermo, Dipartimento di Promozione della Salute, Unità Medico-Infantile, di Medicina Interna e Specialistica di Eccellenza “G. D’Alessandro”, UOC di Malattie endocrine, del Ricambio e della Nutrizione, Palermo, Italy;1University of Milan, Department of Medical Sciences and Community Health, Milan, Italy;1University of Naples-Federico II, Department of Neurosciences, Naples, Italy;1University of Naples-Federico II University, Naples, Italy

Introduction

Acromegaly patients (ACRO) show increased morbidity that affects health and quality of life (QoL). Elderly ACRO are going to increase in the next few years, but evidence regarding their management is lacking.

Aim

To evaluate physical, functional and cognitive performances of elderly ACRO and the relationship with QoL.

Methods

Multicenter case-control study conducted on 42 older ACRO (≥ 65 years) compared to an age- and gender-matched control group (CTR). Each patient underwent a multidimensional geriatric evaluation. QoL was tested with SF-36 questionnaire.

Results

Mean age in both groups was 73 ± 6 years and female gender was most represented (69%). 13 ACRO were in remission and 29 had active disease controlled by medical therapy except for one patient. ACRO showed worse mobility skills, poorer functional status assessment and lower cognitive evaluation scores than CTR (P < 0.05). Age negatively correlated with mobility skills, instrumental and basic daily activities execution (IADL and BADL) and cognitive performance in ACRO (P < 0.05). ACRO presented less satisfactory scores in 5 out of 8 SF-36 questionnaire domains as compared to CTR: physical activity (PA), physical pain (PP), general health (GH), vitality (V), social activities (SA) (P < 0.05). PA, V and SA scores worsened with the increasing number of drugs and comorbidities (P < 0.01). Increasing BMI positively correlated with better PA scores, but no associations were found between BMI and mobility skills. In ACRO, better mobility, IADL, BADL and cognitive performances correlated with more satisfactory PA, PP, GH, V and SA scores (P < 0.01). Mobility skills, IADL and cognitive evaluation strongly correlated with all 8 SF-36 domains in ACRO (P < 0.01). Conversely, no correlations were found in CTR. All comorbidities were more frequent in ACRO than CTR. Musculoskeletal and bone diseases were more frequent in ACRO than in CTR (52% vs. 12%; 64% vs. 10%; P < 0.05) and independently associated with geriatric outcomes in ACRO.

Conclusion

Elderly ACRO show worse performance in mobility skills, functional and cognitive status as compared to no acromegaly patients, supporting increased frailty worsening with aging. Poorer geriatric outcomes directly affect many aspects of QoL and health self-perception. A major prevalence of comorbidities in ACRO group might explain these discrepancies. Our data support the inclusion of a multidimensional geriatric evaluation in routine clinical practice to improve elderly ACRO management and, consequently, ACRO QoL. Further studies are needed to identify the most appropriate geriatric tools.

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P432
A systematic literature review to evaluate extended dosing intervals in the pharmacological management of acromegaly

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Background

Acromegaly is a rare disorder characterized by excess growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Extended dosing intervals (EDIs) of pharmacological treatments may reduce patient burden and costs compared with standard dosing. This systematic literature review (SLR) investigated treatment of acromegaly at EDIs.

Methods

MEDLINE/Embase/the Cochrane Library (2001–June 2021) and key congresses (2018–2021) were searched for relevant literature with a dual reviewer process; included SLR bibliographies were also reviewed. Included publications reported efficacy/effectiveness, safety, humanistic, and economic outcomes in longitudinal/cross-sectional studies in adult patients with acromegaly. Interventions included EDIs of lanreotide autogel (LAR), octreotide long-acting release (OCT), and pasireotide (all administered less often than every four weeks), oral octreotide (less than twice daily), pegvisomant (PEG; less than once daily), and cabergoline (less than twice weekly), with no comparator required. PROSPERO 2021: CRD42021278922.

Results

In total, 35 publications reported on 27 studies: 14 PEG, 9 LAN, and 4 OCT (monotherapies/combination therapies) at EDIs. No identified studies assessed oral octreotide, pasireotide, or cabergoline EDIs. Baseline characteristics differed across studies. As compared with Baseline, treatment at EDIs resulted in reduced IGF-1 levels in 12/16 studies assessing LAN, OCT, or PEG (7–104 patients treated at EDIs) and GH levels in 5/6 studies (LAN/OCT; 15–32 patients). Normalized IGF-1 and/or GH was achieved/maintained in 70–100% of patients in 12/13 studies (LAN/OCT/PEG; 15–124 patients). Proportions of patients experiencing adverse events (n = 4 studies reporting overall events; LAN/OCT/PEG; 8–96 patients) and discontinuing treatment (n = 9; LAN/OCT/PEG; 7–124

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Gene therapy of growth hormone resistant dwarfism in the laron mouse model – comparison of two doses
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Methods
In the present study, we report the results of increasing the dose to four times our earlier reported dose: 16 X 10^10 vector genome per mouse. In both groups of mice, the serum growth hormone (GH) levels decreased, and IGF1, IGF binding protein 3 (IGFBP3) and acid labile subunit (ALS) increased compared to the controls. The mice were monitored for a total of 20 weeks, after which they were sacrificed at different times: 0, 4, 8, 12, 16 and 20 weeks. Mice injected with the same doses of AAV-Luciferase were used as controls. The mice were recorded to have a much higher rate of survival in the experimental group compared to the control group. The results were statistically analyzed using one-way ANOVA and post hoc Tukey's test.

Conclusion
Clinical, safety, and efficacy of the gene therapy were similar and costs lower with EDIs vs standard regimens. Surprisingly, increasing the single dose by four times did not result in a significant increase in the response.

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Liver steatosis in an in vivo model of hyponatremia secondary to SIAD
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Methods
All patients treated with surgery and radiotherapy for NFPMs between 1987 and 2018 with more than 6 months follow-up were identified. A retrospective case note review was performed.

Results
In total, 383 patients were identified, 256 patients (256/383; 67%) were men. The median age was 57 years (IQR 48-67) with median follow-up of 5 years (IQR 2-9). At diagnosis, growth hormone deficiency occurred in 115 patients (115/273; 33%), hypogonadotropic hyponadism in 160 patients (160/375; 43%), and 132 patients (132/375; 36%) to record have adrenal insufficiency and 157 patients (157/375; 42%) developed secondary hypothyroidism. Panhypopituitarism was reported in 100 patients (100/375; 26%). Surgery only was performed in 318 patients (318/383; 83%) while 65 patients (65/383; 17%) needed surgery and radiotherapy to control tumour relapse. The degree of pituitary insufficiency recovery after NFPMs therapy is shown in the table. The combination of surgery and radiotherapy was associated with less likelihood of improvement in the case gonadotropins and TSH deficiencies as well as anterior hypopituitarism to patients who underwent surgery only. Notably, none of TSH deficient patients regained normal thyroid function post irradiation. Younger age was associated with a higher rate of improvement in gonadotropin deficiency (P = 0.004), secondary hypocortisolism (P = 0.01) and anterior hypopituitarism (P = 0.006). Gender and extent of resection of NFPA on postoperative MRI scan was not related to pituitary recovery.

Table 1

<table>
<thead>
<tr>
<th>Total</th>
<th>Surgery</th>
<th>Surgery and radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH</td>
<td>28/115 (26%)</td>
<td>27/99 (27%)</td>
</tr>
<tr>
<td>FSH/LH</td>
<td>36/160 (31%)</td>
<td>35/137 (26%)</td>
</tr>
<tr>
<td>ACTH</td>
<td>41/132 (32%)</td>
<td>38/113 (33%)</td>
</tr>
<tr>
<td>TSH</td>
<td>20/157 (21%)</td>
<td>20/130 (15%)</td>
</tr>
<tr>
<td>Panhypopituitarism</td>
<td>32/100 (32%)</td>
<td>31/87 (38%)</td>
</tr>
</tbody>
</table>

Conclusion
Recovery of pituitary hormone deficit may occur post NFPMs therapy. Factors associated with higher probability of reversal of pituitary hypofunction remain not fully understood. Patients should have regular endocrine evaluation post treatment to assess improvement in pituitary hypofunction and the need for long term replacement therapy.

DOI: 10.1530/endoabs.81.P435

Liver steatosis in an in vivo model of hyponatremia secondary to SIAD
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Hyponatremia is the most frequent electrolytic disorder in clinical practice. It is estimated that in about 50% of cases hyponatremia is secondary to the syndrome of inappropriate antidiuresis (SIAD). Hyponatremia is associated with a worse outcome and with increased mortality in several diseases, including cancer. In vivo and in vitro evidence shows that low [Na+] is associated with neurological and extra-neurological alterations, which include for instance bone demineralization, leading to osteoporosis. In order to better elucidate tissue alterations associated with reduced [Na+], we developed and characterized an in vivo model of hyponatremia secondary to SIAD, induced in a total of 38 Fox nes mice by subcutaneous infusion of the vasopressin analogue 1-deamino-8-D-arginine vasopressin (dDAVP) via osmotic mini pumps for a total of 14 days. Mice were randomly divided into three experimental groups and sacrificed at different times: two groups were infused with 0.3 and 0.5 nM dDAVP, respectively (A and B, n = 11 for each group) and one control group was infused with isotonic saline solution (0.9% NaCl) (C, n = 16). After the initiation of dDAVP infusion, mice gained weight, urinary volume was reduced and urine osmolality increased. Starting from a baseline serum [Na+] of 151 ± 1.57 mEq/l (mean ± SE), a serum
[Na+] of 131.01 ± 5.76 mEq/l and 116.7 mEq/l ± 5.19 mEq/l was achieved in group A and B, respectively, at the end of dDAVP administration. The day of sacrifice different organs were collected, fixed and processed for histological analysis. In particular, we focused on liver, because evident morphological alterations were observed in hyponatremic mice. Specifically, perihepatic steatosis was observed, with accumulation of lipid droplets into hepatocytes and collagen fibers. Western blot analysis of proteins involved in hepatic lipid metabolism confirmed the increased lipogenic status associated with the progressive reduction of serum [Na+]. The expression of the heme oxygenase-1 (HMox1) gene, which we had previously found to be upregulated in low [Na+] significantly increased both in hepatic stellate cells and in Kupffer cells, as confirmed by serial immunohistochemical analysis for α-Smooth Muscle Actin, F480 and HMOX-1.

In view of these original findings, we hypothesize that hyponatremia might be considered a trigger for liver steatosis. This observation has a potential impact on clinical grounds, also because liver steatosis is known to possibly evolve into cirrhosis and ultimately into cancer.

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P436

Growth hormone-releasing hormone (GHRH) promotes survival and proliferation of neural stem cells and reduces amyloid-β-induced toxicity

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Neurogenesis, the process by which new neurons are generated from precursors, persists in discrete regions of the adult hippocampus. The hippocampus is critical for learning and memory and is the main target of Alzheimer’s Disease (AD), which causes massive neuronal death, reduction in neurogenesis, and impairment in cognitive functions. Therefore, preventing neuronal loss or increasing the production of new neurons may represent a potential therapeutic strategy to reduce the AD-induced cognitive decline. Growth hormone-releasing hormone (GHRH) and its agonistic analogs, apart from promoting growth hormone (GH) secretion from the pituitary, exert many peripheral functions, including stimulation of cell survival, cardioprotection and neuroprotection. Furthermore, expression of GHRH, as well as GHRH-receptor (GHRH-R) and its splice variants (SVs), has been demonstrated in different brain regions, including the cerebral cortex, cerebellum, hippocampus, and brain stem cells. To date, however, the role of GHRH on neurogenesis and neuroprotection is still unknown. Thus, we aimed to investigate the role of GHRH on survival, proliferation, apoptosis, and differentiation of rat hippocampal neural stem cells (NSCs), in stress conditions such as growth factor deprivation and amyloid-β peptide 1-42 (Aβ1-42)-induced toxicity, and to define the underlying mechanisms. We found the expression of both mRNA and protein for GHRH in NSCs. GHRH dose-dependently increased cell survival and proliferation, while reducing apoptosis in NSCs cultured under both growth factor deprivation and exposure to Aβ1-42. These effects were blocked by the GHRH-R antagonist JV 1-36. The underlying mechanisms involved Gα12/13/AMP/PKA/CREB signaling, as demonstrated using specific inhibitors, and phosphorylation of Erk1/2, P38k/Akt, and GSK-3β but not mTOR/p70S6K. Furthermore, GHRH counteracted the Aβ1-42-induced phosphorylation of Tau protein and the inhibition of GSK-3β phosphorylation. GHRH also blocked the effect of Aβ1-42 on elevation of the proapoptotic protein BAX and on inhibition of the antiapoptotic protein Bcl-2. In addition, our preliminary results suggest an antiinflammatory role of GHRH, via inhibition in the mRNA levels of inflammatory cytokines (IL-6, TNF-α, INF-γ) and ROS activity. Finally, the role of GHRH was investigated on the differentiation of NSCs into neuronal lineages, such as neurons, astrocytes, and oligodendrocytes. Interestingly, GHRH increased the mRNA and protein levels of the neuronal marker TuJ1/NeuN and the astrocytes marker GFAP while showing no effect on the oligodendrocyte marker Ripk1. Collectively, these results indicate a role for GHRH in preventing neuronal loss and promoting neurogenesis, suggesting therapeutic potential for its agonistic analogs in neurodegenerative diseases, such as AD.

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P437

The screening and management of diabetes mellitus type 2 in patients with acromegaly: a tertiary centre service evaluation

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Introduction
Acromegaly is the result of chronic growth hormone (GH) excess, which leads to decreased insulin sensitivity and increased glucose production, to the extent that the impaired blood glucose regulation (IGR) can be recognised as Type 2 Diabetes Mellitus (T2DM). This project looked to identify whether patients were adequately screened or identified as having T2DM on diagnosis of acromegaly. The secondary aim was to determine whether acromegaly treatment affected glycaemic control in our cohort of patients.

Methods
We included ninety-five patients treated for acromegaly in University Hospital Wales, UK, between 1999 and 2020. Screening IGF-1 and nadir growth hormone followed a 72g oral glucose tolerance test (OGTT) results were taken as evidence of diagnosis of acromegaly. HbA1c at the time of acromegaly diagnosis (Pre), post acromegaly treatment (Post) and most recent recording (Latest) were taken as a representation of glycaemic control. Analysis of this data and the graphs produced was done using Rstudio version 4.1.0, a statistical software.

Results
Nineteen patients were diagnosed and treated for diabetes mellitus before the diagnosis of acromegaly was made. Six patients were newly identified to have a blood glucose within diabetic range at OGTT (2 h plasma glucose ≥ 11.1 mmol/l) and 5 of them underwent subsequent HbA1c testing. However, this was not improved for those with an impaired glucose regulation (IGR) (two-h glucose = 7.8 -11.1 mmol/l and/or fasting glucose = 6.1-6.9 mmol/l) with only 2 out of 16 having a HbA1c result recorded. From the sub-cohort of 26 patients who were identified as having a raised blood glucose measurement on OGTT and a HbA1c reading at acromegaly diagnosis, 15 (58%) had HbA1c reading done 3-6 months after surgical treatment. The results showed a decrease in mean HbA1c post treatment (mean Pre HbA1c=63.5 mmol/mol, mean Post HbA1c = 45.7 mmol/mol, P <0.005). 22 out of 26 patients (85%) who had “Pre”, “Post” and “Latest” HbA1c readings were analysed to determine if acromegaly treatment has a long-term effect on glycaemic control. This showed significant decrease between Pre HbA1c and Post HbA1c (P=0.0210). There was no significant difference between Post HbA1c and Latest HbA1c (P=1.00).

Conclusion
IGR is a risk factor for diabetes mellitus and cardiovascular disease. Our data showed that improvements in the diagnostic OGTT could be made in the care of patients with IGR detected in the diagnostic OGTT for acromegaly and in the follow up HbA1c monitoring for those with established diabetes mellitus or IGR who underwent acromegaly treatment.

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P652

Thinking horses, finding zebras: a rare case report of a giant cell tumor of the skull in a pediatric patient

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Giant cell tumors are rare, benign but aggressive and locally invasive tumors that usually affect the long bones in the limbs, typically presenting during the 3rd or 4th decade of life. Giant cell tumors of the skull are exceedingly rare, and less than 150 cases have been reported to date, of which less than 10 were described in the pediatric population. Here, we present the case of a 14 year old female that progressively developed severe headaches, blury vision and diplopia over approximately 4 months. She was initially directed to the Neurosurgery service, where imaging studies revealed a mass, initially presumed to be a cranioopharyngioma, on the left cavernous sinus topography, that extended into the sella turcica and compressed the pituitary. Complete resection was impossible due to the close proximity of the mass with the internal carotid artery, so endoscopic transnasal partial resection and a biopsy were performed instead. Histopathological examination along with immunohistochemical staining suggested that the mass was a pituitary adenoma. Endocrinological examination revealed partial corticotrop and tirotroph insufficiency, and substitution treatment with hydrocortisone and levothyroxine was initiated, but the patient was non-adherent.

Over the next 6 months, the patient’s symptoms worsened, and she was readmitted to the Neurosurgery service, where imaging studies showed the remaining mass had grown to 3 centimeters maximum diameter. A second
endoscopic transnasal partial resection and biopsy were performed. Second biopsy results suggested a giant cell tumor, but recommended determining PTH levels to rule out a brown tumor. Subsequent endocrinological examination revealed moderately elevated PTH levels (124 pg/ml), and vitamin D deficiency (serum vitamin D = 10.32 ng/ml). PTH levels normalized (64.9 pg/ml) after 6 months of vitamin D treatment (2000 IU daily). Giant cell tumors of the skull bones are exceedingly rare, especially in the pediatric population, but should still be considered in the differential diagnosis of sellar and parasellar masses. This case report is an opportunity to go over the impact of this type of tumor on quality of life, the differential diagnosis process, as well as the therapeutic options and their indications and contraindications in the adult and pediatric population.

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P653

Predicting hypogonadotropic hypogonadism persistence in male macroprolactinoma

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Objective
To study the baseline characteristics predicting hypogonadotropic hypogonadism (HH) persistence in men with macroprolactinoma following medical treatment with cabergoline.

Design
Retrospective cohort study conducted in a tertiary pituitary center.

Methods
Male patients diagnosed with macroprolactinoma and HH that received cabergoline treatment with subsequent prolactin normalization were included: men that achieved eugonadism, and men that remained hypogonadal. Patient’s demographic, clinical and biochemical parameters, sellar magnetic resonance imaging (MRI) and visual fields tests were obtained. Univariate analyses and multivariate logistic regression models for HH persistence were developed to investigate the relative contribution of the predicting factors.

Results
Fifty-eight male patients (age, 49.2 ± 12.6 years) with a median baseline prolactin of 1154 ng/ml (IQR, 478-2763 ng/ml) and adenoma (maximal) diameter of 25.9 ± 14.8 mm were followed for a median of 5.6 years (IQR, 3.0–10.7). All men achieved normoprolactinemia with cabergoline treatment. 12 men (21%) suffered from HH persistence at the end of follow-up, and 46 men achieved eugonadism. Baseline testosterone (1.6 ± 0.7 vs 0.7 ± 0.6 ng/ml; P < 0.01), luteinizing-hormone (1.8 ± 1.5 vs 0.4 ± 0.2 mIU/ml; P < 0.01) and follicle stimulating-hormone (3.4 ± 2.9 vs 0.9 ± 0.7 mIU/ml; P < 0.01) were lower, and prolactinoma diameter (23.7 ± 12.8 vs 34.6 ± 18.9 mm; P = 0.02) was larger in men with HH persistence. In addition, suprasellar tumor invasion (RR = 6.6; 95% CI 1.6–27.8), visual field defect (RR = 3.8; 95% CI 1.5–9.3) and hypopituitarism (RR = 6.3; 95% CI 2.6–14.8) were associated with HH persistence. 42 out of 46 men (91%) accomplished eugonadism within the first year following prolactin normalization. In a multivariate logistic regression model, the presence of either VFD and/or hypopituitarism (OR = 11.5; 95% CI 1.18–71.32) and baseline testosterone levels (OR = 0.12; 95% CI 0.02–0.64) remained independent predictors of HH persistence. Adenoma maximal diameter (OR 1.02; 95% CI 0.96–1.07) did not predict HH persistence.

Conclusion
In our cohort of men with macroprolactinoma that reached prolactin normalization with cabergoline treatment, 21% had HH persistence. Low baseline testosterone levels, visual field defect and pituitary hormone deficiency were independently associated with HH persistence. 91% of men accomplished eugonadism within the first year following prolactin normalization. These findings support informed clinical decisions regarding testosterone replacement initiation in men with macroprolactinomas.

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P654

Pre and post-surgical pituitary dysfunction increase the risk of mortality in patients with non-functioning pituitary tumors: A long-term cohort study

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Introduction
Congenital combined pituitary hormone deficiency (CCPHD) is a rare disorder characterized by an impaired production of two or more hormones of the anterior pituitary gland. It is linked to different genetic mutations and requires an early diagnosis to prevent burdensome developmental consequences. Primary ovarian insufficiency, disparately is the depletion of ovarian function with loss of functional primordial follicles before the age of 40 years due to multiple etiologies including genetic causes. The association between CCPHD and primary ovarian insufficiency has rarely been documented representing thus an uncommon and unexpected condition that merits case report herein.

Case presentation
A 14-year-old female was referred to our department for delayed growth. Born at term with no history of perinatal insult, she was diagnosed with central congenital hypothyroidism in a pediatric unit and L-thyroxine replacement therapy was started. Within the next few years, the patient presented a decrease in growth velocity. Short stature and delayed development were observed. The anthropometric measurements showed weight 28 kgs (between -3SDS and -2SDS) and
Introduction

A mutation in the PROP-1 gene is a rare cause of childhood-onset hypopituitarism. Patients with the disorder usually present with multiple pituitary hormone deficits. The pattern of development and the course of insufficiencies of individual axes remain unclear and affect patients metabolic status. Growth hormone therapy and substitution of other hormones may influence on glucose and lipid metabolism as well.

Aim

To characterize the carbohydrate and lipid metabolism of patients with childhood onset of hypopituitarism caused by PROP-1 mutation on the basis of long term observation in the pediatric/adult endocrinology departments of our university. The mean time of follow-up was 38.3 years (SD 12.8) with the longest observation lasting 62 years.

Methods

A retrospective analysis of metabolic data of 21 patients (12W/9 M) with confirmed PROP-1 mutation was performed. The mean age at the diagnosis was 7.3 years (SD 3.5). All patients present with thyroid, gonadal and somatotropic axis insufficiencies, while secondary hypoadrenalism was diagnosed in 19 cases (in 2 patients – transient).

Results

Body mass index (BMI) was elevated in 11/21 of patients (6/21 – overweight, 5/21 – obesity). At least one lipid abnormality - increased level of total cholesterol (in 20/21, 95.2% of cases, mean value 5.6 mmol/l), low-density lipoprotein (LDL) in 13/21, 61.9% of cases, mean value 3.8 mmol/l) or triglycerides (in 5/21, 23.8% of cases, mean value 1.7 mmol/l) or decreased concentration of high-density lipoprotein (HDL - in 7/21, 33.3% of cases, mean value 1.4 mmol/l) was detected in majority of cases (16/21, 76% of patients). All patients had correct levels of fasting glucose (mean value 4.6 mmol/l) and glycosylated hemoglobin (HbA1c; mean value 5.3%). In one patient oral glucose tolerance test (complete data available for 17/21 of cases) revealed impaired glucose tolerance. Mean values of fasting insulin and C-peptide were 6.92 at/ml (min. 1.76, max. 19.0), and 1.85 ng/ml (min. 0.73, max. 6.58), respectively. HOMA IR was elevated (r = 0.28), whereas IHL did not change significantly after GH replacement in the GHD patients (P = 0.34). Insulin resistance (HOMA-IR) improved after disease control of acromegaly (P < 0.000) and remained unaltered after GH replacement in the GHD patients (P = 0.829). IHL and HOMA-IR correlated positively in the reference group (r = 0.75, P = 0.005) and in GHD patients before (r = 0.61, P = 0.038) and after (r = 0.66, P = 0.020) GH replacement, whereas in acromegaly the correlation only manifested after disease control (r = 0.52, P = 0.038).

Conclusions

1) GH status is a significant modulator of body composition and insulin sensitivity.

2) GH excess reduces total fat mass and intrahepatic lipid content together with induction of insulin resistance.

The data support the notion that GH-induced insulin resistance is unassociated with hepatic lipid accumulation.

DOI: 10.1530/endoabs.81.P657
However, there is no consensus on how to follow these patients after TSS to early diagnose relapses. The aim of the study was to find reliable predictors of recurrence after neurosurgery in CD.

Methods

Fifty-five CD patients (f/m = 43/12, median age 39, IQR 32-49 years) in remission after TSS (median 100, range 36-146 months) were included. Remission was defined by the presence of at least 2 of the following criteria: i) low-undetectable postoperative serum cortisol; ii) prolonged glucocorticoid replacement therapy; iii) normal urinary free cortisol (UFC) and late-night salivary cortisol (LNSC) for at least 12 months after surgery; iv) serum cortisol <50 nmol/l after 1 mg DST. All patients were submitted to desmopressin (DDAVP) test in the diagnostic phase and were re-tested, at least once, 6-12 month after surgery.

Results

Thirteen patients (24%) recurred after a median time of 43 months (IQR 18-65). There were no differences in age and disease severity at time of diagnosis between patients who recurred and those in long-term remission, whereas macroadenomas were more frequently found in recurrent patients (P = 0.003). No differences in historical features were recorded. Early post-operative serum cortisol was markedly lower in patients who remained in remission [55.5 (32.3-97) vs 120 (57-250), P = 0.024], even though there was some degree of overlap between groups. A threshold of 63 nmol/l for serum cortisol was able to identify patient at high risk of relapse with sensitivity (SE) of 77% and specificity (SP) of 69%. Patients with recurrence displayed a greater ACTH and cortisol response to DDAVP test compared to those in prolonged remission (P < 0.0001). An absolute increase in ACTH >7.6 ng/l was identified (AUC = 0.879, 95%CI: 75-100) as the best predictor of recurrence, with SE of 85% and SP of 83%. At 6 and 12 months from TSS, no differences in UFC and LNSC were observed between groups.

Conclusions

The presence of corticotroph macroadenoma is a risk factor for CD relapse. Early post-operative serum cortisol level is a reliable indicator of surgical outcome but DDAVP test is far more accurate to predict future recurrence. The re-appearance of a positive response to this test precedes the increase in LNSC and UFC by several months, thus patients displaying such alteration should be closely monitored.

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P659

Evaluation of copeptin levels during glucagon stimulation test in children with suspected growth hormone deficiency

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Introduction

Glucagon stimulation test is one of the recommended growth hormone provocation tests for diagnosing growth hormone deficiency in children. In adult patients, recent data showed that glucagon administration is able to stimulate the release of copeptin, the stable C-terminal glycopeptide of the AVP prohormone whose evaluation during hypertonic saline infusion represents the gold standard for the differential diagnosis of polyuria/polydipsia. However, similar data on pediatric population are still lacking. Aim of this study was to evaluate copeptin levels during glucagon test in children with suspected GH deficiency and to correlate its secretion with that of glucose, GH and cortisol.

Methods

Twenty-one children (10 females, mean age 10.3 ± 2.9 years) with suspected growth hormone deficiency were studied during glucagon stimulation test (30 µg/Kg, maximum 1 mg intramuscularly). Of these, 20 patients had normal posterior pituitary function, and one patient had well-established central diabetes insipidus. Blood samples for measurement of glucose, GH, cortisol and copeptin were taken at baseline and 60, 90 120, 150 and 180 minutes after glucagon administration.

Results

Median basal copeptin levels in 20 patients without diabetes insipidus were 4.1 pmol/l (interquartile range: 3.3-6.7). During glucagon test, a significant increase of copeptin was recorded 120, 150 and 180 minutes after stimulation (median: 8.1, 10.6 and 8.9 pmol/l, respectively, for all P < 0.01 vs basal) with a peak after 150 minutes (median: 10.6 pmol/l, interquartile range: 5.4-17.9).

Correlation study for repeated measures showed that copeptin was directly associated with cortisol (r = 0.39, P < 0.001 and GH (r = 0.42, P < 0.001), and inversely associated with glucose (r = -0.36, P < 0.001). In a multilevel mixed-effects regression model, copeptin was associated with cortisol (β = 0.375, P = 0.01) and time (β = 0.005, P < 0.001) but not with GH and glucose. No difference in median copeptin levels at any time point between patients with negative and positive response to glucagon test was found. The only patient with central diabetes insipidus showed low basal and stimulated copeptin levels (basal: 1.5 pmol/l, peak: 2.0 pmol/l).

Conclusion

Glucagon administration represents a nonosmotic stimulus of the posterior pituitary also in children, as indicated by increased copeptin levels during the test. Copeptin peak is reached after 150 minutes and its trend seems to be related to cortisol secretion. Further studies are needed in order to clarify the mechanism behind the copeptin stimulation and to confirm the usefulness of this test for the assessment of posterior pituitary function.

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P660

Soluble alpha klotho in adult patients with growth hormone deficiency

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Background

We recently have shown a close association of high concentrations of soluble alpha klotho (sαKL) to disease activity in acromegaly. Small pilot studies suggested that sαKL concentrations might be markers of the timing of disease activity in GH deficiency (GHD) and increase after recombinant human GH (rGH) therapy. Our aim was to evaluate the potential of sαKL as a biomarker in GHD.

Methods

We evaluated sαKL in comparison to the classical biomarkers GH, IGF-I and IGFFBP 3 in different cross-sectional cohorts: adult patients with GHD (AGHD) without (n = 80; A) or with rGH (n = 57; B), patients without GHD having either NFPAs (n = 20; C) or prolactinomas (n = 30; D), and in healthy subjects (n = 199; E). Furthermore, 22 patients were evaluated longitudinally, before and during rGH therapy.

Results

As expected, GH, IGF-I and IGFFBP 3 were lower in AGHD without rGH (A) compared to AGHD with rGH (B). sαKL concentrations in the cohorts were as follows (median [interquartile ranges]; all pg/ml): A: 225 (172-314), B: 325 (254-425), C: 43/12, median age 39, IQR 32-49 years) in remission after TSS (median 100, range 36-146 months) were included. Remission was defined by the presence of at least 2 of the following criteria: i) low-undetectable postoperative serum cortisol; ii) prolonged glucocorticoid replacement therapy; iii) normal urinary free cortisol (UFC) and late-night salivary cortisol (LNSC) for at least 12 months after surgery; iv) serum cortisol <50 nmol/l after 1 mg DST. All patients were submitted to desmopressin (DDAVP) test in the diagnostic phase and were re-tested, at least once, 6-12 month after surgery.

Conclusions

The presence of corticotroph macroadenoma is a risk factor for CD relapse. Early post-operative serum cortisol level is a reliable indicator of surgical outcome but DDAVP test is far more accurate to predict future recurrence. The re-appearance of a positive response to this test precedes the increase in LNSC and UFC by several months, thus patients displaying such alteration should be closely monitored.

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P661
Metyrapone vs osilodrostat in the short-term therapy of endogenous Cushing's syndrome: results from a retrospective single center analysis

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Background
Although surgery is considered the first-line treatment for patients with endogenous Cushing’s syndrome (CS), medical therapy is often required to control severe hypercortisolism. Metyrapone and osilodrostat are inhibitors of 11β-hydroxylase that have not been directly compared yet.

Methods
Retrospective analysis of patients with adrenocorticotropic hormone (ACTH)-dependent and ACTH-independent CS treated with metyrapone or osilodrostat (as monotherapy) for at least one month. Serum cortisol and 24-h urinary free cortisol (24h-UFC) were analyzed at baseline (T0), after 2 weeks (T1), 1 month (T2) and 3 months (T3) of therapy. Furthermore, serum potassium and blood pressure were evaluated.

Results
16 patients with CS (8 under metyrapone and 8 under osilodrostat) were identified. Despite heterogeneity, both groups showed comparable mean 24h-UFC levels at T0 (757.8 µg/24h under metyrapone vs 816.9 µg/24h under osilodrostat; n.s.). From T0 to T1, the decrease of 24h-UFC was less pronounced under metyrapone than osilodrostat (-21.3% vs -68.4%; median drug dose: 1000 mg vs 4 mg). This tendency persisted at T2 (-57.3% vs -50.1%; median drug dose: 1250 mg vs 6 mg). A substantial difference in potassium levels at T3 was identified (-10.9% under metyrapone vs +14.5% under osilodrostat from T0). Furthermore, a more prolonged QTc-interval was observed under osilodrostat than under metyrapone (-455.3 ms vs +432.5 ms). From T0 to T2, the number of antihypertensive drugs decreased under osilodrostat.

Conclusion
Although both of the drugs are efficient in reducing cortisol levels, osilodrostat seems to induce a faster reduction of cortisol levels and a faster control of blood pressure.

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P662
Inferior petrosal sinus sampling for pituitary neuroendocrine tumors localization in cushing’s disease

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Objective
Cushing’s disease (CD) is the most common cause of hypercortisolism after iatrogenic origin, it represents approximately 70% of patients with endogenous Cushing’s syndrome (CS) and ectopic ACTH secretion (10%). CD is caused by a corticotropin-secreting pituitary neuroendocrine tumor (ACTH-secreting Pit-NETs), 95% of cases as a microadenoma. In ACTH-dependent CS, differential diagnosis between CD and ectopic CS must be established. 40% of CD cases, any tumor is observed in the contrast-enhanced pituitary magnetic resonance imaging (MRI), and among the detected lesions, 85-87% are microadenomas Objective: to evaluate the usefulness of inferior petrosal sinus catheterization in the diagnosis of Cushing’s disease, the intrahypophyseal location of the ACTH-secreting Pit- NETs.

Patients and methods
A retrospective observational study was performed in all patients with CS that underwent bilateral inferior petrosal sinus catheterization (BIHSSP) in a single center. Statistical analysis: Chi square test with Yate’s correction s and Cohen’s coefficient k were used as a measure of agreement between the exploratory techniques. Sensitivity, specificity, positive and negative predictive value, and positive and negative probability coefficient were also calculated. Chi-squared test was used to compare categorical data. Statistical analyses were performed using SPSS® statistical software version 20.

Results
BiHSSP was performed in 33 patients, 75.8% women, age 41.79 ± 14.60 years. BiHSSP achieved a sensitivity of 96.67 %, IC 95% (0.80 – 0.99) and a specificity 100%, IC 95% (0.31 – 0.96). Positive predictive value was 100%, IC 95% (0.85 – 0.99) and the negative predictive value was 75%, IC 95% (0.21 – 0.98). The global value or efficiency of the procedure 96.97% IC 95% (0.82 – 0.99). An intersinus gradient ≥ 1.4 was observed in 25 patients. In those who underwent surgery, tumor localization during surgery coincided with BiHSSP results in 80% of cases; Kappa index was 0.60ª. A good agreement between the lateralization result of the BiHSSP and the location by surgery for the location of the ACTH-producing adenoma. No complications were recorded after BiHSSP.

Conclusions
BiHSSP plays a key role in the diagnosis of CD, and its results in the location of the tumor must be taken into account, since it shows good precision when compared with the surgical location of the tumor.

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P663
GH-secreting pituitary adenoma: dura mater invasion is not a predictor of acromegaly persistence after trans-sphenoidal surgery

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Background
Despite the benign nature of pituitary adenomas, microscopic examination of surgical specimens showed that dural invasion occurs in about 42-85% of cases. No studies about dura mater invasion were conducted specifically in acromegaly, so the aim of the present study was to evaluate the relationship between histologically verified dural invasion and the “aggressiveness” features of GH-secreting adenomas.

Methods
A prospective study included all consecutive acromegaly patients that underwent neurosurgery (NS) at the Division of Neurosurgery of the University of Turin, between 2017 and 2020. All patients were operated with a 3DHd endoscope using an endoscopic endonasal approach by a single skilled neurosurgeon. For each patient the following data were collected: 1) clinical, biochemical and morphological data at diagnosis, three months and one year after NS; 2) pathological features (dura mater invasion, immunohistochemical analyses, proliferation index Ki67 and p53, granulation pattern; 3) radiological findings at MRI scan, in particular intensity on T2-weighted images.

Results
35 acromegaly patients enrolled. Eleven patients had dura invasion (31%), while 24 did not have (69%). No significant differences were found in gender and age at diagnosis between INV+ and INV-. No difference was found in IGF-1 levels (INV+: 732 ng/ml, [548-987] ng/ml vs INV-: 664 ng/ml, [394-894] ng/ml) and IGF-1/ULN (2.5, [2.3-3.3] vs 2.4, [1.68 -3.1]). GH levels at diagnosis were higher in INV+ (84.5 µg/ml, [29-153] µg/ml vs 17.2 µg/ml, [4.4-36] µg/ml, P<0.02). ROC curve analysis for GH levels at diagnosis showed that GH > 27 ng/ml was able to distinguish patients with dura mater invasion (AUC 0.760, P=0.006, sensitivity 80% and specificity 73%) and patients with GH > 27 ng/ml at diagnosis had a 10 times higher risk of dura invasion (Odds ratio 10.7; IC 95% 1.74-65.27). No difference was found in morphological, radiological and pathological features. We also analysed predictive parameters of healing. IGF-1 levels at diagnosis (625.5 ng/ml, [391.5 -867.5] ng/ml vs 872 ng/ml, [812 – 1011.5]ng/ml, P=0.03) and proliferation activity (Ki-67 14.5% under osilodrostat from T0). In those who underwent surgery, tumor localization during surgery coincided with BiHSSP results in 80% of cases; Kappa index was 0.60ª. A good agreement between the lateralization result of the BiHSSP and the location by surgery for the location of the ACTH-producing adenoma. No complications were recorded after BiHSSP.

Conclusions
The only parameter significantly associated with the dura mater invasion is GH levels at diagnosis. The dura mater invasion does not affect the possibility of recovery from acromegaly at 12 months. We confirmed that lower IGF-1 levels at diagnosis and lower Ki-67 are significantly associated with healing after surgery.

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Impact of COVID-19 lockdown in patients with acromegaly: an Italian multicenter experience

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Over the last two years, COVID-19 outbreak and lockdown have exerted a remarkable psychological burden in the general population. Such an impact is supposed to be even worse in acromegaly, known to induce a severe psychological impairment due to its somatic disfigurements and systemic comorbidities. The current observational study aimed at investigating the impact of COVID-19 outbreak and lockdown on psychological health in acromegalic patients as compared to non-acromegalic healthy control population. During the last three weeks of lockdown, 246 patients (110 males, 136 females, age 51.4 ± 11.7 years) with history of acromegaly or active acromegaly under treatment from 9 Italian acromegaly referral centers and 246 age, gender, and marital status-matched controls were tele medically administered several psychological questionnaires, aiming at evaluating the spectrum of anxiety (GAD-7) and depression (PHQ-9), and perceived stress (PSS). For all questionnaires, higher score indicated greater psychological impairment. A questionnaire evaluating quality of life in acromegaly, AcroQol, for which the higher score indicates a better quality of life, was administered exclusively to patients. Compared to controls, patients showed a significantly higher prevalence of moderate (P = 0.046) and severe depression (P = 0.015), and severe anxiety (P = 0.024). Both in patient and controls, females showed higher scores in the entire series of psychological tests performed compared to males (P < 0.001). Moreover, male patients showed significantly higher anxiety (P = 0.001), and depression (P < 0.001) scores, whereas female patients showed higher anxiety (P = 0.003) and perceived stress (P = 0.037) scores compared to respective controls. Glucocorticoid replacement (GR) therapy was significantly associated with higher scores of anxiety (P = 0.01), depression (P = 0.037), and perceived stress (P = 0.003), and lower score of AcroQol (P = 0.038). Patients with anxiety, depression, and perceived stress were mostly females (P = 0.05), and patients with anxiety and perceived stress were also associated with low-grade instruction (P < 0.01) and GR therapy (P < 0.01). In conclusions, patients who experienced acromegaly had significantly higher anxiety (P = 0.001), and patients with anxiety and depression (P = 0.05) were observed. A stepwise linear regression analysis showed that the strongest predictors of long-term morbidity were age (B = 0.006), BMI (P = 0.003), glycemia (P = 0.018), and triglyceride levels (P = 0.032), and negatively with HDL (P = 0.009), there were no significant correlations with hormonal levels (P > 0.05). Majority of patients (81.8%) had pituitary microadenoma. Transsphenoideal surgery (TS) was performed in 34 patients (91.9%), with median of 3.2 months after diagnosis. After initial surgical success rate of 82.4% (28 patients), 20 patients (58.8%) kept long-term remission. Remission was achieved by bilateral adrenalectomy in 2 additional patients (22 overall, 59.5%), with follow up of 76.9 ± 60.6 months (1-192). Clinical remission was associated with significant decrease in frequency of overweight/obesity (P = 0.006), depression (P = 0.004), and HTA (P = 0.051) while no significant decrease in frequency of dyslipidemia, IGT/DM and osteoporosis (P > 0.05) was observed. A number of comorbidities remained positively associated with age (P = 0.016), BMI (P = 0.004), glycemia (P = 0.048), and level of triglycerides (P = 0.048), and negatively with HDL (P = 0.019). In separate linear regression analysis the strongest predictors of long-term morbidity were age (B = 0.068, P = 0.019, 95% CI 0.013-0.124) and HDL level (B = -1.218, P = 0.005, 95% CI -2.434-0.001) at diagnosis of CD. Conclusion Cushing’s disease is the most prevalent cause of endogenous hypercortisolism, causing significant morbidity in these patients that remains so even after long-term remission. Life-long follow up of cardiovascular outcomes is needed in these patients.

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Inferior petrosal sinus sampling in differential diagnosis of adrenocorticotropic hormone (ACTH)-dependent Cushing’s syndrome: a tertiary centre experience

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Introduction Inferior petrosal sinus sampling (IPSS) has been considered to be the gold standard for differential diagnosis of Cushing’s Disease (CD) and ectopic ACTH secretion (EAS).

Purpose To describe the experience of our centre in performing IPSS, its safety and efficacy; assess remission rates from transphenoidal surgery and clinical course; approach to the difficulty in the etiologic diagnosis of ACTH-dependent Cushing’s Syndrome.

We retrospectively analyzed 37 patients (91.9% females) aged 39.5 ± 13.9 years (10-70) with diagnosed CD, treated in our institutions, and followed up during 15 years. Each patient was evaluated for presence of comorbidities (overweight/obesity, impaired glucose metabolism (impaired fasting glucose, IGF/impaired glucose tolerance, IGT/diabetes, DM), hypertension (HTA), dyslipidemia, osteoporosis, depression), at the time of diagnosis and during follow up of clinical remission. Spearman’s rank correlation coefficient was used to test associations between comorbidities and age, BMI, biochemical parameters and hormonal levels (basal cortisol and ACTH level, midnight cortisol level). Multiple regression analysis was used to test predictors of long-term comorbidities after CD remission. Statistical analysis was performed by SPSS software.

Results At diagnosis, dyslipidemia, HTA, overweight/obesity, osteopenia/osteoporosis, IGF/IGT/DM and depression were present in these patients with frequencies of 86.5%, 73.0%, 64.9%, 59.5%, 51.4% and 21.6%, respectively. Aside of 4 patients (10.8%), all the other had 2 or more comorbidities. The number of comorbidities positively correlated with age (P = 0.009). BMI (P = 0.003), glycemia (P = 0.018), and triglyceride levels (P = 0.032), and negatively with HDL (P = 0.009), there were no significant correlations with hormonal levels (P > 0.05). Majority of patients (81.8%) had pituitary microadenoma. Transsphenoideal surgery (TS) was performed in 34 patients (91.9%), with median of 3.2 months after diagnosis. After initial surgical success rate of 82.4% (28 patients), 20 patients (58.8%) kept long-term remission. Remission was achieved by bilateral adrenalectomy in 2 additional patients (22 overall, 59.5%), with follow up of 76.9 ± 60.6 months (1-192). Clinical remission was associated with significant decrease in frequency of overweight/obesity (P = 0.006), depression (P = 0.004), and HTA (P = 0.051) while no significant decrease in frequency of dyslipidemia, IGF/IGT/DM and osteoporosis (P > 0.05) was observed. A number of comorbidities remained positively associated with age (P = 0.016), BMI (P = 0.004), glycemia (P = 0.048), and level of triglycerides (P = 0.048), and negatively with HDL (P = 0.019). In separate linear regression analysis the strongest predictors of long-term morbidity were age (B = 0.068, P = 0.019, 95% CI 0.013-0.124) and HDL level (B = -1.218, P = 0.005, 95% CI -2.434-0.001) at diagnosis of CD. Conclusion Cushing’s disease is the most prevalent cause of endogenous hypercortisolism, causing significant morbidity in these patients that remains so even after long-term remission. Life-long follow up of cardiovascular outcomes is needed in these patients.

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Methods
In this single centre retrospective study we included 14 patients diagnosed with ACTH-dependent Cushing’s Syndrome which IPSS were performed between 2011-2021. The diagnosis of CD was made when the basal central/peripheral ACTH ratio was > 2 and/or the rate after CRH/desmopressin stimulation was > 3. With the inter-sinus ratio > 1.3, lateralization was determined.

Results
2 patients whose IPSS failed due to anatomical variation and vasovagal syncope were excluded. In 12 patients, 7 were female patients. Median age: 48.9 ± 11.9 years. Sellar magnetic resonance imaging (MRI) demonstrated pituitary microadenoma in 10 cases. IPSS results were conclusive for diagnosis of CD in 83% of patients (10) and none of them indicated EAS. Lateralization by IPSS and MRI was concordant in 9 out of 10 cases with CD and microadenoma. Inconclusive results in 2 IPSS: 1 blood sample collection into non-EDTA tube; 2) absence of measurement of prolactin and impossibility of assessing correct sampling in the absence of basal central/peripheral ACTH ratio. In 10 of 12 patients whose IPSS showed CD diagnosis, correct lateralization was confirmed by the operation in one patient only. Pathology specimens did not show pituitary adenoma in the other 5 cases. The rate of remission after transphenoidal surgery was 2 out 6 patients.

Conclusions
IPSS is a safe procedure and an effective test in the differential diagnosis of ACTH-dependent Cushing’s Syndrome. In our study, the sensibility of IPSS assessed was 85%, similar to what is described in the previous studies. DDAVP stimulation was equivalent to CRH stimulation. We emphasize the possibility of procedural failures that must be identified. It should be noted that regardless of whether or not there is a pituitary adenoma image on an MRI, IPSS proved to be useful to confirm CD and suggest a lateralization of ACTH secretion.

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P667 Pituitary adenoma in multiple endocrine neoplasia type I (MEN1) syndrome: a single-center study

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Background
Multiple endocrine neoplasia type I (MEN1), is an autosomal dominant inherited disorder with high penetrance, characterized by the onset of multiple tumors, mainly in parathyroid, pituitary gland and gastroenteropancreatic tract. During the course of the disease pituitary adenomas (PA) occur in 20-65%, rarely as first clinical manifestation, and are often described as larger, more aggressive, and more resistant to conventional therapy than their sporadic counterpart. The aim of this study is to analyze clinical characteristics of PA in a monocentric series of MEN1 patients.

Aim
The clinical charts of all patients with MEN1, referred to the Endocrinology Unit at the Federico II University of Naples from January 2000 to June 2021, were retrospectively evaluated, analyzing epidemiological and clinical data. The study included 91 MEN1 patients (F/M 50/41). The prevalence of PA was 49.5% (45 patients) with a slight female preponderance (F/M = 1.36). PA was diagnosed in 92.2% of cases after the diagnosis of MENI. The mean age at diagnosis of PA was 44.6y (13-75y), this was much lower when PA was identified as the first MEN1 manifestation (28y). PA were microadenoma in 60% (27 patients), and macroadenoma in 40% (18 patients). PA were non-secretin in 44.4% (20 patients), PRL-secreting in 42.2% (19 patients), GH-secreting in 22.2% (1 patients), PRL-GH secreting in 8.8% (4 patients), and ACTH-secreting in 22.2% (1 patients). Symptoms of hormonal hypersecretion and/or compression of adjacent structures were detected in 53.4% (24 patients). Among patients with prolactinomas the M:F ratio was 1:1.11 (11/12 patients), and all 12 affected females had associated symptoms (menstrual irregularities, galactorrhea); while only 2/11 male patients had hyperprolactinemia-related disorders (decreased libido, impotence). With regard to therapeutic treatment, cabergoline was used in 40% (18 patients) of PA, while octreotide was used only in 2.22% (1 patient). Transphenoidal surgery was performed in cases of refractoriness or macroadenoma-related symptoms in 15.5% of cases (7 patients), and radiotherapy subsequently was necessary in 2.22% of cases (1 patient).

Conclusion
PA within MEN1 are more common in women and are rarely the first clinical manifestation of the syndrome. Importantly, our data suggest that PA do not seem to be more aggressive than sporadic forms and show good response to medical and surgical therapy. A multidisciplinary approach in specialized centers may improve the clinical history of these patients allowing early diagnosis.

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P668 Ultrasound of the median nerve in acromegalic patients: changes at 1 year follow up

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Background
The aim of our study was to assess changes in the cross sectional area (CSA) of the median nerve by ultrasound in newly diagnosed acromegalic patients 1 year after treatment of acromegaly (transphenoidal surgery, somatostatine analogues). Patients and methods

The study included 30 newly diagnosed acromegalic patients (18 females and 12 males) and 30 healthy controls (18 females and 12 males) matched for age, gender and body mass index. Clinical history, physical examinations, laboratory examinations and ultrasound evaluations were performed at baseline and 1 year after treatment of acromegaly.

Results
The CSA of the median nerve was increased in acromegalic patients compared with controls (13.3 ± 2.2 mm² vs. 7.6 ± 1.8 mm²; P < 0.001). 1 year after the treatment of acromegaly a significant decrease of growth hormone (GH) and insulin-like growth factor I (IGF-I) levels were achieved. The CSA of the median nerve was significantly reduced 1 year after treatment to 11.7 ± 1.8 mm² (P < 0.001). Positive correlation was found between the levels of IGF-I and CSA of the median nerve in acromegalic patients before treatment (r = 0.492, P < 0.006).

Conclusion
This study demonstrates reduction in median nerve CSA 1 year after treatment of acromegaly. This changes are closely associated with the reduction of IGF-I levels. Biochemical control of acromegaly is important factor for normalization of the median nerve size.

Keywords
acromegaly, cross sectional area of the median nerve, growth hormone, insulin-like growth factor I, ultrasound

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P669 From silent to carcinoma: the genomic alterations landscape of whole spectrum macroadenoma corticotrope pituitary tumors and carcinoma

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Corticotrope cells give arise to utmost aggressive and to very rare pituitary neoplasias, including pituitary carcinomas, Crooke’s cell adenomas (CCA), clinically non-functioning silent corticotrope adenomas (SCA) and the Cushing-provoking pituitary adenomas (CD). The molecular etiopathogenesis of these tumors are still poorly understood. Therefore, we carried out whole exome sequencing to better understand the full genomic landscape single nucleotide variants and copy number variations of the pituitary macroadenoma tumors from corticotrope lineage. Carcinomas show SNV in USP8, TP53, AURKA, EGFR, HSD3B1 and CDKN1A. Whereas in CCA SNV in HSD3B1 and CDKN1A were
common however TP53 and AURKA were present in one each, HSD3B1 and CDKN1A SNV were present in all SCA, followed by EGFR and AURKA. They did not show USP8 SNV. As for the only one show USP8 SNV, corresponding to an Nelson syndrome tumor. All CD show TP53 and HSD3B1 SNV. None of the corticotrope tumors showed USP48, BRAF, BRG1 nor CABLES1 SNV. Functioning tumors including carcinoma and CD showed more CNV gains than the non-functioning tumors, carcinoma shares 10q11.22 amplification with benign adenomas, whereas 17q12 characterizes only benign adenomas. The theoretical evolutionary development of the corticotrope carcinoma starting from the silent adenomas, if that’s the case, shows two main clades, the first and smallest, contain two SCA (2/3) and two CD (2/3), these four adenomas shared SNV profile, potentially indicating the genes needed to be altered to make a transition from silent to overt tumors. ATF7IP characterize this clade. The second and largest clade harbors the CCA (1/1), the carcinoma (1/1), one SCA (1/3) and three CD (3/5). Interestingly, in this clade the carcinoma showed a close relation to CCA and a to CD. This clade could represent the molecular alterations required to make the transition from overt adenoma to a carcinoma, or at least to a more aggressive tumor. In this clade there was clustered a Nelson syndrome CD and the carcinoma, which are very aggressive entities. MSH3 gene characterize this clade. Overall, pituitary carcinoma and CD showed more SNV and CNV genomic alterations compared against CCA and SCA.

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P670

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Targeting invasive pituitary adenomas: in vitro studies and in vivo investigations in a murine model of invasive pituitary tumors obtained by orthotopic pituitary GC cells injection

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Context
Surgical removal is the primary treatment option for pituitary adenomas. However, pituitary surgery is frequently incomplete because of invasion of extracellular cerebral structures, notably, of the cavernous sinus. Our objective was to study the molecular basis of the cavernous sinus invasion by pituitary adenomas.

Methods
We analyzed a tissue collection of 19 invasive pituitary adenomas with a sample from the intrasellar portion and a sample from the portion invading the cavernous sinus of each adenoma. We used RNA-sequencing to compare gene expression patterns of the invading and intrasellar portions. The implication of one differentially expressed candidate gene in the invasive behavior was first analyzed in vitro in lactosomatotroph GH3 and gonadotroph LBT2 cells. We used Transwell Assay to analyze the impact of pharmacologic inhibition of the candidate gene on cell migration and invasion. To study the role of this gene on tumor growth and behavior in vivo, we elaborated a model of invasive pituitary adenomas by stereotactic injection of murine somatotroph GC cells into the pituitary gland of female Wistar Furth rats. Twelve adult rats received 20.000 GC cells in each pituitary lobe. Tumor development was assessed fortnightly by 7Tesla MRI. Six of the 12 rats were treated with the pharmacological inhibitor of the candidate gene. Rats were sacrificed 7 weeks after cell injection.

Results
RNA-sequencing identified 159 up-regulated genes and 11 down-regulated genes in the invasive adenoma portions. In vitro pharmacological inhibition of the selected candidate gene decreased cell migration and invasion in GH3 cells (P = 0.0205 and P = 0.0038) and LBT2 cells (P = 0.0345 and P = 0.0131). Amongst the 12 injected rats, 11 (92%) developed invasive pituitary tumors. Tumor growth was rapid, causing death from intracranial hypertensions before the end of the protocol in 7 animals. Pharmacological inhibition tended to slow tumor growth from 30.3 mm²/week to 7.8 mm²/week (P = 0.12) and decreased cumulative mortality (83% in untreated animals vs 33% in treated animals, P = 0.08).

Conclusion
We described the molecular signature associated with the invasive behavior of pituitary adenomas and identified a therapeutic target, which is related to pituitary cells migration and invasion in functional in vitro studies. Pharmacologic inhibition of this target tended to decrease tumor growth and mortality in vivo, however larger numbers of animals are necessary to confirm this pilot observation. Our original approach of orthotopic cell injection into rat pituitaries resulting in tumor development provides a new tool for molecular studies of pituitary tumorigenesis and for pharmacological screening.

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The role of HIF-1α and vegfa polymorphism (G634C) in the development of the aggressive pituitary adenomas

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Introduction
Although pituitary adenomas are considered benign, some have invasive growth, which is one indicator of aggressiveness. Early prognostic markers of aggressiveness may influence the quality of life improvement in patients with aggressive pituitary adenomas.

Objectives
To study the clinical-immunological, molecular-genetic aspects of aggressive pituitary adenomas and to develop new approaches to early diagnosis and treatment.

Materials and methods
83 patients diagnosed with pituitary adenoma were examined. All patients underwent clinical examination and magnetic resonance imaging (MRI), to determine the degree of adenoma invasion by Knops classification. Polymorphism of regions of studied genes in the VEGFA gene of position G634C (rs2010963 locus), the gene HIF-1α (rs11549465 locus) and G197A in the gene IL-17A, made by the allele method - determined by the PCR method.

Results
Genetic analysis of VEGFA polymorphism showed that heterozygote (G/C) mutation in patients with invasive adenomas was found to be twice as high as 32.7% (n = 17.2) compared to a control group of 15.7% (n = 13). Moreover, the C/C homozygote mutation is also observed more in the 7.7% invasive adenoma patient group (n = 4), which supports the evidence that mechanistic progression of invasive adenomas contributes to angiogenesis mutation through the VEGFA pathway. A heterozygous C/T mutation of the HIF-1α gene was found to be significantly higher (P = 0.02) in patients with invasive adenomas compared to controls, with 25% (n = 13) and 9.8% (n = 8), respectively. While in non-invasive adenomas, this mutation was observed about three times lower. Our results clearly support the argument for the regulatory role of HIF-1α within VEGFA in the development of aggressive pituitary adenoma flow.

Conclusions
Thus, genetic analysis can become a predictor of aggressive behavior of pituitary adenomas and the use of genetic markers in clinical practice will contribute to the prevention of complications of aggressive adenomas.

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Transition in endocrinology: predictors of drop-out in a heterogeneous population during long-term follow-up
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Aim
To evaluate: 1) clinical and epidemiological characteristics of outpatients transitioned from Pediatrics Endocrine (PED) to Adult Endocrine Department (AED) in a tertiary Centre; 2) transition process characteristics, and predictive factors of drop-out.

Patients and methods
Demographic, clinical, and transition features of 170 consecutive patients with paediatric onset of chronic endocrine or metabolic disease (excluded type 1 diabetes) who transitioned from PED to AED (2007-2020) were retrospectively evaluated.

Results
The age at transition was 18.4±4 years (F:M = 1.2:1). 93.6% of patients were affected by endocrinopathies (19.4% on a genetic basis), while 6.4% were in follow-up only in a cancer-survivor surveillance protocol. 69.4% of patients had one endocrine disease, 20.0% had 2, and 4.2% of them had 3 or more. 40.0% of subjects suffered also from non-endocrine diseases. The total comorbidity burden was high: 37.1%, 20.6%, and 11.1% of patients had 2, 3, or more diseases. The number of treatments progressively increased and was associated with the number of endocrine diseases (r 0.349, P<0.05). 64.7% of patients were adherent to the follow-up, mainly if they had a high number of comorbidities (x2=13.850, P<0.05). 67.4% of patients were adherent to the follow-up, mainly if they had a high number of endocrine diseases and the etiology (mainly in hypergonadotropic hypogonadism, hypothalamic). Patients with obesity had the low number of visits (x2=14.473, P<0.01) or thyroid disorders (x2=3.618, P<0.04). Having performed one visit only was predictive of drop-out (x2=18.624, P<0.009), regardless of pathology. Among cancer survivors, patients treated for central nervous system tumors had the highest adherence.

Conclusions
This is the first study that analyzed a specific transition plan for chronic endocrine diseases on long-term follow-up. The proposed “one size fits all model” is not adequate in responding to the different needs of patients. A structured transition plan is an emerging cornerstone. The first visit is crucial in building a trusting relationship between patients and healthcare providers and plays an important role in a successful therapeutic intervention.

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Central diabetes insipidus following immunization with BNT162b2 mRNA Covid-19 vaccine
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Introduction
The endocrine complications of COVID-19 remain largely unknown. Cases of central diabetes insipidus (CDI) have been reported after COVID-19, with hypophysitis being the most likely cause. COVID-19 vaccines potential adverse effects may mitigate some of these complications. We present a case of a woman who developed CDI one week after the 2nd dose of BNT162b2 mRNA COVID-19 vaccine.

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Adrenal haemorrhage in a pheochromocytoma - a rare, life-threatening and challenging complication

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Adrenal haemorrhage is a rare, usually life-threatening complication, most commonly connected with primary or metastatic adrenal tumour. Among them pheochromocytoma is the most common cause of spontaneous adrenal bleeding and accounts for nearly 50% of cases. We performed a database search for pheochromocytoma patients, diagnosed and treated in Endocrinology Department, University Hospital in Cracow from 2005 to 2021. 206 patients with pheochromocytoma were identified. Subsequently, 23 cases were excluded due to incomplete medical data necessary to rule out potential adrenal bleeding. Of the remaining 183 patients with histologically confirmed pheochromocytoma, 7 cases with adrenal bleeding were found (3.8% of cases). The group of patients comprise 4 men and 3 women. Median patient’s age was 49 years (range: 36-78 years). The most common manifestation of adrenal bleeding was acute abdominal pain (71.4%). Two patients (28.6%) developed shock, in one case resulted in multiple organ failure (MOF). Hormonal assessment concerning pheochromocytoma were performed in five patients (41.7%). 24-h urinary fractionated metanephrines were significantly elevated in all of them. Most patients (85.7%) had symptoms suggestive of pheochromocytoma before haemorrhage — most commonly paroxysmal hypertension (57.1%). Nevertheless, In four patients diagnosis of pheochromocytoma was made at the time of adrenal haemorrhage based on severe clinical manifestation, hormonal status and imaging. One patient died, before the diagnosis of adrenal bleeding was made. In two patients pheochromocytoma was suspected before the episode of haemorrhage: two months and sixteen months, respectively. Six out of seven patients have diagnostic imaging performed: median largest diameter of the lesion was 7.4 cm (range: 5-11 cm). Five patients had elective surgery, preceded by two-week pharmacological treatment with alpha-receptor blockers. One in case, four-day alpha-receptor blockage was administered, followed by the urgent surgery. In all cases the diagnosis of pheochromocytoma was confirmed in postoperative histopathology or in autopsy. PASS score was defined in 5 patients - in three cases it was no higher than 3, in two cases it exceeded 3. In two other cases, because of massive haemorrhagic changes, it couldn’t be determined. The perioperative survival rate was 85.7%. Adrenal bleeding is a rare complication of pheochromocytoma, which constitutes a diagnostic and therapeutic challenge.

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Pheochromocytoma/paraganglioma metastatic potential prediction

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Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumours, which derive from the chromaffin cells of the adrenal medulla or extra-adrenal sympathetic and parasympathetic ganglia. About 15-20% of those neoplasms could present malignant course. Prediction of PPGL metastatic potential still remains a great clinical challenge, since the sensitivity and specificity of proposed prediction systems are not satisfactory. We performed a retrospective database search for pheochromocytoma and paraganglioma patients, diagnosed and treated in Endocrinology Department, University Hospital in Cracow from 2005 to 2021. 206 patients with pheochromocytoma and 27 patients with paraganglioma were included to the analysis. The mean follow-up period was 93 months (range: 5-360 months). In the whole group, 5 metastatic pheochromocytomas and 2 metastatic paragangliomas have been found. Our objective was to investigate clinicopathological characteristics of the patients with malignant PPGLs in the light of current metastatic potential predictors. The group of patients with disseminated disease comprised 2 men and 5 women. Median patient age was 51 years (range: 19-72). In two patients metastatic disease was observed at the moment of diagnosis, in remaining cases metastases developed 6 to 84 months after the diagnosis (median time 32 months). The most common localizations of metastases were lymph nodes and bones (71.4% for each). The leading symptom of metastatic disease was fatigue (86%). The median size of the primary tumour was 7.7 cm. Hormonal assessment revealed significantly elevated 24-h urinary fractionated metanephrines in 6 patients. The dominant catecholamine profile was adrennergic (57%). In all patients concentration of 3- metoxtyramine was elevated. In one patient with paraganglioma it was the only elevated metabolite in 24-h urine collection. Moreover, chromogranin A level was substantially increased in all cases (minimum 4.8- fold the normal upper limit) and it was positively correlated with the progression of the disease. PASS score was known in three patients with pheochromocytoma, in all cases it was higher than 6. In patients with PPGL detailed analysis of histopathological, clinical, hormonal and imaging results is essential to properly predict the possible course of the disease. In our patients, the most commonly observed metastatic potential predictors were PASS score more than 6, tumour size more than 6 cm, elevation of dopamine metabolite level. A repetitive assessment of chromogranin A concentration during follow-up may have additional value in monitoring of the disease. Due to rarity of the PPGL, the establishment of a new predictive system is difficult and requires multicentre, long-term studies.
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Treatment of cushing’s disease (CD) after primary failure of pituitary surgery or recurrence: evaluation of long-term control by medical treatment

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Introduction

Pituitary surgery is the first line treatment for most patients with Cushing’s disease (CD) but after failure or recurrence after surgery 3 main strategies can be proposed: medical treatment (MT), a 2 nd pituitary surgery, bilateral adrenalectomy (BA). Pituitary radiotherapy is a 4 th strategy, generally combined with one of the 3 others. Medical treatment (MT) emerges as an attractive strategy in acromegaly: results from a 10-year single center experience

Methods

To evaluate long term control of CD with MT after failure of pituitary surgery or recurrence. Treatment of cushing’s disease (CD) but after failure or recurrence after surgery 3 main strategies can be proposed: medical treatment (MT), a 2 nd pituitary surgery, bilateral adrenalectomy (BA). Pituitary radiotherapy is a 4 th strategy, generally combined with one of the 3 others. Medical treatment (MT) emerges as an attractive strategy in acromegaly: results from a 10-year single center experience

Results

The second line treatment was medical treatment (MT) in 28/36 patients (78%) 2 nd pituitary surgery in 5/36 patients (14%) and BA in 3/36 patients (8%). The long-term control was achieved by MT in 21/36 patients (30%), 2 nd pituitary surgery in 8/36 patients (22%) and BA in 14 patients (39%), while 3/36 patients (8%) remained uncontrolled. During the whole follow-up 29 patients received at least one drug and 67 introductions of drug treatment were performed (average 2.3±0.7/patient), using inhibitors of steroidogenesis: ketoconazole (27), metyrapone (1) metyrapone (1). Group A patients had a higher age (55.9 vs 47.9 P=0.06) but were no different regarding sex and initial UFC. All female patients under 35 years ended in-group B. In conclusion, in this study MT was a long-term solution for 38% of the patients who experienced failure or recurrence after pituitary surgery for CD. Steroidogenesis inhibitors appeared more efficient.

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Long-term pasireotide therapy: real life experience of a single referral center

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Pasireotide is a second-line therapy for acromegaly, that allows to obtain disease control in patients with hormone excess. However, uncontrolled disease is a major concern. Currently, few data regarding long-term use of pasireotide are available. The current retrospective study aimed at investigating the efficacy and safety of long-term pasireotide therapy. Sixteen consecutive patients (5 males, 11 females, age 47 ± 11 years) undergoing pasireotide for a minimal period of 36 months, were considered for the current study. In these patients, hormonal (GH, IGF-I), biochemical (fasting glucose and HbA1c), and radiological parameters (tumour maximal diameter and volume) have been considered at baseline and at 6, 12, 36 months, and last follow-up (LUF), during pasireotide therapy. At baseline, GH levels were 4.56 ± 3.82 ng/ml, IGF-I levels were 3.82 ng/ml, IGF-I levels were 1.74 ± 0.72 U/L, resulting 13 patients (81.25%) uncontrolled. Diabetes mellitus (DM) was present in 7 (43.75%), and 4 patients (25%) showed an impaired fasting glucose (IFG) after 6 months of pasireotide, GH and IGF-I levels were significantly reduced compared to baseline (P=0.017 and P=0.001, respectively). At 12 months, all patients achieved disease control (P<0.0001), tumour maximal diameter and volume were significantly reduced (P=0.003 and P=0.019, respectively). Disease control was maintained at 36 months evaluation, being tumour volume significantly further reduced compared to 12 months (P=0.010). Twelve patients (75%) were treated with pasireotide for a longer period (range 42-66 months); all these patients were controlled with a stable size adenoma at LUF. At 6 months, an increase in dose was recorded in 4 patients (25%, P=0.046), no further dose variation have been required. Pasireotide starting dose was significantly inversely correlated to IGF-I at 36 months (r=0.614, P=0.011). Fasting glucose (FG) significantly increased in the first year of pasireotide therapy, particularly in the first 6 months (P=0.005); without a consistent increase in HbA1c (P=0.303) and DM (P=0.285). FG at 6 months was significantly correlated to age (r=0.092, P=0.003), respectively but pasireotide dose (r=0.417, P=0.108). After 6 months, 75% IFG patients developed DM. At 36 months, 80% euglycemic patients at baseline were diabetic, and 20% showed IFG. As consequence, a significant increase in DM (P=0.023), and in the number of metabolic profile in patients with acromegaly resistant to somatostatin analogues (SRLs). Twenty-two patients (9 men,13 women, age 45.54 ± 12.83 years) treated with PEG for 10 years, in monotherapy or in combination with SRLs, were included in the current study. In the whole patient cohort, anthropometric (BMI, systolic and diastolic blood pressure), hormonal (GH, IGF-I, biochemical (fasting glucose and insulin, lipid profile) parameters, and maximal tumour diameter were evaluated before and after 10-years of PEG treatment. After 10-years PEG therapy, IGF-I levels significantly decreased in all the patients (P<0.0001) compared to baseline, with full normalization in 91%. No significant change in dose of either PEG or SRLs was required. Tumour maximal diameter slightly decreased in the whole cohort. Fasting glucose (FG) was significantly increased (P=0.035), whereas HbA1c and diabetes prevalence remained stable. Fasting insulin (FI) and HOMA-IR decreased, HOMA-β was significantly reduced (P=0.013), whereas ISLw was increased. A significant decrease in total (P=0.03) and LDL- (P=0.05) cholesterol, and a slight increase in triglycerides were found. At baseline, GH and IGF-I levels significantly correlated with systolic blood pressure (SBP), FI, HOMA-IR, HOMA-β, and ISLw. Baseline IGF-I correlated with percent change after 10 years (Δ) of FI (r=0.354, P=0.015), and HDL (r=0.045, P=0.045). PEG dose was directly correlated to BMI (r=0.509, P=0.016), and triglycerides (r=0.534, P=0.007), and inversely to age (r=-0.455, P=0.030). Disease duration before PEG was directly related to BMI (r=0.446, P=0.037), and inversely to 10-years HOMA-IR (r=-0.563, P=0.029). HDL (r=-0.424, P=0.049), ΔFG (r=-0.462, P=0.03), ΔI (r=0.546, P=0.05), and ΔFG (r=-0.445, P=0.034). Long-term PEG therapy is effective and safe, without requiring an increase in dose to maintain disease control even after a decade of therapy. PEG beneficial impact on both insulin and lipid metabolism persists after prolonged therapy, PEG treatment should be started as soon as possible in patients resistant to SRLs as the extent of the metabolic improvement is inversely correlated to disease duration before PEG introduction.

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Efficacy, safety and metabolic impact of long-term pegvisomant therapy in acromegaly: results from a 10-year single center experience

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Pegvisomant (PEG) is effective in acromegaly control and exerts a positive impact on glucose metabolism. The current study aimed at investigating the effects of 10-years PEG treatment on disease control, pituitary adenoma size, and

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antidiabetic drugs used \( (p=0.005) \) were observed. Pasireotide therapy is effective in determining disease control, and tumour shrinkage, even after a long period of treatment. Change in FG mainly occur in the first period, depending on age and glycemic status before pasireotide starting.

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**P681**
The burden of adult growth hormone deficiency diagnostic tests: results of a patient experience survey in the UK

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Objectives
To collect qualitative and quantitative information on the burden of adult growth hormone deficiency (AGHD) diagnostic tests for the patient.

Methods
A survey was published on The Pituitary Foundation’s website and social media pages; respondents completed it online using SmartSurvey over period of two months (October-November 2021). 105 respondents took the survey, with 9 screened out after the first question because they had never taken an AGHD diagnostic test.

Results
Of the 96 respondents who completed the survey, 66 answered questions about the insulin tolerance test (ITT), 23 about the glucagon test, and 7 about the GHRH-arginine test. The ITT, whose mechanism of action depends on induced hypoglycaemia, presented both the widest variety of symptoms and, according to scores given by respondents, the most severe, with 9 of the 13 prompted symptoms experienced by the majority of patients who answered questions about it. When ITT patients were asked to rate the severity of the side effects they experienced on a scale of 1-5 (with 5 being the most severe), 5 symptoms — sweating, shakiness, fatigue, feeling dizzy, and feeling weak — had an average score of 3 or above (‘moderate’ or ‘severe’). Although the glucagon test and GHRH-arginine test were overall less burdensome, they still caused some prompted symptoms to be experienced by the majority of patients who underwent them. Only 44% of patients felt well-prepared for their test, and 34.4% did not think the information they received beforehand was useful. Furthermore, questionnaire results were analyzed in acromegalic patients related to gender, BMI, and disease control. ESS score and the prevalence of high SA risk based on BQ were similar between men and women. No significant differences were found for both ESS and BQ score among patients according to the BMI categories. Patients with uncontrolled disease had no differences in questionnaire’s score compared to controlled patients. Patients’ therapy did not influence ESS and BQ results. Acromegaly patients defined at high risk of SA according to BQ presented a significantly higher prevalence of hypertension \( (P=0.002) \), and number of antihypertensive drugs used \( (P<0.001) \), and lower AcroQol \( (p=0.019) \), compared to those at low risk. No differences concerning anthropometric parameters, GH and IGF-I levels, age at diagnosis, and disease duration were found between the two groups. AcroQol was inversely correlated to ESS \((r=-0.326, P=0.012)\) and BQ \((r=-0.310, P=0.018)\) scores. No correlation was found with age both in patients and controls. ESS and BQ are scores validated for SA risk assessment in the general population. The results of this study show that these tools seem to be not suitable for assessing SA risk in patients with acromegaly. Probably acromegalic patients, at higher risk of developing this comorbidity compared to the general population, require a proper questionnaire.

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**P682**
Berlin questionnaire and epworth sleepiness scale as screening tools of sleep apnea risk in patients with acromegaly: comparison of 144 patients and an age-and gender-matched health cohort

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Sleep apnea (SA) is a common acromegaly comorbidity, influencing patients’ quality of life and mortality risk. Despite its importance, SA frequently remains undiagnosed, and its real prevalence seems to be underestimated. The current observational study aimed at investigating the role of Berlin questionnaire (BQ) and Epworth sleepiness scale (ESS) in assessing the risk of SA in this high-risk population, and to compare the results with an age-and gender-matched health cohort. One hundred and forty-four patients with acromegaly (63 men, 81 women, age 56.37 ± 12.94 years), and an equal number of age- and gender-matched health controls were included in the present study. All the subjects had no previous diagnosis of SA. For BQ and ESS, higher score indicated greater SA risk. A questionnaire evaluating quality of life in acromegaly, AcroQol, for which the higher score indicates a better quality of life, was administered only to patients. Patients showed a significantly higher BMI than controls \( (P<0.001) \), whereas there was no difference about hypertension prevalence \( (P=1) \). Comparing patients and controls, no significant difference was found in ESS score \( (P=0.761) \), and prevalence of high SA risk estimated by BQ \( (P=0.623) \). Furthermore, questionnaire results were analyzed in acromegalic patients related to gender, BMI, and disease control. ESS score and the prevalence of high SA risk based on BQ were similar between men and women. No significant differences were found for both ESS and BQ score among patients according to the BMI categories. Patients with uncontrolled disease had no differences in questionnaires’ score compared to controlled patients. Patient’s therapy did not influence ESS and BQ results. Acromegaly patients defined at high risk of SA according to BQ presented a significantly higher prevalence of hypertension \( (P=0.002) \), and number of antihypertensive drugs used \( (P<0.001) \), and lower AcroQol \( (p=0.019) \), compared to those at low risk. No differences concerning anthropometric parameters, GH and IGF-I levels, age at diagnosis, and disease duration were found between the two groups. AcroQol was inversely correlated to ESS \((r=-0.326, P=0.012)\) and BQ \((r=-0.310, P=0.018)\) scores. No correlation was found with age both in patients and controls. ESS and BQ are scores validated for SA risk assessment in the general population. The results of this study show that these tools seem to be not suitable for assessing SA risk in patients with acromegaly. Probably acromegalic patients, at higher risk of developing this comorbidity compared to the general population, require a proper questionnaire.

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**P683**
Pallister-hall syndrome diagnosed in a young man after an acute adrenal crisis

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Introduction
Pallister-Hall syndrome (PHS) is a very rare congenital syndrome, and its exact prevalence is still unknown. The clinical diagnosis is usually made when a hypothalamic hamartoma is associated with polydactyly. Endocrine manifestations consist of hypopituitarism, hypopituitarism, which can affect one or more pituitary axes, and precocious puberty. Here, we report the case of an 18-year-old young man in whom the diagnosis of PHS was delayed until his hospitalization in the endocrinology department for acute adrenal insufficiency.

Observation
The patient was an 18 years old young man who presented to the emergency room with clinical and biological features of an adrenal crisis. The medical history revealed several surgeries: a corrective one for polydactyly, a surgery for testicular ectopia and for a hypothyroid tumour diagnosed at the age of three years complicated with hypopituitarism. He would have received growth hormone for two years from the age of twelve. He was on hormone replacement therapy for hypothyroidism and adrenal insufficiency, and he stopped his treatment for a week. He had no medical follow-up for several years. The patient’s family history was unknown as he was an adopted child. Physical examination showed a height of 157 cm (-3SD), a weight of 68 kg and a BMI of 27.5 kg/m². We noted an inequality of the two lower limbs. External genitalia’s examination revealed a microenvis and hypoplastic testis. PHS was suspected and further investigations were then performed. An otoparyngology examination showed bifid epiglottis and laryngeal cleft. X-rays of the left hand revealed a surgically corrected postaxial type A polydactyly. Pelvic x-ray showed bone demineralisation and Risser stage was 4. Ultrasounds of heart, abdomen and kidneys were normal. The pelvic ultrasound showed hypoplastic testes. Brain MRI revealed a sellar and suprasellar mass measuring 28x25x24 mm corresponding to hypothalamic hamartoma. On biochemical evaluation, the
renal and hepatic functions, blood count, serum calcium and serum phosphorus results were normal. The pituitary assessment showed a thyrotropin and gonadotropin deficiencies

Conclusion

This patient’s presentation shows that PHS may be misdiagnosed given its extremely low prevalence. Practitioners who may see patients with PHS at the young age (pediatricians, surgeons) should be familiar with this disease to avoid late diagnosis which may compromise patient prognosis.

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P684 Pituitary macroadenoma revealed by symptoms mimicking Hakim Adams trial

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Introduction

The clinical presentation of a secretory pituitary macroadenoma usually consists of a tumor syndrome accompanied by visual disturbances with signs of pituitary insufficiency and/or hormonal hypersecretion. Herein we describe an unusual presentation of a mixed secretory adenoma.

Observation

A 69-year-old was referred to our department for the management of a pituitary macroadenoma revealed by a symptomatology mimicking the Hakim Adams trial with gait disorders, sphincter disorders and a dementia syndrome, as well as a right monocular blindness. His past medical history included type 2 diabetes mellitus and hypertension. Physical examination noted a dysmorphic syndrome suggestive of acromegaly. Hormonal investigations revealed a hyperprolactinemia at 4755 ng/ml, a baseline GH of 7.8 ng/ml (>1) with elevated IGF1 levels. Baseline cortisol was at 8.9 µg/dl (nr:5-18) with an ACTH at 36.16 pg/ml (nr:7.22-63.3). TSH and FT4 were at 0.143 mIU/l (nr:0.1-4.5) and 0.67 ng/dl (0.7-1.5) respectively, FSH and LH were at 2.94 IU/l (nr:1.1-1.2) and 13.4 IU/l (nr:2-12) respectively. Brain MRI showed a 5 cm pituitary macroadenoma with supra sellar extension pushing back the optic chiasm and leading to lateral ventricles dilatation upstream and an invasion of the right cavernous sinus. Ophthalmological examination showed palsy and bilateral papillary atrophy. Visual acuity was very low. Visual field showed right monocular blindness and was alegic on the left. The patient was put under Cabergoline at the dose of 1.5 mg per week. The evolution after one week was spectacular with disappearance of the walking, sphincter, and memory disorders with visual improvement, being reduced to a right lateral homonymous hemianopia.

Conclusion

Symptoms mimicking Adams Hakim’s trial are exceptionally in relation with a pituitary adenoma. In case of prolactinoma, medical treatment with dopaminergic agonists may be associated with resolution of those neurological symptoms.

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P685 Immunotherapy-induced endocrinopathies: a case report

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Endocrinopathies are one of the most common side effects induced by immunotherapy. The side effects result from the activation of immune system, which affects not only cancerous but also healthy body cells. In most cases, only one endocrinopathy occurs, but in our presented case we describe multiple endocrinopathies that occurred to a one person. 53-years-old male patient was referred to the Emergency department due to severe hyperglycemia (37.13 mmol/l) and the following symptoms: frequent urination, thirst, general weakness. New-onset diabetes was diagnosed and the patient was admitted to the Department of Endocrinology. After clarification of past medical history oncological disease emerged. In 2013, metastatic right kidney cancer was diagnosed (the tumor was spread to the lungs), the right nephrectomy was performed. Histopathological analysis confirmed clear cell renal cell carcinoma (c-RA, pT3aG3). Systemic therapy with Sunitinib has been initiated. During the course of treatment, in 2016, hypothyroïdism appeared, LT4 treatment was necessary. In 2020, for the reason of disease progression, immunotherapy with nivolumab, as a second line treatment, was initiated and stereotactic radiotherapy for paraaortic lymph nodes was applied. In the Department of Endocrinology, for the treatment of newly diagnosed diabetes mellitus intensive insulin therapy was chosen (HbA1c 18.7%, anti-T2A 1.0k U/l, n 0-7.5k U/l, anti-GAD 0.5k U/l, n 0-5; suspected immunotherapy-induced autoimmune diabetes mellitus). Depending on the patient medical history, was decided to consider other possible immunotherapy-induced endocrinopathies. After additional investigation hypopituitarism, secondary adrenal insufficiency was confirmed (ACTH 0.4 pmol/l, n 1.63-14.5, morning cortisol 47.1 µmol/l, n 147-726). Hydrocortisone replacement therapy was started immediately. Repeated blood tests revealed low levels of testosterone (T 2.22–3.23, n 9.06-30.1). The patient completed an international index of erectile function (IEF) questionnaire and was diagnosed with mild to moderate erectile dysfunction. Mixed hypogonadism was confirmed (hypogonadism due to hypothalamic/pituitary and testicular dysfunction; LH 4.0 IU/l n 1.71-1.2, FSH 10.2 IU/l n 2.18-6.6), testosterone replacement therapy was prescribed. During inpatient treatment, headache and visual disturbances appeared. In assessing the course of the disease, tests results, despite the fact that no changes in the pituitary gland were seen after MRI, hypophysitis was diagnosed. The patient was discussed at multidisciplinary team meeting and it was decided that after adjusting the patient’s condition, immunotherapy can be resumed, continuing the active follow up at the Department of Endocrinology. It is very important to monitor patients throughout and after the treatment of immunotherapy for possible side effects that can lead to serious, life-threatening complications if not diagnosed in time.

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P686 Ruptured Rathke’s cleft cyst (RCC) with irritation of optic apparatus and rapidly evolving panhypopituitarism

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Background

Rathke’s cleft cysts (RCC) are benign intrasellar cysts that originate from the remnants of Rathke’s pouch and contain mucoid material. Most are asymptomatic, but some may compress adjacent structures leading to visual disturbances and endocrinopathies.

Case Report

A 20-year-old gentleman had an MRI Head in view of headaches. This showed a 17.7 mm peripherally enhancing suprasellar lesion with no intrinsic T1 high signal pre-contrast. He presented acutely three weeks later with headaches, blurred vision, sudden onset polyuria, polydipsia, and lethargy. An MR Pituitary showed a 23 mm, lobulated, peripherally enhancing sellar/suprasellar mass with elevation of the optic chiasm. The right optic tract showed inflammatory changes. The normal pituitary tissue was displaced. Blood investigations showed a random cortisol of 93 nmol/l, TSH 0.5 mU/l, T4 8.6 pmol/l, FSH 0.5 nmol/l and central diabetes insipidus with a serum sodium of 139 mmol/l, serum osmolality 293 mmol/kg and urine osmolality of 121 mmol/kg. Pituitary replacement therapy was initiated with hydrocortisone, testosterone (T 2.22, n 3.23, HbA1c 18.7%, anti-T2A 1.0k U/l, n 0-7.5k U/l, anti-GAD 0.5k U/l, n 0-5; suspected immunotherapy-induced autoimmune diabetes mellitus). Depending on the patient medical history, was decided to consider other possible immunotherapy-induced endocrinopathies. After additional investigation hypopituitarism, secondary adrenal insufficiency was confirmed (ACTH 0.4 pmol/l, n 1.63-14.5, morning cortisol 47.1 µmol/l, n 147-726). Hydrocortisone replacement therapy was prescribed. During inpatient treatment, headache and visual disturbances appeared. In assessing the course of the disease, tests results, despite the fact that no changes in the pituitary gland were seen after MRI, hypophysitis was diagnosed. The patient was discussed at multidisciplinary team meeting and it was decided that after adjusting the patient’s condition, immunotherapy can be resumed, continuing the active follow up at the Department of Endocrinology. It is very important to monitor patients throughout and after the treatment of immunotherapy for possible side effects that can lead to serious, life-threatening complications if not diagnosed in time.

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An MR Pituitary showed enlargement of the residual cystic lesion and further encroachment of the optic tract. He underwent urgent redo transphenoidal endoscopic drainage of the cyst. His vision improved significantly post operatively. Visual fields were normal to confrontation. Histology showed a fragment of pituitary gland containing granulation tissue and stratified epithelium compatible with elements of a residual RCC. Conclusion In most RCCs the development of pituitary dysfunction and neuro-ophthalmic deficit are chronic. We present a rare case of a ruptured RCC causing acute visual problems and panhypopituitarism which recurred within a short period after decompression. The patient will remain under close clinical and radiological follow-up.

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P687

Plurihormonal pituitary macroadenoma, co—secreting TSH/GH/and prolactin: a clinical challenge
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Background
Co secreting Thyrotropin/growth hormone pituitary adenomas are rare, and their clinical presentation and long term management may be challenging. Clinically, the majority of plurihormonal pituitary adenomas are silent and diagnosis almost always relies on immunohistochemical analysis of the tumor tissue. Early detection is key to optimize patient management. We report a case of pituitary plurihormonal macroadenoma with overt clinical hyperthyroidism and minimal GH excess symptoms.

Case Report
A 68-year-old female patient was admitted to our university hospital for transesphenoidal surgery due to a Thyrotropinoma diagnosed by one of our colleagues in another hospital. She underwent a thyroidectomy 15 years prior to diagnosis due to multiple bilateral thyroid nodules and she was taking levothyroxine replacement, noting that she presented discordance TSH/T4 levels. On review of previous test she consistently had elevated TSH and T4 levels, and there was no family history of thyroid disease. Slightly high prolactin, IGF-1 and elevated pituitary glycoprotein sSubunit were found during investigation and magnetic resonance Imaging(MRI) showed a sellar mass consisting of a pituitary macroadenoma that measured 31x21x29 mm(trxAPXX) invading both cavernous sinuses and causing compression and superior displacement on the optic chiasm. Early diagnosis was key to optimize patient management. We report a case of pituitary plurihormonal macroadenoma with overt clinical hyperthyroidism and minimal GH excess symptoms.

Conclusion
Co-secretion occurs in 30% of Thyrotropinomas, requiring diligent immunohistochemical analyses of all pituitary hormones to make the correct diagnosis and to alert the clinicians to ensure the right follow up.

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P688

Implications of the 2017 WHO classification in the characterization of GH-secreting pituitary tumors
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Introduction
Somatotroph pituitary adenomas (PAs) represent 10-15% of all resected PAs, exhibiting immunohistochemical (IHC) positivity for GH (growth hormone) and PIT-1 transcription factor (TF). The histopathological (HP) and IHC variability of each PA influences the phenotype, radiological features, and therapy response. Materials and methods
The study included 33 patients with acromegaly, with men: women ratio of 17:16. The HP-IHC characteristics were correlated with the clinical, imaging and laboratory data. Tumour specimens were assessed for anterior pituitary hormones, PIT-1, TPTh and SF-1 TF, Ki-67 labeling index, vimentin and reticulin.

Results
Of all cases, 30 had GH hypersecretion, while 3 had GH and PRL co-secretion. The symptomatology at diagnosis was dominated by the increase in size of extremities, associated with facial changes. Regarding the complications, they were identified right from the diagnosis, almost 50% of patients being hypertensive. Over 90% were macroadenomas. The maximum tumour diameter at diagnosis was positively correlated with suprasellar extension (P 0.001), the latter being also correlated with tumour invasion (P<0.0001). The postoperative tumour size was positively correlated with the postoperative value of random GH (P 0.01), the postoperative control of the residual secretion having a negative correlation with the maximum diameter of the initial tumor. Regarding the biochemical evaluations, a statistically significant correlation was observed between the initial diagnostic values of IGF-1 and nadir GH in OGTT (P 0.02), respectively random GH (P 0.01), correlation maintained postoperatively (P 0.004 and <0.001, respectively). Most PAs were acidophilic, all had a positive IHC expression for GH. As expected, 93.93% had positive expression for PIT-1. PAs with IHC expression positive exclusively for GH accounted for 36.36%, while 13 cases (39.39%) showed a positive expression also for PRL. The expression of the other adenohypophyseal hormones was 12.12% for TSH, 5.05% for ACTH, and 9.09% for LH, respectively. Four cases were plurihormonal PIT-1 positive PAs, all with positive expression for PIT-1. Four cases had unusual IHC hormonal combinations. A particular feature of these PAs was the positive expression of the transcription factor SF-1 in a fairly large number of patients (39.39%). Most had a Ki-67 value below 3%

Conclusions
The IHC classification of PAs, as stated by the WHO 2017 classification criteria, associated with the radiological dimensions and extent influence disease control, and are, probably, the most accurate prognostic factors. The 4 plurihormonal PIT-1 positive PAs associated a good cell differentiation and strongly acidophilic tincoriority, advocating for a well-differentiated, mature tumour variant.

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P689

Peculiar presentation of a TSH-secreting pituitary adenoma: a possible new multiple endocrine syndrome?
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Introduction
TSH-secreting pituitary adenomas (TSHomas) are a rare cause of central hyperthyroidism, accounting for less than 1% of all pituitary adenomas, with a prevalence in the general population of 1-2 cases per million.

Case Presentation
A 45-year-old female patient presented in 2009 with hypertension and tachycardia: blood tests revealed an inappropriately normal TSH with high fT3/fT4 levels and primary hyperaldosteronism. She declined further investigations and was started on nebivolol and hydrochlorothiazide by her GP. In November 2021, aged 58 years, she came to our observation for a compressive multinodular goiter with intrathoracic extension requiring surgery. In spite of a persistent biochemical picture of central hyperthyroidism, she did not complain symptoms of thyrotoxicosis. We ruled out possible interferences in the thyroid function tests and started the appropriate workup.
Diagnostic Investigations
We found an absent TSH response to exogenous TRH stimulation, suggestive for a TSHoma with a MRI showing a 12 mm pituitary macroadenoma. The remaining pituitary function was normal. Moreover, a primary hyperaldosteronism and a mild normocalcemic hyperparathyroidism despite cholecalciferol supplementation were found. No hyperplastic parathyroid glands were found at US scan, while the abdomen CT scan showed a slightly enlarged left adrenal gland. Due to the co-occurrence of a TSH-secreting pituitary adenoma, hyperparathyroidism and adrenal hyperplasia, suggestive of MEN-1, we performed molecular analysis, by a targeted-NGS sequencing custom panel. We did not find variants in the CDKN1B or MEN1 gene, while a heterozygous variant in the gag-A cell-line-derived neurotrophic factor (GDNF) gene, previously reported in Hirschsprung disease, substituting an Isoleucine with a Methionine (p.I211 M) was found.

Discussion and Conclusion
GDNF is a plausible candidate gene for multiple endocrine syndromes, as GDNF family members bind to the GDNF-family-receptor alphas (GFRαs), leading to RET dimerization. In addition, it is expressed in normal pituitary and parathyroid glands and in pituitary/parathyroid adenomas. Furthermore, somatic mutations have been reported in parathyroid adenomas/hyperplasia. Nevertheless, the impact of the p.I211 M variant in the pathogenesis of this case remains unclear. Previous studies showed that this GDNF variant retained its ability to induce RET tyrosine phosphorylation. These results suggest that the p.I211 M variant might act as a disease modifier in conjunction with other genetic lesions (Eketjall, 2002) still not identified in our patient. The curious association of central hypothyroidism with primary hyperaldosteronism and hyperparathyroidism is suggestive of a novel MEN syndrome variant.

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P690
Clinical characteristics at diagnosis and diagnostic delay among newly-diagnosed patients with acromegaly- single-center, pilot study

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Introduction
Diagnostic delay remains significant among the patients with acromegaly, even though the disease awareness has improved over the years. The aim of the study was to investigate the diagnostic delay and symptoms present at diagnosis of acromegaly among the newly-diagnosed patients.

Material and methods
72 consecutive patients diagnosed with acromegaly between 01.2014 and 12.2021 were evaluated. Division into groups based on: gender, age upon diagnosis (≤30 and >30 years of age) and age at the retrospectively estimated onset of symptoms (≤30 and >30 years of age) was made. Clinical and biochemical data at diagnosis were analyzed with IBM SPSS Statistics ver. 27. The study was approved by local Bioethics Committee.

Results
63 patients (56.6% females, mean age 41.13+/−14.03 years) were included in the study. Pituitary tumor was accidentally discovered in 24.2%, the median diagnostic delay was 4 years (IQR 4.0-7.0). There were no statistically significant differences in diagnostic delay, accidental diagnosis between genders and age groups. Acral enlargement was the most frequently reported symptom (90.3% of patients). Headaches, reported by 45.2% patients, were more frequent in females (42.86%) than in males (29.63%)(P=0.031). Snoring was more common among patients with onset >30 years of age than in early onset (28.13% vs 0%, P=0.018). 25.85% patients had visual field impairment due to optic chiasm compression. Menstrual abnormalities were present in 37.14% females; 25.92% males reported decreased libido, with no statistical differences. Those symptoms were more common among patients with onset of symptoms ≤30 years of age than in those with later onset (50% vs 21.88%, P=0.041). Hypogonadotropic hypogonadism was more common in males (74.1%) than in females (16.7%)(P<0.001). 42.8% of females and 29.6% of males suffered from hyperprolactinemia. Secondary hypothyroidism was present in 14.28% of women and 18.5% men. Adrenal axis insufficiency was discovered in only 2 males (7.4%). Nobody was diagnosed with diabetes insipidus. There was no statistically significant relationship between the diagnostic delay and any of the symptoms or any of the pituitary axis insufficiency.

Conclusions
In our study, males tend to underreport the symptoms of hypogonadotropic hypogonadism. Menstrual irregularities or decreased libido are more frequently reported in younger age, while headaches are more common in females. Diagnostic delay did not statistically depend on presence of any of the symptoms nor pituitary insufficiency.

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P691
Very-low-calorie-ketogenic-diet (VLCKD) approach to manage obesity in cranioopharingioma patients

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Background
Cranioopharingioma patients frequently experience severe obesity, unresponsive to caloric restriction or lifestyle modifications. Recently very-low-ketogenic-diets (VLCKD) proved to be a promising lifestyle intervention for obesity management, but no data are available regarding their effect on hypothalamic obesity (HO).

Introduction
We present the outcome of VLCKD protocol applied in young patients with HO following neurosurgery for cranioopharingioma.

Methods
Three patients who developed HO after surgery for cranioopharingioma (1 male, mean weight 125±3.8 kg, mean BMI 43.9±3.9 kg/m²) were treated with VLCKD protocol. All patients had previously undergone largely unsuccessful dietary interventions. BMI, weight, waist circumference changes and adverse effects were assessed during a follow-up period of 7.5±3.7 months (range 3-16 months).

Results
The two female patients presented panhypopituitarism and diabetes insipidus, while the male had multiple pituitary deficiencies (central hypothyroidism, hypogonadotropic hypogonadism and growth hormone deficiency); all patients were on adequate replacement therapy. Both female patients presented visual field impairment. All patients showed non-alcoholic steatoepatitis, hyperinsulinism but not diabetes mellitus, while the male patient also presented hyperuricemia. VLCKD resulted in a significant weight loss (125±2.8 kg vs 112.4±3.6 kg, P=0.008) as well as waist circumference reduction (111±3.8 vs 102.3±3.0, P=0.029). At last follow-up, BMI (43.9±3.9 kg/m² vs 39.4±2.8 kg/m², P=0.14) remarkably decreased, although not significantly. The only side effect registered was persistent hyponatraemia in one female patient, normalising after VLCKD suspension, corticosteroid and desmopressin replacement treatment adjusting.

Conclusions
The use of VLCKD protocol is a promising, safe and effective treatment option for HO in cranioopharingioma patients. Frequent control of electrolytes is mandatory.

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P692
Analysis of the frequency of relapses according to the national registry cushing’s syndrome in Republic of Uzbekistan

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Transsphenoidal pituitary surgery is the method of choice in the treatment of AC/HD, although to date, according to a number of researchers, the method is not ideal. Despite the achievement of immediate postoperative remission in 69-
98% of cases, with an increase in the duration of follow-up after TSS from 5 to 10 years, an increase in the frequency of relapses from 15 to 66% is observed. In this regard, we analyzed cases of ACTH DCS subjected to TSS for 2003-2021, included in the national register. Thus, according to the registry data, over a 18-year period, 222 patients with ACTH DCS were under dynamic observation, of which 128(57.6%). The remaining 94(42.4%) patients were on medication - 54 cases (24.4%), adrenalectomy - 36 (16.2%), including 3 patients (1.3%) in combination with RT, on radiation therapy - 4 patients (1.8%). Every year, there are 2-3 cases of relapse, which aggravate both the course and outcome of the disease. In view of this, the this stage of our research was the search and analysis of possible causes of the development of relapses of the disease in ACTH DCS. The analysis revealed that a total of 53 (41.4%) patients out of 128 treated with TSS developed a relapse in the period 2003-2021. Of these women, the overwhelming majority - 48 (90%) and 5 men (10%). The mean age of the patients was 34.3 ± 2.06 years. The average duration of the remission period was 3.25 ± 0.04 years. Due to the development of recurrence and failure to achieve in 33 cases (62.3%), repeated TSS was performed in 11 patients, radiation therapy in 5 and adrenalectomy in 15 patients, which caused the development of pituitary complications in the form of diabetes insipidus in 2 (3.7%) and panhypopituitarism in 2 (3.7%). Thus, in a cohort of 53 (42.9%) patients with ACTH DCS, who developed a relapse of the disease after TSS, they were aged 34.3 ± 0.16, consisted mainly of females (90%), were characterized by microadenomas (88.6%), insufficient decrease in ACTH and cortisol levels in the early postoperative period (by 1.5 and 1.7 times, respectively), presence of arterial hypertension (26.4%), impaired BMD (63.4%), 26.3%, the presence of central diabetes insipidus (3.7%) and panhypopituitarism (3.7%). As the results of the analysis show, the very state of remission in patients with ACTH DCS is unstable and, for various reasons, they may develop a relapse, the frequency of which increases with an increase in the observation period.

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P693 Multimodal treatment including temozolomide (TMZ) and pasireotide for aggressive, giant silent corticotroph PitNET in a young patient Anna Boguslawska, Łukasz Kluczynski, Magdalena Godlewksa, Ewelina Krzepka, Alicja Hubalewska-Dydycz & Aleksandra Gilis-Jamazanska Department of Endocrinology, Endocrine Oncology and Nuclear Medicine, Jagiellonian University Medical College, Cracow, Poland

Silent corticotroph pituitary neuroendocrine tumours (PitNETs) are a subtype of non-functioning PitNETs, that present positive immunostaining for adrenocorticotropin (ACTH) and/or show the expression of the transcription factor T-PIT without clinical signs of hypercortisolemia. They constitute 20% of all corticotroph PitNETs and manifest in most cases as macroadenomas with suprasellar extension and a higher tendency to apoplexy. We present a 33-year-old male with aggressive course of silent corticotroph PitNET. The patient was admitted to Emergency Department due to severe headaches and vomiting. Headaches (8-9/10 using numbering rate score (NRS)) and worsening vision loss were present one year before the surgery. In computer tomography, a sellar tumour mass (39x33x55 mm) was found with exosaral extension, causing pressure on the cerebral aqueduct of the third ventricle, involving left sphenoid sinus. Additionally, features of cerebral edema were described. The patient was transferred to Neurosurgery Department and, external ventricular drainage was performed due to obstructive hydrocephalus. Two days later, debunking transsphenoidal surgery (TSS) was performed. Histopathology results showed silent adenoma subtype 1 (densely granulated), Ki67 ≤ 1%. Genetic testing was negative for AIP, MEN1 mutations. However, 3 months later, magnetic resonance imaging (MRI) showed progression of PitNET (40x39x30 mm) with increasing hydrocephalus. Subsequently, second TSS was performed, complicated with cerebrospinal fluid leak. Biochemically, persistent multiple pituitary hormone deficiencies and diabetes insipidus was diagnosed. Clinically, severe headaches (9-10/10 using NRS) without improvement after analgesic were observed. The patient was consulted to multidisciplinary pituitary tumour board and radiotherapy was planned. Pasireotide (10 mg) monthly and 0.5 mg of carbozolene were weekly scheduled, however, due to rapid progression of the tumour and the compression of optic chiasm, emergency TSS (05.2021) with the decompression of the optic nerves was performed. After surgery, chemotherapy with temozolomide (starting dose of 150 mg/m2 for 5 days every 4 weeks) was continued. Due to the development of recurrence and failure to achieve in 33 cases (62.3%), repeated TSS was performed in 11 patients, radiation therapy in 5 and adrenalectomy in 15 patients, which caused the development of pituitary complications in the form of diabetes insipidus in 2 (3.7%) and panhypopituitarism in 2 (3.7%). Thus, in a cohort of 53 (42.9%) patients with ACTH DCS, who developed a relapse of the disease after TSS, they were aged 34.3 ± 0.16, consisted mainly of females (90%), were characterized by microadenomas (88.6%), insufficient decrease in ACTH and cortisol levels in the early postoperative period (by 1.5 and 1.7 times, respectively), presence of arterial hypertension (26.4%), impaired BMD (63.4%), 26.3%, the presence of central diabetes insipidus (3.7%) and panhypopituitarism (3.7%). As the results of the analysis show, the very state of remission in patients with ACTH DCS is unstable and, for various reasons, they may develop a relapse, the frequency of which increases with an increase in the observation period.

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P694 Radiological classification of craniohypophysialycoma based on its origin Tanja Škorić Polovina1, David Ozretić2, Mirsala Solak3, Ivana Kraljević1, Tina Dusić4, Anniemárse Balasko5, Karin Zubar Tomšic1 & Darko Kastelan1 1Clinical Hospital Center Zagreb, Dpt of Endocrinology, ZAGREB, Croatia; 2Clinical Hospital Center Zagreb, Dpt of Neuroradiology, Zagreb, Croatia

Recognizing the site of origin of craniohypophysialycoma (CP) along the hypothalamic-pituitary axis is according to pre-operative MR is helpful to understand its growth pattern in relation to hypothalamus, which is critical in the prediction of hypothalamic injury and planning of treatment. We retrospectively classified 29 CP according to MR pre-operative image study using modified classification of Tang et al. (Nature, 8:10215, 2018). According to its relation to pituitary stalk, CP were classified into two types: central and peripheral. Peripheral type was further subdivided into three subtypes: hypothalamic stalk, suprasellar stalk and intrasellar stalk. Central type and hypothalamic stalk peripheral subtype CP were considered to be of hypothalamic origin. We compared types of CP with the development of cognitive dysfunction and obesity after the treatment as markers of hypothalamic injury. Of the 29 CP examined in this study, five were classified as central type, and 24 as peripheral type. Twelve of peripheral type were subclassified as hypothalamic stalk CP, four as suprasellar stalk CP, and eight as intrasellar stalk CP. Cognitive dysfunction was found significantly more often in patients with central CP and hypothalamic stalk CP (3/5 and 4/12, respectively) in comparison to patients with suprasellar and intrasellar stalk CP who did not developed cognitive impairment (P=0.012). Obesity developed in 3 of 5 patients with central CP, 4 of 12 with hypothalamic stalk CP, 1 of 4 with suprasellar stalk CP, and 1 of 8 with intrasellar stalk CP, with no statistical difference between CP types. Our results showed that cognitive impairment as a marker of hypothalamic damage was found only in CPs of hypothalamic origin (classified as central and hypothalamic stalk CP). We conclude that this classification, based on preoperative MR findings, can predict hypothalamic damage. Suprasellar and intrasellar stalk CP may not involve the hypothalamus and therefore can be safely resected with no hypothalamic damage.

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Reproductive and Developmental Endocrinology

P180 European Registries for Rare Endocrine Conditions (EuRRECa): results from the e-Reporting platform for rare conditions (e-REC) Salma Rashid Ali1,2, Jillian Bröye3, Ana Luisa Priego Zurita4, Martine Cools4, Thomas Danne1, Harshini Kattigampola5, Olaf M. Dekkers1, Olaf Hiort6, Agnès Linglart7, Irene Netchine8, Anna Nordenström9, Attila Patöcs10, Alberto M Pereira11, Luca Persani13,14, Nicole Reisch15, Arelene Smyth16, Zdeněk Sumnik17, Domenica Tardisco18, Edward Visser19, Natasha Appleman-Dijkstra20 & Faisal Ahmed21 1Developmental Endocrinology Research Group, School of Medicine, Dentistry & Nursing, University of Glasgow, UK; 2Office for Rare Conditions, Royal Hospital for Children & Queen Elizabeth University Hospital, Glasgow, UK; 3Dept of Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, Netherlands; 4Department of Internal Medicine and Paediatrics, Ghent University, Belgium; Department of Paediatric Endocrinology, Ghent University Hospital, Ghent, Belgium;
Background

European Reference Networks (ERNs) in capturing rare conditions.

There is increasing acceptability of the e-REC platform which can be used to perform regular surveillance of specific events.

P181 Hormonal treatment modification during the long term follow-up of transwomen and transmen individuals: a retrospective observational Italian study

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Background

Persons with assigned either male (AMAB) or female (AFAB) sex at birth might wish to obtain feminization or masculinization, respectively. To this purpose, hormonal treatment with sex hormones must be tailored to each subject. Several studies and the European Society of Endocrinology guidelines tried to identify the optimal hormonal treatment in both AMAB and AFAB subjects. However, the clinical management in the long term follow-up remains challenging. Many treatment adjustments and/or shifts are clinically performed to reach the therapeutic goal, i.e. phenotypic characteristics of the perceived gender, minimizing adverse events.

Aim of the study

To evaluate treatment modifications/shifts required in the long term follow-up of AMAB and AFAB subjects treated with guideline-based hormone therapy adjusted according to biochemical results.

Methods

A retrospective, longitudinal, observational clinical study was carried out at the Andrology Unit of Modena (Italy). All AMAB and AFAB subjects evaluated since 2006 were considered eligible. All clinical consultations performed until January 2022 were collected, including data regarding previous medical history, comorbidities, physical examination, blood examinations, hormonal assessment, and therapeutic choice.

Results

A total of 120 subjects were enrolled, 69 AMAB (57%) and 51 AFAB (43%). AFAB subjects were significantly older (41.1 ± 9.1 vs 33.9 ± 8.8 years, P < 0.0001) and followed-up for longer time (36.8 ± 42.0 vs 23.4 ± 31.2 months, P < 0.0001) than AMAB.

In AFAB subjects, treatment modifications were performed 60 times (26.5%) during follow-up and the dropout rate was 2.0% (1 subject). Mean testosterone serum levels at follow-up were 6.7 ± 6.4 ng/dl. Therapy modifications were neither predicted by testosterone serum levels, nor comorbidities number, nor drug number (Cox logistic regression: 0.384, P = 0.061). In AMAB group, hormonal treatment was modified 164 times (45.1%) during follow-up, with a dropout rate of 24.6% (17 subjects). Mean oestradiol serum levels at follow-up were 49.8 ± 45.1 pg/ml. While therapy changes were not predicted by oestradiol serum levels (Cox logistic regression: 0.778, P = 0.194), they resulted directly related with the number of comorbidities (Cox logistic regression: 0.585, P = 0.025).

Conclusion

Our retrospective long term analysis on AFAB and AMAB subjects highlighted a comprehensive maintenance of sex hormones levels within therapeutic ranges burdened by frequent therapy modifications. These drug adjustments resulted more evident in AMAB subjects, in which treatment changes seemed related to the presence of comorbidities. Considering also the higher dropout rate compared to AFAB, AMAB subjects seem to require a more stringent clinical management during follow-up.

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P182 Defining reference ranges for serum anti-Müllerian hormone (AMH) on a large cohort of normozoospermic adult men highlights new potential physiological functions of AMH on FSH secretion and sperm motility

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Background

Defining reference ranges for serum anti-Müllerian hormone (AMH) on a large cohort of normozoospermic adult men highlights new potential physiological functions of AMH on FSH secretion and sperm motility.
Intranasal kisspeptin administration stimulates reproductive hormone secretion in healthy volunteers and patients with hypogonadism.

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**Background**
Kisspeptin is a critical activator of hypothalamic gonadotrophin releasing hormone (GnRH) neurons and has significant potential to treat common reproductive disorders. To date, kisspeptin has solely been administered to humans via the intravenous or subcutaneous routes, however intranasal administration could offer a novel non-invasive delivery route. We therefore sought to determine the effects of intranasal kisspeptin on reproductive hormone release in humans for the first time.

**Methods**
Randomised, double-blinded, placebo-controlled, cross-over study in 12 healthy men (mean ± SEM age 28.3 ± 1.7 years; BMI 24.5 ± 0.7 kg/m²). After monitored self-administration of intranasal kisspeptin-54 (3.2, 6.4, 12.8 and 25.6 nmol/kg) or 0.9% saline, serum reproductive hormone levels were measured every 15 minutes for 4 h. Subsequently, four women (mean age 29.8 ± 3.7 years; BMI 21.2 ± 1.1 kg/m²) with hypothalamic amenorrhoea (HA) attended for the same protocol comparing intranasal kisspeptin-54 (12.8 nmol/kg) and 0.9% saline. Mean ± SEM was presented. Time profiles of hormone levels were compared using two-way ANOVA, and multiple means using one-way ANOVA.

**Results**
In healthy men, intranasal kisspeptin dose-dependently increased mean luteinising hormone (LH) levels at doses between 3.2-12.8 nmol/kg (P < 0.008 and <0.0001 for 6.4 and 12.8 nmol/kg vs saline, respectively), with the maximal rises occurring 30-45 minutes post-administration. The maximal LH change from baseline was significantly elevated following all kisspeptin doses vs saline (saline: 1.54 ± 0.30 IU/l; 3.2 nmol/kg: 2.46 ± 0.30 IU/l [P = 0.01]; 6.4 nmol/kg: 3.08 ± 0.48 IU/l [P = 0.04]; 12.8 nmol/kg: 4.45 ± 0.59 IU/l [P = 0.002]; 25.6 nmol/kg: 4.07 ± 0.66 IU/l [P = 0.003]). Follicle stimulating hormone (FSH) levels followed a similar trajectory to LH. Kisspeptin at 12.8 nmol/kg increased serum testosterone from 120 minutes onwards (P < 0.02)., with a maximal change from baseline of 4.9 ± 0.7 nmol/l (P = 0.03). In women with HA, intranasal kisspeptin increased mean LH (P = 0.002 vs saline), with the peak levels occurring 30-45 minutes post-administration. The maximal LH change from baseline was 4.06 ± 0.89 IU/l, compared with 0.20 ± 0.38 IU/l for saline (P < 0.03). Intranasal kisspeptin increased mean FSH (P = 0.01 vs saline). No significant changes in downstream serum oestradiol or progesterone were observed during the acute four-h study.

**Conclusions**
We report the first investigation of the effects of intranasal kisspeptin delivery on reproductive hormone release. Our results demonstrate that intranasal kisspeptin robustly and dose-dependently stimulates reproductive hormone release in healthy men and in a patient-group of women with hypogonadism. Given the ongoing development of kisspeptin therapeutics, intranasal kisspeptin offers a novel, safe, effective and non-invasive route of administration for the management of reproductive disorders that would be preferred by patients and clinicians alike.

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**P184**
Effects of testosterone therapy on bone turnover markers and bone mineral density in obese males with type 2 diabetes and functional hypogonadism.

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**Aims**
Both functional hypogonadism (FH) and type 2 diabetes (T2D) negatively affect bone mineral density (BMD). We aimed to evaluate changes on bone turnover markers (BTMs) and BMD in obese males with FH and T2D due to testosterone therapy (TTh).

**Research Design and Methods**
55 obese males with FH and T2D participated in a two-year (first year double-blind, placebo-controlled study, second year follow-up) clinical trial. Participants were randomized into two groups. Group T (n = 28) received 1000 mg testosterone undecanoate (TU) both years of the study while group P (n = 27) received placebo first year and TU second year. BTMs C-telopeptide of type I collagen (CTX) and procollagen I N-terminal propeptide (PINP), estradiol, 25-hydroxyvitamin D, total, calculated free and calculated bioavailable testosterone levels were assessed at baseline, 12 and 24 months. BMD changes were evaluated at baseline and after 24 months using dual-energy x-ray absorptiometry (DXA).

**Results**
Results show decrease in median CTX from baseline of 1055 (676 to 1344) pmol/l to 911 (556 to 1152) pmol/l after one year of TTh (P < 0.001) in group P and from 887 (648 to 1496) pmol/l to 504 (262 to 804) pmol/l after first year of TTh (P < 0.001), then to 372 (165 to 599) after second year of TTR (P < 0.001) in group T. Median PINP did not change from 31.4 (27.1 to 40.3) µg/l at baseline to statistically significant level after one year of placebo (P = 0.006) in group P but decreased to 28.0 (23.6 to 32.0) µg/l after one year of TTh (P = 0.009), then in group T a decrease from 30.9 (21.9 to 35.3) µg/l to 26.2 (18.6 to 32.1) µg/l was observed after first year of TTh (P = 0.005), then to 20.1 (17.8 to 26.5) µg/l after second year of TTR (P < 0.001). DXA showed no changes in femoral neck BMD in 32 patients from both groups. P (n = 16) or T (n = 16) while a statistically significant increase in lumbar spine BMD by 0.075 ± 0.114 g/cm² (95% CL 0.14 to 0.136; P = 0.019) has been observed in group T following two years of TTh.

**Conclusions**
BTMs decreased significantly after TU and improvement of lumbar spine BMD was observed after two years of TTh in obese males with FH and T2D.

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Management of 46, XY 17 alpha-hydroxylase deficiency: a case report
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Introduction
17 alpha-hydroxylase deficiency (17OHD) is a rare autosomal recessive disease caused by mutations in the CYP17A gene, representing 1% of cases of Congential Adrenal Hyperplasia (CAH). The accumulation of mineralocorticoids and the glucocorticoid effect of corticosterone induce high blood pressure (HBP) and hypokalemia.

Clinical Case
A 44 year-old female reporting HBP since the age of 20 years and without chronic medication, presented at the emergency department (ED) complaining of generalized asthenia and polyarthalgia for about two weeks. On examination, she was hypertensive (174/100 mmHg); blood analysis revealed severe hypokalemia — K+ 1.2 mEq/l (3.5-5.1). In the ED, she had an episode of ventricular tachycardia evolving to asystole. After resuscitation, she was transferred to the Intensive Care Unit with rapid clinical improvement under antihypertensive therapy and hydrocortisone. Further laboratory evaluation showed: cortisol <0.4 mg/dl (1.7-19.4), ACTH 213 pg/ml (<46), aldosterone (decubitus) 27.4 ng/dl (1-16), renin <1.8 mU/L (2.8-39.9). Due to these findings, she was transferred to the Endocrinology ward. On examination, she had an uncharacteristic morphotype, BMI 16.7 kg/m² (175 cm; 51.2 kg), cutaneous hyperpigmentation and Tanner stage MIP1. Hormonal evaluation showed: LH 64 mIU/ml (folicular phase 1.8-11.8), FSH 97 mIU/ml (3.03-8.08), estradiol 17 pg/ml (0.1-0.3), progesterone 5.2 ng/ml (0.1-0.3), 17-OHP 0.19 ng/ml (0.21-1.45), total testosterone 0.03 ng/ml (0.11-0.56), CT scan revealed bilateral adrenal hyperplasia (right width 11.5 mm; left width 12.9 mm) and absence of female internal genitalia (explaining primary amenorrhea referred by the patient).

Genetic diagnosis was confirmed by the identification of the c.3G>A p.(Met1?) variant in homozygosity in the CYP17A1 gene. Karyotype analysis was compatible with 46 XY. At the last appointment, the patient was normotensive under dexamethasone 0.5 mg id, spironolactone 50 mg id, olmesartan 40 mg id, nifedipine 60 mg bid and nebivolol 5 mg id; blood analysis revealed severe hypokalemia — K+ 1.2 mEq/l (3.5-5.1). In the ED, she had an episode of ventricular tachycardia evolving to asystole. After resuscitation, she was transferred to the Intensive Care Unit with rapid clinical improvement under antihypertensive therapy and hydrocortisone. Further laboratory evaluation showed: cortisol <0.4 mg/dl (1.7-19.4), ACTH 213 pg/ml (<46), aldosterone (decubitus) 27.4 ng/dl (1-16), renin <1.8 mU/L (2.8-39.9). Due to these findings, she was transferred to the Endocrinology ward. On examination, she had an uncharacteristic morphotype, BMI 16.7 kg/m² (175 cm; 51.2 kg), cutaneous hyperpigmentation and Tanner stage MIP1. Hormonal evaluation showed: LH 64 mIU/ml (folicular phase 1.8-11.8), FSH 97 mIU/ml (3.03-8.08), estradiol 17 pg/ml (0.1-0.3), progesterone 5.2 ng/ml (0.1-0.3), 17-OHP 0.19 ng/ml (0.21-1.45), total testosterone 0.03 ng/ml (0.11-0.56), CT scan revealed bilateral adrenal hyperplasia (right width 11.5 mm; left width 12.9 mm) and absence of female internal genitalia (explaining primary amenorrhea referred by the patient).

Genetic diagnosis was confirmed by the identification of the c.3G>A p.(Met1?) variant in homozygosity in the CYP17A1 gene. Karyotype analysis was compatible with 46 XY. At the last appointment, the patient was normotensive under dexamethasone 0.5 mg id, spironolactone 50 mg id, olmesartan 40 mg id, nifedipine 60 mg bid and nebivolol 5 mg id; blood analysis showed K+ 4.7 mEq/l and aldosterone 20.4 ng/dl.

Conclusion
The association of severe hypokalemia, hypertension, hypocortisolism, oligoamenorrhea and the absence of secondary sexual characteristics favored the diagnosis of 17OHD, confirmed by genetic testing. As in other published cases, diagnosis outside pediatric age is not rare and should be considered in cases of severe hypokalaemia in hypertensive adults and lack of secondary sexual development.

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Glycaemic and metabolic effects of testosterone replacement in hypogonadal men with uncontrolled type 2 diabetes — a randomised double blinded placebo controlled trial — stride study
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The objective of the study was to assess the effect of intra-muscular testosterone on glycemic control, metabolic parameters and hypogonadal symptoms in men with hypogonadism and poorly controlled type 2 diabetes. This is a randomised double-blinded placebo-controlled add-on trial of intramuscular-testosterone undecanoate (Nebido™) administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase-1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase-2 was an open-labelled phase for 6 months and patients on placebo moved on to the treatment group wherein patients in the treatment group continued. Anthropometric measurements, questionnaires and biochemical parameters were assessed at baseline and every three months for a year. Mean age of the cohort was 59 ± 8.9 years (mean ± SD). Mean duration since diagnosis of diabetes was 8.6 years. 17(26%) were on insulin. Baseline cohorts were comparable. There was no improvement in mean HbA1c or fasting plasma glucose(FBG) between the active and placebo groups after 6 months of TRT. No difference was found in HbA1c or FBG at 12 months compared to baseline in the active group either. Our study also showed a significant decrease in serum triglycerides(-0.497 ± 0.213 mmol/L, P = 0.023) and improvement in left hand grip strength(P = 0.025) at 6 months post treatment in the active group compared to placebo group. There was no significant difference in the mean weight, BMI, WC, WHR, fat mass, fat percentage or fat free mass between the groups. Our study is the first ever RCT to show a significant improvement in total AMS(aging male symptom) scores from baseline after 6 months of TU treatment compared to placebo group(P <0.05) in a cohort with poorly-controlled type 2 diabetes and hypogonadism. Another key finding is that the proportion of patients with severe symptoms moving to a less severe category(low/mild/moderate severity) was 46% in the active vs only 28% in placebo(P = 0.0024). Our study concludes that TRT did not have a significant improvement in glycaemic control at 6 months between the active/placebo groups and at 12 months within the active group and may need longer duration to see the positive effects especially in cohort of people who have had long duration of diabetes. There was a significant reduction in triglyceride levels and increase muscular-strength after 6 months of TRT. STRIDE study is the first ever RCT to show a significant improvement in clinical symptoms and symptom severity following testosterone treatment in patients with hypogonadism and type 2 diabetes after 6 months of TRT.

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Overall impact of gender affirming hormone therapy: the portuguese experience
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Introduction
The prevalence of Transgender individuals seeking gender affirming hormone therapy (GAHT) has been increasing. This therapy has been known to be highly effective in the treatment of gender dysphoria and enhancing mental health in this population.

Aim
To evaluate the overall impact of GAHT on self-esteem, well-being and social/familial relations in the Portuguese adult transgender population

Methods
Cross-sectional study conducted in March 2021. Data collected through an online questionnaire that was delivered to adult transgender people living in Portugal who had been under GAHT for at least one year. To answer some of the items on the questionnaire, an ordinal scale ranging from 0 (worst result) to 6 (best result) was used.

Results
A total of 142 individuals (Group T) answered the questionnaire: 101 under GAHT for at least one year. To answer some of the items on the questionnaire, an ordinal scale ranging from 0 (worst result) to 6 (best result) was used.

Discussion
This study reinforces that transgender people report high grades of satisfaction with both the physical and psychological effects of GAHT. This therapy seems to significantly enhance self-esteem, body wellbeing and social/familial relations and to reduce suidical ideation, having an overall great impact on the quality of life of transgender people.

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The objective of the study was to assess the effect of intra-muscular testosterone on constitutional symptoms, sexual symptoms, memory and in men with hypogonadism and poorly-controlled type-2 diabetes. This is a randomised double-blind placebo-controlled add-on trial of intramuscular testosterone undecanoate (Nebido®) administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase-1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase-2 was an open-labelled phase for 6 months and patients on placebo moved on to the treatment group wherein patients in the treatment group continued. Outcomes (AMS, SF-36, IIEF-5 questionnaires, MMSE, Barnsley and NERI questionnaires) were assessed at baseline and every 3 months.

Mean age of the cohort was 59.5 years (mean ± SD). Baseline characteristics were comparable between active/placebo groups. The study also showed that the proportion of patients with severe symptoms moving to a less severe category (low/mild/moderate severity) was 46% in the active vs only 28% in placebo group (P = 0.0024). There was no significant difference in either the SF-36 scores, MMSE scores, BDHQ, NERI or IIEF scores or its domains at baseline and after 6 months of TRT. In phase-2 of the trial, there was a statistically significant reduction in the AMS total score all its subscales before and after TRT in the active arm at 12 months. A significant improvement in libido was also demonstrated. There was a significant reduction in the BDHQ total score (P = 0.07) and two of its sub-domains — Sexual-wellbeing and Emotional-wellbeing (P = 0.002 and P = 0.011 respectively) within the active arm before and after treatment of testosterone at baseline (P = 0.0024). There was significant improvement in the mean scores of physical health domain and health change in over 1-year domain of SF-36 questionnaire (P = 0.014) before and after treatment in the active arm at baseline (0, 3, 6, 9 and 12 months post-treatment. Our trial is the first RCT to show a significant improvement in constitutional symptoms, sexual symptoms, libido, symptom severity, and delayed verbal recall with TRT in a cohort with poorly-controlled type-2 diabetes and hypogonadism.

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P189
Is there a link between polycystic ovary syndrome and transgenerational transmission of a reproductive and metabolic function in male offspring?
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Our previous study showed that polycystic ovary syndrome (PCOS)-like reproductive and metabolic phenotypes induced by maternal dihydrotestosterone (DHT)-exposure, can be passed on in mice from mothers (F0) to daughters (F1),...
granddaughters (F3), and even to great-granddaughters (F4). The female transmission is independent of diet-induced obesity and is mediated by transcriptional and mitochondrial perturbations of oocytes accompanies. How maternal DHT-exposure and obesity affect their male progeny across generations is less known. Based on two clinical studies: a Swedish nationwide register and a Chilean case-control study, we found that sons of mothers with PCOS are more obese and have dyslipidemia. Next, we investigated whether diet-induced maternal obesity and/or prenatal DHT-exposure in mice, mimicking both the lean and the obese PCOS phenotype, result in transgenerational transmission of a PCOS-like phenotype in male offspring via male germline. We find a transmission of reproductive and metabolic dysfunction in F1 and F2 male offspring in both androgenized and obese lineages, respectively, but with stronger phenotype in the obese lineage. Small non-coding RNAs (sncRNAs) sequencing of sperm from F1 and F2 male offspring revealed common differential expressed sncRNAs (DEsncRNAs) across generations in androgenized, obese, and obese and androgenized lineages, with distinct regulatory patterns among lineages. Three of the predicted targets of PIWI-interacting RNA and micro RNAs were also differentially expressed in serum from sons of PCOS mothers. Our results reveal a previously unknown risk of reproductive and metabolic dysfunction in male progeny of PCOS mothers, which is likely caused by epigenetic germline changes by sncRNAs.

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P190
The role of B cells in immune cell activation in polycystic ovary syndrome
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Objective
Age-associated double negative (DN) B memory cells lacking surface expression of CD27 and immunoglobulin D (IgD) are associated with proinflammatory characteristics and higher disease activity in autoimmune diseases. We first characterized B cells phenotypes in women with and without polycystic ovary syndrome (PCOS). We then took an in vivo approach, transferring purified IgG extracted from serum of hyperandrogenic women with PCOS to mice to establish whether self-reactive B cells have a causal effect on the development of a PCOS-like phenotype.

Methods
We initially characterized major B cell lineages in serum of hyperandrogenic women with PCOS and of women without PCOS (controls). We purified IgG from the serum of women with PCOS (PCOS IgG) and controls which was applied in whole blood, spleen, lymph node, ovary, endometrium, visceral adipose tissue.

Results
Immunophenotypic analyses showed a significant remodeling of B cell repertoire in women with PCOS compared with controls: higher frequencies of DN B memory cells were found in PCOS patients (P=0.0002), with declined IgD+ B memory cells (P=0.011). Total testosterone was an independent predicting variable for IgM variability (P=0.01). Transfer of human PCOS IgG into female WT mice resulted in PCOS-like phenotype with higher circulating estrogens and trend of increased androgens, as well as higher body weight (P<0.05). Preliminary results from immune profiling showed an overall increase of DN B cells in mice receiving PCOS IgG, particularly DN2 subsets with a CD21+ phenotype, with increased frequencies of active naïve cells and neutrophils in ovary.

Conclusions
Women with PCOS display an increased peripheral expansion of DN B cells. Exposing mice with IgG from women with PCOS rapidly induced an altered immune cell profile with increased body weight and circulating sex steroids. PCOS may represent a state of inflammatory-cell hypersensitivity and chronic inflammation, resulting in remodeling of the lymphocytes. The ongoing transfer of purified B cells from prepubertal hyperandrogenic mouse model into mice B cell deficient mice (μMT−) will define the overall impact of androgen exposure on B cell phenotypes.

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P191
FSH and bone: comparison between males with central vs primary hypogonadism
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Background
Recent data suggest a direct effect of follicle stimulating hormone (FSH) on the skeletal metabolism. Particularly, it can encourage bone resorption and also inhibit osteoblast differentiation. High FSH levels have been found to correlate with impaired bone health in females, whilst evidence in males remains somewhat poor and conflicting. Intriguingly, men with primary and central hypogonadism might represent a novel study model in this context.

Aims
To investigate the possible association of FSH excess with male osteoporosis.

Patients and Methods
119 men, consecutively referred to Istituto Auxologico Italiano and Newcastle upon Tyne Hospitals, were enrolled in this prospective cross-sectional observational study at the time of the first diagnosis of hypogonadism. All participants had spontaneous pubertal development. Regarding those with hypergonadotropic hypogonadism (Hyper Hipo), patients with a pre-pubertal onset form (PPO) (i.e., Klinefelter syndrome) were distinguished from the ones with an adult-onset form (AO) based on the onset of FSH elevation. Bone mineral density (BMD) at both lumbar spine (LS) and femoral neck (FN) was measured using dual-energy X-ray absorptiometry. The prevalence of morphometric vertebral fractures (VFx) was evaluated by performing spinal radiographs.

Results
Across the whole cohort, LS and FN BMD were directly associated with age at diagnosis and body mass index (BMI), respectively. After adjusting for potential confounders (age at diagnosis, BMI, smoking habits, calculated free testosterone (cfT) and 25OH vitamin D levels) by means of General Linear Model analysis, AO-Hyper Hypo patients showed significantly lower LS BMD and tended to show lower FN BMD values, as compared to those with hypogonadotropic hypogonadism (Hypo Hipo). In men with PPO-Hyper Hipo LS BMD was significantly lower than in AO-Hyper Hipo ones. No significant differences in the prevalence of VFx were found between the groups.

Conclusions
This is the first prospective study comparing men with primary and central hypogonadism in order to better delineate the putative role of FSH on the male bone health. These findings indicate a potential negative effect of FSH excess on the male bone mass, especially at spine. The duration of high FSH levels may also play a part in this setting. Longitudinal studies, involving hypogonadal men on testosterone replacement therapy, are required. Indeed, it would be crucial to identify new risk factors and mediators of male bone

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P192
Simulation via instant messaging - birmingham advance (SIMBA) as a tool to bridge gaps in clinical knowledge and expectations between physicians and patients with polycystic ovary syndrome

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Introduction
Polycystic Ovary Syndrome (PCOS) is the most common endocrinopathy in women. Studies exploring the experiences of people with PCOS reveal inadequate patient access to information and limited insight into healthcare professionals’ (HCP) attitudes regarding the condition. Simulation via Instant Messaging-Birmingham Advance (SIMBA) is a virtual simulation platform proven to increase learners’ confidence in their approach to simulated cases with high acceptance rate and reproducibility. However, participation in previous SIMBA sessions has been limited to HCPs.

Objectives
To assess the effectiveness of SIMBA in improving HCPs’ knowledge on diagnosis and management of health conditions related to PCOS and recognise areas of disparity in knowledge and clinical expectations between HCPs and patients with PCOS.

Methods
Anonymised transcripts based on real-life cases were prepared with expert input and used to train moderators. The transcripts were used to deliver WhatsApp-based simulation to HCPs and parallel Zoom-based workshops to people with PCOS. HCPs were guided through the cases by moderators, eliciting history, proposing diagnoses, and management plans. People with PCOS discussed the same cases and reflected upon case management based on personal experiences. Patient and HCPs convened for a Q&A discussion at the end of the session where cases were discussed by experts and patient reflections were shared. Participants filled in pre and post SIMBA surveys.

Results
25 HCPs and 15 participants participated in the session. HCPs reported a 41% and 49% increase in confidence in the management of simulated cases (skin, weight, fertility and menstrual periods related issues in PCOS: P<0.001) and non-simulated cases (metabolic outcomes, menopause, mental health and endometrial cancer; P<0.001, respectively). HCPs reported that SIMBA improved their professionalism (28%) and communication skills (40%) and had a positive personal (84%) and professional (92%) impact. Participants reported a 17.7% increase in confidence regarding HCPs’ awareness of management options for all cases following the session (P=0.0002). Thematic analysis of participant feedback revealed that 83.3% found the session engaging, organised and insightful. 90% of HCPs agreed that the session improved patients’ understanding of the diagnosis and management of PCOS and 100% believed that the session improved their own understanding of patient experiences.

Conclusion
SIMBA is known to be an effective educational tool that reduces discrepancies in clinical expectations between HCPs and patients and improves HCPs’ confidence in managing simulated cases. It promotes transparent discussion of clinical practice and patient experiences, thereby strengthening doctor-patient relationships.

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P193
Efficacy of very low calorie ketogenic diet in obese PCOS: a randomized controlled study

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Background
Very low-calorie ketogenic diet (VLCKD) was shown to be effective in reducing weight and insulin resistance (IR) in obese patients. Considering that IR is very common in women with polycystic ovary syndrome (PCOS), and that IR worsens hyperandrogenism, ovulatory dysfunction, and body fat accumulation, conceivably VLCKD could alleviate PCOS manifestations in the obese phenotype.

Objective
This study compared the effects of a commercial VLCKD ("PnK method") and the control low calorie standard diet (LCD) on body weight and composition, insulin resistance, ovulation and hyperandrogenism in a population of obese PCOS.

Methods
This is an open-label, monocentric, randomized controlled trial (NCT04801173), supported by Pronokal Health group S.L. Women aged 18-45 years with PCOS diagnosed using the NIH criteria were randomized into the VLCKD or LCD group (15 vs 15). VLCKD group followed the VLCKD for 8 weeks, switching to the LCD for 8 weeks more, while the LCD group followed the LCD for 16 weeks. Ovulation monitoring by progesterone measurement and pelvic ultrasound was done at baseline and at the end of the study (week 16), while a clinical exam, bioelectrical impedance analysis (BIA) anthropometry, and biochemical analyses were performed at baseline, at week 8, and at week 16 of the study. Androgens were measured by tandem liquid chromatography-mass spectrometry. Free testosterone (freeT) was calculated using the Vermeulen formula. Repeated measures general linear model was used to evaluate within- and between-group differences for continuous variables.

Results
2 dropouts occurred in the VLCKD group, 1 in the LCD group. Body weight decreased significantly in both groups, but more so in the VLCKD group – average difference 12.4 kg (−13.6%) vs 4.7 kg (−5.3%) (P<0.001). Significant differences between the VLCKD and LCD groups were also seen in waist circumference (−8.1% vs −2.2%), BIA-measured body fat (−15.1% vs −8.5%), and freeT (−30.3% vs +10.6%), over the course of the study (P<0.004, P=0.02, and P=0.002, respectively). HOMA-IR index also decreased more in the VLCKD group during the first 8 weeks (−36.1% vs −26.1%, P=0.02). At baseline, 5/13 (38.5%) participants in the VLCKD group and 2/14 (14.3%) participants in the LCD group had ovulatory cycles, which diﬀerentially increased to 11/13 (84.6%) and 5/14 (35.7%) at post-intervention monitoring, respectively (McNemar, P=0.031).

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Polycystic Ovary Syndrome (PCOS) is an endocrine disorder affecting 10-15% of women worldwide, characterized by high androgen levels, anovulation and/or diabetes. To define the role of the immune system in the pathophysiology of PCOS, we characterized the immune profile of dihydrotestosterone (DHT)-induced PCOS-like mouse model. Prepubertal female mice implanted with a DHT-pellet displayed reproductive dysfunction, with a disrupted estrous cyclicity and increased anogenital distance, and a metabolic phenotype similar to the comorbidities seen in women with PCOS, with increased body weight and fat mass (EchoMRI), higher fasting glucose and impaired glucose uptake following a meal. Chronic low-grade inflammation is associated with the development of PCOS and metabolic comorbidities seen in women with PCOS, with increased body weight and fat mass. Consistent with our previous findings, the decreased thymic weight in the DHT-induced PCOS model suggests a reduced T lymphocyte population in blood. Interestingly, there was no difference in the number of CD4+ T helper cells, neither in blood nor spleen. The same effect on eosinophils was seen compared to control, whereas infiltration of peripheral NK cells was increased. This is supported by the decreased thymic weight in the DHT-induced PCOS model. In summary, we show that the prepubertal PCOS-like model displays an altered immune profile in a wide range of tissues. Whether these alterations are a result of androgen receptor activation and/or a result of metabolic dysfunctions remains to be elucidated, and it remains to define what impact these immune alterations have on reproductive and metabolic function.

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**P196 Effects of octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane on female reproductive systems in rat**

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In our daily life, humans are exposed to lots of chemicals. Among those chemicals, octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) have been widely used in cosmetics for their functions such as softening, wetting, and viscosity control. However, the effect of these chemicals on the female reproductive systems has not been clearly elucidated. In the case of D4, it was recently recognized as an endocrine disrupting chemical (EDC), but the effect of D5 has been unknown. In vitro study, the human uterus epithelial-like Ishikawa cells, were treated with D4 and D5 to measure cell viability. In both D4 and D5 showed, decreased cell viability at the 10^{-4} M. It means both chemicals are toxic in uterus. In vivo study, female Sprague Dawley rats were exposed to D4 and D5 diluted in corn oil for 2 weeks. At this time corn oil (Vehicle), 60 mg/kg/day (D4), and 100 mg/kg/day (D5) were administrated by using oral injection. Result shows there was no significant difference in uterine epithelial and stromal marker gene expression. On the other hand, ovary folliculogenesis and steroidogenesis gene expression were varied. HE staining results showed that increased uterine glands and ovary follicles number. Therefore, this study suggests that D4 and D5 aggrivated female reproductivity such as miscarriage and implantation failure.

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**P197 Functional analysis of anti-mullerian hormone variants in patients with polycystic ovary syndrome**

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Objective

Recently rare heterozogous AMH genetic variants have been identified in women with polycystic ovary syndrome (PCOS) that result in reduced AMH signaling. However, the exact functional mechanism remains unknown. Therefore, we have performed functional analyses to analyze the processing, secretion and signaling of these PCOS-specific AMH rare variants.

Methods

Six PCOS-specific AMH variants containing mutations (V12G, P151S, P270S, P352S, P362S, H506Q) were selected based on previous findings. The variants were introduced in an AMH expression vector containing either a wild type (AMH-RAG) or optimized cleavage site (AMH-RARR) and co-expressed with the BRE-Luc reporter in the mouse granulosa cell line KK-1. The AMH expression vectors were stably expressed in HEK293 cells for Western blot analysis and ELISA.

Results

Expression of AMH-P151S and AMH-H506Q decreased AMH signaling by ~90% (P <0.001), depending on the presence of a RARR or RAG cleavage site. Signaling of the other four variants was comparable to wild-type (wt)-AMH. Coexpression of the variants with wt-AMH at equal amounts confirmed that AMH-P151S and AMH-H506Q significantly inhibited the signaling activity of wt-AMH by ~30% (P <0.001). Transfection of increasing amounts of these two variants resulted in a further inhibition, which was independent of the cleavage site. To explain this dominant negative effect, we next analyzed the impact of AMH cleavage on AMH signaling. Cells were transfected with an AMH construct containing an inactive cleavage site (AMH-RAGA) in combination with exogenous AMH treatment. We observed that exogenous AMH-induced signaling was suppressed by 30% (P <0.001) in the presence of AMH-RAGA. In contrast, exogenous AMH-induced signaling was not affected when AMH-P151S or AMH-H506Q was transfected. Indeed, Western blot analysis showed that AMH-P151S and AMH-H506Q proteins were only detected in the cell lysate but not in the supernatant, even in the presence of RARR cleavage site. In contrast, wt-AMH and the P352S and P362S variant were detected in both the cell lysate and the supernatant. Further supporting these results, confocal image analysis showed that cells expressing AMH-P151S and AMH-H506Q retained significantly higher cellular AMH protein levels with a highly abnormal

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Results

We compared various cardiovascular (CV), anthropometric, metabolic, and hormonal features of normotensive PCOS patients and healthy women. This case-control observational study involved 249 normotensive PCOS and 85 healthy eumenorrheic women. Based on blood androgen concentrations, PCOS patients were divided into HAPCOS (n = 69) or non-HAPCOS (n = 180) groups. NT-proBNP was measured using Cobas 6000 Analyzer with electrochemiluminescence sandwich immunoassays (Roche Diagnostics GmbH, Germany).

HAPCOS patients had significantly higher NT-proBNP concentration than non-HAPCOS women (34.57 vs. 39.77 pg/ml; P = 0.021) and controls (41.58 pg/ml; P = 0.01). NT-proBNP levels were comparable between non-HAPCOS and controls. HAPCOS patients had also significantly higher peripheral and central systolic BP and pulse pressure (PP), C-reactive protein, low-density lipoprotein cholesterol, triglycerides, glucose, and insulin than non-HAPCOS and healthy women. Still, these results were within normal ranges. However, body mass index (BMI) of HAPCOS subjects was over 4 kg/m² higher than in non-HAPCOS and healthy controls. HAPCOS patients had also significantly higher peripheral and central systolic BP and pulse pressure (PP), C-reactive protein, low-density lipoprotein cholesterol, triglycerides, glucose, and insulin than non-HAPCOS and healthy women. Still, these results were within normal ranges. However, body mass index (BMI) of HAPCOS subjects was over 4 kg/m² higher than in non-HAPCOS and healthy controls.

Conclusions

Our results suggest that the PCOS-specific AMH variants P151S and H506Q disrupt normal processing and secretion of AMH. Our results further suggest that these AMH variants hamper secretion of wt-AMH, explaining the dominant negative effect of these variants on AMH signaling.

P198

Blue Morpho: An international survey investigating differences in emotional and psychosexual wellbeing by ethnicity and birthplace in women with polycystic ovary syndrome

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Objective

This study investigated the association between ethnicity, birthplace and emotional and psychosexual wellbeing in women with Polycystic Ovary Syndrome (PCOS) in the community.

Design

International cross-sectional study.

Methods

Women with a self-reported PCOS diagnosis by a healthcare professional were invited to complete an online Blue Morpho questionnaire between September-October 2020 (UK) and May-June 2021 (India). Four validated questionnaires were included: Hospital Anxiety and Depression Scale (HADS) to examine anxiety and depression; Body Image Concern Inventory (BICI) to assess dysmorphic appearance concerns; Beliefs About Obese Persons Scale (BAO) to investigate beliefs about causes of obesity; and Female Sexual Function Index (FSFI) to assess domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction and pain). Adjusted linear and logistic regression models were used to evaluate the relationship between ethnicity (White vs Non-white) and country of birth (UK vs India), and questionnaires scores and outcomes (Anxiety and/or Depression [HADS ≥ 11] and Body Dysmorphic Disorder [BDD; BICI ≥ 72]).

Results

1008 women with PCOS completed the questionnaire. 44.8% were in the 26-35 age category, 44.9% had an undergraduate degree, 53.9% were single and 84.1% did not have children. The prevalence of anxiety and depression was 60.6% and 24.3%, respectively. Women of non-white ethnicity (60.7%; n = 611) reported higher prevalence of depression (OR 1.96 [95% CI 1.41-2.73]) but lower BDD (OR 0.57 [95% CI 0.41-0.79]) prevalence compared to white ethnic women (38.9%; n = 392). Similarly, women born in India (44.9%; n = 453) had higher prevalence of anxiety (OR 1.57 [95% CI 1.00-2.46]) and depression (OR 2.20 [95% CI 1.52-3.18]) but lower BDD prevalence (OR 0.42 [95% CI 0.29-0.61]) compared to women born in the UK (43.0%; n = 433). Both groups of white ethnic women and women born in the UK reported higher psychological illbeing, higher BCI and BAOP scores. However, overall sexual wellbeing and all FSFI sexual domains, excluding desire, were significantly impaired for both groups of non-white ethnic women and women born in India.

Conclusion

This study reveals the significant influence of ethnicity and birthplace on emotional and psychosexual wellbeing among women with PCOS, focusing on poor body image, weight stigma and sexual dysfunction. This highlights the importance of providing an individualised, holistic multidisciplinary approach alongside clinical care for women with PCOS and improving awareness of the significant influence of ethnicity and birthplace on PCOS related outcomes amongst primary healthcare providers to improve patient care.
P438
Central precocious puberty developed after treatment of Leydig cell tumor: case report
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Background
Leydig cell tumors (LCTs) are the most prevalent hormone-secreting testicular tumors, but overall, a rare testicular tumor subtype. Surgery is the main therapy with a favorable prognosis. Nevertheless, the development of central precocious puberty after surgery of the tumor has been observed on rare occasions.

Case Report
An 8.5-year-old boy presented with symptoms of sexual precocity dating back to 4 years. He had pubic hair (P4), enlarged left testis (G3: right testis 4 cc, left testis 10 cc with a palpable nodule), and stature advance. The hormonal evaluation revealed high levels of testosterone and estradiol and low levels of FSH and LH. Ultrasound of the testes showed an inhomogeneous hypoechoic tumor of the left testis. An inguinal radical orchectomy managed this mass. The pathological diagnosis was a benign LCT. Three months after surgery, the patient presented persistent physical signs of sexual precocity, enlarged right testis, and stature gain of 8.5 cm. His hormonal values confirmed central precocious puberty: the testosterone level stayed high at 2.57 ng/ml facing LH and FSH levels at 3.26 U/I and 4.55 U/I respectively. Ultrasonography ruled out testicular tumor recurrence and brain magnetic resonance imaging excluded a tumor of the hypothalamus or pituitary gland. We started treatment with triptorelin (GnRHa analog). After 3 months of treatment, we observed clinical regression of physical signs and stabilized growth velocity. After 6 months, hormonal assessment showed that testosterone returned to prepuberal range (0.15 ng/ml), FSH and LH levels were 0.11 U/I and 0.43 U/I respectively. At the last follow-up (1 year from the beginning of triptorelin), we note a stature gain of 2 cm and a stabilization of the bone age with no adverse effects.

Discussion and conclusion
Eleven other cases of gonadotropin-dependent precocious puberty after successful treatment of LCTs have been reported in the literature. The mechanism is unknown but is hypothesized due to the rebound secretion of LH after surgery of LCTs and subsequent reduction in androgens, which suppressed the adrenomedullary. The true incidence of central precocious puberty remains unclear because long-term follow-up of children with LCTs is not available. GnRHa analog therapy appears to be the most effective medical treatment in such cases.

Key words
LCTs, central precocious puberty, GnRHa analog.

References

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P439
Coexistence of 46, XX testicular disorder of sex development and 11β-hydroxylase deficiency: In Vivo and In Vitro Studies
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Background
46, XX testicular disorder of sex development (DSD) and 11β-hydroxylase deficiency (11β-OHD) are two extremely rare types of disorder of sex development. No coexistence has been reported yet.

Case Description
Here we reported the first patient diagnosed as the coexistence of 11β-OHD and 46, XX testicular DSD basing on clinical, biochemical, molecular, cytogenetic, and functional experiment findings. A 22-year-old male showed small testes and gynecomastia for 2 years. At the age of 3, he was diagnosed as congenital adrenal hyperplasia (CAH). Adrenal ultrasound suggested the bilateral adrenal hyperplasia (both length*width=2.4*0.9 cm) and X-ray showed accelerated bone age (12.5 years old). Irregular cortisone acetate 6.25 mg per day was prescribed. At 4 years, he had pubic hair (P4), enlarged left testis (4.6 cm×2.4*0.9 cm) and X ray showed accelerated bone age (12.5 years old). Testicular ultrasound showed bilateral testicular dysplasia. To figure out these unexplainable results, whole exome sequencing was performed and revealed two copy number variants: duplication of Xp22.33-q28 spanning 151.32 Mb and deletion of Yp11.2-q11.23 spanning 23.34 Mb. Karyotype test by culuring blood lymphocytes showed 46, XX (100/100). Another disease, 46, XX (151.32 Mb and deletion of Yp11.2-q11.23 spanning 23.34 Mb). Here we reported the first patient diagnosed as the coexistence of 46, XX testicular DSD and 11β-OHD in the same individual. The case illustrates the complexity that might be encountered in the diagnosis of DSD when different genetic defects affecting sex development exist.

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Cardiometabolic risk factors and diabetes mellitus are related with the severity of menopausal symptoms in middle-aged women
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Background
Both surgical and spontaneous menopause are associated with increased cardiovascular disease (CVD) risk. Recent evidence reported that clusters of menopausal symptoms are associated with accumulation of cardiometabolic risk factors. Climacteric symptoms are also known to be affected by lifestyle parameters, ethnicity, the geographical location as well as by the overall health status at the time of the menopausal transition.

Aim
This study aimed to evaluate the association between menopausal symptoms, and lifestyle as well as cardiometabolic risk factors, in a cohort of apparently healthy middle-aged women.

Methods
This study consisted of 2,793 peri- and postmenopausal women (menopausal-age ≤ 15 years), not on menopausal hormone therapy, retrieved from the outpatient Menopause Clinic of the 2nd Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Greece. We assessed demographic and anthropometric parameters (including body mass index, BMI), and obtained fasting blood samples for evaluation of biochemical/hormonal data. The severity of menopausal symptoms was evaluated by the Greene Climacteric scale (GCS). Results
Mixed effect models showed that the total GCS-score associated with BMI (b = 0.12, 95% CI: 0.04 to 0.20), diagnosis of type 2 diabetes (T2DM, b = 2.10, 95% CI: 0.05 to 4.15), older age at menopause (menopausal age ≥ 7 years vs 2 to 7 years, b = -1.24, 95% CI: -2.17 to -0.33), Physical GCS score associated with BMI (b = 0.06, 95% CI: 0.03 to 0.09), central obesity (b = 0.18, 95% CI: 0.02 to 0.34), menopausal status (2 to 7 years vs > 7 years after the final menstrual period vs. perimenopause, b = -0.36, 95% CI: -0.59 to -0.13 and b = -0.65, 95% CI: -0.97 to -0.34, respectively). Psychological GCS-score associated with values of BMI (b = 0.06, 95% CI: 0.00 to 0.11). All previous GCS-scores associated negatively with age. Vasomotor GCS-score associated negatively with menopause-age > 7 years vs younger menopausal age. Poisson mixed models showed that GCS-sexual guideline, c.905_907delinsTT was identified as pathogenic variant, and c.954+7C>T, the novel one, was defined as variant of unknown significance. Pathogenicity of c.954+7C>T were further verified in COST, CHO, and 273T cell lines by in silico methods, which turned out to cause the gain of a cryptic one at the 5bp downstream of the original one. The patient was treated by neoplasy of thoracic aortic aneurysm and added anti-hypertension drugs in addition to glucocorticoid after surgery. Unexpectedly, small testes and gynecomastia came into notice recently. Laboratory tests showed Leydig cell hydrops, hyponatremia and andropenmia. Scrotum ultrasound showed bilateral testicular dysplasia.

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score associated with a younger menopausal age (menopause age 2 to 7 years vs > 7 years, incidence rate ratio (IRR) = 1.53, 95% CI: 1.21 to 1.94), central obesity (IRR = 1.18, 95% CI: 1.00 to 1.39), smoking, diastolic blood pressure, age. Conclusions The results of this study indicate that the severity of menopausal symptoms is associated with obesity, smoking and TDMD, in a large sample of peri- and postmenopausal women.

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P441
Usefulness of routine assessment of free testosterone for the diagnosis of functional male hypogonadism
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Objective
To investigate whether routine assessment of free testosterone improves the diagnostic accuracy of functional male hypogonadism.

Methods
Total and free testosterone (calculated through SHBG assessment) were determined in 372 male patients (median age 44) referring to our department for sexual symptoms (188 patients) or infertility (184 men). Low total and free testosterone were defined as < 0.2311 ng/ml and < 0.4622 ng/ml, respectively.

Results
Hypogonadism, as calculated free testosterone < 63 pg/ml, was found in 47/188 (25.0%) patients with sexual symptoms and in 21/184 (11.4%) with infertility. Total testosterone determination misdiagnosed hypogonadism in 8.4% (12/143) of men with sexual symptoms and in 2% (3/152) with infertility. In subjects with borderline total testosterone (between 2.31 and 3.5 ng/ml), only 24%-7% (19/77) had hypogonadism confirmed by free testosterone levels. No subjects had known conditions altering SHBG. Free testosterone levels significantly correlated with age, haematocrit, gonadotropins, gynecomastia, BMI, and number of co-morbidities, whereas total testosterone associated only with the latter two. Moreover, age, haematocrit, erectile dysfunction, BMI, and low libido were significantly different between men with normal and low free testosterone, whereas only BMI and low libido were significantly different between patients with normal and low total testosterone.

Conclusion
This is the first study evaluating the impact of FT assessment to diagnose functional hypogonadism in men with hypogonadal symptoms or infertility. Routine assessment of free testosterone allows a more accurate diagnosis of functional hypogonadism, especially in men with sexual symptoms. Free testosterone levels associate with clinical and biochemical parameters of androgen deficiency better than total testosterone levels. A first-line assessment of SHBG and calculated free testosterone levels should be performed in all men with symptoms of male hypogonadism, to improve our diagnostic performance.

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P442
Energy deficit as a cause of transient male hypogonadotropic hypogonadism: a successful resolution of a primary infertility
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Introduction
Caloric restriction combined with overtraining can result in a total body energy deficit, which in turn is associated with multiple deleterious endocrine consequences, including hypogonadotropic hypogonadism. This can be a reversible cause of primary infertility, but its occurrence in men is still poorly recognized.

Case Report
We report a case of a 39-year-old male evaluated in an urology appointment for primary infertility. He had a history of psoriasis, previous parotitis with no documented testicular involvement, and obesity 4 years earlier (weight: 110 kg; height: 1.79 m. Body mass index (BMI): 34.3 kg/m²). For that reason, he made lifestyle changes, performing a restricted calories and carbohydrates diet combined with 2 h daily intense physical exercise, with significant and rapid weight loss (currently, weight: 71 kg, BMI: 22.2 kg/m²). For at least 1 year, he had a marked decrease in libido, rare sexual intercourse, vaginal anejaculation since the beginning of attempts at procreation, and significant asthenia, which he associated with work stress and physical activity. No changes in erection were valued. Objectively, he presented hairy distribution according to age and sex, absence of gynecomastia. The vas deferens were bilaterally palpable, the testes were of normal volume, with no apparent lesions and no varicocele, and the penis was without alterations. From further investigation, the analytical study proved hypogonadotropic hypogonadism (Total Testosterone [TT] 2.21 ng/ml [Reference Range [RR]: 2.8-8.0]; LH 1.4 mIU/ml [RR: 1.6-8.6]; SHBG 4.7 nmol/l [RR: 13.71]; Prolactin (7.5 ng/ml [RR: 3.0-15.2]) and TSH (2.11 µU/ml [RR: 0.30-3.18]) were normal. The spermogram showed asthenoteratozoospermia and the scrotal ultrasound showed no changes. The pituitary MRI was normal. The study carried out with the female element did not identify any changes. The hypothesis of hypogonadotropic hypogonadism secondary to caloric restriction and concomitant excessive daily energy expenditure was raised and the patient progressively increased the dietary intake of carbohydrates while maintaining the same frequency and intensity of physical exercise. After 3 months of this modification, the patient reported more energy, complete resolution of libido complaints and greater frequency of sexual intercourse. Analytically, testosterone and gonadotropin levels normalized (TT 2.90 ng/ml [RR:2.8-8.0]; FSH 4.6 mIU/ml [RR: 1.5-12.4], LH 1.6 mIU/ml [RR: 1.6-8.6]) and a pregnancy spontaneously occurred.

Conclusions
The male reproductive axis is very sensitive to caloric deprivation, with clinical and analytical repercussions. This case alerts to this male cause of hypogonadotropic hypogonadism, often overlooked in the investigation of primary infertility. Given its functional nature, this condition is reversible and treated with increased energy intake.

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P443
Y-chromosome disomy and sexual ambiguity
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Introduction
Chromosomal abnormality 47, XXY, despite being present in approximately 1 in 1000 newborn boys, remains less known phenotypically and more than 85% of men are never diagnosed. Males with 47, XXY syndrome are described to be phenotypically normal. They present often a developmental delay, behavioral difficulties and learning disabilities that may be associated with accelerated growth rate and taller stature in adulthood. Endocrine disorders, especially pubertal delay, are rarely described in patients with this karyotype. We report the case of a boy who had at birth sexual ambiguity revealing a 47, XXY karyotype.

Observation
A 13-year-old boy was found at birth to have sexual ambiguity with a 1.5 cm microphallus and empty scrotum. Imaging ruled out the presence of female external genitalia and concluded to bilateral cryptorchidism. 17-OH Progesterone was normal at 0.5 ng/ml ruling out 21-hydroxylase deficiency. Testosterone, DHT, delta 4-androstenedione and DHEA-sulfate were normal with a testosterone/DHT ratio < 20. Genetic analysis revealed 47, XXY karyotype. He received HCG injections and had a surgery for the micropenis and bilateral cryptorchidism. The child does not have psychomotor or growth disorders. He is still prepubescent (Tanner staging: P/G1) with a penis size of 4.5 cm. Hormonal exploration revealed FSH = 0.9 mIU/ml, LH = 0.4 mIU/ml with testosterone < 0.1 ng/ml and a bone age less than 13 years, requiring monitoring to detect early a possible pubertal delay.

Discussion
47, XXY karyotype is a rare anomaly in which gonadal function is generally intact. However, a higher incidence of infertility was noted in men who carry this genetic abnormality. The association of this karyotype with microphallus and...
Kisspeptin improves sexual brain processing in women with low sexual desire
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Introduction
Sexual desire is a key component of the sexual response model. Absence or deficiency of sexual desire can lead to marked distress or interpersonal difficulty, termed ‘hypoactive sexual desire disorder’ (HSDD). HSDD is the most common female sexual health complaint worldwide, affecting up to 10% of women. Despite its detrimental impact on psychological well-being and quality of life, treatment options are currently limited. The hormone kisspeptin is a key endogenous activator of the hypothalamic-pituitary-gonadal axis, with emerging roles in sexual and emotional behaviour, and thus could serve as a novel treatment option in women with HSDD.

Methods
We performed a randomized, double-blind, two-way crossover, placebo-controlled study in 32 premenopausal women with HSDD. We used psychometric, functional neuroimaging, and hormonal analyses to investigate the effects of kisspeptin administration on brain activity, in response to erotic stimuli (erotic videos) and facial attraction (images of faces of varying attractiveness).

Results
Kisspeptin administration resulted in an increase in self-reported ratings of feeling ‘sexy’, compared to placebo, measured using the Sexual Arousal and Desire Inventory (t(32) = 2.27, P = 0.03). On functional MRI, kisspeptin administration deactivated the left inferior frontal gyrus and activated the postcentral and supramarginal gyrus in response to erotic videos (Z = 2.3, P < 0.05). Kisspeptin administration deactivated the secondary somatosensory cortex (Z = 2.3, P < 0.05) and enhanced activation in the posterior cingulate cortex on viewing male faces, which correlated with a reduction in self-reported sexual aversion (r = 0.476, P = 0.005). Kisspeptin resulted in a mean increase in LH of 2.75 IU/l (F1, 62) = 0.084, P = 0.02) and FSH of 0.37 IU/l (F1, 62) = 4.030, P = 0.05) across the 75-minute duration of the study as expected, with no effect observed on downstream circulating estradiol, progesterone or testosterone levels.

Discussion
Our results demonstrate that kisspeptin administration to women with HSDD increases their self-reported ratings of feeling ‘sexy’. Our brain activity changes provide mechanistic insight for this, with deactivation of the left inferior frontal gyrus, likely serving to reduce internal monologue and response inhibition. Furthermore, kisspeptin’s deactivation of the secondary somatosensory cortex can reduce a woman’s focus on herself, her body image, and related negative thoughts, thus augmenting her judgement of male facial attractiveness. Finally, kisspeptin’s actions in the posterior cingulate cortex can serve to increase feelings of romantic love and reward processing, thereby reducing sexual aversion and increasing sexual desire. These behavioural and mechanistic findings in women with HSDD lay the foundations for clinical applications for kisspeptin in psychosocial disorders.

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The effect of gastric sleeve resection on menstrual pattern and ovulation in premenopausal women with class III-IV obesity
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Purpose
Bariatric surgery is very efficacious in treating severe obesity. However, its effect of menstruation and ovulation is currently unknown. The purpose of this study was to assess the effect of gastric sleeve resection (GSR) on menstrual pattern in women with stage III-IV obesity and ovulatory dysfunction compared with conventional management.

Methods
This was a prospective, multicentre, non-randomized trial, in premenopausal women, who fulfilled the criteria for gastric sleeve resection (GSR). Both women with and without polycystic ovary syndrome (PCOS) were evaluated at three, six, nine, 12 and 15 months post-surgery.

Results
Menstrual cycle irregularities were identified in 122 severely obese women (60 with PCOS, 62 non-PCOS). The % total weight loss was greater with GSR than
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Interplay between estrogen signaling and notch pathway in rodent Sertoli cells
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Somatic cells of the seminiferous epithelium, called Sertoli cells, play a key role in germ cell development and maintenance of proper course of spermatogenesis. Although androgens are considered the main regulators of Sertoli cell activity, recent studies indicate that their metabolites, estrogens, also influence Sertoli cell function. Estrogens, act mainly through nuclear estrogen receptors α and β (ERα, ERβ), however non-classical signaling via membrane G protein-coupled estrogen receptor 1 (GPER) was also confirmed. It is well established that direct interactions between the cells in the seminiferous epithelium, including the Notch pathway, are essential for undisrupted spermatogenesis. Notch pathway is activated by binding membranous ligands Delta-like (DLL) or Jagged (JAG) of one cell to surface Notch receptors of the neighboring cell. The aim of this study was to explore the role of estrogens and their receptors in the control of the expression of Notch pathway ligands in Sertoli cells. Experiments were performed on primary Sertoli cells cultures isolated from rat testis (PSC) and mouse Sertoli cell line (TM4). First, the effect of estrogenic stimulation or estrogen action inhibition were examined using 17β-estradiol or estrogen receptor antagonists (ICI 182,780; G-15); respectively. Next, to determine the precise role of each receptor, siRNA silencing was conducted to knockdown the expression of ERα, ERβ, or GPER, qRT-PCR, western blot and immunofluorescence were employed to analyze the expression of DLL1, DLL4 and JAG1. The expression of all studied ligands was increased after stimulation by 17β-estradiol. The increase of either JAG1 or DLL1 expression in estrogen-stimulated cells was inhibited only by ICI 182,780. Knockdown experiments revealed that ERz silence entirely abolished the effect of 17β-estradiol on both JAG1 and DLL1 expression. Exposure to ICI 182,780 and G-15 decreased DLL4 protein expression in 17β-estradiol-stimulated Sertoli cells. Silencing experiments demonstrated that ERα and GPER knockdown effectively blocked estrogen influence on DLL4 protein expression. In summary, our results indicate that the expression of Notch pathway ligands in Sertoli cells is regulated by estrogens. JAG1 and DLL1 expression is controlled mainly via ERα, while DLL4 expression is dependent on ERβ and GPER signaling. Thus, the cooperation between classical and non-classical estrogen signaling pathways may be important for the communication within the seminiferous epithelium via Notch signaling, and thereby for proper spermatogenesis. This study was supported by a grant N18/MNW/000022 (Jagiellonian University, Faculty of Biology). The conference attendance supported by “Jagiellonian Interdisciplinary PhD Programme” POWR.03.05.00-00-Z309/17-00 (The European Social Fund).

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P449 Global impact of PCOS awareness month: challenges and opportunities
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Background September is celebrated as PCOS awareness month worldwide and is aimed at improving the lives of those with PCOS, promoting research, and strengthening advocacy efforts. While significant financial and human resources are invested in promotions during this month, to the best of our knowledge, there is no evidence to show the impact of this initiative. In our study, we evaluated the global digital impact of PCOS Awareness Month, tracking commonly used hashtags as surrogate markers, patterns of associated emotions and identifying key players, collaborations and trending topics associated with PCOS Awareness Month.

Methods We utilised several online tools (Spryml, SocioViz.net, Sprout Social, Sentiment Viz, and Google trends) to study the global impact of PCOS Awareness Month using #PCOS, #PCOSAwareness, #PCOSAwarenessmonth, and a corresponding search query. Network and sentiment analysis was done on the last day of PCOS awareness month to identify common themes and associated topics with the tweets. Google Trends was used to study the web and news search popularity globally to get an overall idea of the internet search trends beyond social media platforms.

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P448 Finasteride inhibits epinephrine synthesis in humans: implication for sexual dysfunction
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Finasteride is a 5α-reductase (5α-R) inhibitor used in clinics to treat androgen-dependent conditions, such as benign prostate hyperplasia and androgenetic alopecia (AGA). It ust has been associated with sexual adverse effects, including sexual complaints. However, to date, no hypothesis to explain such adverse effects has been proposed. This is a consequence of the still incomplete knowledge of the intricate network of motivational, psychological, and molecular inputs that are involved in sexual behavior. In this work, a multidisciplinary approach has been used to evaluate whether finasteride may interact with targets different from 5α-R (i.e., off-target proteins – OTPs). In silico analysis (SPILL-PPBS software and docking/molecular dynamics) indicated that the enzyme phenylethanolamine N-methyltransferase (PNMT), the limiting enzyme in epinephrine production, might be a finasteride OTP. This is interesting, since epinephrine and norepinephrine are involved in erection (Becker et al., 2000, J Urol), and alterations in their levels has been observed in patient with erectile dysfunction (Becker et al., 2002, Urology). An inhibitory assay developed in vitro confirmed that finasteride blocks the human PNMT. Finally, to verify the in vivo interaction, adult male rats were treated with finasteride (1 mg/kg/day s.c. daily for 20 days). Ex vivo analysis indicated that epinephrine levels were decreased by finasteride treatment in adrenal glands, while those of norepinephrine were increased. This, together with no variation in PNMT protein levels, confirmed the hypothesis of a block in epinephrine synthesis. Therefore, we explored if corpora cavernosa (CC) of finasteride-treated rats presented molecular alterations. A decreased protein level of estrogen receptor beta was observed in CC of finasteride-treated rats, in line with evidence in aging and diabetic rats with erectile dysfunction (Shirai et al., 2004, Urology). Moreover, the levels of dopamine, which improve the penis relaxation, were significant decreased in CC tissue after finasteride administration. Overall, the data here presented indicate that finasteride affects epinephrine synthesis by blocking PNMT enzymatic activity in humans. This block can have an impact in sexual behavior, as suggested in an animal model treated with finasteride. In addition, the alterations observed in CC indicate possible impairment of erectile function. Our results suggest possible mechanisms for the sexual dysfunction observed after finasteride treatment in humans and add a piece of knowledge on the mechanisms controlling sexual function in mammals.

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P447 Interplay between estrogen signaling and notch pathway in rodent Sertoli cells
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Somatic cells of the seminiferous epithelium, called Sertoli cells, play a key role in germ cell development and maintenance of proper course of spermatogenesis. Although androgens are considered the main regulators of Sertoli cell activity, recent studies indicate that their metabolites, estrogens, also influence Sertoli cell function. Estrogens, act mainly through nuclear estrogen receptors α and β (ERα, ERβ), however non-classical signaling via membrane G protein-coupled estrogen receptor 1 (GPER) was also confirmed. It is well established that direct interactions between the cells in the seminiferous epithelium, including the Notch pathway, are essential for undisrupted spermatogenesis. Notch pathway is activated by binding membranous ligands Delta-like (DLL) or Jagged (JAG) of one cell to surface Notch receptors of the neighboring cell. The aim of this study was to explore the role of estrogens and their receptors in the control of the expression of Notch pathway ligands in Sertoli cells. Experiments were performed on primary Sertoli cells cultures isolated from rat testis (PSC) and mouse Sertoli cell line (TM4). First, the effect of estrogenic stimulation or estrogen action inhibition were examined using 17β-estradiol or estrogen receptor antagonists (ICI 182,780; G-15); respectively. Next, to determine the precise role of each receptor, siRNA silencing was conducted to knockdown the expression of ERα, ERβ, or GPER, qRT-PCR, western blot and immunofluorescence were employed to analyze the expression of DLL1, DLL4 and JAG1. The expression of all studied ligands was increased after stimulation by 17β-estradiol. The increase of either JAG1 or DLL1 expression in estrogen-stimulated cells was inhibited only by ICI 182,780. Knockdown experiments revealed that ERz silence entirely abolised the effect of 17β-estradiol on both JAG1 and DLL1 expression. Exposure to ICI 182,780 and G-15 decreased DLL4 protein expression in 17β-estradiol-stimulated Sertoli cells. Silencing experiments demonstrated that ERα and GPER knockdown effectively blocked estrogen influence on DLL4 protein expression. In summary, our results indicate that the expression of Notch pathway ligands in Sertoli cells is regulated by estrogens. JAG1 and DLL1 expression is controlled mainly via ERα, while DLL4 expression is dependent on ERβ and GPER signaling. Thus, the cooperation between classical and non-classical estrogen signaling pathways may be important for the communication within the seminiferous epithelium via Notch signaling, and thereby for proper spermatogenesis. This study was supported by a grant N18/MNW/000022 (Jagiellonian University, Faculty of Biology). The conference attendance supported by “Jagiellonian Interdisciplinary PhD Programme” POWR.03.05.00-00-Z309/17-00 (The European Social Fund).

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Results
While we found a growing trend for #PCOS and related hashtags from 2014 to 2020, we noticed a decline in 2021. In each of these years, the largest spike of both impressions and users for #PCOS was seen at the start of September with a declining trend for the rest of the month. Verified users, who have notably more influence, have shown consistently increasing support for the PCOS Awareness Month from 2014 to 2021. On network analysis, the most commonly associated hashtags with the #PCOS were #endometriosis, #fertility, #womenhealth, #PCOS, #fertilityinfertility. Sentiment analysis revealed most of the tweets were linked to subdue but pleasant emotions. 76% of top influencers collaborated with at least one other person during PCOS Awareness Month activities. Geographically, we noted limited engagement in African, Asian, and non-English speaking European countries.

Conclusions
PCOS Awareness Month is an effective strategy to raise awareness with social media playing a crucial role in amplifying the message especially with the usage of hashtags. Further gains can be made by enhancing collaborations between like-minded individuals and organisations to make concerted efforts during PCOS Awareness Month. Our findings also provide an opportunity to understand the current perceptions and expectations amongst the public, which can influence future healthcare investment and research.

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P450
Influence of polycystic ovary syndrome on in vitro fertilization and relationship with the Asn680Ser polymorphism in FSHR gene

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Introduction
Polycystic ovary syndrome (PCOS) is a frequent cause of infertility. Its influence on the results of in vitro fertilization (IVF) is controversial, and generally not isolated from the effect of obesity. A relationship between the FSH receptor (FSHR) polymorphism Asn680Ser and the risk and phenotype of PCOS has been studied with conflicting results.

Objectives
To analyze the influence of obesity and PCOS on the gonadal axis and IVF results.
To assess the influence of Asn680Ser on the risk of PCOS and IVF.

Material and Methods
Retrospective analysis of patients with PCOS by Rotterdam criteria with and without obesity and controls with tubal infertility, undergoing 1st IVF after a short ovarian stimulation cycle with GnRH antagonist.

Results
Sample with 212 patients: 72 without obesity, with PCOS (group A); 75 without obesity or PCOS (B); 36 with obesity and PCOS (C); 29 with obesity, without PCOS (D). Mean age 33.5±3.7 years with homogenous distribution between groups (P=0.207) and similar body mass index in the non-obese (A 23.8±2.9 vs B 23.3±2.7 kg/m², P=0.203) and in the obese groups (C 33.9±3.0 vs D 33.1±1.1 kg/m², P=0.495). The PCOS groups had: higher gonadotropins, LH/FSH ratio, testosterone, antral follicle count and anti-Müllerian hormone; lower luteal phase estradiol and progesterone (P<0.001 for all analyses). In the IVF results, the differences were more pronounced in the groups with vs without obesity, C and D (vs A and B) had: fewer mature oocytes (6.3±5.3 vs 5.7±2.9 vs 9±1.2 vs 6.8 and 6.7±5.2, P=0.035), less blastocysts (1.1±1.6 and 0.5±0.8 vs 1.7±2.3 and 1.6±2.2P=0.031) and lower embryo transfer rate (45.7 and 41.4 vs 68.8% and 69.3, P=0.007). In those who transferred embryos, the probability of pregnancy did not differ (P=0.197). In multivariate analysis, only obesity had an individual contribution to the transfer probability (P=0.001). The Asn680Ser polymorphism (analyzed in 113 cases) was present at a similar rate in patients with and without PCOS (65.7 vs54.4%, P=0.225) and was not associated with the likelihood of embryo transfer or pregnancy (P=0.452 and 0.174, respectively).

Discussion
Differences in IVF results were particularly related to obesity, suggesting that, although the hormonal changes associated with PCOS can be overcome by controlled ovarian stimulation, addressing obesity is essential for the success of IVF. In this population, Asn680Ser was not associated with the risk of PCOS or IVF outcomes.

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P451
Association between basal androgen concentrations and number of follicles on the day of triggering final oocyte maturation in poor responders undergoing IVF - a prospective study

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Purpose
Androgens promote early follicular development and granulosa cell proliferation by augmenting follicle-stimulating hormone (FSH) receptor expression in granulosa cells. Several retrospective studies have evaluated the association between basal androgen concentrations and follicular development in women undergoing ovarian stimulation for in vitro fertilization (IVF) with conflicting results. The aim of this study was to investigate whether basal androgen concentrations are associated with the number of follicles on the day of triggering final oocyte maturation in poor responders undergoing IVF.

Methods
This prospective study was performed between 02/2020 and 01/2022 in 103 poor responders according to the Bologna criteria. Androgens, including total testosterone, sex hormone-binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), Δ4- androstenedione and 17-OH progesterone (17-OHP), were measured at the initiation of ovarian stimulation. Ovarian stimulation was performed using a fixed dose of 300 IU of recombinant gonadotrophins and gonadotrophin releasing hormone (GnRH) analogues. Triggering of final oocyte maturation was performed in the presence of three follicles ≥ 11 mm. Primary outcome measure was the number of follicles ≥ 11 mm on the day of triggering final oocyte maturation. The association between androgen concentrations and the number of follicles ≥ 11 mm on the day of triggering was evaluated using generalized estimating equations, accounting for female age and body mass index (BMI). Values were expressed as a coefficient (coef) or mean (95% confidence interval).

Results
Female age was 41.9 (41.2-42.6) years, while BMI was 26.1 (24.9-27.3) kg/m². The number of follicles ≥ 11 mm on the day of triggering final oocyte maturation was 6.1 (5.3-7.0). The number of COCs retrieved was 3.9 (3.2-4.6), the number of MII oocytes was 3.4 (2.8-3.9) and the number of 2pn oocytes was 2.5 (2.1-2.8). No significant association was found between basal testosterone (coef: -0.008, 0.019 to +0.003, P=0.17), 17-OHP (coef: -0.044, 0.391 to +0.303, P=0.80), SHBG (coef: -0.002, -0.007 to +0.002, P=0.25), Δ4-androstenedione (coef: -0.101, -0.306 to +0.104, P=0.33) concentrations and the number of follicles ≥ 11 mm. In contrast, a significant negative association was found between basal DHEAS (coef: -0.011, -0.019 to -0.003, P=0.007) concentrations and the number of follicles ≥ 11 mm on the day of triggering final oocyte maturation.

Conclusions
Higher DHEAS concentrations were associated with the development of fewer follicles ≥ 11 mm. Given the significant negative association between DHEAS concentrations and the number of follicles on the day of triggering final oocyte maturation, future studies on DHEAS supplementation should consider basal DHEAS concentrations.

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P452
Need for transgender care education among polish endocrinologists

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Background
A significant body of research indicates that transgender and gender-nonconforming persons represent an underserved population susceptible to health care disparities. The attitudes and knowledge of medical doctors toward transgender people have important implications for the future quality of healthcare for transgender patients.

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Specific Aim
The aim of this study was an assessment of coverage of transgender care issues in training curricula of endocrinologists in Poland, including educational and practical experience while providing health care to transgender persons.

Methods
An anonymous survey was sent via electronic mail to the members of the Polish Society of Endocrinology. Survey questions were designed to assess the transgender health issues coverage during training, personal experience with transgender patients and attitudes toward gender-affirming interventions.

Results
A total of 110 endocrinologists responded to the online survey, 74 fully answered questionnaires (67.27%) were analysed. The majority of respondents were between the ages of 35-54 (n = 50; 67.57%) with minimal 10 years seniority. Years in practice were not associated with the level of transgender care training. Among respondents, 21 doctors (28.28%) provided hormonal gender-affirming interventions for transgender patients. The vast majority of endocrinologists did not receive any training on the care of transgender patients, including communication skills (n = 54; 72.97%) and therapeutic recommendations (n = 37; 50.00%). Assessment of willingness to provide health care to transgender persons revealed that 22 respondents (29.73%) have concerns in this area. In this group, most doctors (n=15; 68.18%) did not have any previous experience with transgender patients. The main indicated obstacle was lack of experience and competence (n = 19; 82.61%). Endocrinologists, who provide hormonal gender-affirming interventions represent a higher level of participation in training on the care of transgender patients (OR = 4.0, P < 0.003) and acceptance of hormone interventions as well as surgical procedures (OR = 6.6, P < 0.002).

Conclusion
Medical school and residency curricula are lacking in the content of transgender care. As a result, personal and professional comfort levels while providing medical care to transgender and gender non-conforming persons could be inadequate. Efforts should be made to provide the proper education on health care issues related to gender incongruence.

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Introduction

Follicle-stimulating hormone (FSH) is a glycoprotein that support reproduction by regulating ovarian follicular growth and development. Recent studies demonstrated that proliferative signals mediating folliculogenesis are mediated by the G protein-coupled estrogen receptor (GPER) expressed in ovarian tissues throughout the follicular phase. In granulosa cells, GPER forms heteromers with FSHR, reprogramming cAMP-induced death signals to AKT-dependent, anti-apoptotic/ proliferative events, fundamental to sustain oocyte survival. Since GPER is mainly located in the endoplasmic reticulum, we may hypothesize it modulates FSH signals via heteromerization and retention of FSHR in the cytoplasm.

Aim

In this study, we analysed FSHR/GPER heteromers trafficking through early and late endosomes and its impact on FSH-mediated signalling from endocytic compartments.

Methods

HEK293 cells were transfected with FSHR- and GPER-coding plasmids and treated by 10 nM FSH, in the presence or absence of receptor internalization blockade by Dynasore. cAMP production and FSHR interaction with specific endosome markers, i.e. Ras-related proteins (Rab) 5, 7 and 11, were evaluated at different time-points (0-20 min) by bioluminescence resonance energy transfer (BRET). Results were compared by Kruskal-Wallis test and Dunn’s post-hoc test (P < 0.05; n = 5) and showed as means ± SEM.

Results

FSH treatment of FSHR-only expressing cells resulted in the receptor internalization mediated by β-arrestins, and in FSHR localization into Rab7-positive endosomes, addressing it to lysosomes. No FSH-induced compartmentalization of the receptor into early- and recycling-endosomes (Rab5 and Rab11 markers) was found. Conversely, FSHR/GPER co-expression reduces the basal FSH trafficking through Rab5 and Rab11-marked endosomes, prevents FSH-induced FSHR-Rab7 interaction and drives FSH internalization mainly through β-arrestin recruitment (FSHR-β) or FSHR/GPER-expressing cells; P < 0.05).

This event might be essential for FSH-induced signalling modulation. Indeed, as previously described, the FSH treatment of FSHR-expressing cells induces intracellular cAMP increase, while it does not in FSHR/GPER co-expressing cells (AUC FSHR = 85.51 ± 8.4 vs AUC FSHR + GPER = 36.06 ± 7.4; P < 0.05). Interestingly, in FSHR/GPER co-expressing cells where internalization was inhibited by Dynasore, FSH induces a CAMP response, oppositely to what demonstrated in Dynasore-untreated cells (AUC Dynasore-treated FSHR + GPER = 101.1 ± 16.11; P < 0.05) and suggesting the requirement of the heteromer internalization to inhibit a CAMP production.

Conclusion

In conclusion, these results suggest that GPER blocks FSHR-mediated cAMP production via compartmentalization of receptors into specific endosomes. These data strengthen the existence of FSHR membrane partners modulating its mode of action, possibly impacting ovarian physiology.

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P456

Common and unique transcriptional regulation in target tissues and oocytes across poly cystic ovary syndrome-like mouse models

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Yu Pei and Sanjiv Risal are joint first authors. Elisabet Stener-Victorin and Quoelin Deng are joint corresponding authors. Polycystic ovary syndrome (PCOS) affects around 15% of women of reproductive age and the key feature of the syndrome is hyperandrogenism. To understand the complex pathophysiology of PCOS, more than 30 PCOS-like models have been developed to mimic certain pathophysiological features. So far, not much is known about the common and unique molecular and cellular features among the most used PCOS-like mouse models. The overall aim of this study is to compare three hyperandrogenic PCOS-like mice models that are commonly used to understand the molecular pathology across inflicted tissues: hypothalamus, subcutaneous adipose tissue, ovary, and metaphase II (MII) oocytes among the prenatally androgenized (PNA) model (F1 offspring), the prepubertal androgenized (PAP) model, and the theca-cell specific nerve growth factor overexpressing mouse model (17 NF).

We performed bulk RNA sequencing of tissues and single-cell RNA sequencing of MII oocytes across the models and identified differential expressed genes (DEGs) in each tissue and model. The greatest number of DEGs was found in the ovary followed by adipose tissue whereas hypothalamus is least affected in all models. In addition, ovary and adipose tissue were most affected in PPA model compared to other models. We found several common DEGs were involved in lipid metabolism and steroid hormone binding with strong ovary, adipose tissue and hypothalamus in all models. Moreover, we conducted weighted gene correlation network analysis (WGCNA) to identify functional correlated gene modules across all models and revealed common biological pathways for hub genes including gonad development, cell-cell communication, hormonal metabolism and lipid metabolism in ovary and adipose tissue. Notably, greatest transcriptional alteration was also observed in MII oocytes in the PMA model, with DEGs in gonad development and germ cell development, likely due to fetal programming effects. Currently, we are investigating crosstalk between tissues and oocytes and comparing these findings with relevant human tissues.

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P457

A systematic review and meta-analysis assessing psychosexual wellbeing in people with polycystic ovary syndrome

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Background

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder, with an estimated prevalence of 10-15% worldwide. PCOS can have adverse consequences on the emotional wellbeing of the patient. However, evidence exploring the relationship between PCOS and psychosexual wellbeing, specifically sexual function, and dysmorphic appearance concerns, is largely inconclusive.

Aim

A systematic review and meta-analysis were undertaken to assess differences in sexual function and dysmorphic appearance concerns among people with and without PCOS.

Methods

Electronic databases (MEDLINE, EMBASE, APA PsycInfo, PUBMED, Web-of-Science Core Collection, and CENTRAL) were searched through August 2021. Observational studies (cross-sectional, case-control, cohort) and Randomised Control Trials (RCTs) were included. Outcome measures included validated questionnaires or Visual Analogue Scales (VAS) reporting on sexual function or dysmorphic appearance concerns. Methodological quality was assessed by adaptation to the Newcastle-Ottawa Quality Assessment Scale (NOS). The inverse variance method, based on a random- or fixed-effects model (Review Manager, Version 5) was used to perform meta-analyses.

Results

The search yielded 5964 publications and 53 full-text articles were included, of which 38 (71.7%) assessed sexual function outcomes, and 15 (39.5%) assessed dysmorphic appearance concerns using validated scales, in people with PCOS. 27 studies used the Female Sexual Function Index (FSFI) to assess domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain). Meta-analysis of 11 comparative cohort studies (793 PCOS women and 1507 controls) revealed no significant differences between PCOS and controls in sexual desire (P = 0.11); satisfaction (P = 0.05); pain (P = 0.56); arousal (P = 0.05) and total

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Conclusions
COVID-19 can result in short-term impaired sperm and T production. Available data cannot clarify long-term andrological effects. Low T observed in the acute phase of the disease is associated with an increased risk of being admitted to the Intensive Care Unit or death. The use of mRNA COVID-19 vaccines does not seem to affect sperm quality.

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P696

Comparison of three different AMH assays with AMH levels and follicle count in women with polycystic ovary syndrome

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Anti-Müllerian hormone (AMH) levels strongly correlate with the number of antral follicles in the ovary. In women with polycystic ovary syndrome (PCOS), this is reflected by significantly increased serum AMH levels. AMH levels are therefore suggested as a proxy for polycystic ovary morphology (PCOM) in PCOS diagnosis. Different assays are available to measure serum AMH levels. However, lack of a gold standard and the use of different antibodies to detect AMH have led to inter-assay variability. Little is known about inter-assay correlation in women with increased AMH levels, especially in PCOS. Hence, our aim was to investigate the correlation of AMH values between different AMH assays and with total follicle count (TFC) in a large cohort of PCOS patients. Serum AMH levels were measured in 1660 PCOS patients, diagnosed using the Rotterdam criteria. AMH levels were measured by three different AMH assays: (1) Gen II ELISA [Beckman Coulter]; (2) picoAMH assay [Ansh Labs]; and (3) Automated Elecsys assay [Roche]. Patients were divided in subgroups based on the reported AMH cutoff values for PCOM: low AMH (<2.80 ng/ml), mid AMH (2.80–7.04 ng/ml) and high AMH (>7.04 ng/ml). Passing-Bablok regression was used for the comparison between assay methods. Spearman’s correlation rank was used to assess the correlation between AMH levels and TFC. The inter-assay correlations over the total range of AMH levels were: Gen II vs Elecsys: 0.81; picoAMH vs Gen II: 0.81; picoAMH vs Elecsys: 0.94. Stratification in three AMH subgroups revealed an AMH level dependent inter-assay correlation. A strong inter-assay correlation was present in both low and high AMH subgroups, ranging from 0.62–0.90. The correlation in the mid AMH level subgroup was only moderate, with correlation coefficients ranging between 0.28–0.56. A positive correlation was present over the total range of AMH levels and TFC, with correlation values ranging from 0.57–0.62. However, subgroup analysis showed that independently of assay method used, the correlation decreased in all three AMH subgroups and became moderate at best with coefficients ranging between 0.11–0.45. In conclusion, in our cohort of PCOS patients both inter-assay correlation and correlation between AMH level and follicle count depend on the range of serum AMH level. While a high AMH level may reflect the presence of PCOM, our results suggest that it does not accurately reflect the total number of follicles in PCOS. This once more emphasizes the need of a standardization of AMH measurement.

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P697

Clinical/biochemical characteristics of functioning gonadotroph adenomas in women presenting with ovarian hyperstimulation

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Background
Functioning gonadotroph adenomas (FGA) are rare benign pituitary tumours. Several case reports suggest that FGA may present with features of ovarian hyperstimulation in women. However, a lack of aggregated clinical experience of FGA precludes the meaningful guidance of management in affected women.

Conclusions

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FSFI score (P = 0.27). PCOS women scored significantly lower on lubrication (SMD = -0.16; P = 0.001) and orgasm (SMD = -0.16; P = 0.02), indicating impaired sexual function. Included studies used 13 different validated scales to assess dysmorphic appearance concerns among people with PCOS. Meta-analysis of 3 comparative cohort studies (406 PCOS women and 394 controls) using the Multidimensional Body-Self Relations Questionnaire Appearance Scales (MBSRQ-AS) to assess appearance concerns was performed. PCOS women scored significantly lower on the appearance evaluation (SMD = -0.78; P = 0.0001) and significantly higher on appearance orientation (SMD = 0.22; P = 0.0004), indicating higher overall dissatisfaction with physical appearance.

Conclusions

People with PCOS experience a greater degree of sexual dysfunction and body image concerns implying psychosexual wellbeing needs to feature in clinical assessment of people with PCOS. Further studies are needed to identify ways to minimise this impact.

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P695

Andrological effects of SARS-Cov2 infection: a systematic review and meta-analysis

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Background
Since the preliminary epidemiological data concerning the coronavirus disease 2019 (COVID-19) has been available, clear sex disparity has been evident, with males, although not more frequently affected, often experiencing worse outcomes when compared to women. The short and long-term andrological effects of coronavirus disease 2019 (COVID-19) have not been clarified. The aim of the present study is to systematically review and meta-analyse all available data regarding possible short- and long-term andrological effects of COVID-19. In addition, information regarding the safety of the COVID-19 vaccines on sperm quality was investigated.

Methods
All prospective and retrospective observational studies reporting information on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA semen and male genitalia tract detection, as well as those reporting data on semen analysis and hormonal parameters in infected/recovered patients without any arbitrary restriction were included.

Results
Out of 204 retrieved articles, 35 were considered, including 2092 patients and 1138 controls with a mean age of 44.1 ± 12.6 years, and mean follow up 24.3 ± 18.9 days. SARS-CoV-2 mRNA can be localized in male genitalia tracts during the acute phase of the disease; mean crude detection rate (DR) was 8/5(12%). Meta-regression analysis showed that DR was not influenced by patient age or by disease severity or associated morbidities. DR was significantly higher in those studies assessing the viral mRNA presence in the semen less than 11 days after the diagnosis (P = 0.02). When all studies were considered, COVID-19 was associated with a significant reduction of total sperm count, sperm concentration and total sperm motility, whereas no difference in sperm morphology or progressive motility was observed. Moreover, SARS-CoV-2 infected patients were characterized by reduced total T levels, whereas no difference in either LH or FSH levels was observed. Sensitivity analyses confirmed the negative effects of SARS-CoV-2 infection on T levels only for those studies that included patients in the acute phase (mean difference in total T levels -2.19 [-7.08;-1.20] nmol/l; P = 0.001).

Conclusions

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P698

The biochemical investigation of PCOS: a UK wide survey of laboratory practice

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Background

Polycystic ovary syndrome (PCOS) is a heterogenous condition that affects approximately 12% of females. The diagnosis can be complex and biochemical tests are routinely relied upon to help identify hyperandrogenaemia and to exclude other conditions. However, although national and international guidelines advocate the use biochemistry tests, little information is provided as to which tests should be used and which other endocrinopathies should be excluded.

Objectives

To gather information about what tests UK laboratories routinely use to investigate PCOS, what reference ranges are applied, and which other conditions are routinely excluded.

Design

A national survey consisting of 32 questions was compiled by clinical scientists and clinicians. This was circulated to NHS clinical laboratories via UK NEQAS and The British Endocrine Society with online access available between June — December 2021. Supplementary to the survey, UK NEQAS distributed three cases for interpretation to complement their steroid hormone scheme.

Results

The survey attracted responses from 81 participants. Of these, 90% identified that testosterone would be included in an initial screen with only 50% using it in combination with SHBG to provide a free androgen index. Of the conditions that are not routinely excluded, 74% would not add TSH to investigate hypothyroidism and 84% would not consider adding 17OHP to exclude late onset CAH. Testosterone analysis is commonly performed by immunoassay in the UK with only 12% of respondents using LC-MS/MS. Reference ranges for testosterone varied with the most commonly used being a manufacturer derived <1.7 nmol/l and the highest reported being a luteal upper limit of 6.0 nmol/L. Several participants (64%) identified that they would send high testosterone to an LC-MS/MS laboratory for confirmation, the concentration at which this occurred ranging from >1.2 nmol/l to > 5 nmol/l. Androstenedione was only included by 16% of participants in the initial screen with the majority using LC-MS/MS for its measurement and the upper limit of normal ranging from 4.6 to 14.3 nmol/l. The results from the clinical interpretation provided varied responses.

Conclusions

There is significant variation across the UK in the investigation of PCOS. This is apparent in which tests are offered by biochemistry laboratories, what reference ranges are used and, as a direct consequence of these, what interpretation is applied. This potentially further complicates the investigation and diagnosis of PCOS and represents an inequality across the healthcare system. There is a requirement for clear guidance on what tests should be used to investigate PCOS.

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P699

Cyproterone associated meningioma in a poly cystic ovarian syndrome patient - a rare occurrence in our cohort

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Introduction

Meningiomas are the most common brain tumours and they express progesterone receptors. Cyproterone acetate (CPA) is a synthetic progestogen approved for use as an anti-androgen in Polycystic Ovarian Syndrome (PCOS). We report a case of meningioma probably resulting from long-term CPA treatment and a review of our PCOS cohort for further cases.

Case report

A 47-year-old lady with PCOS was treated with CPA 100 mg once daily for hirsutism and androgenic alopecia for 15 years (cumulative dose-exposure = 193g). She developed reduced vision in left eye; an MRI brain revealed a 6-cm left supra-orbital meningioma alongside 2 small separate lesions (0.8 cm & 0.3 cm). CPA was stopped and large mass was resected; histology confirmed Grade 2 meningioma. Smaller lesions were conservatively managed.

Quality Improvement project

To identify further cases of meningioma, a retrospective electronic records review of consecutive PCOS patients who were on either CPA or Dianeette (CPA 2 mg + Ethinyl Estradiol 35 mg) in University Hospitals of Leicester from 1980 to 2021 was undertaken. n = 1302 patients received either CPA or Dianeette as current or past treatment (CPA = 508; Dianeette = 794) with a cumulative dose-exposure of 56g/patient. 78/508 CPA patients are currently under active follow-up; 20 are currently on CPA (100 mg = 14; 50 mg = 6). CPA was stopped in rest due to lack of efficacy, tolerability, compliance, and/or lost to follow-up. Up-to-date imaging & records review of 508 CPA-cohort detected one meningioma occurrence which is described above. No meningioma cases were noted in the Dianeette cohort.

Discussion

First described in 2008 and confirmed in a recent French study, there is a 11-fold higher dose-dependent risk of meningioma with 36g to 60g cumulative CPA exposure compared to <3g. In June 2020, Medicines and Healthcare products Regulatory Agency (MHRA) issued guidance to minimise risk of meningioma, limiting high dose (50-100 mg) license for only prostate cancer and male hypersexuality. It is plausible that meningioma is co-incidental in our patient as incidence is 6-10 in 100,000 background population. However, recognised association, potent progestogenic effect and high-dose exposure may potentially incriminate CPA. Given solitary incidence in our cohort, remaining 19 CPA patients are closely monitored, MHRA guidance explained with an option offered to swap to alternate treatment.

Learning points

1) To be aware of meningioma side effect risk in high dose CPA (>50 mg/day) treated patients and consider cessation/swapping to alternate treatment.

2) CPA should be stopped in high risk patients such as PMH of meningioma, radiotherapy or Neurofibromatosis-2 genetic mutation.

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P700

Fetal exposure to anti-müllerian hormone triggers a transgenerational epigenetic transmission of polycystic ovary syndrome (PCOS) defects in adulthood

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Background

Anti-Müllerian hormone (AMH), a member of the transforming growth factor-β superfamily, is expressed in the female reproductive tract from the fetal period to adulthood. AMH is released from the developing ovary and acts on the Müllerian duct to inhibit their development. In males, AMH is produced by Sertoli cells in the seminiferous tubules and is involved in the regulation of the onset of puberty and spermatogenesis. AMH is also a potent androgen antagonist that can inhibit the effects of androgens on the reproductive system. AMH is a potential therapeutic target for the treatment of PCOS, as it may be involved in the regulation of androgen production and ovarian function.

Aims

The aim of this study was to investigate the effects of AMH on the development of the female reproductive tract in a transgenic mouse model. The study aimed to determine whether AMH has a transgenerational effect on the development of the female reproductive tract and whether this effect is mediated by changes in the epigenetic landscape.
Pignata, Brunella Bagattini, Lucia Montanelli, Patrizia Agretti, Digitale Selvaggio, Rosa Di Fraia, Francesca Allosso, Aldo Marrone

with 123-I and perchlorate discharge test: 6 patients presented a partial iodine (20.8%), 20 showed hyperthyrotropinemia (41.7%) and 18 were euthyroid Results follow-up.

We evaluated the need for L-T4 therapy at retesting and during clinical reassessment with thyroid function profile, imaging evaluation with ultrasound, and clinical reassessment after withdrawal of levothyroxine (L-T4) therapy, through a cohort of pregnant women with PCOS and control women revealing that AMH is significantly more elevated in the former group vs the latter. Pregnant mice were treated with AMH to model our clinical findings and investigate the neuroendocrine phenotype of their female progeny across multiple generations. Using this new preclinical PCOS model revealed that fetal exposure to excess AMH drives a transgenerational transmission of the major reproductive and metabolic PCOS alterations across multiple generations via altered landscapes of DNA methylation. Furthermore, findings revealed the existence of common epigenetic signature in a cohort of mothers and their daughters suffering from PCOS as well as in PCOS-like mice, which could serve as markers for early detection of the syndrome. Furthermore, the efficiency of an epigenetic-based therapy used in this preclinical model of PCOS, offers a promising therapeutic avenue to improve the management of PCOS patients. Collectively, our results challenge the concept of PCOS originating in utero and appear to consolidate the role of AMH as a trigger of the pathogenesis. This work further points to PCOS-like mouse model as an excellent preclinical tool to investigate both neuroendocrine disturbances of PCOS and how developmental programming effects are transmitted, while offering a therapeutic avenue for the treatment of the disease.

Key words: PCOS, Fetal programming, AMH, GnRH, Transgenerational Transmission

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P701

Evolution of congenital hypothyroidism with in situ thyroid gland in children and adolescents

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Background

In recent years, increasing cases of congenital hypothyroidism (CH) with in situ thyroid gland are identified. Outcome of children affected from CH with normally situated thyroid of normal size is still unknown. The objective of our study is to describe the natural history of this specific form of CH. Patients and methods: We retrospectively evaluated clinical, biochemical and instrumental data of 74 patients with diagnosis of CH with in situ thyroid gland, referred to our center after positive neonatal screening. After 3 years of age, 48 patients performed a clinical reassessment after withdrawal of levothyroxine (L-T4) therapy, through biochemical evaluation with thyroid function profile, imaging evaluation with neck ultrasound and, in most cases, a scintiscan with 123-I and perchlorate discharge test. We evaluated the need for L-T4 therapy at retesting and during follow-up.

Results

48 patients performed clinical reassessment: 10 had overt hypothyroidism (20.8%), 20 showed hyperthyrotropinemia (41.7%) and 18 were euthyroid (37.5%) after L-T4 withdrawal for 4 weeks. 32 patients performed a scintiscan with 123-I and perchlorate discharge test: 6 patients presented iodine organification defect, while 4 patients had a total defect. 28 children (58.3%) resumed therapy immediately after clinical reassessment, while 20 (41.7%) suspended it. Follow-up data after retesting (median duration of 10) were available in 44 patients. Between children who had suspended therapy at retesting, 4 resumed therapy during follow-up, while in the group of children who had resumed therapy at retesting, 9 suspended it. At the end of follow-up, 22 patients (50%) were untreated and 22 (50%) were still taking therapy. We observed no statistical differences between CH children who suspended or continued L-T4 in first serum TSH levels, sex ratio, or birth weight. Serum TSH at clinical reassessment showed a significant difference between two groups.

Conclusions

over a third of patients had a normal thyroid function off L-T4 therapy when retested after 3 years of age. During subsequent follow-up, half of our patients underwent to suspension of L-T4. Therefore, a clinical reassessment after 3 years of age should be performed to evaluate the need of L-T4 substitution and avoid unnecessary prolonged treatment. However, it is not possible to predict whether these subjects will need therapy again, so long-term follow-up studies are needed.

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P702

Non-alcoholic fatty liver disease prevalence in Klinefelter syndrome

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Non-alcoholic fatty liver disease (NAFLD) is becoming more common over the world. Its predisposition for evolving to cirrhosis and hepatocellular cancer, as well as its link to extrahepatic symptoms, puts patients and clinicians under a double burden. Several studies have found a link between NAFLD and many endocrinopathies, demonstrating a substantial bidirectional link between NAFLD and hypogonadism, in both men and women. In men with T2DM, NAFLD is linked to reduced total testosterone, however this is owing to a common soil of insulin resistance/obesity rather than the degree of liver necroinflammation or fibrosis. No data are available regarding Klinefelter syndrome (KS), the most common chromosomal condition associated with hypogonadism and NAFLD.

Methods

Thirty-five KS on Testosterone (T) replacement treatment were recruited. All patients underwent physical examination, full liver function tests, fasting glucose, triglycerides, cholesterol, blood cell counts, viral markers (HBV, HCV, HIV) and liver ultrasonography. The presence of autoimmune liver disease was assessed. The body mass index (BMI: kg/m2) was recorded for all patients. Insulin resistance index (HOMA-IR), and renal function were calculated. Conventional ultrasonography was performed to assess liver dimension, hyper echogenicity as compared to the right kidney parenchyma, distal attenuation, and the presence of areas of focal sparing. Prevalence of steatosis, using non-invasive methods in relation to anthropometric, biochemical, virological and ultrasound was estimated.

Results

Prevalence of steatosis in KS was 51%. BMI was 28.4 ± 1.3 and HOMA-IR 3.8 ± 1.0 (Mean ± SEM). T, 393.3 ± 22 ng/dl, and SHBG, 31 ± 2 nmol/l, serum levels were in the normal range. AMA, ANA and ASMA were negative. AST, ALT, and gamma GT were slightly increased in 11.1%, 44.4% and 31.1%, respectively. No patient shows signs of advanced liver disease. Total and LDL cholesterol were normal (174 ± 9 and 112 ± 7, Mean ± SEM, respectively). Serological markers for HBV, HCV, HAV infection were negative.

Conclusions

The prevalence of NAFLD increases by up to 80-90% in cohorts of individuals with dysmetabolic conditions such as overweight/obesity, T2DM, and metabolic endocrinopathies, demonstrating a substantial bidirectional link between NAFLD and hypogonadism, underscoring the primary role of metabolic factors in its development. These data are consistent with our preliminary findings in KS patients in whom the prevalence of steatosis was relevant in 51% of cases. The prevalence of autoimmune liver disease was excluded, and viral markers were negative, while KS were overweight and exhibited insulin resistance, despite normal T levels. However, the main pathophysiological mechanisms linking hypogonadism to NAFLD are complex and still under investigation, and more data are needed to better understand this condition.

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Early changes in androgen hormones in individuals with spinal cord injury: a longitudinal study

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Background

Individuals with spinal cord injury (SCI) are at increased risk of hypothalamic–pituitary–gonadal axis disruption. We aimed to explore changes in androgen hormones during the first inpatient rehabilitation and identify factors associated with their levels among participants from the Swiss Spinal Cord Injury Cohort (SwiSCI) cohort.

Methods

We measured sex hormones using Enzyme Linked Immunosorbent Assay in persons with a newly acquired SCI that participated in the SwiSCI study. We used univariable linear regression analysis to explore the association between clinical and injury characteristics and androgen hormones (total testosterone (TT), free testosterone (FT), sex hormone-binding globulin (SHBG), dehydroepiandrosterone (DHEA), and dehydroepiandrosterone sulfate (DHEAS)) at baseline. Longitudinal changes were explored using linear mixed models adjusted for age, body anthropometrics, injury characteristics, and medication use. Analyses were stratified by sex.

Results

We analyzed paired samples of 86 individuals with SCI [70 males (81%), 16 females (19%)] with median age of 51 years (IQR 36-64) and median rehabilitation duration of 5.6 months (IQR 4.2-7.5). At baseline, increasing age, body mass index, injury severity, and medication use were associated with lower TT, DHEA, and DHEAS and higher SHBG respectively. Increased upper extremity spasticity was linked with lower TT, DHEA and DHEAS and higher handgrip strength was associated with higher FT. TT in males in the beginning of the rehabilitation was in low normal range. At the end of rehabilitation, TT and DHEAS increased in males. We found no differences in hormone levels among individuals with different injury etiology, body composition, nor total spinal cord independence measure (SCIM). Due to limited number of women, female-specific findings should be interpreted with caution (Table 1).

Conclusions

We observed gradual increase in androgen hormones over a period of rehabilitation which was linked with improved functional recovery. Future studies to explore whether testosterone and DHEA supplementation may improve neurological and functional recovery as well as metabolic parameters during first inpatient rehabilitation.

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Lessons from a patient with the 48XXXXY karyotype: Not just another case of Klinefelter’s syndrome

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Introduction

The 48XXXXY karyotype is an infrequent (incidence about 1/50000 male births) sporadic aneuploidy of the sex chromosomes, classically considered as a variant of the Klinefelter syndrome (47XXY). Although many of their characteristics are shared, patients with the 48XXXXY karyotype suffer from additional endocrinological and neuropsychological disturbances which are not part of the classic Klinefelter syndrome. Hereby we present a clinical case.

Methods

Review of the patient’s clinical records and of the relevant literature.

Case Presentation

A male, 27 year old patient, previously diagnosed of left renal agenesis, hypothyroidism and cognitive impairment of unknown etiology with a 66% legal disability was referred to our Endocrinology Clinic from the Urology Dept., for workup of testosterone deficiency. He had undergone a standard vasectomy, but his testicles were reported as partially atrophic and his total testosterone was 0.96 ng/ml (normal range 2.8 - 10.7 ng/ml). The anamnesis disclosed cognitive impairment since childhood, with speech development at the age of 4 years and enuresis until 12 years. Growth was normal, having reached target adult height, and the development of secondary sexual characters was normal except for absence of facial hair. The patient had normal erections and maintained regular sexual activity. The physical examination disclosed dysmorphic facial features, bilateral gynecomastia, penis of normal size, testicular volume of 10-12 mL, scarce pubic and axillary hair, gynoid fat distribution, short trunk with long limbs and bilateral cubitus valgus. Lab tests were compatible with hypergonadotropic hypogonadism, with total testosterone 0.82 ng/ml, FSH 36 mU/ml and LH 34.6 ng/ml, normal 2.8 - 10.7 ng/ml) and 24 mU/ml. Acetazolamide 500 mg BID was prescribed for a week. The patient was asymptomatic at discharge. One month after the discharge, transdermal testosterone was reinstated, with a daily dose of 50 mg, with no adverse effects, recovery of the target hormonal levels and normal hematocrit.

Conclusions

HH is a rare complication of testosterone therapy, which we had not previously found in our extensive experience with testosterone treated transsexual patients. In our patient it was related to accidental overdosing, but it has occasionally been reported with standard treatment. It is a potentially severe complication, which may impair the patient’s daily activities and in the worst case scenario cause permanent blindness. The risk of HH must be considered in male transsexual patients but only very rarely may result in a contraindication for gender-affirming therapy.

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while others such as unilateral renal agenesis are less often associated with it. Other developmental abnormalities involving the cardiac, neurological and genitourinary systems may be present. This case underscores the heterogeneity of the syndrome. TXSSXY is considered a rare variant of Turner syndrome (47XXY) with additional somatic and cognitive disturbances, and usually requires multidisciplinary care and follow-up.

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**P706**

**Alterations in lipid composition are linked with decreased motility in human spermatozoa**

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Infertility is a growing concern in Western countries. Several factors, including lifestyle habits and increased prevalence of chronic disorders associated with hormonal alterations, increased chronic inflammation and systemic oxidative stress (such as obesity and diabetes mellitus), are contributing to the reduction of reproductive potential among males in modern societies. Evidence suggests these factors negatively impact human sperm quality resulting in a combination of alterations in specific sperm features, namely in their motility. Asthenozoospermia is a common cause of fertility reduction and is characterized by a reduction in sperm motility (sperm total motility <40%). Sperm lipid metabolism is crucial for sperm motility and morphology as well as for sperm-oocyte interactions, although the relevance of lipid content of human spermatozoa is poorly understood. In this work, we aimed to compare sperm lipidome from asthenozoospermic and normozoospermic men. Sperm samples from the male partner of couples seeking fertility counselling (n=57) were collected and sperm parameters were assessed accordingly to WHO guidelines. Sperm polar lipid content from asthenozoospermic (n=17) and normozoospermic men (n=39) were analysed by liquid chromatography-mass spectrometry. A total of 245 lipid molecular species were identified and quantified in sperm samples from both groups. Using a PCA model, we found a distinct lipid composition in sperm samples of asthenozoospermic men. Asthenozoospermic sperm content in LPLs suggests altered lipid metabolism in these men, which might be associated with alterations in sperm membrane fluidity and consequent decrease in sperm motility. Moreover, LPL levels suggest that increased inflammation and oxidative status might be in the aetiology of asthenozoospermia. Our results suggest that alterations in lipid metabolism might be a potential cause for chronic disorders-related sperm motility and male infertility.

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**P707**

**The role of hypothalamic markers in the development of POI following COS (in vivo)**

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Introduction

Premature ovarian insufficiency (POI) is a pathological condition, which accompanying with loss of ovarian function in women under the age of 40. This is mainly caused by hypergonadotrophic amenorrhea, infertility and ovarian deficiency. POI affects 1% of women. The specific causes can be genetic disorders, autoimmune, infectious-toxic and iatrogenic factors, but the exact mechanism is unclear yet. According to different authors, the idiopathic form accounts for 50 to 90% of cases. Increased cases of menstrual irregularities (amenorrhea), following infection with COVID-19. This abstract review the study conducted on the role of hypothalamic peptides such as kisspeptin and BDNF in the pathogenesis of premature ovarian insufficiency as a consequence of COVID-19. The pandemic has significantly impacted the mental health of women, and it can affect women’s reproductive health. This is due to stress during the pandemic. It is very important to identify markers of menstrual disorders after covid-19. The aim of the study was to study the concentrations of kisspeptin and BDNF in blood plasma in patients with POI following coronavirus disease.

Methods and results

The study included 2 groups: 44 women with diagnosed POI following COVID-19 (age 30 ± 2 years) and 15 women with regular menstrual cycle as control group (age 33 ± 3). The KISS1 and BDNF levels were measured using enzyme linked immunosorbent assay kit (ELISA KIT). In control group tests were performed in follicular phase (days 3-5). In the group with POI the level of kisspeptin was lower (268.35 ± 16.78 pg/ml) than in control group (312.95 ± 31.84 pg/ml, P < 0.005). The concentration of BDNF was also lower in group with POI (215.48 ± 37.67 pg/ml) than in control group (402.91 ± 34.12 pg/ml). The kisspeptin and BDNF plasma levels are correlated negatively with period of amenorrhea. Decreased levels of kisspeptin and BDNF in the blood correlated with the occurrence of premature ovarian insufficiency and were as risk factor for its occurrence. It showed that patients with POI were more likely to have deficiency of kisspeptin and BDNF and higher levels of FSH.

Conclusion

This study confirms the relationship between kisspeptin, BDNF and the occurrence of POI in women following COVID-19. This study provides important potential opportunities for understanding the pathology of POI.

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**P708**

**The medical treatment of polycystic ovary syndrome: effects of inositol isomers and metformin on clinical, metabolic and hormonal profile**

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Polycystic ovary syndrome (PCOS) is characterized by menstrual irregularities and clinical and biochemical hyperandrogenism, and is associated with insulin resistance, visceral obesity and metabolic disorders. The aim of the current study was to compare the effects of inositol isomers (INO) and metformin (MET) on the clinical, metabolic and hormonal aspects of PCOS. In 94 PCOS women, clinical (weight, BMI, waist circumference - WC, menstrual intervals, Ferriman-Gallway score - FGS), metabolic (fasting glucose and insulin, HOMA-IR, HOMA-beta, lipid profile) and hormonal (FSH, LH, estradiol (E2), androstenedione (A), testosterone (T)) parameters were retrospectively investigated before (T0) and after 6 months (T6) of treatment with INO (Group 1, n = 36) or MET (Group 2, n = 58). INO was administered in the 3 following formulations (F): F1, myo-inositol 1000 mg + D-chiro-inositol 200 mg; F2, myo-inositol 1100 mg + D-chiro-inositol 276 mg; F3, myo-inositol 1000 mg + alpha-lipoic acid 800 mg. At T0, FGS and hormonal profile were similar between Group 1 and 2 except for HDL (P = 0.002) and FSH (P = 0.002), which were higher in Group 1, whereas weight (P < 0.001), BMI (P < 0.001), WC (P < 0.0001), menstrual intervals (P = 0.011), fasting insulin (P = 0.001), HOMA-IR (P = 0.001), HOMA-beta (P = 0.001) and triglycerides (P = 0.001) were significantly reduced compared to baseline, with a trend to a decrease for weight, BMI, A, HOMA-IR and triglycerides. The effects of INO
formulations were similar, except for percent increase in E2, which was significantly higher (P = 0.027) in F1, compared to F3. At T6, in Group 2, weight (P < 0.0001), BMI (P < 0.0001), WC (P < 0.0001), menstrual intervals (P < 0.0001), FGS (P < 0.0001), HOMA-IR (P = 0.002), total cholesterol (P = 0.002), LDL (P < 0.0001), triglycerides (P < 0.0001), A (P = 0.003) and T (P = 0.005) were significantly reduced, whereas HDL (P < 0.0001) and HOMA-beta (P < 0.0001) were significantly increased, compared to baseline. Noteworthy, percent decrease in weight (P < 0.0001), BMI (P < 0.0001) WC (P = 0.018), HOMA-IR (P < 0.0001), total cholesterol (P = 0.046), LDL (P = 0.015) and triglycerides (P = 0.041), and percent increase in HDL (P = 0.012), were significantly higher in Group 2, compared to Group 1. In conclusion, INO and MET are effective

**P710**

**Age- and body mass index-adjusted association between insulin sensitivity and risk factors for cardiovascular disease in polycystic ovary syndrome**

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**Introduction**

Impaired insulin sensitivity accompanies polycystic ovary syndrome (PCOS). Women with PCOS are usually at risk of premature cardiovascular disease, which increases with age and body weight. We studied the link between insulin sensitivity measured by the Matsuda Insulin Sensitivity Index (MISI) adjusted to body mass index (BMI) and age in otherwise healthy PCOS women.

**Methods**

250 adult women with PCOS of reproductive age (18-43 years old) underwent measurements of MISI, lipid profile, resting heart rate, peripheral and central systolic and diastolic blood pressure. Patients were divided into tertiles of MISI (T1 (<4.74), T2 (4.74-8.35) and T3 (≥8.35), respectively). Their data were compared by the Analysis of Covariance (ANCOVA) adjusted for patients' BMI and age. Only the results with a P-value <0.05 are shown as Estimated Marginal Means +/- Standard Error in the following order: T1, T2 and T3.

**Results**

Better insulin sensitivity (patients with higher MISI values) was associated with lower plasma concentration of total cholesterol (188.2 ± 3.8, 175.3 ± 3.5 and 176.2 ± 3.6 mg/dl), low-density lipoprotein cholesterol (106.0 ± 3.4, 93.6 ± 3.1 and 91.8 ± 3.2 mg/dl), triglycerides (96.3 ± 5.3, 77.5 ± 4.8 and 76.2 ± 5.0 mg/dl), and resting heart rate (76.9 ± 1.5, 73.1 ± 1.4 and 70.0 ± 1.4 beats/minute) independent of age and BMI. Similar associations were not found for high-density lipoprotein cholesterol, peripheral and central systolic and diastolic blood pressure.

**Conclusions**

A less atherogenic lipid profile and lower heart rate, regardless of the effects of age and BMI, are observed in PCOS women with better insulin sensitivity. The clinical meaning of these findings requires further studies.

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**P709**

**Serum testosterone mirrors inflammation parameters in females admitted with covid-19 disease**

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**Background**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is showing a rapid and continuous evolution in terms of new waves, the spread of variants and the evidence of reinfections. The growing heterogeneity of clinical presentation requires the identification of underlying pathogenic mechanisms to allow a better risk stratification. Previous studies analysed the role of sex hormones in disease severity demonstrating in male patients the association of low testosterone (T) levels with unfavorable outcome of COVID-19. Conversely, data concerning the role of T in women with SARS-CoV-2 infection are scant and limited to small cohorts.

**Purpose**

To investigate the relationship between serum T values and clinical presentation and outcome of SARS-CoV-2-related pneumonia in a population of adult females admitted to hospital due to coronavirus disease 19 (COVID-19).

**Methods**

All adult females hospitalized for COVID-19 in our Institution during the period between November 1st 2020 and February 28th 2021 were evaluated for arterial partial pressure oxygen (PaO2)/fraction of inspired oxygen (FiO2) ratio, serum T and inflammatory parameters (IL-6 and procalcitonin) at study entry, need of ventilation during hospital stay and in-hospital mortality. Berlin criteria were used to define acute respiratory insufficiency (ARI).

**Results**

The study included 101 women (mean age 76.8 ± 13.8 years, mean BMI 27.3 ± 6.3 kg/m² and mean T 1.33 ± 1.3 nmol/l). A significant correlation was observed between serum T levels and IL-6 (P < 0.044) and procalcitonin (P < 0.001). At hospital admission 55% (n = 56) of subjects were diagnosed with ARI. No significant association was found between serum T levels and ARI (P = 0.227). Mean duration for hospital stay was 14.2 days, and mortality was 23% (n = 25). Subjects who died had significantly higher age (83.7 ± 10.5 vs 74.6 ± 14.1, P = 0.033), IL-6 (98.3 ± 95.3 vs 35.9 ± 39.2, P = 0.021) and procalcitonin levels (1.7 ± 4.0 vs 0.3 ± 1.7, P = 0.001) as well as significantly lower IT3 levels (2.89 ± 0.55 vs 3.70 ± 0.80, P = 0.007) as compared to survivors. No significant difference was observed in serum T levels among the two groups (P = 0.604).

**Conclusion**

Opposite to what observed in male subjects, this study provides a first preliminary evidence about the role of higher serum T levels in females as a mirror of higher inflammatory phenotype and worse COVID-19 disease course, possibly reflecting a massive adrenal cortex activation in response to systemic inflammation.

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population. Transgender individuals first attended between 2015-2020 were younger (28 vs 17 years, \(P<0.001\)), had a higher academic level (secondary education or higher in 85.5% vs 37.5%, \(P=0.001\)) and consume less anxiolytics than those first attended the preceding years (2009-2014).

Conclusions

The proportion of transgender people in the Basque Country is 2.4 per 10,000. Transgender population in the Basque Country is at risk for several morbidities. Individuals who have sought gender-affirming therapy between 2015-2020 have a better profile at baseline (younger age, higher academic level, and less psychoactive drugs use) than those first attended between 2009-2014, which likely reflects the positive changes that have taken place in our area regarding integration and improved medical care to this population.

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P712

Phenotypic and genotypic heterogeneity of sexual development disorders 46, XY in the Tunisian population

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Introduction

Sexual disorders 46 XY DSD are responsible for a range of phenotypic disorders, ranging from an ambiguous phenotype to a complete female phenotype. In this context, we report a cohort of 22 46 XY patients with a female phenotype in order to establish a phenotype-genotype correlation.

Results

The average age at diagnosis was 15.5 years (E: 7 days-33 years). The reason for consultation was primary amenorrhea in 16 cases (72.7%), sexual ambiguity in 5 cases and inguinal hernia in 1 case. The standard karyotype showed a homogenous chromosomal formula compatible with a male genetic sex, i.e. 46,XY, in 95% of cases and a mosaic formula, i.e. 46, XY/45, X in two cases. The diagnosis of gonadal dysgenesis was chosen in 4 patients (18.18%) in front of a completely female phenotype with ectopic gonads and frankly low levels of testosterone and HMA compared to age contrasting with increased FSH. Full LH resistance was retained in 3 patients with a female complete phenotype and low testosterone levels contrasting with high LH levels with histological Leydig cell agenesis, the biomolecular study of LH resistance confirmed the presence of a nonsense mutation Q525X in the second extracellular loop. A testicular steroidogenesis abnormality affecting the conversion of 

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\Delta 4-\text{androstenedione to testosterone was reported in 8 patients with a TES}^{\text{O}}/\text{D}^{\text{A}} < 0.8 
\]

ratio after HCG, a molecular abnormality of the 17a-HSD3 gene was confirmed as homozygous in (c.618C>A) in 4 patients and as heterozygous composite (Pc206X/Pp133R) in 4 others. A biomolecular abnormality of androgen resistance with the presence of a homozygous mutation of exon 5 (R753X) was identified in 5 patients with an evocative phenotype associated with high levels of testosterone and LH. Finally, a biomolecular abnormality of the 5’ reductase gene was mentioned in 2 patients with an ambiguous phenotype associated with a base-increased Testo/DHT ratio and less LH resistance. A homozygous mutation of exon 4 (p.C222T) was confirmed in a single patient.

Conclusion

The abnormalities of sexual differentiation cover a wide spectrum of phenotypic and genotypic abnormalities and pose a real problem of etiological diagnosis. To be sure, advances in molecular biology are of great value in understanding the etiopathological links between clinical aspects and the cascade of sexual differentiation.

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P714

Serum concentrations of 17-hydroxyprogesterone and dehydroepiandrosterone sulfate in women with polycystic ovary syndrome and their relation to the parameters of glucose metabolism

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Introduction

Polycystic ovary syndrome (PCOS) is characterized by menstrual disorders, hyperandrogenism and polycystic ovaries on ultrasoundography. This hormonal disorder is also strongly associated with insulin resistance. The diagnosis of PCOS can be established after the exclusion of other causes of mentioned symptoms, such as non-classic congenital adrenal hyperplasia (NCAH). To date, several studies suggest the increased serum concentration of 17-hydroxyprogesterone (17-OHP) in PCOS, even in the absence of NCAH; however, its impact on glucose metabolism has not been discussed widely in the literature.

Aim of the study

The aim of the study was the evaluation of serum 17-OHP and dehydroepiandrosterone sulfate (DHEA-S) concentrations in women with PCOS and the assessment of their relation to the parameters of glucose metabolism.

Materials and methods

We analyzed 35 PCOS women and 19 control subjects, matched for BMI (24.87 ± 4.51 kg/m2) and age (25.35 ± 4.56 y.o.). In women with PCOS, NCAH was excluded by the ACTH stimulation test. The participants were reviewed for

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anthropometric measurements, the clinical signs of hyperandrogenism, complex hormonal profile, oral glucose tolerance test (OGTT) and ovarian ultrasound parameters. The increase in 17-OHP concentrations in the ACTH-stimulation test (17-OHP delta value), the homeostasis model assessment of insulin resistance (HOMA-IR), Matsuda index and free androgen index (FAI) were calculated.

Results

The women with PCOS were distinguished by statistically higher baseline concentration of 17-OHP, FAI, the level of DHEA-S, serum glucose concentrations at 60 min and 120 min of OGTT, as well as insulin concentration at 120 min of OGTT (all P < 0.01) and higher testosterone level (P = 0.014) in comparison to the control group. In PCOS-affected women, we found the correlation between the 17-OHP delta value and Matsuda index (r = 0.77, P = 0.002), as well as testosterone and insulin at 60 min of OGTT (r = 0.5, P = 0.042). Moreover, we observed that FAI correlated with fasting insulin concentration (r = 0.76, P < 0.001), as well as HOMA-IR (r = 0.67, P = 0.005). Additionally, in a whole study group, we observed the correlation between glucose concentration at 60 min of OGTT and baseline level of 17-OHP (r = 0.39, P = 0.006), 17-OHP delta value (r = 0.44, P = 0.017), testosterone (r = 0.29, P = 0.048), FAI (r = 0.4, P = 0.016) and DHEA-S (r = 0.34, P = 0.049). We also found the relationship between DHEA-S and insulin concentration at 120 min of OGTT (r = 0.34, P = 0.049), as well as the baseline level of 17-OHP (r = 0.48, P = 0.004) in a whole study group.

Conclusion

Serum 17-OHP and DHEA-S concentrations are elevated in PCOS-affected women and their levels might be related to the parameters of glucose metabolism.

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**P715**

**Early career clinicians’ knowledge about lifestyle management of PCOS and the current practices of implementing it in clinical practice - does more need to be done?**

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**Objective**

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine conditions affecting women of reproductive age. Current estimates place the condition as more common than Type 2 Diabetes Mellitus (T2DM). Recent studies have shown several long term comorbidities associated with PCOS, thus making it essential that all physicians, regardless of training and specialty, understand and empower women with PCOS to adopt evidence-based behavioural changes. This study set out to establish an understanding of evidence-based lifestyle management of PCOS and the current practices of implementing it in clinical practice amongst final year medical students and newly graduated healthcare professionals.

**Design**

A survey was constructed using evidence-based recommendations in the national guidelines for PCOS.

**Method**

We invited final year medical students and non-specialist junior doctors in the UK to complete an online survey between September 2020 and January 2021. The findings were reported as frequency and proportion.

**Results**

A total of 67 participants took part in the survey (41 female and 25 male; medical students (21%), foundation doctors (64%) and senior house officers (15%); 54% from London deanery and 27% from the West Midlands deaneries). 54% (n = 36) knew the correct prevalence of PCOS. Although 70% (n = 47) knew biochemical androgen excess is a sign of PCOS, only 43% (n = 28) and 1% (n = 1) knew free testosterone and free androgen index respectively, were the tests of choice to diagnose this. Instead, androstenedione (52% (n = 35) and DHEAS (43% (n = 29) were the most common biochemical tests of choice by this cohort. Interestingly, 55% (n = 37) said they would use AMH as a test to diagnose PCOS. Although most of the participants knew that BMI 94% (n = 63) and waist circumference 95% (n = 64) required routine monitoring between 6-12 months for PCOS, only 6% (n = 4) were aware of the national recommendations for exercise. 36% (n = 26) identified obesity and T2DM as the most common long term effects of PCOS.

**Conclusion**

Effective evidence-based lifestyle advice and patient empowerment are crucial for enhanced clinical outcomes in people with PCOS. Our study highlights that physicians and medical students have a limited understanding of the international evidence-based recommendations for PCOS. Our future work will focus on understanding the current educational opportunities for medical students and junior doctors about lifestyle advice and patient empowerment. With this information, we will work with all involved stakeholders to improve access to these programmes for medical students and early career clinicians.

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**Thyroid P200**

**Thyroid dysfunction related to SARS-CoV-2 vaccination: the experience of a single center in Milan**

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**Background**

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic disease (Covid-19) has caused millions of deaths worldwide, thus a massive SARS-CoV-2 vaccination campaign has been launched since the end of 2020. Viruses and vaccines can induce adverse thyroid effects; SARS-CoV-2 infection and vaccines have been associated with several thyroid disorders, especially subacute thyroiditis (SAT) and Graves’ disease (GD). We aimed to study the occurrence of thyroid diseases following SARS-CoV-2 vaccination in our Centre.

**Methods**

From February 2020 onwards we have recorded all consecutive cases of SAT of any cause, noting if occurred shortly after SARS-CoV-2 infection or vaccines. We have also retrospectively extended this analysis to GD and Graves’ orbitopathy (GO). Our patients underwent blood tests for thyroid function, inflammatory markers, anti-SARS-CoV-2 antibodies and thyroid ultrasound scan.

**Results**

Up to December 2021 we have registered 15 patients with thyroid dysfunction occurring shortly after SARS-CoV-2 vaccination: 8 SAT and 7 GD, of which 3/7 (43%) also developed GO and 3/7 (43%) associated autoimmune acute hepatitis. Importantly, we observed an increased number of SAT diagnoses from June 2021 onwards, when the vaccination campaign was extended to the Italian general population. Patients’ mean age was 53 years (range 23-83 years) and females were 9/15 (60%). 3/15 (20%) patients had a previous history of thyroid disease (one subclinical hypothyroidism, one transient gestational hyperthyroidism and one Hashimoto’s thyroiditis) and 10/15 (67%) patients had a positive family history of thyroid disorders. Patients received all SARS-CoV-2 vaccination types (8 Pfizer, 5 AstraZeneca, 1 Johnson&Johnson, 1 Moderna); symptoms were developed following the first dose (mean +6 days) in 10/15 (67%), the second (mean +6 days) in 4/15 (27%) and the third (mean +4 days) in 1/15 (7%) patients. A previous documented SARS-CoV-2 infection occurred in 4/15 (27%) patients several months before the vaccination.

**Conclusions**

SARS-CoV-2 vaccines seem to be associated with the onset of SAT or GD. Possible mechanisms involve the interaction of the spike protein with the ACE-2 receptor expressed in thyroid tissue, a cross-reactivity of the spike protein with thyroid self-proteins or an immune reaction induced by adjuvants (ASIA syndrome). The majority of patients had a positive family history for thyroid disorders, thus a genetic predisposition is likely involved. Until more safety data about SARS-CoV-2 vaccines will be available, caution and strict monitoring of individuals predisposed to thyroid disorders or autoimmunity is suggested, especially those with low risk factors for Covid-19 disease.

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P201
Indications and extended follow-up of radiofrequency ablation for treatment of hyperthyroidism caused by solitary autonomous functioning thyroid nodules

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Background
Hyperthyroidism caused by autonomous functioning thyroid nodules (ATN) is usually treated with I-131. Recently, radiofrequency ablation (RFA) has emerged as a promising alternative but it is not yet incorporated in guidelines.

Aims
Assessment of efficacy of RFA treatment in patients with hyperthyroidism caused by ATN and factors that may affect treatment success.

Methods
Retrospective analysis of patients treated for hyperthyroidism caused by ATN with RFA, when follow-up of at least one year was available. Results of patients with a single toxic adenoma (STA) are compared with patients with a toxic multinodular goitre (TMG) and a dominant hyperactive nodule on scintigraphy and ultrasound. Proportions were compared by the chi-squared test. Cure was defined as thyroid medication-free biochemical euthyroidism.

Results
48 patients (36 STA, 12 TMG) were included, 85% were female, mean age was 55 (range 27-80). The median nodule volume was 12 ml at baseline. Median energy delivered during RFA was 0.6 KCal/ml. One year post RFA 29 patients (60.4%) were cured after a median of 3.2 months (range 0.1-11). Median volume reduction was 68% (range 21-99). One patient, with a history of hemihypothyroidism, developed hypothyroidism. 18 patients (37.5%) were hyperthyroid one year post RFA. Baseline and RFA parameters were similar for STA and TMG patients. The one-year cure rate was higher among STA patients compared to TMG: 72% vs 25% (P<0.05), respectively. 13 patients with persistent hyperthyroidism received re-RFA. 9 (69%) of them were cured at last follow-up (median 12 months post re-RFA). Extended follow-up was available for 31 patients (25 STA and 6 TMG). 3 STA and 1 TMG patients developed late recurrent hyperthyroidism between 24-37 months post-RFA. Of all 48 patients, cure was achieved in 86% of STA patients and in 33% of TMG patients after 1 or 2 RFA sessions at last available follow-up after first intervention (median 20 months after first intervention).

Conclusion and discussion
The efficacy of single session RFA session was nearly 3 times higher in STA patients compared to TMG. These data confirm that RFA is an effective treatment option for these patients. Cure was defined as thyroid medication-free biochemical euthyroidism. In STA patients, the efficacy of RFA is nearly 3 times higher than in TMG patients.

P202
Deiodinase Type I regulation in fatty liver disease

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Background and Aim
Hepatic thyroid hormone (TH) signalling plays an important role in onset and progression of liver diseases. Patients with altered thyroid hormone regulation in the liver, leading to a local hypothyroid, are at higher risk of developing non-alcoholic fatty liver disease (NAFLD). Treatment with thyroid hormones proved to be a promising therapy for these patients, slowing the progression of NAFLD to non-alcoholic steatohepatitis (NASH), a more advanced stage of the disease characterized by inflammation and occasional fibrosis. The action of thyroid hormone in the liver is regulated by TH transporters, deiodinases, and receptors. Among these, deiodinase type 1 (Dio1) is a major player, converting the

P203
Transoral endoscopic thyroidectomy (TOETVA) in thyroid cancer, our view as endocrinologists

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Background
Recent progress in surgical technology has resulted in new techniques as transoral endoscopic thyroidectomy (TOETVA) that is an option for patients’ cosmetic requests. We evaluated patients with thyroid cancer who underwent thyroidectomy by TOETVA approach and their follow-up. Retrospective study, 5 patients were included. Bethesda classification in FNAC resulted: 2 patients with VI category (CAT), 2: V CAT and 1: III CAT. All patients were operated by TOETVA between 2020-2021. Median age: 48 years (36-64). Median nodules size was: 13.5 mm (7-23). No patients presented adenopathies. Total thyroidectomy was performed by TOETVA in 4 patients, one patient required conversion to open thyroidectomy. Hemihiyroidectomy was performed in the patient with III CAT, the pathology report resulted in follicular carcinoma and she was later operated by conventional approach. Median size of malignant tumors was 14.7 mm (12-21). Of the 2 patients with VI CAT. 1 had a classical papillary carcinoma, the other one had a follicular variant of papillary carcinoma. The other two patients with V CAT. 1 had a classical follicular carcinoma and the other one had a nodular goiter; the patient with III CAT had a clear cell variant of follicular carcinoma. In 3 patients the thyroid capsule was absent in some areas, predominantly in the posterior margin. In 4 patients were noted electrosurgery effects and tissue atrophy. Postoperative complications were: inferior lip insensitivity (5/5), hypogeusia (4/5), mild to soft pain and hematoma in the neck (5/5), suffocating hematoma (1/5), hypoparathyroidism (3/5); all complications were transient. Four patients underwent I-131 therapy; post-therapeutic WB was shown and nodular uptake in the neck compared with the patients with conventional thyroidectomy. Stimulated thyroglobulin (TG) was normal in 3 patients and 1 had elevated TG. In the follow-up, only the patient with clear cell variant of follicular carcinoma had increased TG and presented recurrence in the neck, so she was operated again and later received radiotherapy. The remaining patients had normal ultrasonography and TG below 1.

Conclusion
Patient selection is very important in TOETVA approach. The cosmetic objective of TOETVA was reached; the complications were different, probably related to the learning curve required for surgeons. Except the patient with the aggressive follicular carcinoma, the patients’ follow-up was satisfactory. However, we need more patients and longer follow-ups to determine if the higher and different RA uptake in the neck scan and the histological findings have an impact in the long follow-up of these patients.

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**P204**

Thyrotoxicosis due to African herbal supplements: does iodine contamination play a role?  
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**Case Presentation**

In our endocrinology outpatient clinic, in the period between September 2017 and October 2021, six patients, originally from Western Africa, were referred due to abnormal thyroid function tests with suppressed TSH and elevated fT4 and/or fT3. In all patients thyroid antibodies were negative. No fever, painful swelling of the thyroid or recent URTI were reported. The patients hadn’t used any medication containing iodine nor had recently underwent a radiological study. On thyroid scintigraphy, in all patients a reduced to absent radio-iodine uptake could be seen. Ultimately, it came to light that all six patients had been taking African natural supplements. In one patient a complete 24-h urinary iodine excretion was performed, which was significantly elevated with a value of 1115.8 μg/l, confirming iodine excess. After discontinuation of the supplements, in all patients a normalization of the thyroid function tests could be obtained.

**Discussion/conclusion**

Some herbal remedies used in traditional African medicine seem to cause hyperthyroidism. Characteristics of this kind of hyperthyroidism are reduced to absent radio-iodine uptake on thyroid scintigraphy, absent thyroid autonomy, a normal thyroid ultrasound and a spontaneous restoration of euthyroid state with discontinuation of the supplements. Our hypothesis is that this type of thyrotoxicosis is caused by an increased iodine exposure due to use of natural supplements used in traditional African medicine. We suspect that the African supplements, imported from Western Africa to Europe, are treated with iodine-containing compounds to improve the preservability. Iodine-induced hyperthyroidism, or the Jod-Basedow syndrome, is therefore a cause of thyrotoxicosis that therefore must certainly be kept in mind in certain ethnic groups. If a thorough questioning of the supplement use doesn’t reveal the intake of natural remedies, then an urinary iodine excretion can sometimes provide a conclusive answer if iodine excess is suspectedly involved in the thyrotoxicosis.

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**P205**

Association between thyroid autoimmunity and gestational diabetes mellitus in euthyroid women  
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**Objective**

Pregnant women with autoimmune (subclinical) hyperthyroidism have an increased risk of developing gestational diabetes mellitus (GDM). However, this association remains controversial in euthyroid women with thyroid autoimmunity (TAI). Therefore, the aim of the study was to determine the association between TAI and GDM in euthyroid women in a logistic regression analysis with adjustments for baseline/demographic parameters.

**Methods**

Cross-sectional study in 1447 euthyroid women who performed their entire clinical/biological work-up and oral glucose tolerance test (OGTT) in our center. At median 13 (11-17) weeks of gestation, TSH, free T4 and thyroid peroxidase antibodies (TPOAb) were measured, baseline characteristics recorded and an OGTT was performed between 24-28 weeks of pregnancy. Exclusion criteria were pre-pregnancy diabetes, assisted pregnancies, and women with (treated) thyroid dysfunction before or after screening. The diagnosis of GDM was based on 2013 WHO criteria.

**Results**

Two hundred eighty women were diagnosed with GDM (19.4%), 26.1% in women with TAI and 18.9% in women without TAI (P = 0.006). TAI was associated with GDM (adjusted odds ratio (aOR) 1.69 (95% CI, 1.01-2.82); P = 0.046). Maternal age > 30 years, pre-pregnancy BMI ≥ 30 kg/m2 and another than Caucasian background were also associated with GDM, aOR 1.93 (95% CI, 1.46-2.56); P < 0.001, 2.03 (95% CI, 1.46-3.01); P < 0.001 and 1.46 (95% CI, 1.03-2.06); P = 0.034, respectively.

**Conclusions**

In our cohort, the presence of TAI in euthyroid pregnant women was associated with an increased risk of developing gestational diabetes mellitus in euthyroid women. In line with literature data, higher age and obesity were associated too. Future studies should focus on treatment options that might decrease the development of GDM in euthyroid women with TAI.

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**P206**

Discordance between fT4 and TSH concentrations during levothyroxine treatment  
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**Introduction**

Physicians in our hospital notified the laboratory staff of a number of patients at the outpatient clinic with increased free T4 (fT4) concentrations without (complete) suppression of thyroid stimulating hormone (TSH). This phenomenon appeared to occur more frequently following implementation of a new automated fT4 immunoassay. The discordance between T4 and TSH concentrations may be explained by analytical issues (not further explained here), incorrect reference intervals, or patient-related factors (e.g. medication, population). We aimed to establish the contribution of the possible factors involved.

**Methods**

First, reference intervals of the current Cobas (Roche) and former Delfia (Perkin Elmer) fT4 immunoassays were re-evaluated by using blood samples of healthy volunteers. Second, TSH (Cobas, Roche) and fT4 requests and the frequency of discordant pairings (i.e. fT4 above the upper limit of normal and TSH 0.02 – 5.0 mU/l) of patients from Amsterdam UMC were retrospectively analysed using a Delfia fT4 and Cobas fT4 cohort. Third, we performed a literature search to assess whether time of blood draw and time of levothyroxine (L-T4) ingestion may contribute to higher fT4 concentrations in L-T4 users.

**Results**

The original reference intervals belonging to the Delfia and Cobas assay were confirmed. The Delfia (n = 176, 5.5%) and Cobas cohort (n = 295, 8.6%) showed comparable frequencies of discordance. Interestingly, approximately 80% of the discordant results belonged to L-T4 users. Review of the literature showed that fT4 concentrations may vary depending on time of blood draw and, therefore, time of L-T4 intake. Besides, fT3/fT4 ratios are different in L-T4 users vs healthy controls and indicate an adapted regulation of the thyroid axis in those patients.

**Conclusion**

Discordance between fT4 and TSH concentrations was not related to the introduction of a new fT4 immunoassay. The increased fT4 concentrations with discordant TSH could not be explained by analytical issues or incorrect reference intervals, but may be explained by L-T4 intake. Physicians and laboratory specialists should be aware that patients treated with L-T4 may have fT4 concentrations above the reference interval, which was significantly elevated with a value of 1.03-2.06). However, not taking any medication and without any history of recent radiological imaging studies, the confirmation of iodine excess as the cause of the thyrotoxicosis is difficult. Especially in patients with a penchant for traditional medicine and natural supplements, a thorough inquiry about supplement use is key to establishing a correct diagnosis.

**References**

- **K** 5.0
- **P** 2.03
- **R** 1.46
- **Z** 0.034

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**P207**

Thyroid autoimmunity observed in a local center hospital of northeast Japan – Association with the nuclear power plant accidents  
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Background

Our hospital is located 40 km from the nuclear power plants (Tokyo Electric Dai-ichi; NPP) exploded in northern east Japan disaster (2010.3). After the explosion, yearly radiation dose reached to 1-10 mSV in our city and 10-50 mSV in most polluted areas (next to our city). In former ESE congress, we reported cytological analysis of nodular goiter (NOD). In the present study, patients’ thyroid autoimmunity was analyzed whether there is any difference between pre- and post-NPP accidents. Patients and methods: 1.625 new patients (pts; 6.242 exams; 2007-2021). Ultra-sonogram (US) and hormonal assay for anti-thyroglobulin (aTg), thyroid peroxidase antibody (TPO), anti-TSH receptor antibody (TSH-R) and, in case of HY, thyroid stimulating antibody (TS) were performed at their visits. Fine needle aspiration cytology (FNA) was, if necessary, performed for NOD. Clinical diagnosis: Hyperthyroidism (HY), 420 pts (26%, 1,592 exams), chronic thyroiditis (HA), 160 (10%, 642), NOD 1,045 (65%:solid 27%, cyst 12%, multiple 15%). Data was compared between pre-NPP (A, 2007-2009) and post-NPP period(B1-B3, 2010- 2021). Significance was determined by Ka2 or student t-test (significance P<0.05).

Results

1) Age: A, 55 ±18 years (n=1,295); B1 (2010-2013), 55 ±16 (n=1,796); B2 (2014-2017) 59 ±16 (n=1,495); B3 (2018-2021) 57 ±17. (B2B3 vs A, P=0.01).
2) Gender: female(%), A 21.4%; B1 29.6%; B2 23.6%; B3 25% (B< B2B3 P=0.004). 3) aTg (A, B1, B2, B3) (%): A 151 (n=1,472), B2 153 (n=1,230), B3 151 (n=1,230). (A< B2B3, P<0.0001). 4) Autoimmunity(%) : a) All periods; TP(aTg + TPO +); 10%, TP(aTg + TPO + TSH-R): 30%, (P< 0.0001). b) Period-A-B (all pts): TP(aTg + TPO + A); 18%; B1 21%; B2 29% B3 25% (A< B2B3 P=0.004). c) Period-A-B (pts): TP(aTg + TPO +); A 20% (n=97), B2 21% (n=147), B3 28% (n=253). (B, A, P<0.0001). 5) TSH-R positive(%): A 34% (n=206), B1 27% (n=232), B2 21% (n=151), B3 22% +21% (n=196). (A>B, <0.0001). 6) NOD: Autoimmune positivity(%): Solid: 41%, cyst 52% a) aTg: A 12% (n=162), B1 42% (n=246), B2 13% (n=230), B3 44% (n=298). (A< B1B3, P<0.0001). b) TSH-R: +; A 5.5% (n=162), B1 4% (n=246), B2 14% (n=230), B3 9.1% (n=296). (A<B, P<0.0001).

Discussion

There was a slight increase of aTg+ TPO+ pts and decrease of TSH-R+ pts. This phenomenon is similar to the results of Chernobyl inhabitants’ analysis. However, there are various factors influencing autoimmunity, aging, gender, residence or some others. Conclusions

No apparent effect of NPP accidents was observed in thyroid immunity. To confirm the radiation effects, more elaborated environmental study is needed.

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P208

Estimating incidence and case fatality of thyroid storm in Germany between 2007 and 2017: A claims data analysis

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Background

Given the general lack of descriptive epidemiological studies on thyroid storm, we aimed to estimate the incidence rate and case fatality of thyroid storm in Germany based on a large claims database.

Methods

Using the German Pharmacoepidemiological Research Database (GePaRD) we identified patients with at least one inpatient discharge diagnosis of thyroid storm (International Statistical Classification of Diseases and Related Health Problems, 10th revision, German modification; ICD-10-GM E05.5) between 2007 and 2017 and calculated age-standardized and age-specific incidence rates in males and females. We defined deaths occurring within 30 days of the diagnosis as thyroid storm-associated and determined case fatality by sex and age group.

Results

Overall, we identified 1,690 patients with an incident diagnosis of thyroid storm (72% females). Mean age was 60 years (standard deviation: 18.6 years). The age-standardized incidence rate per 100,000 persons per year was 1.4 (95% confidence interval [CI] 1.2 to 1.7) in females and 0.7 (95% CI 0.5 to 0.9) in males. In females ≤60 and >60 years of age, the incidence rate was 0.9 (males 0.4) and 2.7 (males 1.7), respectively. The case fatality of thyroid storm was 1.0% in males ≤60 years (females: 1.4%) and 16.7% in males >60 years of age (females: 10.9%).

Conclusion

Incidence rates of thyroid storm were markedly higher in females than in males and were three times higher in persons >60 years compared to younger age groups. Case fatality was below 2% in persons aged >60 years and markedly higher in older persons (males: 17 times, females: 8 times).

Keywords: thyroid storm; incidence; case fatality; Germany

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P209

Patients with autoimmune thyroiditis present similar immunological response to COVID-19 BNT162b2 mRNA vaccine with healthy subjects, but vaccination may affect thyroid function

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Background

This is the first study, that aimed to: a) compare immune response, namely the kinetics of neutralizing antibodies (Nabs), after vaccination with BNT162b2 mRNA vaccine between patients with autoimmune thyroiditis and controls, and b) to investigate changes in thyroid function in healthy subjects with no history of thyroid dysfunction before and after vaccination.

Methods

The entire study consisted of two sub-studies. In the first sub-study, Nabs levels after BNT162b2 mRNA vaccination were compared between 56 patients with autoimmune thyroiditis and 56 age and gender-matched healthy controls from the day of the first vaccination until a period of up to three months after the second vaccination. In the second sub-study, thyroid hormones (T3, T4, TSH) and anti-TPO or anti-TG. 72 healthy subjects with no history of thyroid disease were examined before (D1) and one month after completion of the second vaccination (D50).

Results

Among patients with autoimmune thyroiditis, the median neutralizing inhibition on D22, immediately before second vaccination was 62.5%. One month later (D50), values increased to 96.7%, while three months after the second vaccination, Nabs titer remained almost the same (94.5%). In the healthy group, median Nabs levels at D22 were 53.6%. On D50 the median inhibition values increased to 95.1%, while after three months they were 89.2%. The statistical analysis did not show significant differences between two groups (P-values 0.164, 0.390, 0.105 for D22, D50 and three months). Regarding changes in thyroid function, the mean value for T4 before vaccination was 89.797 nmol/l and one month after the second vaccination was 89.11 nmol/l (P-value = 0.649). On D1 the mean T3 value was 1.464 nmol/l, which dropped to 1.389 nmol/l on D50 (P-value = 0.004). For TSH, mean levels were 2.064 mIU/ml on D1 and fell to 1.840 mIU/ml one month after the second vaccination (P-value = 0.037). Despite decrease, all thyroid hormone levels remained within the normal range. No changes were found for anti-TPO or anti-TG.

Conclusions

This study provided evidence that patients with autoimmune thyroiditis present similar immunological response to COVID-19 BNT162b2 mRNA vaccine with healthy subjects, while vaccination may affect thyroid function.

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24th European Congress of Endocrinology

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Despite being the most successful definitive treatment for GD and offering the best response in terms of quality of life, thyroideotomy is rarely performed worldwide. Few studies evaluate its complication rate and potential prognostic factors for complications. We report our last ten years’ experience. Incidence of temporary and permanent hypoparathyroidism, temporary and permanent recurrent laryngeal nerve (RLN) injury and incidental malignancy were recorded, looking for predictors of their occurrence. Biochemical trends of TSI and TSH levels after surgery were also examined. From 1798 thyroideotomy surgeries, 162 patients undergoing total thyroideotomy for GD were collected. Median age was 44.4 years and 78.4% were female. Thirty percent of the patients needed calcitriol at discharge, and one year later this rate was 5.2%. Twelve percent of patients had injury to one RLN following surgery, with permanent damage in 1.9%. Active Graves’ orbitopathy (GO) was the second leading reason for surgery (26 cases). GO activity improved in 50% but worsened after thyroideotomy in 6 cases. Mean thyroid weight was 41.4 g and 13 glands showed incidental malignancy, all but one PTC. Prior to surgery, 94.8% of patients had measurable TSI titres (ELISA) and these were persistent 6 and 12 months after surgery in 86% and 62%, with lower titres. Median time to halve TSI titres was four months. One month after surgery, previously suppressed TSH was detectable in 75.2% of patients. There were no recurrences of hyperthyroidism. Univariate analysis showed that glandular weight, lower postoperative calcium, higher preoperative alkaline phosphatase, and parathyroid tissue in the surgical specimen were associated with immediate postoperative hypoparathyroidism, whereas higher TSI titres were associated with a higher incidence of RLN damage. Incidental carcinomas were associated with the presence of severe OG. In multivariate logistic regression, only perioperative PTH and calcium dynamics predicted the need for calcitriol, whereas preoperative [TSI] maintained the predictive value of RLN damage (OR 4.80 per 1 IU/L 1.07). OG lost predictive value for the detection of incidental cancers. Neither the finding of incidental malignancy nor the presence of parathyroid glands, nodular disease or germinal centres in histological specimen were associated with increased complication rates. Underused thyroideotomy is a safe alternative to radioiodine in GD, with a low rate of complications. It discloses occult carcinoma in 8% of GD. Surgical hyperparathyroidism is associated with perioperative calcium and PTH dynamics and this study finds a novel association between preoperative TSI level and transient LNR damage.

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P211

SARS-CoV-2 Vaccine-Associated Subacute Thyroiditis: Insights from a Systematic Review
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Introduction
Subacute thyroiditis (SAT) is an inflammatory disease of the thyroid gland causing transient thyrotoxicosis, characterized by neck pain and symptoms of thyroid hormones excess. Viral infections are considered the main trigger of SAT. SAT has also been described after vaccination against HI N1 vaccine, seasonal influenza virus vaccine, Human Papillomavirus vaccine, and hepatitis B vaccination; more recently, a rising number of cases of SAT following SARS-CoV-2 vaccination, to highlight main features and increase the awareness of this condition.

Methods
original reports of SAT developed after SARS-CoV-2 vaccination (mRNA, viral vector, or inactivated virus vaccines) were retrieved from a search of electronic databases. Individual patient data on demographics, medical history, type of vaccine, workup and therapies were collected. Wilcoxon rank-sum, Kruskal-Wallis and chi-squared tests were employed for comparisons.

Results
29 articles including 48 reports were retrieved, 3 additional cases evaluated by the Authors were described and included for analysis. Of the 51 patients, 38 (74.5%) were women, median age was 39.5 years (IQR 34-47). Patients developed SAT after a median of 10 days (IQR 4-14) after the vaccine shot. Baseline thyroid exams revealed thyrotoxicosis in 88.2% of patients, decreasing at 31.6% at follow-up. Corticosteroids were used in 56.4% of treated patients. Patients undergoing non-mRNA vaccines were most frequently Asian (P=0.019) and reported more frequently weight loss (P=0.021). All patients with a previous diagnosis of thyroid disease belonged to the mRNA vaccine group.

Conclusions
SARS-CoV-2 vaccine-associated SAT is a novel entity, that should be acknowledged by physicians. Previous history of thyroid disease may predispose to develop SAT after mRNA vaccines, but further studies and larger cohorts are needed to verify this suggestion. SARS-CoV-2 vaccine-associated SAT is usually of mild/moderate severity and could be easily treated in most cases, thus it should not raise any concern regarding the need to be vaccinated.

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Identifying the use of clinical and radiological parameters to assess moderate-severe Graves’ Orbitopathy – a multi-centre analysis of the characteristics of patients with Graves’ Orbitopathy
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Background
Early diagnosis and surveillance of Graves’ Orbitopathy (GO) is essential to prevent severe, sight-threatening complications and long-term disability; therefore, it is highly desirable to identify risk factors and early predictors of severe disease. GO is clinically assessed using the Clinical Activity Score (CAS) and the EUGOGO Severity Scale (ESS), which are subjective, qualitative tests that are used to evaluate the activity and severity at the anterior orbit. However, we propose the use of radiological characteristics, such as specific muscle enlargement, to predict the progression to severe disease. Therefore, we evaluated the clinical and radiological features of GO in patients presenting to multi-centre multidisciplinary teams in London and identified factors predictive of severe disease.

Method
A retrospective patient cohort study of 356 patients referred to three multidisciplinary (MDT) clinics in London between 2012 and 2021 was investigated. Patient characteristics were statistically analysed to investigate group-wise differences and correlations to help predict subsequent disease activity. From this analysis, odds ratios were produced for both clinical and radiological parameters.

Results
Median age was 46.0 years (interquartile range: 36-55), 79.2% female, 41.2% Asian. Out of 356 patients, 43.0% had moderate-severe or sight-threatening disease. GO was clinically assessed using the Clinical Activity Score (CAS) and the EUGOGO Severity Scale (ESS), which are subjective, qualitative tests that are associated with more severe disease. On analysis of radiological parameters, superior rectus-levator complex muscle involvement was also associated with more severe disease (OR 1.90 (1.03-3.50)).

Conclusion
These results suggest that cases of higher severity disease were more prevalent in the older demographic and the male population. The presence of radiological superior rectus-levator muscle involvement was associated with a higher incidence of moderate-to-severe disease. This provides an additional significant radiological criterion for diagnosing moderate-to-severe disease and providing all-important early intervention for these patients. This highlights the merit of both clinical and radiological assessment for the diagnosis and surveillance of Graves’ Ophthalmopathy.

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P213

Tuberculosis and myxedema coma – clinical case
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Introduction
Tuberculosis and myxedema coma (MC) are rare conditions with few case reports described. They are described in the literature as rare cases, and both are associated with an increase in mortality. Tuberculosis is described as an infectious disease secondary to a deficiency in thyroid hormone levels and increased catabolism; however, MC is due to the combined effects of hypothyroidism and chronic inflammation. This case report describes a patient with active pulmonary tuberculosis who presented with MC.

Case Description
A 65-year-old woman with a history of pulmonary tuberculosis presented with acute onset of fever, myalgia, and fatigue. On examination, she was found to be tachycardic with normal blood pressure. Laboratory evaluation revealed a low thyroid-stimulating hormone (TSH) level and elevated thyroid-binding globulin (TBG) level, consistent with hypothyroidism. Chest X-ray showed active pulmonary tuberculosis. The patient was treated with standard antitubercular therapy and thyroid hormone replacement. However, her clinical condition did not improve, and she developed acute respiratory distress syndrome (ARDS). Despite supportive care, the patient died after 3 weeks of hospitalization.

Discussion
This case highlights the importance of early diagnosis and management of both tuberculosis and hypothyroidism. The combination of these two conditions can lead to severe complications and high mortality. The timely initiation of appropriate therapy is crucial to improve outcomes.

Conclusion
This case report serves as a reminder of the importance of recognizing and managing both tuberculosis and hypothyroidism to prevent severe complications and improve outcomes.

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P214
Severe refractory active thyroid eye disease: an unmet clinical need in Europe

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Introduction
Moderate to severe thyroid eye disease (TED) has a significant impact on quality of life. In some cases, TED is resistant to systemic glucocorticoids, the mainstay of treatment since the 1950s, requiring alternative therapies. We describe here a patient with active severe TED who is refractory to various treatments.

Case presentation
A 48-year-old non-smoker male, with a long history of psoriasis, vitiligo and atrophic gastritis, presented in May 2019 with Graves’ thyrotoxicosis and was treated with methimazole. In July 2020, following 14 months of euthyroidism, he started experiencing eye pain, proptosis, and diplopia, with a clinical activity score (CAS) of 6/7. TSI (thyroid stimulated immunoglobulin) levels were 16.2 IU/l (normal range < 1.75 IU/l). He was treated with oral methylprednisolone for 3 months, showing a small response in eyelid swelling, but developed a 15 kg weight gain, proximal myopathy, peripheral edema, restlessness, and insomnia. In November 2020, he underwent total thyroidectomy. After a brief period of hypothyroidism, which was corrected with levothyroxine, he had TED improvement (CAS 4/7) and TSI normalization. In March 2021, a few weeks after COVID vaccination, his TED deteriorated significantly (CAS 6/7), while TSI rose to 4.45 IU/l. Administration of a total dose of 4.5 gr methylprednisolone in 12 weekly intravenous infusions resulted in a reduction of eyelid swelling, some pain relief, and TSI normalization. Throughout this period, he received artificial tears and oral selenium, while he remained euthyroid. However, he gradually developed worsening diplopia and several side effects, including a 7 kg weight gain, irritability, and insomnia. Tocilizumab, a monoclonal antibody against interleukin-6 (IL-6) receptor, was started intravenously (8 mg/kg). After three monthly infusions, there was significant improvement in eyelid swelling and pain, but no effect on proptosis and diplopia (CAS 5/7). Severe arthralgias and intractable pruritus necessitated discontinuation of treatment.

Conclusion
This case illustrates the therapeutic challenges around severe refractory active TED. Glucocorticoids and tocilizumab improved soft-tissue inflammation, but had minimal impact on proptosis and diplopia. There is an unmet clinical need in Europe for therapies with efficacy against proptosis and diplopia, such as teprotumumab, a monoclonal antibody against the insulin-like growth factor-I receptor. Teprotumumab, approved in 2020 by the US Food and Drug Administration for TED, is still not routinely available in Europe. In a rapidly evolving treatment landscape of TED, it is essential to ensure patient access to therapeutic advances targeting the underlying pathogenetic mechanisms in order to improve patient outcomes.

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P215
Is there a familial predisposition to severe amiodarone-induced thyrotoxicosis? Report of two cases
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Introduction
Amiodarone-induced thyrotoxicosis (AIT) occurs in up to 6% of patients taking this medication in iodine sufficient areas and in up to 10% of patients in iodine deficient areas and has a high rate of mortality, that can reach 50% in untreated severe forms. There are two main types (1 and 2) described, although usually we find mixed types, with both components. Below, we describe the cases of two brothers that developed severe mixed forms of amiodarone-induced thyrotoxicosis.

Case Report
The first case was a 61-year-old male with ischemic cardiomyopathy and atrial fibrillation which was successfully ablated in 2017 and was treated with amiodarone until September 2018. In April 2019, he was admitted to hospital because of a severe mixed AIT with initially good response to medication, which enabled discharge home with continued medical management. However, he was immediately re-admitted to the hospital due to worsening symptoms and increasing levels of thyroid hormones and required amiodarone continuous infusion and urgent total thyroidecomy. The second case was a 60-year-old male with recurrence of atrial fibrillation successfully ablated a few years prior and also treated with amiodarone until December 2020. In August 2021 he began to experience palpitations and independently decided to start amiodarone for 2 weeks. Two months later he was admitted with severe AIT, despite medical treatment. He was treated with amiodarone continuous infusion and two sessions of plasmapheresis before total thyroidecmy.

Discussion
We report two cases in the same family with severe mixed AIT. They both needed urgent thyroidecmy and amiodarone continuous infusion, useful four days before surgery to rapidly block conversion between T4 and T3, decreasing the active form of the hormone. Furthermore, in one of the cases plasmapheresis was used, being a procedure that decreases blood levels of thyroid hormone up to 40-50%. Although both cases could be explained by underlying thyroid autonomy or iodine deficiency and a Job-Basedow phenomenon, we can’t rule out the existence of familial predisposition to AIT. There is not literature describing genetic alterations potentially involved in increasing production of thyroid hormones secondary to amiodarone administration. For that reason, it would be useful to report those familiar cases of AIT, from now on, so that we can investigate which factors are involved.

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P216
Keep calm and call the surgeon: a case series of urgent thyroidectomy in thyrotoxicosis
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P217
A combining pre-surgical thyroid risk score (TRS) for nodules with indeterminate cytology
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Background
Cytology is the gold standard method for the differential diagnosis of thyroid nodules, though 25–30% of them are classified as indeterminate and, in some cases, surgery is required for a definitive diagnosis.

Aim
In order to reduce unnecessary thyroid surgeries, we set up a ‘thyroid risk score’ (TRS) to increase the diagnostic accuracy in a large series of patients with indeterminate cytology and to apply it to a validation series.

Methods
The pre-surgical TRS derived from the sum of the scores assigned at cytology, namely EU-TIRADS classification, nodule measurement, and molecular characterization (24 different genetic alterations, including point mutations and copy number variations). A 50 patients have been enrolled to date for the model validation.

Results
66/136 analyzed nodules underwent surgery and 20/86 (30.3%) were malignant.

Conclusions
In conclusion, for the first time, we generated and applied a score combining a cost-effective molecular assay with already validated tools, harboring different specificities and sensitivities. The combination of different parameters reduced the number of false negatives inherent to each classification system. The TRS > 6.5 was highly suggestive for malignancy and retained a high accuracy in the identification of patients to be submitted to surgery. A proper role of the TRS can also be predicted in the evaluation of large nodules routed to surgery in most cases. Indeed, in the era of mini-invasive procedures, a low TRS could favor the possibility to submit older patients and cases with co-morbidities to these techniques. The validation series will give more insights into the accuracy of our present TRS cut-off.

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Conclusions
In low-risk DTC patients, the response to treatment with 30 mCi is like that with higher doses. High pre-ablation Tg and AbTg should guide us to use higher doses of I131.

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P219
Utility of liquid biopsy in indeterminate thyroid nodules
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Background
Indeterminate thyroid nodules pose a diagnostic dilemma and the patients often undergo unnecessary surgeries or repeat surgery. Currently different molecular methods for detection of driver mutations are being used for better characterisation of these nodules. These methods are costly and not widely available all over the world. Currently use of liquid biopsy by measurement of cell-free DNA (cfDNA) levels from plasma has been useful in diagnosis and follow-up of cancer or other organs/tissues. We have analysed cfDNA levels in patients with thyroid nodules to explore the possibility of establishing a cut-off level for identification of malignancy and its application in the indeterminate category of nodules.

Methods
Patients underwent ultrasonography (USG) and USG-guided fine needle aspiration as well as surgery, where indicated. CfDNA was extracted from plasma by using a commercially available kit. Quantification and purity of the isolated cfDNA was measured by determining absorbance at 260 nm and 280 nm in duplicate using a Nano Drop Spectrophotometer. Surgical biopsy and histopathology were taken as gold standard for diagnosis. In initial analysis (determination of cut-off), cfDNA levels were compared between Bethesda 2 and Bethesda 5 to establish a cut-off value that could differentiate malignant from benign nodules. In the subsequent analysis, the aforementioned cut-off was applied (validation of cut-off) to those with indeterminate nodules to check ability to predict malignancy.

Results
Fine needle aspiration (n = 207) yielded patients with Bethesda 2 (n = 112) Bethesda 5 & 6 (n = 34) who underwent histopathological confirmation. Cell-free DNA levels in these 2 groups were 23.09 ± 8.47 and 90.26 ± 9.00 (ng/ml) respectively. A cfDNA cut-off of 64.05 ng/ml, with area under the curve of 0.993 (95% CI, 0.98-1.0) with 100% sensitivity and 96.4% specificity was established to predict malignancy. Indeterminate group (Bethesda 3 & 4 n = 61) underwent surgery (malignant n = 33), (benign n = 28), and using the previously identified cut-off for cfDNA, we were able to identify malignant lesions with a sensitivity of 100% and specificity of 96.4%. There was a very strong agreement between cfDNA-based classification with histopathology-based classification of benign and malignant nodules (Cohen’s kappa 0.96; P < 0.001).

Conclusion
Liquid biopsy by using plasma cfDNA could be a useful test in differentiating benign and malignant nodules in indeterminate category and help in better management.

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P220
Alpelisib-induced thyroiditis in a patient with metastatic breast carcinoma
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Background
Alpelisib is a novel phosphotyrosinolinositol 3-kinase (PI3K) inhibitor which, in combination with fulvestrant, has been shown to increase progression-free survival in patients with HR+/HER2-PIK3CA mutated advanced breast cancer[1]. Hyperglycaemia, including alpelisib-induced diabetic ketoacidosis is a known adverse effect, along with rash, diarrhoea and stomatitis. No other associated endocrinopathy has been reported to date. Case presentation: We present the case of a 50-year-old woman with metastatic breast cancer was referred from the Oncology service with a two-week history of fatigue, tremors, palpitations, sweats and myalgia, associated with raised free T4 and free T3, and suppressed TSH. Two months prior, she had been commenced on the novel Phosphotyrolinositol 3-kinase (PI3K) inhibitor, alpelisib, combined with fulvestrant, due to progression of her disease on first and second-line therapies. Alpelisib was held once abnormal thyroid function was noted. On examination the patient was tachycardic and tremulous. The thyroid was tendent to palpation without a discernible goitre. TSH <0.02 mIU/l (0.2-4.2), FT4 62.4 pmol/l (12.0-22.0), FT3 25.1 pmol/l (3.1-6.8). Anti-TSH receptor and anti-thyroid peroxidase antibodies were undetectable. She was commenced on proton pump for symptom relief. Ultrasound showed a diffusely heterogeneous gland without increased vascularity. Technetium 99 m radionuclide uptake scan showed diffusely reduced radiotracer uptake, consistent with thyroiditis. Although her hyperthyroidism initially improved with cessation of alpelisib, it deteriorated again with recommencement. The patient was commenced on prednisolone 30 mg once daily. This was weaned as her thyroid function improved, allowing for recommencement of alpelisib treatment. She currently remains euthyroid. Summary: This is the first reported case of alpelisib-induced thyroiditis in a patient treated for metastatic breast carcinoma. We have demonstrated efficacy in treatment with steroid therapy, allowing for continued treatment with this agent. Activation of the PI3K pathway has been shown to inhibit sodium-iodide symporter expression and function within thyroid follicular cells[2]. However, the patient's endocrinology of alpelisib-induced thyroiditis remains to be elucidated.

Bibliography

2. Garcia, B. and P. Santisteban, PI3K is involved in the IGF-I inhibition of symporter expression and function within thyroid follicular cells[2]. However, the pathophysiology of alpelisib-induced thyroiditis remains to be elucidated.

Introduction
Hyperthyroidism is a very common condition, and its treatment is relatively easy with levothyroxine (LT4). However, cases of resistant hyperthyroidism were reported despite high doses of levothyroxine. The aim of this study was to evaluate the usefulness of the levothyroxine absorption test to confirm or exclude a disorder of thyroid hormone absorption.

Methods
There was a retrospective study including patients who were admitted to our department between January 2018 and December 2021 for resistant hyperthyroidism under high-dose of levothyroxine (≥ 2.7μg/kg/day). Levothyroxine absorption test was performed on all patients. The percentage of levothyroxine absorption was calculated using the following formula: % LT4 absorption = [(peak ΔT4 x volume distribution) / administered dose of LT4 (μg)] x 100

(Volume distribution (dl) = 0.42 x body mass index). Normal absorption was defined by a % LT4 absorption > 60 %.

Results
Seven patients (5 women and 2 men) were enrolled in this study. Their mean age was of 39 ± 11.3 years [27-62]. Their mean body weight was 85.4 kg [72-98] with a mean body mass index of 30.5 kg/m² [25.4-36]. The average duration of hyperthyroidism was 10 years [2-20]. The mean dose of levothyroxine was 5.3 μg/kg/day. At baseline (TO), the mean TSH level was 278.8 μIU/l (nr: 0.35-4.95) and the mean FT4 level was 0.59 ng/dl (nr: 0.7-1.5). During the levothyroxine absorption test, the mean peak of FT4 was 0.80 ng/dl. The average % LT4 absorption was 4.5%. It was < 60% in all patients consistent with the diagnosis of malabsorption. Etiological investigations showed negative celiac disease serology for all patients and a helicobacter pylori gastritis in six patients.

Conclusion
Our results illustrate the interest of the levothyroxine absorption test to confirm the diagnosis of malabsorption and avoid diagnosing wrongly a pseudo-malabsorption.

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24th European Congress of Endocrinology

P222
Risk factors for acute kidney injury in patients with severe hypothyroidism
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Objective
This study aims to investigate the factors affecting development of acute kidney injury (AKI) due to severe hypothyroidism.

Methods
This retrospective observational study involved patients with primary hypothyroidism and thyroid stimulating hormone (TSH) levels of more than 50 mIU/L at their review in the endocrinology outpatient clinic, between January 2015 and April 2021. Factors affecting the development of AKI were examined by logistic regression analysis.

Results
A total of 100 patients, 20 (11 male, 9 female) in the AKI (case) group and 80 (23 M, 57 F) patients in control group, were included in our study. The median age of the case group (56 years, interquartile range (IQR) 44.3–68.5) was significantly higher than the control group (49 years, IQR 32.3–60; P = 0.027), and the ratio of males to females was significantly higher in the case group (P = 0.001). Multivariate logistic regression analyses showed that hypothyroidism diagnosed after the age of 60 years (odds ratio (OR) 59.674, 95% confidence intervals (CI) 5.955–598.031; P = 0.001), free triiodothyronine (FT3) < 1.3 pg/ml (OR 17.151, 95% CI 2.491–118.089; P = 0.004) and creatine kinase (CK) > 1000 U/L (OR 1.522, 95% CI 1.602–82.848; P = 0.015) were predictors for the development of AKI due to severe hypothyroidism (Table 1).

Conclusion
We recommend close follow-up and monitoring of patients with AKI caused by severe hypothyroidism if aged > 60 years, CK > 1000 U/L or FT3 < 1.3 pg/ml.

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P223
Assessment of the Quality of life in patients with well-controlled primary hypothyroidism: is there a relationship between quality of life and the TSH level?
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Introduction
Poorly controlled hypothyroidism is a chronic disease frequently associated with an impaired quality of life (QoL). However, persistent symptoms may be observed in well-controlled hypothyroid patients, impacting their QoL. The aim of our study was to assess the QoL in patients with well-controlled primary hypothyroidism and to evaluate the relationship between the TSH level and the QoL.

Methods
A cross-sectional study was conducted in the outpatient clinic of our department in December 2021. Patients with well-controlled primary hypothyroidism (TSH level between 0.35–4.94 mIU/L), and aged less than 65 years were enrolled in this study. Clinical and paraclinical data were collected from medical records. QoL was assessed using the SF36 questionnaire.

Results
Seventy patients (65 women and 5 men) were enrolled in this study. Their mean age was 51.2 ± 9.6 years. The mean duration of hypothyroidism was of 6.7 years. Primary hypothyroidism was secondary to Hashimoto’s thyroiditis, thyroidectomy, and radioactive iodine therapy in 55%, 23%, and 14% of cases, respectively. The average dose of levothyroxine was of 97.32 µg/day (25-225). Mental health score (r = 0.24, P = 0.045) and social role functioning score (r = 0.257, P = 0.032) were negatively correlated with the TSH level. The QoL was good in 52% of patients and moderate to poor in 48% of patients. The mean TSH level was significantly lower in patients with good QoL than in those with moderate to poor QoL (P = 0.024). On the other hand, role limitation due to emotional problems score and the SF36 total score were significantly higher in patients with TSH level < 2.5 mIU/L than in those with a TSH level ≥ 2.5 mIU/L. A TSH level < 2.5 mIU/L was significantly associated with a better QoL. (Odds Ratio 2.83, P = 0.035, 95% CI: 1.06–7.58).

Conclusion
In patients with well-controlled primary hypothyroidism, mental health and social role functioning scores were negatively correlated with TSH level. A TSH level < 2.5 mIU/L was positively associated with a better QoL. However, many other factors may impact the QoL of patients with hypothyroidism. Therefore, further studies involving larger sample sizes would be useful to confirm our findings.

DOI: 10.1530/endoabs.81.P223

Table 1 Univariate and multivariate binary logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>Lower</th>
<th>Upper</th>
<th>p</th>
<th>OR</th>
<th>Lower</th>
<th>Upper</th>
<th>p</th>
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<td>0.121</td>
<td>0.902</td>
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<td>59.674</td>
<td>5.955</td>
<td>598.031</td>
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<td><strong>Age &gt; 60 years</strong></td>
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<td>0.080</td>
<td>0.621</td>
<td>0.004*</td>
<td>0.006</td>
<td>0.002</td>
<td>0.006</td>
<td>0.006</td>
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<td><strong>Age &gt; 60 years at diagnosis of hypothyroidism</strong></td>
<td>0.127</td>
<td>0.035</td>
<td>0.462</td>
<td>0.002*</td>
<td>1.3 pg/ml</td>
<td>0.080</td>
<td>0.019</td>
<td>0.345</td>
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<td><strong>DM</strong></td>
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<td>0.042</td>
<td>0.580</td>
<td>0.006*</td>
<td>11.522</td>
<td>1.602</td>
<td>82.848</td>
<td>0.015*</td>
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<tr>
<td><strong>HT</strong></td>
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<td>0.023</td>
<td>0.235</td>
<td>&lt; 0.001*</td>
<td>17.151</td>
<td>2.491</td>
<td>118.089</td>
<td>0.004*</td>
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<td><strong>Hyperuricaemia</strong></td>
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<td>0.024</td>
<td>0.503</td>
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<td>0.082</td>
<td>0.739</td>
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<td>0.080</td>
<td>0.019</td>
<td>0.345</td>
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<tr>
<td><strong>FT3 &lt; 1.3 pg/ml</strong></td>
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<td>0.083</td>
<td>0.700</td>
<td>0.007*</td>
<td>0.241</td>
<td>0.083</td>
<td>0.700</td>
<td>0.009*</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; HT: hypertension; CK: creatine kinase; FT4: free thyroxine; FT3: free triiodothyronine.

*Statistically significant (P < 0.05).

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25 cases and full thyroid recovery or chronic thyroiditis/hypothyroidism were observed in 72% and 28% of cases, respectively. From June to December 2021, the percentage of SAT in files was 1.5%. SAT diagnoses increased (P=0.03) in 2021 compared with the 2000-2020 period. The median age of SAT patients in 2021 (54 years; 50-61) was higher (P=0.05) than in the 2000-2020 period. To date, 6 women have been followed up for 2-4 months. In 2 women, a decrease in thyroid volume was noted, while in 4, TSH was suppressed or increased; in the remaining 2, L-T4 was ongoing. Pain, palpatiation and aggravating disappeared after treatment. Subclinical hypothyroidism (ScH) and Graves’ disease (GD), are both characterized by the presence of circulating thyroid antibodies and inflammation by autoreactive lymphocytes in the thyroid gland and sometimes the orbit. One of the most studied mechanisms underlying AITD is the imbalance between immune activation and immune homeostasis of CD4+CD25+ T cells or T effector cells (Teff) and CD4+CD25+FOXP3+ regulatory T cells (Treg). Histone deacetylases (HDACs) are enzymes that exert posttranslational modifications at protein level. HDAC9 interacts with FOXP3, the master regulator of Tregs, leading to an imbalance in Treg function. We have recently reported an increase expression of HDAC9 in Treg cells from AITD patients. Objective To investigate the in vitro effects of HDAC inhibitors (trichostatin A (TsA) a pan-inhibitor, TMP-269 a class IIa inhibitor and the FDA approved pan-inhibitor, suberanilhydroxamic acid (SAHA/Vorinostat)) on human freshly isolated CD4+CD25- T effector cells from AITD patients. Methods Toxicity assays were evaluated using LIVE/DEAD Viability-Cytotoxicity Kit on T cell proliferation by each inhibitor. Treg suppression assays were carried out in healthy controls and AITD patients. CD4+CD25+ Tregs were isolated from fresh PBMC using CD4+CD25+ Regulatory T Cell Isolation Kit (Miltenyi Biotec). To evaluate proliferation T eff cells were CFSE-labeled, and added to wells in serial dilutions giving Treg/Teff ratios of 0.1; 1:1; 1:2; 1:4 and 1:8 and in the presence or absence of differing concentrations of HDAC9 and using DMSO as control. Results Toxicity assays revealed that TMP269 and SAHA demonstrate the same viability and viability as control cells. On the contrary, TsA decreased significantly the viability at the minimal concentration used, discarding this inhibitor from our assays. Suppression assays using the TMP269 inhibitor did not showed significantly effects on the proliferation of CD25- T cells. However, SAHA caused a mild to moderate impairment of CD25- division. Conclusions Among all the inhibitors assessed, SAHA did not exert a toxic effect in cells and had a significantly decrease on Teff proliferation compared to TMP269. Our study also showed that the impaired proliferation of CD4+CD25-Teff cells by SAHA, was not only by a specific Treg mediated effect, but also by the decrease in the CD4+CD25- cell division rate. These findings suggest that HDAC inhibition by SAHA may serve as a possible treatment of inflammation in AITD. DOI: 10.1530/endoabs.81.P225

**P227**

**Thyrotoxicosis-associated anemia at baseline and after methimazole treatment**

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**Background**

Overt newly diagnosed hyperthyroidism is frequently associated with mild anemia. However, there are limited data on long term evolution under methimazole treatment. Our aim was to study the baseline characteristics and evolution of anemia in the hyperthyroidism setting.

**Methods**

We retrospectively assessed 58 consecutive patients [46 (79.3%) women] presenting with newly diagnosed overt thyrotoxicosis (43 Graves disease, 9 toxic nodular goiters, 4 toxic adenomas and 2 drug induced hyperthyroidism) in our practice. Of these, 30 were reassessed after 4-6 months of methimazole treatment. No patient had treatment for anemia. We measured thyroid-stimulating hormone, free thyroxine, hemoglobin (Hb), hematocrit, red blood cells, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration at both baseline and 4-6 months assessments. Anemia was defined by a Hb value <12 g/dl in women and <14 g/dl in men.

**Results**

At baseline, 19 patients (32.76%) had normochromic normocytic anemia, of whom 14 (73.83%) were women. Mean Hb was 11.5 ± 0.25 g/dl and 12.4 ± 0.97 g/dl.
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g/dl in women and men respectively. FreeT4 (39.53±20.2 pmol/l) inversely correlated with Hb in women (r=0.45, P<0.05), but not in men. All patients (25 women, 5 men) that were assessed after 4-6 months of methimazole treatment had normal Hb levels (including 7 women and 1 man with anemia at baseline).

Conclusions
Our study demonstrated that hyperthyroidism is frequently associated with mild normochromic normocytic anemia. 4-6 months of methimazole treatment leads to resolution of anemia.

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P228
When patients with DTC can be discharged to primary care
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Purpose
To evaluate if patients with low- or intermediate-risk differentiated thyroid cancer (DTC) can be discharged to primary care.

Material and Methods
The clinical records and evolution of 346 patients with DTC who had undergone surgery between 1995 and 2020 with a follow-up after a mean of 7.6 ± 6.1 years were retrospectively reviewed. All had a low or intermediate risk of recurrence as defined under the 2015 ATA risk stratification system and a minimum follow-up of one year. Biochemical (thyroglobulin) and structural (imaging findings) yearly evaluations were used to statistically classify patients based on their response to treatment as excellent, indeterminate, biochemically incomplete or structurally incomplete. Primary outcome was the assessment of disease recurrence (biochemical or structural) as defined under the 2015 ATA guidelines.

Results
Throughout follow-up, 14.7% (n=51) patients presented disease recurrence. When classified by initial risk of recurrence (low or intermediate) it was seen that 4.53% (11/243) of low-risk patients and 39.81% (41/103) of intermediate-risk patients presented recurrence. This difference was statistically significant (P<0.001) with no statistically significant difference in follow-up times between the two groups (P=0.34). Moreover, when examined in terms of response to treatment, it was seen that only 1% (2/193) of low-risk patients with an excellent response to treatment presented recurrence. The majority of patients presented disease recurrence in the first five years of follow-up, 98% (50/51), the mean time to recurrence being 9.38 ± 18.68 months.

Conclusions
Low- and intermediate-risk DTC patients exhibiting an excellent response to treatment have a minimal recurrence risk that could offer the possibility of discharge to primary care follow-up after a five-, or a more cautious ten-year, follow-up period. The 2015 ATA risk stratification system proves to be an accurate and useful tool for the prediction of recurrence both postoperatively as well as at specific points during follow-up.

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P229
An innovative synthetic support for cytological and immunocytochemical assessment in cytologically indeterminate thyroid nodules.

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Background
Fine needle aspiration (FNA) is the diagnostic procedure of choice in the evaluation of thyroid nodules. Nodules with indeterminate cytological categories, Tir3A and Tir3B according to Italian cytological classification, pose diagnostic challenges in clinical practice and are frequently submitted to diagnostic surgery. CytoFoam Core (CF) (DiaPath, Martinengo, Italy) uses an absorbent foam device inserted into the needle hub to collect the cytological sample aspirated during FNA. The specimen is formalin-fixed and paraffin-embedded similarly to the microhistological material obtained with core-needle biopsy.

Aim of the study
To assess diagnostic efficacy of CytoFoam core, compared to traditional cytology, in re-evaluating thyroid nodules classified as Tir3A. Post-surgical histology was used as reference standard.

Method
Retrospective study on 89 patients with a first indeterminate cytological report who were referred to the Department of Endocrinology of Regina Apostolorum Hospital (Albano L. Rome, Italy) for a second FNA. FNA was performed after at least one month under ultrasound guidance with a 23G needle according to the established procedure. During the second procedure, both traditional cytological (TC) smears and a single-pass CF specimen were obtained for each patient. On CF samples immunocytochemical staining for Galectin-3, HBME-1, and CK-19 was also performed. Forty-five patients eventually underwent surgery, and their histological diagnoses were compared to the TC and CF reports. Four parameters were blindly and independently compared by two cytopathologists with specific thyroid expertise: inadequacy rate, rate of persistent indeterminate (Tir3A and Tir3B) reports, rate of malignancy in persistently indeterminate nodules, and rate of cancer in lesions cytologically classified as malignant.

Results
Non-diagnostic samples were 8/45 (17.7%) in TC vs 5/45 (11.1%) in CF samples (P=0.4). Persistent indeterminate samples were 27/45 (60%) in TC vs 16/45 (35.5%) in CF samples (P<0.005). The rate of malignancy in persistently indeterminate nodules was 8/16 (50%) in CF group vs 9/27 (33.3%) in TC group (P=0.4). Five/45 (11.0%) samples were classified as benign by TC vs 16/45 (35.0%) samples by CF (P<0.005). All these nodules resulted benign at post-surgical evaluation. Five/45 (11.0%) samples were classified as suspicious for malignancy/malignant in TC group against 8/45 (18.0%) samples in CF (P=0.4).

Post-surgical evaluation confirmed malignancy in all these cases.

Conclusion
CytoFoam core demonstrated greater diagnostic accuracy than TC in repeat FNA assessment of cytologically indeterminate nodules. CF increased the conclusive diagnosis rate and decreased the number of cytologically indeterminate cases. A large prospective study is needed to confirm this pilot study results.

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P230
Development of a new ultrasound score to predict thyroid nodule malignancy

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Introduction
Thyroid cancer remains a relatively rare entity. Radiological scoring systems aim to stratify the risk of malignancy based on morphological criteria. The objective of this study was to develop a new score based on ultrasound criteria to predict thyroid nodule malignancy risk.

 Patients and methods
This was a retrospective study including 200 thyroid nodules (100 malignant nodules and 100 benign nodules). The report of the thyroid ultrasound and the sum of the ORs of the ultrasound criteria for each nodule.

Results
The clinical records and evolution of 346 patients with DTC who had undergone surgery between 1995 and 2020 with a follow-up after a mean of 7.6 years were retrospectively reviewed. All had a low or intermediate risk of recurrence as defined under the 2015 ATA guidelines.

To assess diagnostic efficacy of CytoFoam core, compared to traditional cytology, in re-evaluating thyroid nodules classified as Tir3A. Post-surgical histology was used as reference standard.

Method
Retrospective study on 89 patients with a first indeterminate cytological report who were referred to the Department of Endocrinology of Regina Apostolorum Hospital (Albano L. Rome, Italy) for a second FNA. FNA was performed after at least one month under ultrasound guidance with a 23G needle according to the established procedure. During the second procedure, both traditional cytological (TC) smears and a single-pass CF specimen were obtained for each patient. On CF samples immunocytochemical staining for Galectin-3, HBME-1, and CK-19 was also performed. Forty-five patients eventually underwent surgery, and their histological diagnoses were compared to the TC and CF reports. Four parameters were blindly and independently compared by two cytopathologists with specific thyroid expertise: inadequacy rate, rate of persistent indeterminate (Tir3A and Tir3B) reports, rate of malignancy in persistently indeterminate nodules, and rate of cancer in lesions cytologically classified as malignant.

Results
Non-diagnostic samples were 8/45 (17.7%) in TC vs 5/45 (11.1%) in CF samples (P=0.4). Persistent indeterminate samples were 27/45 (60%) in TC vs 16/45 (35.5%) in CF samples (P<0.005). The rate of malignancy in persistently indeterminate nodules was 8/16 (50%) in CF group vs 9/27 (33.3%) in TC group (P=0.4). Five/45 (11.0%) samples were classified as benign by TC vs 16/45 (35.0%) samples by CF (P<0.005). All these nodules resulted benign at post-surgical evaluation. Five/45 (11.0%) samples were classified as suspicious for malignancy/malignant in TC group against 8/45 (18.0%) samples in CF (P=0.4).

Post-surgical evaluation confirmed malignancy in all these cases.

Conclusion
CytoFoam core demonstrated greater diagnostic accuracy than TC in repeat FNA assessment of cytologically indeterminate nodules. CF increased the conclusive diagnosis rate and decreased the number of cytologically indeterminate cases. A large prospective study is needed to confirm this pilot study results.

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Congestive heart failure as a first-time presentation of thyrotoxicosis in COVID-19 positive patient

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Background

The clinical manifestations of thyrotoxicosis do not always correlate with the extent of thyroid biochemical abnormalities. Here, we report the case of a COVID-19 positive patient who presented with congestive heart failure as a first-time presentation of thyrotoxicosis.

Case report

A 40-year-old female presented to Emergency Department with two days history of lower limb oedema and abdominal distension. She denied dyspnoea, chest pain, palpitations, weight loss or heat intolerance. She had history of cervical cancer 3 years prior, treated with oophorectomy and hysterectomy and 10 pack-year smoking. On clinical examination, diffusely enlarged thyroid gland, irregularly irregular pulse and signs of congestive cardiac failure (raised JVP, gallop rhythm, reduced air entry in lower zones of the lungs, pitting oedema up to hips bilaterally) were observed. ECG showed atrial fibrillation with atrial flutter; chest X-ray showed bilateral moderate pleural effusion. Laboratory work-up revealed deranged liver biochemistry (bilirubin 38 µmol/l, ALT 13 U/l, GGT 120 U/l, alkaline phosphatase 339 U/l), normal troponin, elevated d-dimer (1340 ng/ml), markedly elevated pro-BNP (7421 pg/ml), markedly elevated free T4 73 pmol/l (range 8.3-19 pmol/l), free T3 27 pmol/l (range 3.8-6 pmol/l) and suppressed TSH <0.01 mU/l (range 0.38-5.33 mU/l). She had positive SARS-CoV-2 PCR on surveillance testing but no symptoms of COVID-19 infection. Transesophageal echocardiogram demonstrated left ventricular dysfunction (ejection fraction 35%), impaired right ventricular systolic function, dilated left and right atria. CT pulmonary angiogram/abdomen/pelvis showed no evidence of pulmonary embolism but demonstrated moderate to large bilateral pleural effusion with extensive free intra-abdominal fluid, an enlarged thyroid gland and heterogeneous liver parenchymal enhancement. She was treated with IV magnesium, IV furosemide and anticoagulation on admission, later commenced on oral carbimazole 20 mg bd, propranolol and IV furosemide infusion (180 mg/24hr) for further diuresis. Heart failure medications were adjusted as per management.

Discussion

Our case highlights that thyrotoxicosis can present with congestive cardiac failure with no classical symptoms of hyperthyroidism. Thyrotoxicosis values should be considered in cases with a new presentation of heart failure. There is evidence that COVID-19 may be associated with high risk of thyrotoxicosis. It remains unclear if COVID-19 infection was coincidental or precipitated thyrotoxicosis with heart failure in our case.

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P232

Levothyroxine Replacement Therapy overuse. Factors suggesting treatment discontinuation

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Background

Levothyroxine (LT4-Rx) is one of the most prescribed drugs worldwide and the vast majority of patients receive long-term treatment. However, in a recent study of 291 subjects we found that 60% of this cohort were euthyroid two months after LT4-Rx discontinuation1.

Aim of the study

A prospective clinical cohort follow-up study was carried out. In 688 subjects (82% females) aged 48.01 ± 15.96 years (range 17-84 years) on LT4-Rx without a solid diagnosis of hypothyroidism, the treatment was abruptly interrupted. The treatment indications and corresponding percentage for LT4-Rx were classified as nodele(s) (33%), indefinite (27%), post-partum (7%) and Hashimoto’s (33%). Follow up for a short period of time occurred in 54% of subjects (< 4 months, Group A) and long-term follow-up was achieved in the remaining (up to 60 months, Group B). The studied subjects were evaluated at the time LT4-Rx was discontinued. 2 months later and at the end of follow-up. At each time point, estimation of TSH, FT4 levels and thyroid ultrasound was performed. A TSH value of ≥ 4.5 IU/ml was considered as underlying hypothyroidism.

Results

Among the entire cohort, n = 158 subjects became hypothyroid, while the remaining n = 530 remained euthyroid off LT4-Rx (23 vs. 77%, P < 0.001). On subgroup analysis, 40% of subjects comprising Group A became hypothyroid, whereas the corresponding value for Group B was 3%. In Group A, the reason for LT4-Rx, LT4 dose, LT4 dose/BMI, TSH levels and the existence of thyroid autoantibodies (ATA) were significantly different in those who became hypothyroid. No difference among any parameter evaluated was disclosed in Group B. Subjects with diagnosis of Hashimoto’s, positive ATA, higher TSH values and higher LT4 dose had significantly higher probability to become hypothyroid. Furthermore, in Group A, 15.4% became hypothyroid with baseline TSH > 3 IU/ml vs. 5.4% with baseline TSH < 3 IU/ml (P < 0.001); the corresponding values for Group B were 44.4% vs. 10.0% (P < 0.001), respectively.

Conclusions

These findings suggest considerable overuse of thyroxine administration. In cases of uncertainty, the existence of nodules, a low-normal TSH value, a relative small T4 dose and the absence of ATA are strong indicators of euthyroid patients on LT4-Rx and accordingly treatment discontinuation is strongly advised. Furthermore, in the case that a subject does not become hypothyroid 2-4 months post treatment discontinuation, then the likelihood to develop hyperthyroidism long term is insignificant.


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P233

A case of severe hypothyroidism causing reversible chronic kidney disease

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Introduction

Despite hypothyroidism being seen in patients with kidney disease, it is rarely the underlying cause. We present a rare case of chronic kidney disease (CKD) secondary to severe hypothyroidism that was totally reversed on commencement of Levothyroxine. The mechanism is multifactorial, and importantly involves the pre-renal and direct renal effects of thyroid hormones.

Case report

A 37-year-old Caucasian male presented to the endocrine clinic in March 2020 after a GP friend mentioned that he did not look well. The patient did not feel unwell himself, however on direct questioning complained of cold intolerance, fatigue, puffy eyelids, and weight gain over the preceding years. Most notable to the patient was hair loss on the body and scalp which had left him bald. The
Subacute thyroiditis following mRNA anti-SARS-CoV-2 vaccination in a patient with solitary kidney: a case report

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Introduction
Massive anti-SARS-CoV-2 vaccination campaigns have been established as the cornerstone of confronting the current COVID-19 pandemic. Subacute thyroiditis (SAT) comprises an inflammatory process in the thyroid gland, mostly due to viral infections of the upper respiratory tract, although it may rarely occur after vaccine administration. To date, a few cases of SAT related to anti-SARS-CoV-2 infection have been reported globally. Hereby, we present the case of a patient with solitary kidney who developed SAT, mild thyroid autoimmunity activation and subsequent permanent hypothyroidism after mRNA-based anti-COVID-19 vaccination.

Case report
A 79-year old male patient with solitary kidney due to nephrectomy after drug-induced acute renal failure presented for evaluation in terms of newly detected subclinical hyperthyroidism and neck pain starting 20 days ago. The patient had a known history of mild subclinical hyperthyroidism diagnosed 2 years ago without laboratory-confirmed autoimmune etiology (negative thyroid-related autoimmune antibodies) and without levothyroxine supplementation. Neck pain and tenderness as well as slow grade fever with intermittent episodes of hypothermia had an onset 10 days after the first dose of the mRNA vaccine Comirnaty and continued after administration of the second dose 2 weeks before the patient’s visit. The neck ultrasound revealed a pattern typical of subacute thyroiditis with bilateral volume growth and diffuse hetero-echogenicity and inhomogeneity accompanied by reduced blood flow; the adjunctive laboratory evaluation showed elevation of the inflammatory markers (CRP, ESR) with thyroid volume and the hypoechoic inflammatory zones.

Conclusion
Despite being commonly encountered and well understood individually, hypothyroidism is an underappreciated reversible cause of renal impairment and the interaction between thyroid hormones and the kidneys are rarely remembered. Patients can be asymptomatic even with severe hypothyroidism and CKD; the treatment is sufficient replacement with Levothyroxine which can show profound kidney improvement — as with our patient this can happen within only two months. Hence, clinicians should ensure that renal function tests be performed on initial diagnosis of hypothyroidism to ensure that this reversible complication can be adequately managed with Levothyroxine.

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Thyrotoxic periodic paralysis: a case report
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A rare complication of thyrotoxicosis among Asians is Thyrotoxic Periodic Paralysis (TPP), with an incidence of approximately 2% in patients with thyrotoxicosis from any cause. TPP is characterized by sudden onset of hypokalemia and muscle paralysis. Hypokalemia in TPP results from an intracellular shift of potassium induced by the thyroid hormone sensitization of Na+/K+ ATPase rather than depletion of total body potassium. Treatment of TPP includes correcting the underlying hyperthyroid state, prevention of potassium shift by using non-selective beta-blockade, and replacing potassium. TPP is curable once a euthyroid state is achieved. We describe here a rare case of TPP in a young Chinese man who presented with sudden bilateral lower limb weakness. A 23-year-old gentleman of Chinese origin, presented to the outpatient department with complaint of bilateral lower limb weakness for one day. Motor examination revealed normal bulk and reflexes bilaterally but power was 2/5 in both the lower limbs. His initial electrolytes showed severe hypokalemia of 1.3 mmol/l (Range: 3.5-5.1 mmol/l). Hypokalemia was rapidly corrected with IV potassium. His symptoms subsequently improved and patient was discharged. At discharge his potassium level was 4.1 mmol/l. Follow up was advised but patient was lost to follow up. Three weeks after the initial presentation, patient again presented to the emergency department with complaints of sudden onset of bilateral lower limb weakness. Motor examination of the lower limb revealed decreased tone and power was 1/5 bilaterally. No goiter, lid lag and lid retraction noted. Rest of the systemic examination was unremarkable. Laboratory findings were significant for a potassium of 1.3 mmol/l. Potassium (K) was replaced intravenously (IV) and when rechecked, the potassium level was 5.2 mmol/l. Patient lower limb weakness also improved clinically. Endocrinology was consulted as laboratory workup revealed a suppressed TSH (<0.010 uIU/ml). We advised checking FT3, FT4 and thyroid receptor antibodies (TRAB), FT4 was markedly elevated at 4.24 ng/dl (Range: 0.89-1.76 ng/dl) and TRAB was positive 8.85 IU/l (Range: 0-1.75 IU/l). Endocrine team recommended initiating anti-thyroid medication, Neomarzole 15 mg two times a day. He was discharged as soon as K levels normalized. Potassium on discharge was 4.9 mmol/l. It is important to consider TPP as a differential in a patient presenting with low
potassium levels and neurological symptoms as management initially with propranolol and of the underlying thyrotoxicosis is essential in definitive treatment of the recurrent periodic paralysis.

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P237
A case of the uncommon Marine-Lenhart syndrome
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Background
The combination of a toxic adenoma and Graves’ disease compose the Marine-Lenhart syndrome. This condition is estimated to occur in 0.8-2.7% of Graves’ disease patients and only few cases are reported in the literature.

Patient findings
A 29-year-old female patient was referred to our outpatient clinic due to subclinical hyperthyroidism and a newly discovered thyroid nodule on the right thyroid lobe. She had no thyreotoxic symptoms and the clinical examination was unremarkable. Her initial blood tests were: TSH 0.01 mU/l (reference 0.16-4.25 mU/l), fT3 8.3 pmol/l, (reference 3.6-6.4 pmol/l), fT4 15.6 pmol/l (reference 12.3-20.2 pmol/l) and TSH-Receptor-Ab titers < 0.30 U/l (reference < 1.75 U/l). The thyroid ultrasound and scintigraphy revealed a toxic adenoma in a right sided goiter. Following a radiiodine ablation with 200 MBq 131-I was performed. follow-up ultrasound after six months revealed a 70% volume reduction of the formerly toxic adenoma of (2.6 ml, pre-therapy 8.7 ml). Two months later at the regular after-therapy follow-up, a manifest hyperthyroidism was revealed [TSH 0.004 mU/l, (reference 0.10-4.00 mU/l), fT3 28.1 pmol/l (reference 3.0-9.5 pmol/l) and fT4 21.4 pmol/l (reference 10.0-28.0 pmol/l)] and the TSH-Receptor-Ab titers were elevated [1.85 U/l (reference < 1.75 U/l)]. The patient was still completely asymptomatic. The thyroid scintigraphy was repeated and showed a symmetrical, elevated radionuclide uptake, leading to the diagnosis of Graves’ disease. A thyrostatic therapy with carbimazole was initiated and continued for 8 months, until the thyroid function markers in the blood were normalised.

Conclusion
The existence of both a toxic adenoma and a Graves’ disease in the same patient has been termed as Marine-Lenhart syndrome. This coexistence may be observed simultaneously or in different stages, according to the bibliography. In cases where radioiodine treatment of a toxic adenoma is indicated, attention is required, because it may trigger the Graves’ disease, as shown in this case. Every new presentation of hyperthyroidism should be investigated as a new pathology, as it may reveal a new underlying condition indicating the need for different therapeutical pathways.

Photos
Thyroid scintigraphy 09.06.2020

Thyroid ultrasound 09.06.2020

Thyroid ultrasound 18.01.2021

P238
The use of body composition measured by CUN-BAE as a simple tool to predict the LT4 titration after total thyroidectomy in patients with benign and malignant thyroid disease
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Background
Patients who require levothyroxine (LT4) supplementation after total thyroidectomy often have difficulty achieving target TSH levels. Several studies have attempted to develop a dosing schedule considering different factors such as age, gender, weight, or body mass index (BMI) as potential determinants of the correct dose of LT4. The objective of this study is to determine if a scheme that uses the percentage of body fat (%BF) measured by CUN-BAE is more accurate to correctly predict levothyroxine dose requirements.

Methods
Data from 143 patients who underwent total thyroidectomy for benign and malignant disease at our institution between 1993 and 2021 were retrospectively reviewed. Two new dosing formulas, CUN-BAE Model 1 and CUN-BAE Model 2, were designed using Poisson’s regression. These dosing models were applied to our cohort and

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compared with other dosing schemes proposed in the literature. The accuracy of each model was established by determining the proportion of correct estimates.

Results
CUN-BAE-1 and CUN-BAE-2 accurately estimated 61.5% and 62.9% of LT4 doses, respectively. These results slightly improve the precision of previous methods such as the Poisson regression proposed by Zaborek et al based in several factors including BMI (estimated 60.1%) and the weight-based model (estimated 59.9%) of correct doses.

Conclusion
— The use of %BF calculated by the CUN-BAE formula to adjust the dose of LT4 after total thyroidectomy is a simple and accurate method that improves current formulas based on weight or BMI.

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P239

Frequency of autoimmune thyroid disease in polycystic ovary syndrome: case-control study

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Introduction
Polycystic ovary syndrome (PCOS) is a common endocrine pathology in women with a high prevalence varying between 5 and 20%. Autoimmune thyroid diseases (AITD) are the most prevalent organ-specific autoimmune diseases, particularly in young women. The purpose of our study was to determine the prevalence of AITD in a group of patients with PCOS compared to a control group.

Patients and Methods
103 women were recruited into the study, aged between 18 and 46 years. They were divided into two groups matched for age and body mass index. The first group included 51 women with PCOS and the second group included 52 healthy volunteers. Serum-free thyroxin (FT4), thyroid-stimulating hormone (TSH), anti-thyroid peroxidase antibody (anti-TPO) levels were evaluated. The diagnosis of Hashimoto’s thyroiditis was made when the participant had hypothyroidism coupled with high level of anti-TPO.

Results
The age and the body mass index were comparable between the two groups (29.6 ± 6.5 vs. 29.2 ± 6.1 years, P = 0.81; 30.3 ± 6.5 vs 29.3 ± 8.9 Kg/m2, P = 0.19). The TSH, FT4 and anti-TPO anti-TPO levels were similar in both groups (P = 0.41, P = 0.35, P = 0.41, respectively). The frequency of Hashimoto’s thyroiditis was significantly higher in the PCOS group (21% vs 4%, P = 0.01). In patients with PCOS and controls, the percentages of positive anti-TPO, subclinical hypothyroidism were similar (P = 0.21, P = 0.27, respectively). Graves’ disease and subclinical hypothyroidism were not found in the two groups.

Conclusion
Hashimoto’s thyroiditis is a frequent condition in PCOS patients. Therefore, the assessment of TSH and anti-TPO should be considered in patients with PCOS during follow-up even in the absence of overt symptoms.

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P241

Compare the effects of levothyroxine therapy vs liothyronine/levothyroxine combination therapy on cardiac biomarkers in 364 patients with hypothyroidism

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Methodology
Between Jan’20 to Jan’21, 364 patients on thyroid replacement therapy were included in the study and analysed retrospectively. They were divided in 2 groups: T4 group (189 on levothyroxine therapy (T4) therapy) & T3 group (175 on levothyroxine/liothyronine combination therapy (T3/T4)). Hypothyroidism was defined as TSH > 4.2 mIU/ml or on > 2 occasions > 2 weeks apart irrespective of their thyroid antibody (anti-TPO Ab) status or TSH > 4.2 if symptomatic or positive Anti-TPO Ab. Patients were evaluated every 2–3 months for 6 months for CV markers [body mass index-kg/m² (BMI), systolic (SBP), diastolic (DBP) [mm in Hg], Lipid profile mg/dl (TC, LDL, TG, HDL), hs-CRP (mg/l)]. Baseline characteristics were analysed using descriptive statistics. Data was analysed using SPSS 26 and represented as mean ± standard error & independent sample t-test was used. P value < 0.05 was considered significant (S).

Results
Baseline characteristics were well matched in both groups except DBP (mean ± SD) (T4 77.72 ± 9.601 vs T3/T4 81.69 ± 10.87, P < 0.00) & LDL (T4 105.121 ± 33.868 vs T3/T4 114.687 ± 33.916, P < 0.02). T4 group (baseline to 6 months): there was a S reduction in SBP (3.31 ± 0.941, P = 0.01), TSH (4.452 ± 0.9762, P = 0.00), TC (12.75764 ± 3.72702, P = 0.00), TG (8.45775 ± 4.38677, P = 0.05). Difference between T4 & T3/T4 at 6 mths: There was no difference in hs-CRP mg/l (T4 0.2947 ± 0.3071 vs T3/T4 0.3844 ±

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P242
Dyslipidemia in subclinical hypothyroidism : a case control study
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Subclinical hypothyroidism (SCH) represents a mild or compensated form of primary hypothyroidism. Although the relationship between SH and lipid profile have been reported in several studies, the results are conflicting. The objective of the present study is to assess dyslipidemia among patients with SCH. Our study included 107 patients vs 108 sex matched controls. Clinical information and medical history were obtained through a questionnaire from all SCH patients and normal control subjects. Blood samples were collected and analyzed for thyroid-stimulating hormone (TSH), free thyroxine (FT4), total cholesterol (T-Chol), serum triglycerides (STG), low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C). Results: average CT and LDL-C were significantly higher in patients respectively: 1.91 ± 0.385 vs 1.77 ± 0.294 (IC 95% 1.84 ± 0.02), and 1.19 ± 0.341 vs 1.09 ± 0.258 (P = 0.01). The average value of TG was higher in patients 1.23 ± 0.69 Vs 1.14 ± 0.527 (IC 95% 1.10)but the difference was not significantP=0.28. No correlation was found between TSH and lipidic parameters. Our study concluded that SCH is associated with elevated CT and LDL – CT. Therefore the assessment of lipidic parameters is highly recommended in theses patients

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P243
Resistant Graves’ thyrotoxicosis with adverse cardiovascular effects
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A 61-year-old lady presented to her general practitioner in July 2018 with weight loss, loose stools, hair loss, increased anxiety and dry eyes over several weeks. Blood tests revealed Graves’ thyrotoxicosis (TSH < 0.10 mU/l, (RR) 0.30-0.50 mU/l; Free T4 (T4) 26.1 pmol/l, RR 11.5–22.7 pmol/l; Free T3 (T3) 11.8 pmol/l, RR 0.0-7.0 pmol/l, thyroid receptor antibodies > 40.0U/l, RR 0.0-1.8 U/l, thyroid peroxidase antibodies 173.0 iu/ml, RR 0.0-33.9 iu/ml). There was also evidence of mild Grave’s orbitopathy. She was commenced on carbimazole 15 mg once daily (od) and propranolol 20 mg three times daily. As thyrotoxicosis worsened, the dose of carbimazole was gradually increased to 60 mg od (December 2019-January 2020). Thyrotoxicosis did not improve (T4 45.1 pmol/l, FT3 19.2 pmol/l), thus, a month later, aqueous iodine I drop three times a day (5 mg) was added first, followed by 1-month course of prednisolone 20 mg per day. No treatment response occurred, so the patient was referred for radioiodine treatment (RAI), that was delayed by the COVID-19 pandemic. In April 2020, the patient suffered an acute inferior ST elevation myocardial infarction (STEMI). This was treated with primary percutaneous coronary intervention, complicated by recurrent stent thrombosis and cardiac arrest. The patient received a 2-day course of Amiodarone to control the ventricular arrhythmias, which interestingly normalised her fT4 and fT3. The patient remained on carbimazole 60 mg od. A surgical thyroidectomy was considered a high operative risk due to the recent STEMI. A month later, the patient was re-admitted with severe congestive cardiac failure. At that time, there was evidence of new hypothyroid (T4 4.4 pmol/l, TSH 8.10 mU/l). Thus, the dose of carbimazole was reduced to 5 mg once daily. In July 2020, a recurrence of thyrotoxicosis occurred. RAI was administered in July 2020 with 2 weeks of 30 mg per day prednisolone cover for Grave’s orbitopathy. Recurrence of thyrotoxicosis occurred as soon as the carbimazole was stopped. Carbimazole 60 mg was restarted and tapered down over the following year, until the carbimazole requirement plateaued at 1.5 mg/10 mg alternate days. A second radioiodine dose was administered in July 2021 and the carbimazole stopped a month later. By September 2021, the patient had developed profound hypothyroidism (TSH 76.70 mU/l, low T4 3.8 pmol/l, FT3 < 3.0 pmol/l) and levothyroxine replacement was initiated. This represents a case of Grave’s disease which was resistant to treatment with carbimazole, odine and first dose RAI. Thyrotoxicosis contributed to cardiac complications (STEMI and heart failure). Additionally, the temporary thyroid function suppression following the amiodarone clearly illustrates the Wolff-Chaikoff phenomenon.

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P244
A case of severe thyrotoxicosis in acute setting presenting with hypercalcemia and deranged liver function test
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Background
Thyroid hormones may affect bone calcium metabolism either by a direct action on osteoclasts or by acting on osteoblasts which mediate osteoclastic bone resorption. Hyperthyroidism induces an accelerated bone loss, causing hypercalcemia and may thereby increase the risk of low energy fractures. Increased IL-6 levels and hyperadrenergic state due to thyrotoxicosis, are also implicated in hypercalcemia.

Case
A 33 year old who is a known case of Graves’ thyrotoxicosis presented to the accident and emergency because of poor control of her thyrotoxicosis symptoms and previous history of asthma, for which she is on Propranolol (40 mg BD) and Carbimazole (10 mg OD). Thyroid examination revealed nodular goitre more enlarged on the right side and fine tremors were present in both hands, bilateral pedal oedema. Bloods revealed deranged thyroid function test and liver function: TSH: < 0.01 mU/l, FT4: > 100 pmol/l, FT3: 49.4 pmol/l, Calcium: 2.84 mmol/l, ALT 36.3 IU/l. Patient suffered with constant nausea, poor appetite, weakness, myalgia, mood changes and many other symptoms indicative of poor control. So her Carbimazole dosage was stepped up to 30 mg OD and she was put on a short course of Prednisolone to counteract the impending thyroid storm. Her blood tests 6 weeks after this showed: TSH: < 0.01 mU/l, FT4: 26.6 pmol/l, FT3: 9.5 pmol/l, with normal calcium: 2.53 mmol/l and normal ALT 17 IU/l.

Discussion
It has been reported that hyperthyroidism is associated with mild to moderate hypercalcemia in approximately 20% of total patients. The serum calcium levels are often increased by mild to moderate range and it rarely exceeds 3.0 mmoI/l in hyperthyroidism associated hypercalcemia. The case presented here demonstrates the importance of timely control of calcium level by adequate anti thyroid treatment which was critical. A follow up appointment has also been arranged for her prior to which certain blood tests like Serum PTH and Vitamin D have also been requested in addition to the routine blood tests. However the quick normalisation of calcium level in her blood following optimisation of her anti thyroid treatment points towards thyrotoxicosis as the cause.

Conclusion
Though this is a rare case, clinicians should be aware of the association of hypercalcemia with hyperthyroidism because timely treatment can save the lives of patients and it should not be ignored after ruling out the other causes of hypercalcemia.

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COVID-19 outbreak and de-escalation of thyroid cancer diagnosis and treatment

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Background
The COVID-19 outbreak in Italy forced the health system to cancel all non-urgent outpatient activities, to avoid further spreading of the disease inside the healthcare facilities. At our institution, for cancer patients the hospital allowed treatments and consultations: the medical team, however, identified patients whose procedures could be postponed. Even after May 2020, the capacity for non-urgent thyroid surgeries was reduced. These events enhanced our efforts to reduce overdiagnosis and overtreatment of non-threatening thyroid cancers, as was already suggested by current practice guidelines. The aim of this analysis was to describe the features of patients submitted to thyroid surgery with a final diagnosis of cancer before and after the Italian lockdown.

Methods
Single-center subgroup analysis of a prospective observational study (NCT04031339), approved by the institutional review board. The records on all patients being followed up in our center were analyzed. The cohort was split in two groups: the first one, before the COVID-19 lockdown (March 2019-February 2020, group A), and the second one during and after the lockdown (March 2020-February 2021, group B). The early response to treatment was assessed 6 to 12 months after initial treatment, according to the American Thyroid Association guidelines.

Results
Group A consisted of 58 patients, while group B of 38 patients, due to a reduction of the number of thyroid surgeries. There were no difference in age (group A: 48 years, 36-61; group B: 52 years, 33-61; P=0.9), gender distributions (females 74.1% and 65.8%, respectively), and known risk factors (i.e., family history of thyroid cancer, previous neck irradiation). Also, the histotype distribution was similar in the two cohorts (P=0.46). However, in the cohort of patients submitted to surgery after COVID-19 outbreak, the median tumor size was higher: 14 mm (IQR 10-25 mm) vs 9 mm (IQR 6-20 mm; P=0.01), and the rate of micrometastasas was lower (12 [31.6%] vs 33 [56.9%], P=0.02). Furthermore, the ATA risk stratification distribution was different (P=0.036), with less low-risk and more high-risk cancers (19.4% vs 5.5%). This is consistent with a reduction in overtreatment of low-risk diseases. However, the early response to treatment was not affected (P=0.73), as the vast majority of patients had no evidence of persistent disease after treatment (A, 51.7% and B, 57.9%).

Conclusions
The “forced” reduction of thyroid surgeries due to COVID-19 outbreak improved the adherence to international practice guidelines, with decreased overtreatment: the short-term outcomes were not negatively impacted.

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Thymic hyperplasia associated with Graves’ Disease: lessons from the resolution of six individual cases

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Objective
Since the relationship between thymic hyperplasia (TH) and Graves’ Disease (GD) is of paramount importance for diagnostic and therapeutic choices, a wider knowledge of this association is required for endocrinologists in routine clinical practice. Our aim was to assess the prevalence, the clinical features, and the response to treatment of GD-related TH in an Academic referral centre.

Methods
Consecutive cases of GD-related TH at University Hospital “L. Vanvitelli” between January 2019 to December 2021 were retrospectively reviewed. Cases could be included whether: a) TH was initially suspected by symptoms or neck ultrasound (nUS) but confirmed and followed-up also by neck and chest (nc) computed tomography (CT)/magnetic resonance (RM); b) the imaging follow-up time was at least of six months; c) we had complete data at diagnosis of GD and after therapy (i.e., demographic, clinical, laboratory and imaging details).

Results
Among 144 newly diagnosed GD patients, TH was detected in six patients (6/144, 4.2%). Patients with GD-related TH were female with mean age 34.7 years (age range 23-48 years). Typical cardiovascular and neurological symptoms of thyrotoxicosis were reasons for the consultations, and mild oculomotor involvement was present in three patients. No other pathologies affected our patients but multiple sclerosis was previously diagnosed in one case. At nUS mean thyroid volume was 25.2 ml (range 14-36 mL). Mean laboratory values were: FT3 12.5 pmol/l (range 11-18 pmol/l), FT4 32.2 pmol/l (range 28-40 pmol/l), thyroid storm receptor antibodies (TRAb) 9 IU/l (range 5-16 IU/l, positive ≥ 1.5 IU/l). In all the six cases TH was asymptomatic and initially identified by nUS as a hypoechoic (relative to thyroid tissue) trapezoidal mass with smooth margins and a reticulated pattern located at jugular notch with partial extension in superior mediastinum. In all the six cases confirmation of TH was obtained by the ncRM, which displayed at T2 images a homogeneous well-defined and lobulated soft tissue mass in the mediastinal prevascular space dislocating epaioytic vessels with a mean maximum diameter of 50 mm (range 44-56 mm) that disappeared after therapy. The average time for TH disappearance was nine months (range 6-14 months), and this was obtained after euthyroidism restoration (i.e. two cases by methimazole, three cases by radiodine and one case by surgery).

Conclusion
Based on our experience, thymic hyperplasia was not infrequent in the GD setting and it was incidentally detected at nUS. TH regressed with the treatment of GD along with euthyroidism restoration.

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Staying cool in the heat – the role of thyroid hormone receptor α in thermoregulation

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A normal thyroid status is crucial for normal tissue and organ functioning, including temperature homeostasis. The tissue-specific actions of TH on body temperature regulation and thermogenesis are largely modulated via thyroid hormone receptor TRα. Consequently, mice expressing a mutant TRα have defective heat response to a range of stimuli, including excessive heat loss via the tail. To test whether this peripheral heat loss is the sole reason of TH role in thermoregulation, we measured bradycardia and a reduced body temperature at 22°C ambient temperature due to excessive heat loss via the tail. To test whether this peripheral heat loss is the sole reason for the hypothermia, we housed TRα-mutants at 30°C, where tail heat loss is minimized. Using infrared thermography, we revealed that the heat loss effect via the tail could be reversed; however, body temperature surprisingly still remains lower during the inactive phase in TRα-mutants. The observed lack of a compensatory brown fat activation suggests that the central regulation of temperature homeostasis may be impaired in TRα-mutants indicating a lower central body temperature set-point, also at 30°C. Whether the expression of mutant TRα in the brain can indeed lower the central body temperature set-point will be tested in future experiments.
P461
The effect of over- and undertreatment of hypothyroidism on hospitalization outcomes of patients with decompensated heart failure
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Background
Hypothyroidism has profound effects on cardiac function, however, the effect of over- and undertreatment of hypothyroidism on hospitalization outcomes of patients with acute exacerbation of heart failure (HF) has not been evaluated yet.

Methods
We conducted retrospective cohort analyses of outcomes among 231 consecutive patients with treated hypothyroidism who were admitted to the internal medicine departments of Shamir Medical Center with HF from 2011 to 2019. Patients were divided into three groups according to their TSH levels — normal (TSH 0.4-4 mIU/L), over-treated group (TSH <0.4 mIU/L), and undertreated group (TSH >4 mIU/L). The main outcomes were functional deterioration, in-hospital mortality, and recurrent hospitalization within three months.

Results
Among 231 patients, 106 were euthyroid, 14 were overtreated, and 111 were undertreated. Patients’ mean age was 79.8 ± 9.4 years. Heart failure with reduced ejection fraction was found in 41.1%, hypertension in 91.3%, and COPD in 26.8% of patients. The most common triggers to HF decompensation were anemia, infection, and low compliance for treatment. In-hospital mortality occurred in 4.7% in euthyroid patients, 14.3% in the overtreated group, and 10.7% in the undertreated group (P = 0.183). Differences in 30- and 90-days mortality were not significantly different as well. Functional deterioration during hospitalization was found in 9.4% in the euthyroid patients, non in the overtreated group, and 6.3% in the undertreated group (P = 0.288). There was no significant difference in recurrent hospitalization within 3 months between the three groups (P = 0.438). However, when evaluating patients with extreme values of TSH (<0.4 mIU/L or >10 mIU/L), we found higher 90 days mortality (30.4% vs 15.1%, P = 0.016), as compared to patients with normal or mildly increased TSH (0.4-10 mIU/L).

Conclusion
Our results show that mild under- or overtreatment of hypothyroidism did not have a significant detrimental effect on mortality, functional deterioration, or rehospitalization of patients with acute decompensated HF. However, significant over- and undertreatment do cause adverse hospitalization outcomes. Larger cohorts are needed to establish the relationship between treatment targets and hospitalization outcomes of patients who are at risk for hospitalization for HF.

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P462
Impact of COVID-19 vaccination on incidence of Graves’ disease
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Several reports of Graves’ disease (GD) onset after COVID-19 vaccination were recently published. The mechanism underlying GD occurrence in these cases could be related to the autoimmune syndrome induced by adjuvants (ASIA), a condition triggered by several vaccine adjuvants and excipients leading to dysfunctional immune response causing different conditions and endocrinopathies in genetically predisposed subjects. In Italy, population campaign for COVID-19 vaccination started in December 2020 and by the end of December 2021 more than 80% of citizens were vaccinated. The aim of our study was to evaluate for the first time the impact of COVID-19 vaccine on incidence of GD in 2021. Of the 33 first-diagnosis of GD in our Center in 2021, in 16 (48.5%) patients, 2 males (12.5%) and 14 (87.5%) females, GD temporally occurred before the vaccination and in 17 patients (51.5%), 5 males (29%) and 12 females (71%), after the first or second vaccine dose. In 14 (83%) patients, GD occurred in the first four weeks after vaccination, in 1 (6%) after 8 weeks and in 2 (11%) after 12 weeks. All 5 male patients with GD after vaccine injection presented symptoms and signs onset and subsequent GD diagnosis in the first four weeks after vaccination. All 33 patients started anti-thyroid treatment. After three months of therapy, TSH was normalized in 7 out of 14 (50%) patients in whom GD occurs after vaccine administration, whereas tT4 and tT3 levels were available in 13 and 12 and within the normal reference range in 11 and 1 patients (85% and 92%), respectively. Anti TSH-receptor antibodies were negative in 2 out of 6 patients (33.3%) with post-vaccine GD. Possibly COVID-19 vaccine-related GD (within 4 weeks after vaccine administration) accounted for more than 50% of the cases observed in our 2021 monocratic experience. Moreover, since one third of post-vaccine GD were males, our observation strengthens the hypothesis of a causal vaccine-GD relationship since males are usually less affected by GD. In conclusion, for the first time we report a remarkable impact of COVID-19 vaccination in GD diagnosis in a single-center experience. Our report can improve awareness of thyrotoxicosis diagnosis by primary-care physicians and endocrinologists, particularly in patients with marked and persistent symptoms, such as fever, palpitations and asthenia, occurring after vaccination.

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P463
Management of suspicious neck lymph nodes in patients with differentiated thyroid carcinoma
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The management of loco-regional metastases in patients with differentiated thyroid carcinoma is still debated. Current American Thyroid Association guidelines state that in this context the main goal is to differentiate between low-volume metastatic disease that will progress and that remaining stable over time.

Aim of our study was to evaluate the behavior of suspicious or cytologically confirmed lymph node metastases, detected after initial treatment (i.e. thyroidectomy with or without cervical lymphadenectomy and radiodine treatment), in patients with differentiated thyroid carcinoma. Secondary endpoints were the analysis of predictive factors useful to precociously recognize the lesions with a more aggressive behavior. We retrospectively evaluated 95 patients, who were followed-up with serum tumor biomarker evaluation and neck ultrasound every 6-12 months, who had a persistent finding of suspicious neck lymph nodes and a minimum follow-up of 12 months. The lymph-nodal disease was considered aggressive when (a) there was a growth of at least 5 mm in the longest diameter at ultrasound, (b) appearance of at least one new suspicious lymph node, (c) at least one lymph-node was PET-FDG avid. After a mean follow-up of 9 years, 7595 (79%) patients had a stable disease, while 2095 (21%) had progressive loco-regional disease. Patients with a more aggressive disease were more frequently male (50% vs 25.3%, P = 0.03), older (mean age was 54.3 vs 38 years old, P = 0.003), and with a larger primary tumor (31.8 vs 20 mm, P = 0.000). We did not find significant differences regarding TNM, histology, papillary thyroid cancer variant, extrathyroidal extension, ablative radiodine dose, stimulated thyroglobulin at first radioactive iodine, positive thyroglobulin antibodies after initial treatment, finding of distant metastases at the end of follow-up. At the end of follow-up, 16/20 patients with progressive loco-regional disease had a structural disease despite further treatments (i.e. lymphadenectomy, external beam radiotherapy, radiodine treatment, tyrosine kinase inhibitors). Our study report that a high majority of patients with cervical lymph node metastases can be safely followed-up with serial neck ultrasound and serum tumor biomarker evaluation. In case of suspicion, a PET-FDG scan may be necessary. The remaining 20% of patients, in particular male, older patients, and with a larger tumor size at surgery, may have lymph node metastases with an aggressive behavior requiring additional treatments.

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P464
Steroid treatment in the management of destructive thyrotoxicosis induced by PD1 blockade
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Efficacy of immunotherapy.

Methods

We conducted a case-control study, comparing the course of thyrotoxicosis of 6 patients treated with oral prednisone at the dosage of 25 mg/d (tapered to discontinuation in three weeks) and an enlarged thyroid volume to that of 12 patients with similar thyroid volume who were left untreated.

Results

The levels of thyroid hormones were lower in subjects treated with prednisone compared to those untreated at time 7, 14, 21, 28, 35, 42, 60 and 90 days (P<0.05 at each time). The median time to remission of thyrotoxicosis was 24 days in patients treated with steroids and 92 days in untreated patients (P<0.001). At 6 months, the rate of evolution to hypothyroidism was similar in the 2 groups (56% in steroid vs 91% in untreated group, P=0.74) and no difference was found in tumor progression (P=0.89).

Conclusions

A short period of prednisone therapy is useful to restore more quickly euthyroidism in patients with a poor performance status and a severe destructive thyrotoxicosis. The benefit of this treatment, however, cannot be assessed at 6 months.

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P465

Change in body fat distribution after total thyroidectomy in euthyroid patients and its relationship with serum adiponectin and leptin levels

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Objective

Euthyroid patients undergoing thyroidectomy were reported to gain weight than their matched counterparts. The etiology is still unknown. Serum adiponectin and leptin levels are related to fat mass and thyroid hormones. We aimed to evaluate the influence of thyroidectomy on body composition, serum adiponectin, leptin levels in euthyroid obese and non-obese patients who underwent total thyroidectomy for goiter.

Methods

We conducted a prospective observational study in a training hospital. Twenty-one euthyroid normal-weight patients (10F/5M, mean age 43.5 ± 8.4 y), 19 obese patients (17F/2 M, mean age 44.3 ± 8.7 y) and 22 healthy controls (21F/1 M mean age 40.4 ± 10.2) were included in the study. Main anthropometric measures, body fat distribution by bioelectrical impedance analysis, preportal venous fat thickness, plasma glucose (FPG), insulin, lipids, thyroid hormones, leptin, and adiponectin levels were evaluated before and after surgery. L-thyroxine treatment was started immediately. All patients were maintained in a euthyroid status throughout the study, and patients were re-evaluated three months after the achievement of euthyroidism.

Results

At baseline, obese patients had significantly higher BMI, waist circumference (WC), total fat mass, lean body mass, and SC fat thickness than normal-weight subjects and healthy controls (P<0.001 for all). Obese patients had higher visceral fat mass than normal-weight patients at a Plevel of 0.051 (11.0 ± 4.5% vs. 8.4 ± 3.9%). Serum fasting insulin and leptin levels and HOMA-IR values were significantly higher in obese patients (P<0.05 for all). In contrast, all groups had comparable FPG and adiponectin levels (P>0.05 for both). Mean TSH and free T4 levels were also similar. Although BMI and WC remain unchanged (P>0.05), the visceral fat mass increased significantly after surgery (8.4 ± 3.9 vs. 10.0 ± 4.1 in normal-weight; 11.0 ± 4.5 vs. 15.5 ± 6.0 in obese; P<0.05). Despite a significant increase in TSH levels, the values remained normal in both groups. Both groups did not show any significant change in serum FPG, insulin, leptin, and adiponectin levels (P>0.05 for all).

Conclusions

Total thyroidectomy caused increased visceral fat mass despite no change in clinical anthropometric measures in patients who had a thyrotoxicosis due to goitre. This change was unrelated to serum adiponectin and leptin levels.

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P466

Predictive factors of success of radiometabolic therapy in Graves’ disease

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Objective

Predictive factors of success of radiometabolic therapy (RAI) in Graves’ disease (GD). Our study aimed to establish prognostic factors affecting RAI outcome and to investigate if a tailored dosimetric approach based on the application of the “effective biological dose” (BED) offered a higher chance of success. Materials and methods

Our cohort comprised 365 GD patients (280 women and 85 men; age 49 ± 14 years) treated with RAI in the period 2001-2021. Patients were allocated into two groups: “failure group” in case of persistence of hyperthyroidism for more than six months post-RAI or hyperthyroidism relapse; “success group” in case persistent euthyroidism or hypothyroidism were achieved after treatment. A multivariate analysis was performed to predict a multivariable model of success; a BED threshold value was derived using a ROC curve.

Results

Success was achieved in 80% of cases. No significant differences emerged between the two groups when analyzing demographic data (age, sex), smoking habit, GD duration and ongoing medical therapies, presence/severity of ophthalmopathy, RAI uptake and the applied formula for dosimetry calculation. Negative predictive factors for success were higher thyroid volume, nodules (presence and volume) and disease severity at diagnosis, and a higher effective half-life of radionuclide. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated absorbed dose at 3 months, a higher orbitopathy, RAI uptake and the applied formula for dosimetry calculation. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated absorbed dose at 3 months, a higher effective half-life of radionuclide. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated absorbed dose at 3 months, a higher effective half-life of radionuclide. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated absorbed dose at 3 months, a higher effective half-life of radionuclide. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated absorbed dose at 3 months, a higher effective half-life of radionuclide.

Conclusions

Our study suggests that the outcome of RAI is influenced by clinical, biochemical, ultrasonographic and dosimetric factors, which interact with each other in a complex way. It is a delicate balance, in which no factor, considering individually, can predict the treatment approach. A multidisciplinary approach is necessary, to better understand the different interactions and confounding factors.

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P467

Vitamin D levels in patients with Graves’ orbitopathy

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Introduction

Graves’ disease (GD) is an autoimmune thyroiditis frequently associated with development of Graves’ orbitopathy (GO). GD patients have lower vitamin D
levels compared to the general population. Whether low vitamin D levels are associated with GO is still controversial. The aim of our study was to assess the vitamin D levels in patients with GO and the clinical outcome.

Methods
This was a single-center observational study in an outpatient clinic of autoimmune endocrinopathies at a Tertiary, General, University Hospital. Patients with GO and increased levels of thyroid-stimulating immunoglobulin (TSH > 1.75 IU/l) were included in the study. Clinical activity score (CAS) was evaluated according to the European Consensus Report. Patients were divided in two groups according to CAS (inactive CAS < 3 and active CAS ≥ 3). Laboratory tests for TSH, T3, FT4, TSI, TgAbs, TPOAbs, complete blood count, liver enzymes and 25OHvitamin D levels were performed in all patients.

Results
A total of 78 patients (71.8% females) with a mean age of 53.9 ± 13.3 years were analyzed. The mean follow-up was 3 ± 9.04 years. The median TSI levels were 5.65 IU/l and the mean CAS was 3 ± 1.42. 47% (37/78) and 26.9% (21/78) of the patients had positive anti-TPO and anti-Tg antibodies, respectively. 23.1% (18/78) of the patients had undergone total thyroidectomy, 10.3% (8/78) had thyroid cancer, 29.5% (23/78) had other autoimmune diseases, and 69.2% (54/78) had smoking history. Overall, mean 25OHVitamin D levels were 21.98 ± 1.38 ng/ml. When analyzed based on disease activity, mean 25OHVitamin D levels were 21.05 ± 7.8 ng/ml in patients with inactive GO (CAS < 3) and 22.51 ± 10.72 ng/ml in patients with active GO (CAS ≥ 3). Overall, CAS was significantly associated with TSI levels, diplopia and years of the disease (P = 0.011, P = 0.025 and P = 0.035, respectively). 25OHVitamin D levels were significantly associated with anti-TPO and the disease duration in patients with active GO (P = 0.05).

Conclusions
In our study, we found a correlation of vitamin D levels with anti-TPO and disease duration in patients with active GO. However, further prospective studies are needed to confirm whether there is a correlation between GO activity and vitamin D levels.

DOI: 10.1530/endoabs.81.P467

**P468**

**From hyper to hypothyroidism: pitfalls in graves’ disease following DRESS syndrome**

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**Background**
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon severe systemic hypersensitivity drug reaction. Several studies have described the occurrence of newly developed endocrine autoimmune diseases following DRESS syndrome resolution. However, little attention has been paid by endocrinologists to this disorder. Here, we report a case of a patient with Graves’ disease following DRESS syndrome.

**Clinical case**
A 70-year-old man with urinary tract infection was treated with co-trimoxazole. Two weeks later, he presented to the dermatology outpatient clinic with a pruritic dermatosis, fever and peripheral lymphadenopathy. Physical examination revealed erythematous maculopapular lesions affecting his trunk and limbs and laboratory tests showed leukocytosis, eosinophilia and thrombocytopenia. Diagnosis of DRESS syndrome was made by the dermatologist, and treatment with glucocorticoids was initiated and allowed a gradual recovery. One year later, he presented his follow-up appointment with fatigue, heat intolerance and palpitations. The blood tests revealed a Graves’ hyperthyroidism with suppressed TSH (< 0.01 uU/ml), elevated free T4 (2.07 ng/dl; N:0.85-1.7 ng/dl) and positive TSH receptor antibodies (TRAbs) (137 U/l; N: <1.22). He was referred to the endocrinology outpatient clinic, with a suspected newly onset Graves’ disease succeeding DRESS syndrome resolution. By the time of his first endocrinology appointment, two months later, the laboratory evaluation revealed hyperthyroidism (TSH 33.1 uU/ml; free T4 0.67 ng/dl) with persistent positive TRAbs (128 U/l). The patient started levothyroxine and, to this date, he remains euthyroid under 100 mg per day.

**Discussion**
There are several reports of newly developed Hashimoto’s thyroiditis as sequelae of DRESS syndrome. What is original about this case is the association between Graves’ disease and DRESS syndrome, a more uncommon association, and also the coexistence of stimulating and inhibiting TRAbs, leading to a rapid shift from hyperthyroidism to hypothyroidism, a rare condition in Graves’ disease. We believe that endocrinologists should be aware of this association and that involvement of endocrine glands should be monitored in patients with a history of DRESS syndrome.

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**P469**

**Graves’ disease and polymorphisms in proinflammatory cytokines genes**

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**Methods**
25OHvitamin D levels were performed in all patients. 25OHvitamin D levels were significantly associated with anti-TPO and the disease duration in patients with active GO (P = 0.05).

**Conclusions**
In our study, we found a correlation of vitamin D levels with anti-TPO and disease duration in patients with active GO. However, further prospective studies are needed to confirm whether there is a correlation between GO activity and vitamin D levels.

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**P470**

**McCune-Albright syndrome diagnosed in adulthood with GNAS mutation-related hyperthyroidism and elevated anti-TPO antibodies. Case report.**

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McCune-Albright syndrome (MAS) is a rare mosaic disorder caused by a postzygotic activating mutation in the GNAS gene encoding the G protein alpha subunit. Although clinical manifestations may be heterogeneous, MAS is often
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Hyperpigmentation in Graves’ disease

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Introduction

Hyperpigmentation is a clinical sign that can be associated with different endocrine disorders. It is commonly seen in Addison’s disease and has rarely been reported in Graves’ disease. The exact physio pathological mechanism of this sign is not well established in hyperthyroidism. We describe two cases of Graves’ disease accompanied by diffuse hyperpigmentation.

Case report

Case 1 was a 63-year-old female admitted to the endocrinology department for the management of a thyroid crisis. The physical examination didn’t find signs of thyroid eye disease or goiter, we instead noted diffuse hyperpigmentation. Laboratory investigations confirmed the diagnosis of hyperthyroidism showing a 6-fold elevation of FT4 (7.7; normal: 0.9-1.7 ng/dl) and low serum thyroid-stimulating hormone (TSH <0.001 mIU/L) with positive anti-TSH receptor antibodies. Hepatic function tests revealed cytolysis and cholestasis. Addison’s disease and autoimmune hepatic diseases were eliminated. The patient received radioiodine treatment after preparation with antithyroid drugs. She regained euthyroidism with normalization of her liver function tests, but hyperpigmentation persisted.

Case 2 is a 52-year-old male patient who presented to our department with Graves’ disease. He had clinical signs of hyperthyroidism a few months before admission with a concomitant change of his skin color. On physical exam, we noted irregular tachycardia with goiter. The patient had diffuse hyperpigmentation. Hyperthyroidism was biologically confirmed; high serum free T4 (10.3 ng/dl) with low serum thyroid-stimulating hormone (TSH <0.001 mIU/L). Anti-TSH receptor antibodies were positive. The rest of the explorations revealed cholestasis with normal transaminase levels. The patient was treated with radioiodine with clinical and biological amelioration. However, hyperpigmentation remained.

Discussion

Hyperpigmentation is rarely described as a clinical sign of hyperthyroidism. Its physiopathological mechanism is not well elucidated. It has been hypothesized that thyrotoxicosis is associated with an increased ACTH release causing overproduction of melanin and that melanocytes express TSH receptors resulting in their proliferation when stimulated with TRAb. More studies are needed to understand the relationship between skin color modification and thyroid function status.

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P472

Cervical lymph nodes metastases in differentiated thyroid cancer: impact on clinical outcome

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Background

Cervical lymph node metastases at histology are common findings in differentiated thyroid cancer (DTC); however, their impact on clinical outcome is debated.

Material and method

1332 DTC patients, performed the first 131I treatment between January 2010 and September 2012 and were divided into 2 groups: absence (Nx/N0) or presence (N1) of lymph node metastases at histology. The latter group was further split in central compartment (N1a) or lateral-cervical compartment (N1b) metastases.

Clinical outcome, according to 2015 ATA guidelines, was defined as: post-operative and post 131I (median time from surgery: 6 months), first evaluation after 131I (median time from 1.8 months) and at last evaluation (median time since 131I: 83 months).

Results

1064 (79.9%) patients were in the Nx/N0 group and 268 (20.1%) in the N1 group. N1 patients were more frequently males (35.8 vs 27.3%, P<0.01) and younger (median age 40 vs 47, P<0.01). Several pathological features were prevalent (P<0.01) in the N1 group: multifocality (63.4 vs 46.8%), mETE (67.9 vs 24.6%), vascular invasion (28 vs 8.9%) and intermediate ATA risk (94.8 vs 36.5%). The incomplete structural response rate was higher in N1 group, in all times of follow-up (P<0.01); despite N1 patients significantly experienced higher 131I activities and more neck re-operation. N1b (n=142, 53%) patients, compared to N1a (n=126, 47%), had higher prevalence of mETE (74.6 vs 59.5%, P<0.01) and vascular invasion (33.1 vs 22.2%, P<0.05) and lower pathological thyroiditis (21.1% vs 35.7, P<0.01). Regarding treatment, N1b patients experienced higher 131I activities and more neck re-operation. Structural incomplete response rate was significantly higher at post-operative (16.2% vs 6.3%, post-131I 26.1 vs 8.7%) and at first assessment after 131I (24.3% vs 9.6%). Conversely, at the last evaluation, significance was not reached (17.9% vs 10.4%, P=0.08).

Conclusions

Cervical lymph node metastases at histology are associated with more aggressive features in DTC. Despite the higher activity of the 131I administered and the more frequent surgery on neck, the N1 patients showed a higher structural incomplete response rate at each time of the follow-up. N1b patients, compared to N1a, experienced more frequent and aggressive treatments during the follow-up with higher incomplete structural response rate.

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Potential risk factors for post-treatment recurrence in patients with intermediate-risk differentiated thyroid carcinoma

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Introduction

The recurrence rate of intermediate-risk differentiated thyroid carcinoma (DTC) ranges between 5% and 20% and the therapeutic strategy requires further evaluations.

Aim

We therefore investigated the potential risk factors for post-treatment recurrence of intermediate-risk DTC at 1 and 3 years from diagnosis.

Methods

This retrospective observational study included 121 patients who underwent thyroidectomy for intermediate-risk DTC between January 2017 and December 2020 in two Italian centres (Endocrinology, Diabetes and Metabolism - Department of Medical Sciences, University of Turin, Turin, Italy; 2Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; 3University of Turin, Turin, Italy; 4Università del Piemonte Orientale, Novara, Italy)

Results

Most of patients were females (M/F:1/3) with an age at diagnosis > 55 years in 69% of cases. Overall, 92 patients (76.0%) underwent RAI treatment. This subgroup had a higher prevalence of microscopic extrathyroidal extension (mETE) of the tumour (53.3% vs 31.0%, P = 0.03) and clinical lymph node metastasis at diagnosis (74.4% vs 45.0%, P = 0.01), as well as higher number (13.5 ± 4.5 vs 13.8 ± 1.7, P = 0.02) and dimensions (12.2 ± 8.4 vs 6.0 ± 0.7, P = 0.01) of metastatic lymph nodes than patients who did not undergo RAI. Tumour relapse was observed in 18.1% and 20.7% of cases at 1 and 3 years from diagnosis, respectively, without significant differences between subgroups.

Discussion

In our study, mETE and clinical lymph node metastasis represent the main indicators for referring patients to RAI. Stimulated thyroglobulin levels in patients undergoing RAI, and the age at diagnosis are the only factors that independently influence the risk of recurrences in patients with intermediate-risk DTC.

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Levothyroxine dose adjustment after total thyroidectomy using an artificial intelligence methodology

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Introduction

Finding the optimal levothyroxine (LT4) dose regime to ameliorate the abnormally low levels of natural thyroid hormones, especially for thyroidectomized patients, is still challenging. Many researchers have studied various LT4 dosage regimen clinically; and ultimately, they proposed multiple variants affecting LT4 requirements including age, gender, body weight, body mass index (BMI), and body surface area (BSA). However, prescribing the most appropriate LT4 dose regime for different patients remains ambiguous.

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Repeating thyroid FNAC: inter-observer agreement among high- and low-volume thyroid services in Naples metropolitan area and correlation with the EU-TIRADS

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Objective

Our institution (University Hospital “L. Vanvitelli” - Naples, Italy) is a high-volume (HV) center in Naples metropolitan area and many patients are referred there to repeat thyroid fine-needle aspiration cytology (FNAC) after initial FNAC performed in low-volume institutions (LV). The aims of the study were to 1) to examine the inter-observer agreement between HV and LV institutions according to the Italian thyroid cytology system, and 2) explore how the discordant FNAC reports were distributed among the European Thyroid Imaging and Reporting Data System (EU-TIRADS) categories.

Methods

All consecutive cases of repeated FNAC performed at University Hospital “L. Vanvitelli” from January 2016 to December 2021 were retrospectively reviewed. Cases could be included whether: a) the second FNAC diagnosis was achieved by HV cytologists blind of the previous LV report; b) HV FNAC sample was independently evaluated by two observers; c) nodule could be classified according to the EU-TIRADS by two endocrinologists reviewing ultrasound (US) blind of FNAC reports. Fleiss‘ kappa (k) was used to assess the inter-observer agreement, and categorical variables were compared by chi-square testing. P < 0.05 was considered statistically significant.

Results

A total of 124 nodules from 124 adults (mean age 49 years; mean maximum diameter 19 mm) were evaluated. Initial FNAC reports at LV were: 4 (3.2%) 

TIR1c, 64 (51.6%) TIR2, 48 (38.7%) TIR3A, 8 (6.5%) TIR3B, 0 TIR4, 0 TIR5. At repeated FNAC, pathological diagnosis was unchanged in 64 (51.6%) cases including TIR2 and TIR3A results. A downgraded FNAC diagnosis (i.e., TIR2 vs TIR3A, TIR2 vs TIR3B) was observed in 36 (29%) nodules. An upgraded FNAC diagnosis (i.e., TIR3B vs TIR2, TIR3B vs TIR3A, TIR4 vs TIR3A, TIR4 vs TIR2) was recorded in 24 (19.4%) nodules. The overall FNAC reports were significantly different between the HV and LV institutions. The inter-observer agreement between LV and HV institutions was poor (k = 0.13). Changed FNAC reports were significantly more frequent in nodules at intermediate/high-risk (i.e., EU-TIRADS 4/5) than in those at no/low risk (EU-TIRADS 2/3) [i.e., 32/48 (66.7%) and 28/76 (36.8%), respectively]. Downgraded FNAC results were significantly more frequent in EU-TIRADS 2/3 (P = 0.001) while upgraded FNAC were present only in EU-TIRADS 4/5 (24/24, 100.0%).

Conclusion

The inter-observer agreement among LV and HV thyroid services was poor. The EU-TIRADS 4 and 5 categories included all the nodules with FNA results reclassified as higher risk (i.e., TIR3B-TIR4-TIR5) by the high-volume cytology service.

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Levothyroxine dose adjustment after total thyroidectomy using an artificial intelligence methodology

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Introduction

Finding the optimal levothyroxine (LT4) dose regime to ameliorate the abnormally low levels of natural thyroid hormones, especially for thyroidectomized patients, is still challenging. Many researchers have studied various LT4 dosage regimen clinically; and ultimately, they proposed multiple variants affecting LT4 requirements including age, gender, body weight, body mass index (BMI), and body surface area (BSA). However, prescribing the most appropriate LT4 dose regime for different patients remains ambiguous.
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Thyroid nodules and glucose metabolism derangements: does sex matter?
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Background
Glucose metabolism derangements (GMD) and thyroid nodules (TN) are the most frequent endocrine disorders. A relationship between these conditions has been suggested, but data are still controversial and no evidence was reported regarding sex differences.

Aim
To evaluate the distribution of impaired fasting glucose (IFG), normal glucose tolerance (NGT), impaired glucose tolerance (IGT), type 2 diabetes (T2DM) and TN according to sex.

Methods
Retrospective analysis of 342 patients who underwent both an oral glucose tolerance test and a thyroid ultrasound at our Institution. Only patients with normal TSH levels, with or without replacement therapy (RT), were included.

Results
Most patients were females (78%) and were ≥ 50 years old. No mean age differences were found among sexes in the whole group and among the different GMD categories. IGT/T2DM rate was higher among patients ≥ 50 years old as compared to younger patients in both sexes (males 66.7% vs. 34.5%, P < 0.01; females 43.2% vs. 20.8%, P < 0.001). Males presented IGT/T2DM more frequently than females (54% vs. 33%, P < 0.01) even when considering only the 193 patients ≥ 50 years old (67% vs. 43%, P < 0.01). No differences between sexes were found concerning IFG or insulin resistance. Total TN prevalence was 61%, with no differences between the sexes. TN prevalence assessed in GMD classes did not show any significant difference. However, within the female group, TN prevalence was significantly higher in ≥50 years old subjects as compared to younger females (72% vs. 51%, P < 0.01) and in IFG group as compared to no-IFG group (79% vs. 57%, P < 0.01). When considering only ≥50 years old females, we confirmed that TN prevalence was higher in the IFG group as compared to no-IFG group (87% vs. 63%, P < 0.01). Median thyroid volume (TV) was found significantly higher in males as compared to females (13 vs. 10 ml, P < 0.01) in the whole group and among the different GMD categories, except for the IFG group.

Conclusions
Age was confirmed as a risk factor for TN occurrence and GMD. In males, IGT/T2DM prevalence is higher, but no relationship was found with TN occurrence. Furthermore, they showed higher TV in most of GMD categories. Older females present more frequently TNs that occurred more often in patients with IFG. More studies are needed to further explore the relationship between TN and glucose metabolism disorders in order to identify higher-risk population sub-groups.

*The first two Authors equally contributed to the study

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The effects of aging on thyroid C-cells in male rats
Branko Filipović1, Vladimir Ajdzanović2, Jasmina Živanović1, Gagliardi1, Alberto Gobbo1, ROBERTA ROSSI2, Martina Rossi2, EJEA P461—27/4/2022—14:27—SIVA—14_594005N—XML StyleD – pp. 1–19

Thyroid C-cells, as a second type of endocrine cell population within thyroid, produce and secrete peptide hormone calcitonin (CT). This hypocalcemic hormone acts as an inhibitor of bone resorption. The aging is a complex process that alters various cellular functions. Therefore, the aim of this study was to examine the aging-related changes in the structure and function of CT-producing thyroid C-cells in male Wistar rats, using histomorphometric, ultrastructural and biochemical analysis. The investigation was performed on three groups of male rats: adult (3-months old), middle-aged (16-months old) and old (24-months old).

The peroxidase-antiperoxidase method was applied for localization of CT in the thyroid C-cells. Stereological analysis was performed using Olympus microscope (BX-51), equipped with a microcator, a motorised stage and a CCD video camera, and controlled by the newCAST stereological software package. Blood serum samples were analyzed for determination of CT, testosterone (T), calcium (Ca²⁺) and phosphorus (P) concentrations. We found a significant increase in the volume density (Vv) of thyroid C-cells in both middle-aged and old rats, all compared to adults. The percentage of smaller volume range C-cells (both 500-1000 m³) markedly decreases with aging. By ultrastructural analysis we found that the average number of secretory granules per C-cell was significantly increased in both middle-aged and aged rats, all compared to adults. Unlike the C-cells of adult rats, these granules in older, especially in old animals, had a content of fairly low density. By the biochemical analysis, we detected a significant increase in serum CT levels, while serum T was markedly reduced in both middle-aged and old rats, all in comparison with adults. Serum Ca²⁺ concentration significantly decreased in middle-aged rats compared to adults, while concentration of serum Pwas lower in both middle-aged and old rats, all related to adult group. Our findings show that aging process increases the Vv of thyroid C-cells, with a simultaneous change in percentage of cells with larger and smaller volume range, and an increase in the number of both cell types. These changes, accompanied by modulation of the cellular ultrastructure and an increase in serum CT levels, reflect the structure and function of CT-producing thyroid C-cells in our aging model.

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Role of irisin as modulator of antioxidants in two models of non-thyroidal illness syndrome
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We attempted to adjust an appropriate LT4 dose regime for a total thyroidectomized virtual-patient by means of fuzzy logic system (FLS) methodology, an applicable artificial intelligence technique. THYROSIM 3.0, a free web application developed by UCLA Biocybernetics Laboratory, was utilized as a model of feedback control of hypothalamus-pituitary-thyroid axis. In order to evaluate patient responses to LT4 monotherapy, we simulated our total thyroidectomized virtual-patient by setting T3 and T4 secretory parameters at 1% while receiving dynamic oral LT4 dosages post-surgery. In addition, with an assumption that no supplement was administrated, the absorption rate of oral LT4 was set to 88%. Fuzzy logic controller was developed using MATLAB software ver. 2019. The discrepancies of TSH value at day n and one-step time back TSH value (at day n-1) in regard with the TSH set point were considered as the controlled variables while LT4 daily dosages was considered as the manipulated variable.

Results
According to our proposed algorithm, our developed FLS recommends a LT4 monotherapy dose regime for the assumed total thyroidectomized virtual-patient on a daily basis as presented in the following table. The resulting doses provided by FLS are indicated as “Precise FLS LT4 dose” while available doses are presented by rounding the precise dose considering 25 μg intervals in respect with the smallest increment between LT4 dosing strengths.

<table>
<thead>
<tr>
<th>Day</th>
<th>Recommended FLS LT4 dose (μg)</th>
<th>Available LT4 dose (at 25 μg intervals)</th>
<th>TSH error (mIU/l) (calculated by FLS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>377.87</td>
<td>375</td>
<td>50.05</td>
</tr>
<tr>
<td>2</td>
<td>307.86</td>
<td>300</td>
<td>20.82</td>
</tr>
<tr>
<td>3</td>
<td>241.83</td>
<td>250</td>
<td>12.35</td>
</tr>
<tr>
<td>4</td>
<td>207.31</td>
<td>200</td>
<td>8.29</td>
</tr>
<tr>
<td>5</td>
<td>180.45</td>
<td>175</td>
<td>5.81</td>
</tr>
<tr>
<td>6</td>
<td>166.31</td>
<td>175</td>
<td>4.30</td>
</tr>
</tbody>
</table>

Day > 6: ca. 159.66 150 ca. 3.38

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Radioactive iodine treatment in thyrotoxicosis—audit, Southampton general hospital

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Hyperthyroidism is common and in iodine-sufficient parts of the world the prevalence of overt hyperthyroidism is estimated to be 0.2% to 1.3%. The treatment options include antithyroid medication (ATD), thyroid surgery, or Radioactive iodine (RAI). The latter is increasingly used as a first line definitive treatment for hyperthyroidism. We reviewed the outcomes of patients who received RAI at our tertiary nuclear medicine department over a 4-year period (May 2015 to Dec 2019) and who are under the care of our unit to ensure we have relevant follow up data. We identified 146 Patients who received RAI: 119 Female (82%), 27 Male (18%) with a mean age of 51.3 years. 45.9 % of patients had Grave’s Disease, 11.7% had single toxic adenoma (STA), 40.4% had Toxic Multinodular Goitre (MNG) and 2% had mixed disease (MNG & Graves). Outcome post-RAI: 129 patients (88.5%) achieved remission from thyrotoxicosis after a single dose. 7.5% (5 patients with Graves’ disease - GD, and 6 patients with MNG) needed 2 doses of RAI to achieve remission. 5 patients (3.4%; 3 with MNG, one patient with mixed disease, and one with GD) did not respond after 2 doses of RAI and were still on ATD. The remission rates after the first dose per diagnosis were: 91 % for GD, 83 % for MNG, 66% for mixed disease, and 100% for STA. 74.6% of the treated patients developed permanent hypothyroidism after responding to RAI. The risk of developing hypothyroidism was higher in GD patients who responded to treatment, of which 95.5% developed hypothyroidism, followed by patients who had STA (82.3%) with only 47.5 % of patients with MNG developing subsequent hypothyroidism. The average time to develop hypothyroidism after RAI was 3.6 months, however, this tended to be longer with patients who had MNG. In conclusion, RAI is an effective treatment for thyrotoxicosis, which is associated with a high rate of hypothyroidism and a small rate of failure. Our Patients were closely followed up post-treatment as per standard recommendations.

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Unexpected alterations in thyroid status: a case of alemtuzumab-induced Graves’ disease with fluctuating course

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Introduction
Alemtuzumab is a humanized anti-CD52 monoclonal antibody approved for the treatment of relapsing—remitting multiple sclerosis (RRMS). Through an immune reconstitution mechanism, it leads to thyroid autoimmunity in 35% of cases, with Graves’ disease (GD) being the most common presentation. Alemtuzumab-induced GD exhibits distinctive clinical and immunological features, with rarely reported cases of fluctuating thyroid status with documented both blocking (TAb) and stimulating (TSAb) TRAb.

Case description
A 48-year-old woman, diagnosed with RRMS at the age of 33, underwent the first and second cycle of alemtuzumab in 2019 and 2020, respectively. Neither the patient nor her relatives had history of thyroid disease. Clinical and medication history were otherwise unremarkable. Almost 12 months after treatment, she complained about exacerbated fatigue, and was referred to the endocrinology appointment for altered function tests. Clinical examination revealed a non-pulsatile goiter, with no evident signs of orbitopathy (Clinical Activity Score 0). Laboratory workup showed TSH 0.004 mIU/ml (0.4-4), T4 2.2 ng/dl (0.7-1.5), T3 5.1 µg/dl (1.8-4.2), TRAb 110 U/l (<10), TSAb 40 U/l (<0.1) and anti-TPO 916 U/l (<5.6). Thyroid ultrasound excluded nodules. She started treatment with methimazole (MMI) 5 mg/day. Two months after, analytical follow-up revealed TSH 0.29 mIU/ml, T3 2.1 µg/dl, FT4 0.60 ng/dl and was told to stop MMI. The patient was reevaluated in 2 months, under no therapy, with worsening of fatigue and palpbral edema, with TSH 93 mIU/ml, FT4 <0.40 ng/dl, FT3 <1.0 pg/ml, TRAb 98 U/l, TSAb 7.3 U/l. At this point she started levotiroxine (LT4) with progressive doses up to 75 microgram/day. Six months later, TSH was <0.004 mIU/ml, FT4 1.4 ng/dl, TRAbs 3.1 U/l, TSAb 2.7 U/l and LT4 was stopped. Thereafter, thyroid function kept switching unexpectedly between hyper and hypothyroidism, and was finally proposed to treatment with radioidine (RAI). Six weeks after RAI, with no other therapy, TSH was 68 mIU/ml, FT4 <0.40 ng/dl, TRAbs 10 U/l, TSAb 7.5 U/l, and LT4 was re-started in progressive doses.

Conclusion
We present a case of alemtuzumab-induced GD with unexpected fluctuations from hyperthyroidism to hypothyroidism, not explained by omission or changes in therapy. There was evidence of periods were TRAb level were rising but TSAb levels were decreasing, which may be explained by the presence of TAb in circulation. Our case report emphasizes the need for close monitoring of thyroid function in patients with alemtuzumab-induced GD, as maintaining euthyroidism in these patients may represent a challenge.

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Thyroid incidentalomas: which features in internal medicine?

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Background
Thyroid nodules (TN) are common. Their prevalence increases with age. A thyroid incidentaloma (TI) is defined as a non-palpable TN detected fortuitously during a radiological investigation performed for reasons unrelated to the thyroid gland. Although they are mostly benign, the risk of malignancy is estimated from 7% to 15% of nodules. The objective of this study is to investigate the characteristics of TI in a cohort of patients admitted in an internal medicine department.
Methods
A descriptive retrospective study identifying 48 records of TN in patients hospitalized in an internal medicine department between 2016 and 2021. Then we studied cases of TI.

Results
Among the 48 cases of TN, 50% were incidentalomas. There was a clear female predominance (gender ratio: 0.17). The mean age was 50.8 years old (ranging between 29 and 73). The patients had a medical history of chronic renal failure in 6 cases, Systemic Lupus in 4 cases, Crotin disease in 1 case, sarcoidosis in 1 case, myelodysplastic syndrome in 1 case and AL amyloidosis in 1 case. TI were mostly detected by neck ultrasound. Only 12.5% were discovered by chest CT scan. These investigations were performed in order to examine lymph nodes (45.83%), parathyroid glands (33.33%) lung parenchyma (32.5%) or parotid glands (8.33%). Ultrasonography, performed in all patients, showed: a solitary nodule (41.7%), a multilobular goiter (29.2%) and lymphadenopathy (14.6%). According to the European Thyroid Imaging Reporting and Data System (EU-TIRADS), TN were classified as EU-TIRADS 2 (4.1%), EU-TIRADS 3 (75%), EU-TIRADS 4 (12.5%), and EU-TIRADS 5 (8.3%). Thyroid function test was abnormal in 5 cases: 3 cases of hypothyroidism and 2 cases of hyperthyroidism. Fine needle aspiration biopsy, performed in 6 patients, revealed: benign cystology in 3 cases, atypia of undetermined significance (occult tumor) in 1 case, cytology suspicious for malignancy in 1 case, and was unsatisfactory in 1 case. Thyroidectomy was conducted in 9 cases, revealing a malignant origin in 2 patients (papillary carcinoma in both cases). Therapeutic modalities were surgery (29.2%), radioactive iodine (14.6%) and monitoring (54.2%).

Conclusion
In our study, incidentalomas were discovered in 50% of TN cases. Among them, 2 cases were malignant (8.3%). Thus, screening for thyroid nodules, by cervical ultrasound, seems necessary for internal medicine patients, so as not to miss thyroid cancer, mainly at a subclinical stage.

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P483
Thyroid dysfunction in patients presenting metabolic syndrome
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Introduction
Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance, high triglycerides plus high-density lipoprotein (HDL) cholesterol and hypertension. A developing collection of proof proposes that metabolic condition is related to endocrine problems including thyroid brokenness. Thyroid brokenness in metabolic condition patients might additionally add to cardiovascular illness hazard subsequently expanding mortality. This study was done to survey thyroid capacity in metabolic disorder patients and assess its relationship with the parts of metabolic condition.

Methods
This cross-sectional study was carried out among metabolic syndrome patients at selected hospital in Bihar from June 2020 to March 2021. We selected 346 patients who satisfied National Cholesterol Education Program-Adult treatment Panel III models. Anthropometric estimations (height, weight, waist circumference) and circulatory strain were taken. Fasting blood tests were analysed to gauge glucose, triglyceride (TG), high thickness lipoprotein (HDL) cholesterol and thyroid chemicals. Patients were supposed to be euthyroid assuming all thyroid chemical levels fell inside the reference range [TSH: 0.47-5.0 mIU/l; FT4: 0.71-1.85 ng/dl]. Subclinical hypothyroidism (SCH) was thought of if TSH > 4.0 mIU/l with normal FT3 and FT4. Subclinical hypothyroidism was the commonest followed by obvious hypothyroidism. Also, thyroid capacity is related to certain parts of metabolic disorder (high thickness lipoprotein cholesterol and triglycerides). Further review is expected to assess the system of this relationship.

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P484
Assessing cognitive functions among elderly patients with subclinical hypothyroidism
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Background
The consequences of overt hypothyroidism on the central nervous system are well known. Interestingly, there is less proof in regards to the impacts of subclinical hypothyroidism (SCH) on the cognitive functions among elderly subjects. Studies from various countries including India have shown a variable association between SCH and cognitive dysfunction. This study planned to survey the event of cognitive impairment among the older Indian subjects who were introducing subclinical hypothyroidism.

Methods
The participants were 126 elderly subjects (age > 60) with SCH and a similar number of age-matched euthyroid controls. Subclinical hypothyroidism was defined as a serum TSH level of more than 4.0 mIU/l with normal FT3 and FT4. Members were met by a solitary onlooker. Cognitive capacity was evaluated by Mini-Mental State Examination (MMSE) and clock drawing test (CDT). MMSE has the most extreme score of 30 and scores ≤ 24 are suggestive of cognitive impairment. For CDT a score of 3 addresses a cognitive shortfall, while a score of 1 or 2 is viewed as typical. Information was dissected by utilizing SPSS and Pwert of < 0.05 was huge.

Results
The mean age of the patients’ group was 66.3 years and BMI 27.0 kg/m2 which were tantamount to controls who had a mean time of 68.1 years (P=0.17) and mean BMI 26.0 kg/m2 (<P=0.24). Any remaining benchmark factors including sex proportion, co-morbidities, family background of dementia, smoking, liquor use, schooling and exercise were likewise similar in both the groups. The mean TSH was 7.7 in the understanding group and 2.8 in the control bunch (<P=0.06). The MMSE score was 26.4 in the understanding group and 27.7 in controls (<P=0.35). The patients had a mean CDT of 2.31 and control 2.41 (<P=0.67). Cognitive impairment by MMSE (score ≤ 23) was seen in 28.2% of patients and 26.8% of controls (<P=0.65), additionally the cognitive impairment by CDT (score of 3) was available in 31.3% of patients and 29.8% of controls (<P=0.48).

Conclusion
Hypothyroidism is known to cause a decrease in cognitive capacities. Studies have tended to the relationship of cognitive impairment with subclinical hypothyroidism with variable outcomes exceptionally in old subjects. In the current review, we have observed that the commonness of cognitive impairment in old subjects with SCH is like the age-matched controls. Subsequently, the expected advantage of LT4 treatment, whenever involved with a point of working on cognitive capacities in this vulnerable group, becomes suspicious.

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P485
Thyroid pyramidal lobe detection by ultrasound in 500 consecutive patients
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Background
The thyroid pyramidal lobe (TPL) represents a normal anatomical variation of the thyroid gland. Intraoperative TPL identification is of paramount significance, taking into account that the remnant TPL leads to higher thyroglobulin, could contain thyroid carcinoma foci and lead to recurrence.

Methods
We conducted a prospective single-center, single-operator study to identify TPL in 500 consecutive patients undergoing thyroid ultrasound for any indication. We extended the standard technique to actively search for TPL. The findings reported

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were presence and site of the TPL (right vs left), presence of incidentally discovered nodules in TPL and thyroglobulin duct cysts (TGDC). We excluded patients who underwent thyroid surgery or radioiodine therapy.

Results

Of the 500 consecutive patients, TPL was identified in 113 (22.6%), 4 had TGDC, 2 had hemiagenesis of the left thyroid lobe. Forty-nine patients (43.4%) presented with left-sided TPL, 64 (56.6%) with right-sided. In 4 patients (3.5%), we identified incidental asymptomatic nodular lesions within TPL.

Conclusions

We suggest to routinely screen for thyroglobulin duct remnants (TPL or TGDC) during thyroid ultrasound. This may reduce the rate of postoperative remnant TPL, obtain lower postoperative thyroglobulin levels and potentially lead to less frequent radioiodine therapy indication. Incidental discovery of thyroid nodules within TPL could also play important role in patient management. We observed a higher prevalence of the right-sided TPL in our study, which differs from previous reports stating more frequently left-sided TPL.

P486
Resistance to methimazole in a patient with Graves’ disease
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Introduction

Graves’ disease (GD) is caused by TSH receptor antibodies (TRAbs) which stimulate thyroid activity. Initial treatment usually relies on antithyroid drugs (ATDs), mainly methimazole, carbimazole or propylthiouracil (PTU). These drugs inhibit the enzyme thyroperoxidase, blocking the synthesis of T3 and T4. Definitive therapeutic options include radioactive iodine and total thyroidectomy which are usually reserved for patients who do not tolerate or respond to ATDs, or for those who relapse or do not achieve remission after a course of ATDs. Here, we present a GD patient who suffered from remarkable resistance to ATDs requiring an early definitive therapy in order to solve her thyrotoxicosis.

Clinical case

A 57-year-old female presented with a 1-year history of palpitations, increased sweating, anxiety, insomnia and weight loss. Laboratory work-up confirmed hyperthyroidism: TSH <0.01 mIU/l, FT4 2.33 ng/dl (0.7-1.9). The titration of TRAbs was 8.55 IU/l (< 2.13) confirming the diagnosis of GD. Methimazole was commenced and progressively titrated up to 70 mg/day (i.e. fourteen 5 mg-tablets), which the patient has reassured us to be fully compliant with. Nevertheless, she remained in hyperthyroidism, and under methimazole 70 mg/day her thyroid function tests were: TSH <0.005 mIU/l, FT4 2.56 ng/dl and FT3 9.76 pg/ml (2.0-4.4). This prompted us to consider an early definitive therapy, and the patient was then proposed for total thyroidectomy. Lugol’s solution was added to her ATD therapy, and her thyroid function has improved over the following two weeks, with FT4 and FT3 serum levels dropping from 2.00 and 9.76 down to 1.57 and 4.39 ng/dl, respectively. After controlling her thyrotoxicosis, she underwent an uneventful total thyroidectomy.

Discussion

This case highlights the uncommon, but possible, scenario of resistance to high-dose ATD therapy in patients with GD. In these cases, poor compliance to therapy should always be suspect, but other possible explanations include: i) decreased intestinal absorption; ii) impaired thyroid uptake; iii) greater metabolism and excretion of ATDs. High dietary intake of iodine can also impair the action of ATDs, and may further contribute to resistance to high-dose ATDs. Lugol’s solution inhibits thyroperoxidase through Wolff-Chaikoff effect, thus blocking the synthesis and release of T4 and T3, as well as it reduces the vascularization of the thyroid gland. Hence, Lugol’s solution must be used in GD patients prior to thyroidectomy, particularly in patients unresponsive to ATDs, as illustrated here.

P487
Pazopanib-induced hypothyroidism in a patient with adrenal metastasis of renal cell carcinoma
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Introduction

Pazopanib is a tyrosine kinase inhibitor (TKI) considered to be a first-line treatment in adult patients with metastatic clear cell renal cell carcinoma (ccRCC). Thyroid dysfunction, namely hypothyroidism, is now recognized as being an important but potentially manageable side effect induced by such therapy. With this case we aimed to recall an endocrinological complication that can emerge during treatment with TKIs and highlight the importance of a thorough follow-up.

Case report

A 51-year-old man, whose past history and family history were irrelevant, was diagnosed with stage 1 ccRCC in 2001. A left radical nephrectomy was performed. In 2013 a lesion with 24 mm in diameter was first recognized in his right adrenal. In 2015 he was referred to the endocrinology outpatient clinic due to an increase in the lesion diameter to 51 mm, the CT scan showed a density of +30.9 Hounsfield Units. Laboratory findings excluded autonomous hormone secretion. Due to suspicious radiological findings and rapid tumor growth without evidence of hormonal hypersecretion, a biopsy of the adrenal mass was performed, revealing a ccRCC metastasis. The patient was submitted to a right adrenalectomy and started pazopanib 800 mg daily as adjuvant therapy, along with hydrocortisone and fludrocortisone as substitution therapy. He developed primary hypothyroidism 16 months after he started pazopanib. Anti-thyroid antibodies were normal, and the hypothyroidism was interpreted in relation to pazopanib. Furthermore, due to progressive disease pazopanib was substituted by another drug, however the hypothyroidism did not remit, and the patient remains under levothyroxine substitution therapy at the dose of 50 mg daily for 5 years now.

Discussion

High dietary intake of iodine can also impair the action of ATDs, and may further contribute to resistance to high-dose ATDs. Here, we present a GD patient who suffered from remarkable resistance to ATDs requiring an early definitive therapy in order to solve her thyrotoxicosis.

P488
Autoimmune thyroiditis, quality of life and underlying symptomatology
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Introduction

Autoimmune thyroiditis caused by autoimmune thyroiditis (AIT) is a disease that can originate physical, psychological and behavioral symptoms. Quality of life (QoL) and psychopathological symptoms in thyroid diseases and its relation with thyroid function remains unclear. In hypothyroidism there is a discussion about the normal range of TSH and Free T4 values and in which way its fluctuation influences the patient in its daily activities.

Objective

To analyze the QoL and physical and psychological symptomatology of patients with AIT.

Methods

We analyzed a sample of 145 patients with AIT with a mean age of 54.2 ± 15.3 years, 89.7 % were female and 63.4 % were married. We assessed thyroid function tests, thyroid antibodies, lipid profile, high-sensitivity C-reactive protein, B12 vitamin, folic acid and applied several questionnaires, namely: the Thyroid Dependent Quality of Life questionnaire (ThyDQoL), the Thyroid Symptom Rating Questionnaire (ThySRQ), the Thyroid Treatment Satisfaction Questionnaire (ThyTSQ) and the Brief Symptom Inventory (BSI). Statistical analysis was performed with the One-way ANOVA test and Pearson’s correlation test. P values ≤ 0.05 were considered as statistically significant.

Results

In this sample we found that patients had a mean BMI of 28.4 ± 5.2 Kg/m² and TSH 2.69 ± 4.84 µU/ml, FT4 1.15 ± 0.40 ng/dl. Patients reported a mean QoL of 15.3...
value of -2.11 points (range from -9 to 1). In regard to the ThySRQ, 46.2% of patients have noticed at least moderately memory problems, 50.4% of patients reported at least being moderately tired and 62.7% showed some kind of depressed feelings. In concern with ThyTSQ, 85.5% demonstrated being worse with treatment and 82% believes that treatment is working well. In terms of correlations, we found positive correlations between TSH and weight gain ($r = 0.19; P = 0.02$) and loss of appetite ($r = 0.27; P = 0.001$). Free T3 correlated negatively with depression ($r = 0.22; P = 0.009$), skin problems ($r = 0.19; P = 0.01$) and loss of appetite ($r = 0.22; P = 0.007$). Antithyroglobulin antibodies were negatively correlated with colder body sensation ($r = -0.17; P = 0.04$) and antiperoxidase antibodies correlate itself with voice problems ($r = -0.22; P = 0.01$).

Conclusions
In this study we can clearly see that despite the normal range of the TSH this disease negatively influences the QoL in AIT patients. We also noticed that there are certain symptoms that suffer a more direct influence of thyroid function. Further studies are needed to analyze the symptomatology that contributes to worsening of the QoL in these patients.

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P489

cGMP is not involved in thyroid cancer cell death
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Introduction
Type 5 phosphodiesterase (PDE5) inhibitors (PDE5i) lead to intracellular cyclic-guanosine monophosphate (cGMP) increase and are used for clinical treatment of erectile dysfunction. Studies found that cGMP may up/downregulate the growth of certain endocrine tumor cells, suggesting that the use of PDE5i could impact the risk of certain tumors, such as colorectal cancer.

Aim
We evaluated if PDE5i may impact thyroid cancer cell growth in vitro.

Materials and methods
We investigated caspase 3 activation by bioluminescence resonance energy transfer (BRET), in malignant (K1) and benign (Nthy-ori 3-1) thyroid cell lines, expressing a specific biosensor. Cells were treated with the PDE5i vardenafil or the analog did not impact cell viability of both malignant and benign thyroid cell lines, nor the phosphorylation of ERK1/2 ($P \geq 0.05$).

Results
BRET experiments revealed that both vardenafil and 8-br-cGMP effectively induced dose-dependent intracellular cGMP increase ($P < 0.05$) in both the K1 and Nthy-ori 3-1 cell lines, as well as in reference COS7 cells. However, no caspase 3 activation occurred between PDG, 83.5% vs -untreated cells, at all concentrations and time-points tested ($P \geq 0.05$), in contrast to the results obtained using thapsigargin ($P < 0.05$). These results match those obtained upon cell treatment with 8-br-cGMP, which failed in inducing caspase 3 cleavage in all the cell lines ($P \geq 0.05$). Moreover, they reflect the lack of caspase 3 cleavage, evaluated by Western blotting, as well as missing nuclear fragmentation. Interestingly, the modulation of intracellular cGMP levels with vardenafil or the analog did not impact cell viability of both malignant and benign thyroid tumor cell lines, nor the phosphorylation of ERK1/2 ($P \geq 0.05$).
in body fluids, especially during the activation periods of diseases in which cellular immunity plays a major role in the pathogenesis. The most potent stimulator of neutrophin synthesis is IFN-γ, which is a Th1 cytokine, and it has been suggested that serum neutrophin levels are a sensitive marker of endogenous IFN-γ release. In our study, a similar result with the literature was found, such as the detection of high neutrophin levels in immune system-related diseases.

Keywords: neutrophin, Graves, hyperthyroidism.

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P492
Simulation of the plasma level of thyroid hormones for a total thyroidectomized virtual-patient treated by BMI and BSA-based LT4 monotherapy dose regimen
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Introduction
Several levothyroxine (LT4) monotherapy dose regimen have been already proposed by different medical scientists which may result in various daily LT4 doses. Comparing the consequences of such dose regimen are rather difficult since they have to be applied on either the same patient or a large study groups. Therefore, a straight forward method would be to simulate the plasma level of thyroid hormones of virtual-patients treated by various dose regimen.

Method
In this study, the resulting plasma levels of thyroid hormones were compared for a total thyroidectomized virtual-patient treated by BMI and BSA-based LT4 monotherapy dose regimen adopted from Elfenbein et al., 2016 and Al-Dhahri et al., 2019 respectively. Our virtual-patient was considered as a 37 years old male with 72 kg weight and 170 cm height. The BMI of this patient would be 24.9 m^2. In order to evaluate patient responses to LT4 monotherapy dose regimen, we simulated our total thyroidectomized virtual-patient by setting T3 and T4 secretion parameters at 1% using THYROSIM 3.0 while receiving static oral LT4 dosages post-surgery. In addition, with an assumption that no supplement was administrated, the absorption rate of oral LT4 was set to 88%.

Results
Considering the proposed dose regimen by BMI and BSA our virtual-patient should receive static LT4 dose of 1.9 and 1.4 µg/kg respectively. Parameters to compare these two dose regimen for a period of 30-days are presented in the following table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BMI</th>
<th>BSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to reach normal TSH level</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Time to reach normal T3 level</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>TSH out of normal range</td>
<td>14</td>
<td>30</td>
</tr>
<tr>
<td>T3 out of normal range</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>T4 out of normal range</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Discrepancy between TSH at day 30 and normal TSH (1.93)</td>
<td>1.93</td>
<td>7.11</td>
</tr>
<tr>
<td>Discrepancy between T3 at day 30 and normal T3 (1.35)</td>
<td>-0.51</td>
<td>-0.59</td>
</tr>
<tr>
<td>Discrepancy between T4 at day 30 and normal T4 (78.21)</td>
<td>8.35</td>
<td>-9.95</td>
</tr>
</tbody>
</table>

Discussion/Conclusion
Thyroid dysfunction after vaccination is a rare phenomenon. However, clinicians should be aware that thyroiditis might be an underreported adverse effect of COVID-19 vaccines. Further research is needed to investigate the prevalence and the mechanisms of thyroiditis after COVID-19 vaccination. Based on the finding of these cases we recommend performing Thyroid function test post Covid-19 vaccination to monitor for thyroid dysfunction.

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P493
Rare presentation of thyrotoxicosis post CoVID-19 vaccination in acute setting
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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 has led to unparalleled burden on national and global healthcare systems. Vaccines were viewed as way of combating Covid 19 pandemic. This led to development and implementation of vaccination programmes worldwide. Several vaccines have been approved for use in worldwide including Pfizer-BionTech, Oxford-AstraZeneca vaccine and Moderna vaccine. Disturbingly, the speed at which these vaccines been approved suggest limited studies regarding their efficacy and possible side effects were carried out. Following their widespread use in general public, a problematic trend of post Covid-19 vaccine manifestations are become more apparent and are being reported with increasing frequency. One such manifestation of post Covid-19 vaccination is new onset of autoimmune diseases such as immune thrombocytopenia, IgA nephropathy, rheumatoid arthritis and rarely thyroid dysfunction.

Case series
1. A 49-year-old male presented with shortness of breath and palpitations 2 weeks after AstraZeneca vaccine. The patient also reported significant weight loss. On examination, the patient was tachycardic and palpable thyroid nodules. Blood test results can be seen in table 1, Ultrasound scan of thyroid gland which demonstrated bilateral thyroid nodules with peripheral vasculature. The patient was subsequently diagnosed with Graves’ disease and started on treatment with iv hydrocortisone, propranolol, carbimazole. With endocrine team follow up scheduled. 2. A 53-year-old female referred by her GP with deranged thyroid function tests. Patient reported significant weight loss, lethargy, hair loss and ongoing spikes in temperature at night with associated night sweats. The patient indicated her symptoms started 2 weeks after administration of AstraZeneca vaccine. On examination she was found to be tachycardic and visible anterior neck swelling suggestive of goitre. Further to this she underwent Ultrasound scan of Thyroid gland which demonstrated atrophic thyroid gland with right thyroid nodule. The patient was treated with steroids, propranolol, carbimazole.

Discussion/Conclusion
Thyroid dysfunction after vaccination is a rare phenomenon. However, clinicians should be aware that thyroiditis might be an underreported adverse effect of COVID-19 vaccines. Further research is needed to investigate the prevalence and the mechanisms of thyroiditis after COVID-19 vaccination. Based on the finding of these cases we recommend performing Thyroid function test post Covid-19 vaccination to monitor for thyroid dysfunction.

Patient 1 Patient 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BMI</th>
<th>BSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>&lt;0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>T4</td>
<td>&gt;100</td>
<td>61.5</td>
</tr>
<tr>
<td>CRP</td>
<td>1</td>
<td>70</td>
</tr>
<tr>
<td>TSH RECEPTOR AB</td>
<td>9.56</td>
<td>0.31</td>
</tr>
<tr>
<td>TPO AB</td>
<td>&lt;4</td>
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DOI: 10.1530/endoabs.81.P493

P494
Female papillary thyroid cancer survivors are at increased risk of hyperproliferative pathology of the reproductive system
Tetiana Tatarchuk1, Mykola Tronko2, Panagiotis Anagnostis3, Liudmyla Kalugina1, Natalia Pedachenko2, Anna Danylova1 & Tetiana Kuchmenko1
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Coronavirus disease 2019 (COVID-19) pandemic has led to unparalleled burden on national and global healthcare systems. Vaccines were viewed as way of combating Covid 19 pandemic. This led to development and implementation of vaccination programmes worldwide. Several vaccines have been approved for use in worldwide including Pfizer-BionTech, Oxford-AstraZeneca vaccine and Moderna vaccine. Disturbingly, the speed at which these vaccines been approved suggest limited studies regarding their efficacy and possible side effects were carried out. Following their widespread use in general public, a problematic trend of post Covid-19 vaccine manifestations are become more apparent and are being reported with increasing frequency. One such manifestation of post Covid-19 vaccination is new onset of autoimmune diseases such as immune thrombocytopenia, IgA nephropathy, rheumatoid arthritis and rarely thyroid dysfunction.

Case series
1. A 49-year-old male presented with shortness of breath and palpitations 2 weeks after AstraZeneca vaccine. The patient also reported significant weight loss. On examination, the patient was tachycardic and palpable thyroid nodules. Blood test results can be seen in table 1, Ultrasound scan of thyroid gland which demonstrated bilateral thyroid nodules with peripheral vasculature. The patient was subsequently diagnosed with Graves’ disease and started on treatment with iv hydrocortisone, propranolol, carbimazole. With endocrine team follow up scheduled. 2. A 53-year-old female referred by her GP with deranged thyroid function tests. Patient reported significant weight loss, lethargy, hair loss and ongoing spikes in temperature at night with associated night sweats. The patient indicated her symptoms started 2 weeks after administration of AstraZeneca vaccine. On examination she was found to be tachycardic and visible anterior neck swelling suggestive of goitre. Further to this she underwent Ultrasound scan of Thyroid gland which demonstrated atrophic thyroid gland with right thyroid nodule. The patient was treated with steroids, propranolol, carbimazole.

Discussion/Conclusion
Thyroid dysfunction after vaccination is a rare phenomenon. However, clinicians should be aware that thyroiditis might be an underreported adverse effect of COVID-19 vaccines. Further research is needed to investigate the prevalence and the mechanisms of thyroiditis after COVID-19 vaccination. Based on the finding of these cases we recommend performing Thyroid function test post Covid-19 vaccination to monitor for thyroid dysfunction.

Patient 1 Patient 2

<table>
<thead>
<tr>
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<tr>
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<tr>
<td>TSH RECEPTOR AB</td>
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<td>&lt;4</td>
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</tbody>
</table>

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P494
Female papillary thyroid cancer survivors are at increased risk of hyperproliferative pathology of the reproductive system
Tetiana Tatarchuk1, Mykola Tronko2, Panagiotis Anagnostis3, Liudmyla Kalugina1, Natalia Pedachenko2, Anna Danylova1 & Tetiana Kuchmenko1
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P495

A rare case of a non-secretory medullary thyroid carcinoma
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Introduction
Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor (1-2% of all
tyroid carcinomas), which arises from calcitonin-producing C cells. Calcitonin
(Ct) and calcitoninogen C-segment antigen (CEA) are used as tumor markers in the
follow-up of patients with MTC. Non-secretory forms of MTC are very rare,
accounting for less than 1% of the cases.

Case Report
A 53-year-old man underwent left thyroid lobectomy for a 1.1 cm thyroid nodule
subjected to fine-needle aspiration (twice), which cytology revealed a “follicular
lesion of undetermined significance. Histological examination showed a
multifocal MTC (1.2 cm and 0.4 cm) and C-cell hyperplasia. Immunohistochem-
istry revealed cytoplasmic positivity for CT, chromogranin and synaptophysin,
and nuclear positivity for TTF1. Totalization of thyroidectomy and lymph node
dissection of the central compartment were performed. Histopathological analysis
revealed C-cell hyperplasia and absence of lymph node metastasis in 26 lymph
nodes. Preoperatively, there was no elevation of CT or CEA (CT 2.84 pg/ml (NR:
0.40-18.90) and CEA 2.4 ng/ml (NR: <5.0)). A dilution test for CT was performed
and showed no evidence of interference caused by heterophile antibodies. The
measurement of fractionated 24-h urinary metanephrines and phospho-calcium metabolism did not show any changes. The search for mutations in the RET gene was negative. In the postoperative study, CT and CEA measurements remained within the normal range. 18F-DOPA positron emission
tomography (PET) was requested, which revealed a moderate uptake located in
the topography of the duodenal arch. The patient was referred to the
Gastroenterology outpatient clinic. He underwent endoscopic ultrasound and
abdominal computerized-tomography scan. No duodenal or locoregional lesions
were observed. The patient is currently under surveillance, with no clinical,
analytical or imaging evidence of recurrent disease.

Conclusion
The reported cases of non-secretory MTC are rare and present a heterogeneous
clinical course, which makes it difficult to predict its behavior. It is not clear what
is the best way to monitor these patients, as the use of tumor markers is limited.
Alternative methods for monitoring are needed to optimize the follow-up of these
patients.

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P496

Outcomes of low-risk differentiated thyroid cancer submitted to
radioactive iodine ablation - a comparative analysis in a single tertiary centre
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2Centro Hospitalar Lisboa Central, Endocrinology, Diabetes and Metabol-
ism department, Lisbon, Portugal; 3Hospital CUF, Endocrinology Depart-
ment, Lisboa, Portugal; 4Instituto Português de Oncologia de Lisboa
Francisco Gentil - IPOPFG, Endocrinology Department, Lisbon, Portugal

Introduction
The update of 2015 American Thyroid Association (ATA) guidelines recommend
that radioactive iodine (RAI) ablation therapy should be used in line with patients’
risk stratification. However, there is no consensus on benefits of post-operative
RAI ablation in patients with low risk differentiated thyroid cancer (DTC). The
aim of this study is to compare the outcomes of patients with low risk DCT
submitted to RAI ablation with those who were not.

Methods
This is a retrospective study of patients with low risk DTC followed in a tertiary
cancer centre between 2016-2019. Clinicopathological features were collected.
Clinical outcomes of patients submitted to RAI ablation were compared to a
group control. The risk factors considered for recurrence were: multifocality,
minimal extrathyroidal extension (ETE), N1 micrometastases (≤5 nodes with <
0.2 cm in largest dimension), suspicious or non-specific findings on post-
operative ultrasound (US), positive non-stimulated serum thyroglobulin (Tg) and
positive Tg antibodies (ATG) levels. Recission was defined as no evidence of
disease /indeterminate response and disease recurrence as biochemical or
structural evidence of disease, at last follow-up, based on ATA criteria.

Results
739 patients were included (77.9% female) with a mean age of 53.7 ± 15.9 years-
old and a mean follow-up of 3.6 ± 1.2 years. RAI ablation was performed in
45% (n = 331). Recurrence was observed in 4.2% (n = 14) of the patients
submitted to RAI ablation and in 2.9% (n = 12) of the cases that underwent
surveillance (P = 0.342). Multivariate analysis showed that only post-op Tg -
Tg > 1 ng/ml [P < 0.001; hazard ratio (HR): 9.5; 95% confidence interval
(95% CI): 3.0-30.0], Tg between 0.2-1 ng/ml (P = 0.008; HR: 5.3; 95% CI: 1.6-
18.1) and suspicious findings on post-op US (P < 0.001; HR: 8.7; 95% CI: 2.8-
27.8) were independent risk factors for recurrence.

Conclusions
Our results demonstrated no differences in clinical outcomes between RAI
ablation and surveillance after surgery in low-risk DTC patients, reinforcing that
these patients do not benefit from RAI ablation. Positive non-stimulated serum Tg
levels and suspicious findings on post-operative ultrasound were the only factors
associated with recurrence.

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P497

Impact of 2015 ATA guidelines in 131I prescription in low-risk DTC
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Joana Simões-Pereira5, Helena Vilari5 & Valeriano Leite5
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and Metabolism Department, Lisboa, Portugal; 2Armed Forces Hospital
Lisbon, Endocrinology Department, Lisbon, Portugal; 3Hospital CUF,
Lisbon, Lisbon, Portugal; 4Instituto Português de Oncologia de Lisboa
Francisco Gentil, Endocrinology Department, Lisbon, Portugal

Background
To minimize potential harm from overtreatment of low-risk thyroid cancers, the
2015 American Thyroid Association (ATA) Guidelines recommend that
radioactive iodine (RAI) ablation should not be routinely used in low-risk
differentiated thyroid carcinoma (DTC). The present study aims to evaluate trends
in RAI therapy in a tertiary center after the update of these Guidelines.

Methods
Data from patients followed in a tertiary center with low-risk DTC between 2016
and 2019 were analyzed. Risk stratification was based on 2015 ATA staging criteria.
Multifocality, minimal extrathyroidal extension, ≤5 pathologic N1 micro-
metastases (<0.2 cm in largest dimension), non-specific findings or suspicious
lymph nodes on post-operative ultrasound (US), non-stimulated serum
thyroglobulin (Tg) >1 ng/ml and positive anti-Tg were considered potential
risk factors for recurrence.

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Variation of anti-TSH receptor antibodies after iodi ne-131 therapy
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Introduction
Graves’ disease (GD) is a systemic autoimmune disease characterized by lymphocyte activation and synthesis of anti-TSH receptor antibodies (TRABs). Higher values of TRABs are associated with a higher risk of Graves’ ophthalmopathy and dermopathy. Iodine-131 therapy (RAI) is one of the well-established options in GD, but it can cause a transient increase in TRABs.

Objectives
To evaluate the evolution of TRABs after RAI; to identify factors associated with a more marked increase in TRABs.

Material and methods
Retrospective analysis of a sample of patients with GD undergoing RAI. Information on demographic data, antithyroid drug therapy (ATD), TRAB values over time (pre-RAI and at 1, 3, 6 and 12 months after RAI) and response to RAI were collected.

Results
We analyzed 86 episodes of RAI, involving 75 patients, mostly female (80.0%), 84.9% corresponded to 1st therapies and 15.1% to subsequent therapies. Age at RAI administration was 40.9 ± 17.2 years, mean 3.0 ± 3.0 years after diagnosis, and 82.6% were under ATDs. The pre-therapeutic TRABs had a median value of 17.2 years, mean 3.0 vs 1.0 ± 2.0 months, higher estimated glaucomatous damage (57.5 ± 32.7 vs 43.0 ± 25.0 g, \( P = 0.024 \)) and were more frequently of the female gender (60.8 vs 29.4%, \( P = 0.029 \)). There was no significant difference in administered dose (11.0 ± 4.6 vs 10.0 ± 4.4 mCi, \( P = 0.384 \)). In multivariate analysis, female gender and the estimated glaucomatous damage maintained a statistically significant relationship with the probability of duplication of the TRABs (\( P = 0.015 \) and \( P = 0.017 \), respectively).

Discussion
Most patients registered an elevation of the TRABs post-RAI. Female patients with larger glaucomatous damage may be especially at risk for higher elevations. These data may have implications for the extrathyroidal manifestations of Graves’ disease.

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Immune check point inhibitors- induced thyroid disorders -would you recognize them?
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1Queen’s Hospital, London, United Kingdom; 2Queen’s Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom

Introduction
Development and progression of cancers is multifactorial encompassing several mechanisms that aid its proliferation. One of the hallmarks of cancer progression is inhibition of the immune system. Cancer cells can activate different immune checkpoint pathways that are pathways that harbour inhibitory or stimulatory mechanisms that enabled self-tolerance and assist with immune response. Through activation of immune checkpoint pathways cancers can suppress immune response against it. Monoclonal antibodies that target immune checkpoin tsgs have garnered immense interest in management of solid tumours. The mechanism of action immune checkpoint inhibitors is that they block inhibitory molecules on T-Cells. However, they also downregulate immunomolecular tolerance to self-antigens, inducing immune related adverse events (IRAEs). IRAEs have been reported in several organs including the endocrine glands including the thyroid and pituitary glands. Here we present cases of two patients which developed hypothyroidism following immune checkpoint inhibitor therapy for their metastatic carcinoma.

Case presentations
Case-1. An 80-year-old gentleman with a background his of metastatic squamous cell carcinoma of the lung was given pembrolizumab (anti-PD-1) treatment. He subsequently developed transient hyperthyroidism (characterised by TSH -69.10
mU/l, FT4 0.5 Pmol/l). Five months post therapy he became hypothyroid, elevated TSH and low FT4). He was subsequently started on levothyroxine and became euthyroid.

Case-2: A 63-Year-old male with history of metastatic cancer of the colon was started on azetolizumab (anti-PD-L1). Post therapy the patient developed severe hypothyroidism characterised by myopathy and myositis. Before immunotherapy the patient was euthyroid with normal levels of TSH and FT4. Subsequent blood test post treatment showed high levels of TSH >150 mU/l and FT4 6 Pmol/l. He was treated with high dose of levothyroxine to get him back to his baseline.

Discussion/Conclusion
Thyroid toxicity post immune checkpoint inhibitor therapy is being reported with increasing frequency, based on literature this complication irreversible with patients requiring continuous therapeutic management and follow up which can put increased pressure on patients, who are often under increased mental strain in dealing with their cancer treatment. Based on the case reported here we recommend baseline thyroid function test should be done at initiation of therapy, periodically after immunotherapy and during each cycle of infusion.

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P501
Thyroid involvement in the context of sars-cov-2 infection
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Introduction
The SARS-CoV-2 virus has severely affected humanity. The disease causes pneumonia which may be severe. In many cases, patients, especially if they have comorbidities, may have a fatal outcome. The disease affects all organs and the variability of its manifestations has attracted intense scientific interest.

Aim
The aim of the study was to describe the case of a patient who developed subacute thyroiditis after infection with the SARS-CoV-2 virus.

Case description
A patient, female, aged 52 years, developed signs of respiratory infection with a mild clinical picture and fatigue. Hospitalization was not necessary. Sixty days later, she developed signs of subacute thyroiditis with pain in the area of the thyroid gland radiating to the ears, hyperidrosis, tachycardia and intense fatigue. Laboratory investigations revealed IgG Ab COVID-19 31.9 (normal values <1) (ELISA), IgM Ab COVID-19 10.6 (normal values <1) (ELISA), CRP 4.27 mg/l (normal values <0.5 mg/dl), ESR 85 mm/h and TSH 0.03 mU/l. A thyroid ultrasonogram was performed which revealed hypoechogenic areas. Non-steroidal-anti-inflammatory drugs were administered which led to pain relief. A month later the patient presented with tachycardia, pain in the area of the thyroid and fatigue. Methylyprednisolone was administered 16 mgx2 daily and propionate 20 mgx2 daily and the patient improved. However, a month later the patient presented with disease relapse. Methylyprednisolone 16 mgx2 was administered and the patient improved and is now asymptomatic.

Conclusions
The disease caused by the SARS-CoV-2 virus affects all organ systems. The virus enters cells by attaching to the ACE2 (angiotensin converting enzyme 2) which acts as a receptor for the virus. It has been observed that thyroid cells express the ACE2. It appears that the SARS-CoV-2 virus infects thyroid cells via the ACE2. Cases of subacute thyroiditis, a post-infectious disease, have been described mainly in female patients after SARS-CoV-2 infection. In conclusion, it appears that the SARS-CoV-2 virus may affect the thyroid gland.

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P502
Comparing non-diagnostic FNA results in thyroid nodules
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Introduction
Multiple specialities teach and perform ultrasound-guided fine-needle aspiration biopsy (USG-FNA) of thyroid nodules, including Radiology, Endocrinology, and Pathology. Contrasts in cytopathology results might connect with various USG-FNA procedures just as complications in the knobs assessed. The study planned to play out a nitty-gritty investigation of USG-FNA results among these different showing administrations at a solitary scholarly clinical focus.

Methods
We performed a review outline survey of patients who went through USG-FNA of a thyroid knob at a solitary scholarly clinical focus from 2015-to 2017, barring patients with hyperthyroidism. Cytopathology results were arranged by the Bethesda framework and separated by the performing strength (Radiology, Endocrinology, and Pathology). Segment, clinical, and ultrasound factors were likewise analysed to additionally research contrasts between the performing specialities.

Results
Of the 356 total thyroid nodules examined by USG-FNA, 167 nodules were biopsied by Radiology, 119 by Endocrinology, and 70 by Pathology. Onsite cytopathology assessment was accessible to Radiology and Pathology, but not to Endocrinology during this period. The appropriation of Bethesda results was different between the three performing administrations (P<0.05). The pace of a Bethesda I (non-indicative) cytopathology result was 3.6% for Radiology, 10.1% for Endocrinology, and 11.4% for Pathology (P<0.05). Contrasts between the pace of harmless (Bethesda II), uncertain (Bethesda III-IV), or high-hazard (Bethesda V-VI) results were not measurably critical. The Radiology-performed USG-FNA group included 58.9% knobs found unexpectedly contrasted with 43.9% and 32.8% for Endocrinology and Pathology, separately (P<0.001). A larger part of knobs was somewhat or dominatingly cystic in the Radiology (53.4%) and Pathology (55.5%) gatherings, however not in the Endocrinology group (34.6%), which just arrived at a measurable pattern (P=0.07). No other huge contrasts

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P716
Antenatal thyroid hormone therapy and antithyroid drug use in Norway from 2004 to 2018
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Thyroid disease during pregnancy is associated with adverse pregnancy outcomes and suboptimal fetal development. During the last decades, guidelines for diagnosing thyroid disease during pregnancy have changed considerably, and there has been increased awareness. This study aimed to describe the prevalence of thyroid disease treatment over time among pregnant women in Norway. We combined historical data from the Medical Birth Registry of Norway and the Norwegian Prescription Database, identifying pregnant women using thyroid therapy before, during and after pregnancy from 2004 to 2018. A total of 855,067 pregnancies were included in the analyses. The proportion of women using thyroid hormone replacement therapy during pregnancy increased from 1.46% (n = 800) in 2004 to 3.57% (n = 1940) in 2018. The proportion of women using antithyroid medications also increased from 0.04% (n = 20) in 2004 to 0.10% (n = 56). During these 15 years, the mean maternal age increased by 0.9 years. When adjusting for age, the risk for being on thyroid hormone replacement therapy during pregnancy increased by an average of 5% per year (odds ratio 1.05, 95% confidence interval 1.05–1.05). The reasons behind the increased use of thyroid therapy could be many. Firstly, an enhanced focus on better diagnostics lead to an increased prevalence of thyroid disease, which is evident by the results of a repeated population-based cross-sectional study in Norway. However, one of the key clinical issues in this field is the definition of gestational thyroid disease. A second reason could be the increase in inadequate iodine intake among the pregnant population. Recent study from Norway found that pregnant and postpartum women with mild-to-moderate iodine deficiency had altered thyroid. Furthermore, experimental and epidemiological studies have shown that a wide spectrum of environmental contaminants has the potential to adversely affect the hypothalamic-pituitary-thyroid axis, resulting in reduced maternal thyroid hormone synthesis affecting fetal neurodevelopment. Another possible contributor to the increased use of thyroid therapy could be that euthyroid women, with thyroid autoantibodies, use thyroid hormone treatment. The proportion of
babies born after assisted reproductive therapy has increased by 2.2% during the studied period. During the recent 15 years, there has been a substantial increase in the use of thyroid hormone therapy in Norwegian pregnant women. We speculate that this could be due to an increased awareness in combination with overdiagnosis because of inappropriate diagnostic criteria. To truly understand the possible causes and consequences of this development, further research is warranted.

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P717

**DICTER1** mutations in pediatric thyroid nodules
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**Objectives**

Mutations in the **DICTER1** gene represent driver events in development of pediatric thyroid nodules, malignant as well as benign. The occurrence of these mutations has been reported in differentiated thyroid carcinomas, poorly differentiated thyroid carcinomas, non-invasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTPs), multinodular goiters and follicular adenomas. The aim of this study was to detect mutations in **DICTER1** gene in a large cohort of pediatric thyroid nodules and correlate found mutations with clinicopathological data with a focus on prognosis of disease in patients with papillary thyroid carcinoma (PTC).

**Methods**

The study consisted of 132 thyroid nodule samples from 124 pediatric patients (age 6-20 years). The cohort included 110 PTCs, 2 NIFTPs and 20 benign nodules. DNA was isolated from fresh frozen thyroid tissues using the Allprep DNA/RNA/miRNA Universal kit and the QIAcube Connect Extraction System (Qiagen, Germany). DNA was used for next-generation sequencing on MiSeq sequencer (Illumina, USA) using the Nextera XT DNA Library Prep Kit (Illumina). Mutations in the **DICTER1** gene were visualized in Integrative Genomics Viewer (Broad Institute, USA) and evaluated by VarSome platform (Sapherton SA, Switzerland).

**Results**

Pathogenic **DICTER1** hotspot mutations (E1705K, D1709 N, E1813D) in 7 of 132 (5.3%) pediatric thyroid samples were detected. Six of them were PTCs (follicular variant), from which 5 were encapsulated. Five PTC patients received only one dose (100 mCi) of radiodine treatment and are in remission. Only in one case, the patient received three doses of radiodine (2× 100 mCi, 1× 120 mCi). This patient had a 60-mm carcinoma and angioinvasion was described only in this patient. The **DICTER1** alteration was also found in one NIFTP case. All **DICTER1**-mutated tumors did not possess other driver mutations (in the **BRAF** gene, **RAS** genes, fusion genes).

**Conclusion**

In summary, **DICTER1** mutations are important molecular markers in pediatric thyroid nodules. Almost all our **DICTER1**-mutated carcinomas represented low-risk malignancies and patients had an excellent response to the treatment. However, one patient had an incomplete response to treatment due to the advanced stage at the time of diagnosis. In conclusion, **DICTER1**-mutated tumors appear to be indolent, but should not be underestimated.

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P719

**Serum FT3 levels and FT3/FT4 ratio as predictors for poor prognosis in hospitalized COVID-19 patients**
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**Background**

Thyroid dysfunctions are among the most common immune-related adverse events (irAEs) following the administration of immune checkpoint inhibitors (ICIs) for malignancies. The pathogenesis of thyroid irAEs remains unclear and the clinical course can be multifaceted.

**Aim**

Aims of this study were a) to describe the incidence and the clinical course of thyroid irAEs b) to determine the association between thyroid irAEs and overall survival (OS).

**Methods**

We performed a single-center retrospective study of cancer patients treated with anti-PD-1/PD-L1 from January 2018 to December 2020. Demographic data, thyroid function tests (serum thyrotropin, TSH; free thyroxine FT4; free triiodothyronine, FT3) and thyroid ultrasonographic findings (if available) were retrieved at baseline and at regular intervals after starting ICIs. Patients were excluded if a) they had abnormal thyroid function at baseline b) were on anti-thyroid drugs or levothyroxine (LT4) replacement c) had missing data.

**Results**

One hundred sixty-six cancer patients were considered for potential enrollment, and after assessment of inclusion and exclusion criteria, 112 were enrolled. The mean age was 67.9 (10.6) years, and 82 patients (73.2%) were males. Lung cancer accounted for 65.8% of all cancers, followed by melanoma (16.2%), squamous cell carcinoma (9.9%), genitourinary cancers (6.3%) and other cancers (1.8%). Among all patients, 97 (86.6%) were treated with a PD-1 blockade, whereas 15 (14.4%) received a PD-L1 inhibitor. Previous treatments had been performed in 72 patients (79.1%). During the study period, 25 patients (22.3%) developed thyroid irAEs with a median time to onset of 5.1 months (IQR 6.7). Two of them (8%) initially presented with hyperthyroxinemia and 23 (92%) with hypothyroidism. Patients with hypothyroxinemia had an earlier median time to onset compared to those who had hypothyroidism (1.3 ± 5.2 months, P = 0.045). Overall, 19 patients (76%) required LT4 replacement. Systemic steroids were not required in all cases. Thyroid ultrasonography, performed in 19 patients at thyroid irAEs onset, revealed a slightly increased thyroid volume in patients with hypothyroidism and a reduced volume in hyperthyroid patients (18.1 ± 8.4 mL, P = 0.01). Multivariable Cox regression analysis revealed that the occurrence of thyroid irAEs was independently associated with better OS (HR 0.3, CI 95% 0.1-0.7, P = 0.006).

**Conclusion**

This study confirms that thyroid irAEs occur with a high frequency in routine clinical practice and with heterogeneous clinical presentation. It also supports that thyroid irAEs may represent a predictive biomarker of better response to ICIs.

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P718

**Clinical presentation and significance of thyroid dysfunctions secondary to PD-1/PD-L1 blockade cancer immunotherapy**
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**Background**

The coronavirus disease 2019 (COVID-19) can involve multiple organs and systems, including the endocrine system. In particular, thyroid dysfunctions are frequently seen in COVID-19 patients. The aim of this study was to evaluate thyroid function in hospitalized COVID-19 patients and to correlate thyroid function with inflammatory status, blood count parameters and mortality.

**Materials and methods**

Data of COVID-19 patients admitted to the hospital of Pescara between October 2020 and March 2021 were retrospectively evaluated. Serum thyrostim (TSH), free thyroxine (FT4), free triiodothyronine (FT3), FT3/FT4 ratio, thyroid antibodies (TGAb, TPOAb), inflammatory and blood count parameters (C-reactive protein, CRP, interleukin-6, IL-6; red blood cell, RBC; white blood cells, WBC; platelets, PLT; neutrophil to lymphocytic ratio, NLR) were analyzed and compared between survivors and non-survivors.
Results

Three hundred thirty-four adult COVID-19 patients were considered for potential enrollment, and after assessment of inclusion and exclusion criteria, 264 were enrolled. The median age was 74.4 (20.6) years, and 167 patients (63.5%) were males. The average hospital stay was 9 days. Of the 264 enrolled patients, 101 (38.2%) died of COVID-19 complications. The characteristics of survivors and non-survivors are shown in table 1. Serum FT3 levels and FT3/FT4 ratio were significantly lower in non-survivors compared to survivors. Instead, inflammatory and blood count parameters, except for RBC, were significantly higher in survivors. Notably, FT3 levels and FT3/FT4 ratio negatively correlated with CRP and NLR (r = 0.2, P = 0.05). In Kaplan-Meier and Cox regression analyses, low FT3 levels (FT3 less than 2.5 pg/ml) were independently associated with mortality (HR: 1.7, CI 95% 1.01–2.96, P = 0.042).

Conclusions

FT3 levels and FT3/FT4 ratio correlate negatively with inflammatory markers and may be predictive for poor prognosis in hospitalized COVID-19 patients.

P721

Does the risk of new metabolic changes among thyroid cancer survivors depend upon thyroid function?

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Background

Various components of metabolic syndrome (MS) significantly increase the risk of thyroid cancer (TC). Moreover, thyroid cancer survivors (TCS) are at increased risk of new components of MS (MSC). The role of thyroid function in this context has not yet been determined. We investigated changes in selected MSC and their association with thyroid function during a two-year follow-up among TCS.

Materials and Methods

This retrospective, nested case-control study used data from a single academic hospital. The one-hundred and fifteen participants had undergone total thyroidectomy, radioactive iodine treatment and thyroid-stimulating hormone-suppressive L-thyroxine therapy for two years due to differentiated TC.

Results

The numbers of MSC in the entire cohort at baseline compared to those after a two-year follow-up were as follows: none in 58.3% patients vs 30.4% patients, respectively, 1 in 20.9% vs 35.5%; 2 in 11.3% vs 16.5%; 3 in 7.8% vs 13.9%; 4 in 1.7% vs 1.7%; and 5 in 0% vs 1.7%. The incidence of MSC increased during the two-year follow-up period in 51 TCS (cases), while none of the 64 TCS (controls) developed any new MSC. The multivariate logistic regression analysis showed that TCS with a FT3/FT4 ratio greater than 0.22 (lower tertile) had a significantly increased risk of a new MSC (odds ratio 2.73, 95% confidence interval 1.14–6.48, P = 0.025).

Conclusions

Our study demonstrated that an FT3/FT4 ratio greater than 0.22 is correlated with detrimental metabolic changes among TCS.

P722

Clinicopathological characteristics and response to therapy in patients with tall cell variant papillary thyroid carcinoma in an institution: analysis of 109 cases

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Objectives

1. Characterization of patients with tall cell variant papillary thyroid carcinoma (TCV-PTC) at diagnosis (Dx) compared to patients with classic papillary thyroid carcinoma (c-PTC);
2. Evaluation of response to therapy (RT) in the (TCV-PTC) cohort
   Experimental design: Retrospective observational study

   Materials and methods
   Patients submitted to surgery for PTC in our institution since 2010 were evaluated. Clinicopathological characteristics at dx were compared between TCV-PTC and c-PTC. Subsequently, the RT in the TCV-PTC cohort was evaluated. Continuous variables (v) were used to compare continuous variables and chi square or Fisher in categorical variable. Logistic regression was used for multivariate analysis.

   Results
   From 1475 patients with PTC, 1040 (70%) correspond to c-PTC and 109 (7%) to TCV-PTC. Table 1 compares the clinicopathological characteristics most relevant at Dg. In multivariate analysis, RT was independently associated with a higher probability of ETE and LNF-Inv in the pathology report. RAI was given to 86% of patients. Of the 68 patients in whom it was possible to evaluate RT (median follow-up 21 months), 66% presented excellent RT, 16% indeterminate RT and 7% structural incomplete RT. RT was significantly better in patients with tumors ≤2 cm without lymph node metastases (LNM) at Dg (Table2).

   Table 1: Clinicopathological characteristics at diagnosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TCV-PTC</th>
<th>c-PTC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Median, range)</td>
<td>46 (19-77)</td>
<td>42 (6-86)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>83%</td>
<td>76%</td>
<td>0.10</td>
</tr>
<tr>
<td>Tumoral size</td>
<td>43%</td>
<td>29%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>47%</td>
<td>23%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Extra-thyroidal invasion (ETE+)</td>
<td>46%</td>
<td>23%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Linvvascular invasion (LNF-Inv) (+)</td>
<td>5%</td>
<td>1.4%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Necrosis (+)</td>
<td>55%</td>
<td>70%</td>
<td>P&lt; 0.05</td>
</tr>
<tr>
<td>pT (AJCC 2017)</td>
<td>55%</td>
<td>28%</td>
<td>21%</td>
</tr>
<tr>
<td>pT1a</td>
<td>5%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>pT3a</td>
<td>8%</td>
<td>0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>pT4</td>
<td>4%</td>
<td>4%</td>
<td>0.7%</td>
</tr>
<tr>
<td>pN0/Nx</td>
<td>67%</td>
<td>66%</td>
<td>0.7</td>
</tr>
<tr>
<td>pN1a</td>
<td>24%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>pN1b</td>
<td>9%</td>
<td>12%</td>
<td></td>
</tr>
</tbody>
</table>

   Table 2: RT according to AJCC-2017

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>pT1a/pT1b-N0/Nx</th>
<th>Otros</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent RT</td>
<td>31/38 (82%)</td>
<td>14/30 (46%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Indeterminate RT</td>
<td>7/38 (18%)</td>
<td>9/30 (30%)</td>
<td></td>
</tr>
<tr>
<td>Structural incomplete RT</td>
<td>0</td>
<td>7/30 (23%)</td>
<td></td>
</tr>
</tbody>
</table>

   Conclusions
   At diagnosis, TCV-PTC has a higher probability of ETE, LNF-Inv, necrosis and larger tumor size. Despite that, RT seems to be good in patients with tumors ≤2 cm without LNM. Studies with longer follow-up and larger number of patients are needed to confirm these observations.

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P724

Congenital central hypothyroidism diagnosed in-utero
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Introduction
Congenital central hypothyroidism (CH), is characterized by low levels of thyroid hormones and TSH. It is not possible to diagnose this condition by neonatal screening programs based on TSH measurements, hence it is often missed. The assumption that CH is usually a mild condition has been refuted, and more than 50% of all newborns with CH have moderate to severe disease. Early diagnosis and treatment lead to better neurodevelopmental outcomes. Isolated CH is a rare condition with an estimated prevalence of 1-13/1000. More than 90% of cases are due to pathogenic mutations in five known genes: thyroid releasing hormone receptor (TRHR), thyroid stimulating hormone beta subunit (TSHB), immunoglobulin superfamilly member 1 (IGSF1), transducin (beta)-like X-linked (TBLIX) and in insulin receptor substrate 4 (IRS4) genes. Mutations in both IGSF1 and TBLIX can lead to X-linked isolated CH. IGSF1 mutations are also associated with low PRL, variable GH deficiency, metabolic syndrome, and postpubertal macroorchidism.

Case description
A 40-year-old pregnant woman with a past medical history of hemihyphoidecetm due to goiter, was diagnosed with CH at the age of 20 years. Prolactin levels were low, adrenal function was preserved and pituitary imaging was normal. She reported having had lactation problems after her first pregnancy. The family history was unremarkable and there is no known consanguinity. Genetic evaluation: A prenatal CMA (chromosomal microarray) revealed a normal
male karyotype 46XY with a 250kb deletion on chromosome X; arr (hg19) Xq26.1- Xq26.2 (130.181.100-130.431.733)*. This deletion encompasses two omni genes: ARHGAP56, IGF1 and was later confirmed to be inherited from the patient. Central congenital hypothyroidism was diagnosed clinically in the newborn boy, and treatment with thyroid hormone replacement was initiated, there was no need for steroid replacement therapy.

Discussion

X-linked IGF1 deficiency syndrome is the main etiology for Congenital CH. As far as we know, this is the first described case of a molecular diagnosis made in utero. Such early diagnosis enables focused surveillance of the fetus, regarding thyroid size, bone age and heart rate. Hydropsis was described in 20% of neonates with CH. Prenatal diagnosis enables early treatment with thyroid hormones and steroids if needed, and reduces the risk of neurodevelopmental problems.

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P725

TIRADS system: what does clinical practice tell us?

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Introduction

Thyroid nodules have a high prevalence in the adult population (20-76%). In 2018, the American College of Radiology proposed an ultrasonographic classification score of thyroid nodules - Thyroid Imaging Reporting and Data System-TIRADS, with 88% of sensitivity and 94% of specificity to predict malignancy. Since then, several studies report sensitivity values of 70.9-97% and specificity of 30-98%. We pretend to compare TIRADS score with cytologic results based on Bethesda classification.

Methods

This is a retrospective study of patients with thyroid nodules submitted to fine-needle aspiration (FNA) in an endocrinology department, during 16 months. Cytologic results (Bethesda classification) and TIRADS score (TR) were evaluated. TR score was calculated at the time ultrasound-guided FNA was performed. All Bethesda I (non-diagnostic) results were excluded.

Results

A total of 143 FNA of thyroid nodules were analysed, from 123 patients (57.7% female) with a mean age of 64 ± 14.3 years old. The nodules’ mean dimension was 24.6 ± 9 mm. 61.5% of nodules were classified as TR 4, 27% TR3, 7% TR5, 2.1% TR1 and 1.4% TR2. 90.2% of FNA were Bethesda II (benign) and 9.8% were Bethesda III. 24.6% of nodules were Bethesda II and 20% were Bethesda III. Compared TIRADS score with cytologic results based on Bethesda classification.

Discussion

The study was a retrospective cohort study of patients treated with first series of prednisone (5-15 mg BD) and TSH 5.9 mIU/l (0.35-4.2). Cases with uncontrolled hyperthyroidism were treated with antithyroidal medications (3 patients). TSH was 0.04 mIU/l (0.27-4.2) and FT4 12.6 pmol/l (9.0-20.0), Free T3 3.9 pmol/l (2.6-4.9) and 90.2% were Bethesda II (benign) and 9.8% were Bethesda III. 24.6% of nodules were Bethesda II and 20% were Bethesda III. This is a study of patients with thyroid nodules submitted to fine-needle aspiration (FNA) in an endocrinology department, during 16 months. Cytologic results (Bethesda classification) and TIRADS score (TR) were evaluated. TR score was calculated at the time ultrasound-guided FNA was performed. All Bethesda I (non-diagnostic) results were excluded.

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P727

Alemtuzumab induced thyroid disease: a Danish cohort study

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Objectives

Alemtuzumab, a monoclonal antibody against CD52, is used in the treatment of multiple sclerosis. A side effect to the treatment is development of autoimmune thyroid disease. The aim was to evaluate the rate, type and course of thyroid disease in Danish patients with multiple sclerosis (MS) previously treated with Alemtuzumab.

Methods

The study was a retrospective cohort study of patients treated with first series of alemtuzumab for multiple sclerosis (MS) in the Capital and Zealand regions (population: 2.6 million) in Denmark between 2014 and 2018 (n = 60). The following data was collected from patient records: known previous thyroid disease, date of first series of alemtuzumab, onset date of thyroid dysfunction, blood sample result of thyroid hormones and thyroid antibodies and thyroid scintigraphy and ultrasound to determine type of thyroid disease, type of treatment, duration and course of thyroid dysfunction.

Results

The follow-up period was median 58.5 months (31-83, range). Thyroid disease occurred in 24 of the 60 patients (40%), with a median onset at 24 months after the first alemtuzumab treatment (1-63, range). Graves’ disease (GD) occurred in 18 of 60 patients (30%) and three of these also had silent or postpartum thyroiditis with undetectable thyroid receptor antibodies (TRAB) before onset or after remission of GD. Isolated silent or subacute thyroiditis occurred in two of 60 patients (3%), unclassified hyperthyroidism (due to lack of information) in two of 60 patients (3%) and toxic multinodular goitre also in two of 60 patients (3%). An unusual or unpredictable course of GD was observed in 12 patients, with a rapid change in serum hormone concentrations unrelated to changes in

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P728

Graves’ eye disease associated with SARS-CoV2 infection

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Introduction

SARS-CoV2 infection or vaccination against SARS-CoV2 has been linked to the onset or recurrence of Autoimmune and subacute thyroiditis resulting in thyroid dysfunction.

Case

We describe a case of Thyroid eye disease temporally associated with SARS-CoV2 infection in a 48 year old female with a one-year history of subclinical hypothyroidism without interval thyroid hormone replacement or SARS-CoV2 vaccination. Two months following PCR confirmed SARS-CoV2 infection, the patient presented with eye irritation and oedema. Direct ophthalmological assessment led to a diagnosis of thyroid eye disease. CT orbit confirmed bilateral proptosis with increased intracranial fat. TSH was 0.01 mU/l (0.27-4.2) and FT4 18 pmol/l (12-20). Carbimazole 10 mg BD was commenced as she complained of palpitations, heat intolerance and tremor. TFFs three months later indicated T3-thyrotosnosis (TSH <0.01 mU/l (0.35-4.94), FT4 14.3 pmol/l (9.0-20.0), Free T3 6.3 pmol/l (2.6-4.9) with elevated TSH Receptor Antibody 3.5 UI (0.0-4.0) in keeping with a diagnosis of Grave’s Disease. The patient was referred to Endocrinology for clinical assessment. At that assessment, nine months following eye symptom onset, the patient was clinically and biochemically euthyroid on Carbimazole 5 mg BD (TSH 3.24 mU/l (0.35-4.94), FT4 11.8 pmol/l (9.0-20.0), Free T3 3.9 pmol/l (2.6-4.9), Anti TPO 108.1 IU/ml (5-60). She was an ex-smoker of 2 years with no family history of autoimmune. Of note the patient reported L-thyroxine replacement until 4 years prior to presentation. Review of available TFFs one year prior, off L-thyroxine, showed TSH 8.7 mU/l (0.27-4.2), T4 13.4 pmol/l (12-22), thyroid antibodies unavailable. Mild non-tender goitre was evident on exam with palpbral oedema and conjunctival injection without exophthalmos or lid retraction. Carbimazole was stopped. Although still troubled by eye irritation the patient remains clinically and biochemically euthyroid on review 12 months following onset of eye symptoms (TSH 2.85 mU/l (0.35-4.94), FT4 12.8 pmol/l (9.0-20.0), Free T3 4.5 pmol/l (2.6-4.9) with reducing titres of TSH Receptor Antibody 1.2 IU/l (0.0-4.0).

Conclusion

There have been numerous published cases of new or recurrent Graves’ disease and Subacute thyroiditis following SARS-CoV2 infection. In our case, the rapid response to antithyroidal medications and predominant ophthalmic symptoms perhaps point to a dual diagnosis of acute thyroiditis and Graves’ Eye Disease.

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medication, e.g. sudden changes from hyperthyroidism to hypothyroidism, being the most common. Some of these patients were treated with antithyroid hormone or thyrroxine titration regimen, while others were switched to block and replace treatment. Full remission of GD, defined as undetectable TRAB, was at the time of data collection only seen in four patients.

Conclusion
Data from this Danish population was in accordance with recent published studies and supports previous observations of both unusual, long-lasting and unpredictable courses of GD in a subgroup of patients. Hypothetically, some of these may benefit from block and replace treatment, to stabilize an otherwise clinically inappropriate fluctuating GD.

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P728
A rare etiology for thyrotoxicosis — case report
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Introduction
Hyperthyroidism and thyrotoxicosis can have multiple etiologies, varying from the most frequent described in clinical practice (Graves disease, toxic nodular goiter, thyroiditis) to very rare causes such as anaplastic thyroid cancer, thyroid lymphoma, amyloidosis or even secondary malignancy of the thyroid gland. Case report
A 53-year-old man presented to our department for progressive goiter enlargement in the last two months which was accompanied by dysphagia and dysphonia. The patient had a history of smoking for almost 40 years and also mentioned that in the last two weeks he lost in weight approximately 3 kg. The clinical exam was in normal limits, with the exception of multiple laterocervical adenopathies and the enlarged, firm thyroid gland which was painful and presented local inflammatory signs. The paraclinical investigations showed an acute inflammatory syndrome (ESR 42 mm/h, CRP 85.2 mg/l, Fibrinogen 606 mg/dl) with thyrotoxicosis (TSH - 0.01 mIU/ml, free T4 4.13 ng/dl and total T3 - 278 ng/dl) and negative autoimmunity. The thyroid ultrasound showed a pseudomultifocal heterogeneous aspect with decreased blood flow and multiple non-inflammatory laterocervical adenopathies, largest one being almost 2 cm. In addition, thyroid scintigraphy showed no hyperfunctioning areas while the computed tomography of the neck and thorax discovered a right apical pulmonary nodule of 35/36/46 mm. During his hospital stay he received anti-inflammatory treatment with dexamethasone and ibuprofen. His largest right laterocervical adenopathy was surgically removed and sent to the anatomical pathology department who described a ganglionar metastasis of pulmonary carcinoma with clear large cells.

Conclusions
This was a rare case of thyrotoxicosis which required a professional multidisciplinary team in order to offer an appropriate diagnosis and treatment. Secondary malignancy of the thyroid gland is quite rare, and especially in the form of thyrotoxicosis which probably was caused by a destructive invasion of thyroid tissue with malignant cells, similar to a “thyroiditis.”

Key words: thyrotoxicosis, secondary malignancy, pulmonary carcinoma

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P729
Hyperthyroidism and ischemic stroke in a young adult
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1Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; 2Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia

Introductions
Moyamoya disease is a rare angiopathy characterized by a progressive stenosis of the intracranial internal carotid arteries (ICA). First described in 1957, its pathophysiologic mechanisms are still not well understood. Its association with various systemic diseases is termed moyamoya syndrome.

Observation
A 21-year-old female patient, with a family history of hyperthyroidism, was admitted initially with stroke. The clinical examination revealed hemiparesis of the right hemisphere and dysarthria, in addition to a moderate goiter and tachycardia. Cerebral CT scan with contrast showed bilateral stenosis of the intracranial ICA with 78% in the left and 30% in the right ICA, confirming the diagnosis of moyamoya angiopathy. Biological analysis on admission and prior to the imaging procedure revealed suppressed TSH level and 10-fold increase in serum PT4. The diagnosis of Graves’ disease was made upon the presence of anti-TSH receptor antibodies; 5 IU/l (< 2 IU/l) and high thyroid technetium-99 m pertechnetate uptake. Thyroid peroxidase antibodies were also positive and 32-fold elevated (1600 IU/ml). The patient received 30 mg of ulinazine in addition to rehabilitative management with improvement of its poststroke hemiparesis.

Discussion
Moyamoya syndrome represents one-third of moyamoya angiopathy and is associated with well-recognized conditions like neurofibromatosis type 1, Down syndrome, sickle cell disease but also autoimmune diseases. Autoimmune thyroiditis are increasingly reported in the literature in patients with moyamoya angiopathy suggesting a possible role of the immune process in the pathogenesis of this disease.

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P730
Effect of levothyroxine replacement therapy on testosterone, LH, FSH levels in men with overt hypothyroidism
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Introduction
The prevalence of hypothyroidism overtly ranges from 5% to 11%. Though Hypothyroidism is less common in males as compared to females but deficiency of thyroid hormone affects almost all metabolic organs of the body, which includes changes in growth hormone, steroid metabolism, sexual function, antioxidative function.

Aim
The aim of our study was to assess the levels of total testosterone LH, FSH levels in males with overt hypothyroidism pre and post levothyroxine therapy. In our study we included 51 patients with overt hypothyroidism, with mean age 40.2 years (32-56 years). 50% of patients had low testosterone level at baseline, low testosterone level associated with hypothyroidism has not been well documented in several studies with varying prevalences. In our study only 5 patients had low LH level at baseline while FSH level of all the patients was normal at baseline, semen analysis could not be done due to non-consent of patients. In our study after attainment of euthyroidism or after 4 months of replacement of levothyroxine therapy 70% of hypogonadic patients had their testosterone level normal, more than 80% of patients with low ADAMS score showed improvement in their parameters.

Conclusion
Thyroid hormone deficiency affects all tissues of the body, including multiple endocrine changes that alter growth hormone, corticotrpin, glucocorticoids, and gonadal function. Primary hypothyroidism is associated with hypogonadotropic hypogonadism, which is reversible with thyroid hormone replacement therapy. The same has been seen in our study also that after levothyroxine replacement there was significant improvement in free testosterone level, significant improvement in ADAMS score, although predominance of hypogonadotropic hypogonadism was not that significant but still some degree of relevance was observed. So according to the results we concluded that overt hypothyroidism can induce hypogonadism or low testosterone levels in men that is reversible with thyroid replacement therapy. Importantly, some of the clinical manifestations of primary hypothyroidism in men may be due in part to a reduction in free testosterone. Further evaluation of this potential clinical interaction would require a controlled trial of androgen replacement in the hypothyroid state. However, hypogonadotropic hypogonadism with thyroid replacement is reversible with full restoration of normal thyroid function.

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P731

Epidemiological, clinic-pathological, evolutionary profile of differentiated thyroid carcinoma in adolescents and young adults: About 161 cases

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Introduction
Adolescent and young adult differentiated thyroid cancers are frequently under diagnosed forms. They would be characterized by their aggressiveness and the presence of particular histological forms. The aim of the study was to describe the characteristics of thyroid carcinoma in adolescents and young adults by analyzing the clinical, histological, therapeutic and evolutionary characteristics.

Materials and methods
We conducted a retrospective study in Endocrinology and Diabetology department of Ibn Rochd University Hospital of Casablanca between 1986-January 2022, including 161 cases of thyroid cancer in young adults under 30 years among all thyroid differentiated cancers (927 patients). This group of patients was compared to a second one aged between 30 and 45 years (386 patients). The statistical analysis was performed by the software SPSS version 25.0

Results
Mean age at diagnosis was 22.7 years (10-29), with a clear female predominance (91.3%). Familial thyroid neoplasia was found in 1.8% of patients. Predominant mode of discovery was multinodular goiter suspected in 62.1% of cases and lymph node metastases in 9.3% of cases. All patients underwent total thyroidectomy associated with lymph node dissection in 21.1% of cases. Papillary carcinoma was the predominant histological type in 95% of cases. Recurrences were found in 6.1% of cases: locoregional recurrence (4.3%) and pulmonary metastases (1.8%). The analytical study had shown that the following prognostic factors including multifocality, capsular invasion and bilaterality were significantly higher in the group of young patients compared to the older one (P < 0.001), and that the occurrence of metastases were earlier.

Conclusion
Differentiated cancers of the young subject are becoming more and more frequent and invasive. The precocity and frequency of local and distant metastases reflect particularly aggressive forms as reported in the literature.

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Increased incidence of primary hyperparathyroidism in patients with papillary thyroid cancer. Just a coincidence or a new syndrome. I have problems defining the rationale of the study Why PHP and thyroidectomy were performed at the same time

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Presence of primary hyperparathyroidism (PHPT) in patients with thyroid disease has been previously reported. However, co-existence of PHPT and papillary thyroid cancer (PTC) has been reported very rarely, mainly in the form of isolated case reports. Since the pathophysiological mechanisms of the two diseases are theoretically quite different, no causal relation between these diseases has been inferred. The aim of this study was to investigate the presence of PHPT in individuals who underwent thyroidectomy for suspected thyroid cancer or large nodular goiter.

Patients and Methods
A retrospective observational study involving 3230 patients (24% men, mean age 49.8 years, and 76% women, mean age 47.7 years) who underwent total thyroidectomy in the Department of Endocrine Surgery, Euroclinic Hospital, Athens, Greece, over a period of 13 years (2005-2018). The patient groups were categorized according to histopathological criteria of the parathyroid and thyroid glands.

Results
1945 patients (64%) had large benign nodular goiter, while 978 (32%) had papillary thyroid carcinoma. Among patients with benign nodules and those with papillary carcinoma respectively 16 (11 women/5 men) and 38 (33 women/5 men) had PHPT. The relative risk for coexistence of PHPT and PTC was 2.0 (95% CI 1.7 to 2.4, P = 0.0001). The age groups between 30 and 60 years were associated with the highest relative incidence (82% of PHPT, while there was sexual dimorphism, with a ratio of 4.4:1 in women vs. men.

Conclusions
Our study found that coexistence of PHPT and PTC is relatively common. As primary hyperparathyroidism is a chronic disease that is associated with many complications and requires early diagnosis and treatment, this co-morbidity should be considered in all patients requiring thyroidectomy for cancer. Further investigation of the possibly shared pathogenetic mechanisms between primary hyperparathyroidism and papillary thyroid carcinoma is warranted.

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P734
Short and long-term efficacy of image-guided laser and radiofrequency ablation therapies: a prospective monocentric and single-operator study

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Methods
For this prospective monocentric, single-operator study 41 consecutive patients who underwent either ultrasound-guided laser (USG-L) (25 cases) or radiofrequency (USG-RF) (16 cases) ablation were enrolled. All patients had large, predominantly solid nodules with previous benign. THY2 cytological diagnosis. Subsequently, they underwent follow-up assessment with B-mode, color-Doppler and contrast-enhanced sonography at 1-2 months (first follow-up) and 1-, 2- and 3 years after ablation, with evaluation of the volume reduction ratio (VRR). Results

The median volume (MV) of the nodules undergone USG-L was 15.7 ml (range 0.75–91.58 ml). At the first follow-up the MV was 10.08 ml, with a median VRR of 44.06% (P < 0.05: 34.17-53.94%), while at the 3-year follow-up the MV was 4.08 ml and the median VRR 88.09% (P < 0.05: 80.83-95.36%), with positive correlation between patients’ age and 3-year VRR (r = 0.43, P = 0.031). In the cohort treated with USG-RF, the MV of nodules was 28.65 ml (range 9.81-109.89 ml) before ablation, and 13.89 ml at the first follow-up, with median VRR of 46.80% (P < 0.05: 38.44-55.17%). At 3-year follow-up the MV was 5.17 ml, and the median VRR 80.84% (P < 0.05: 73.60-88.08%). The difference in number of cases and pre-ablation size between the two groups do not allow to perform statistically significant comparisons. No immediate or late complications occurred, apart from a moderate local discomfort immediately at the end of the procedure, lasting 24-48 h, in almost all patients. No nodular regrowth was detected and no replacement therapy had to be administered to any patient during the 3-year follow-up.

Conclusion
In accordance with the literature, our study confirms that both USG-L and USG-RF can safely achieve significant and long-lasting size reduction of large benign thyroid nodules. Further studies are needed to evaluate specific features, such as nodular volume and shape, can affect the procedure outcomes and to compare the effectiveness of the two modalities of treatment.

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P736
Thyroid hormones and platelet activation in COVID-19 patients

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Background
The relationships between thyroid hormones (TH) and platelets (PLT) have not been fully established. Physiological concentrations of L-thyroxine (T4) activate human PLT resulting in ATP release and aggregation. On the other hand, subclinical hypothyroidism has been frequently associated with hypercoagulability, in particular mean platelet volume (MPV), a marker of platelet activation, has been found higher in patients with subclinical hypothyroidism. A possible prothrombotic action of TSH has also been hypothesized. COVID-19 is a pleiotropic virus known to exert its effects in many endocrine glands, including the thyroid. In fact, both direct and indirect mechanisms of Sars-CoV2 infection can render the thyroid dysfunctional. In COVID-19 patients hyperactivated platelets, with an increased MPV, and a low T3 syndrome have been described.

Aim
The aim of this study is to evaluate the relationships among TSH, FT3, FT4 and FT3/FT4 ratio and the MPV in 104 patients affected by COVID-19 on admission to the emergency room.

Methods
104 patients (46 males, 58 females) with real-time polymerase chain reaction testing-confirmed COVID-19 admitted to the Policlinico Umberto I hospital of Rome were included in the analysis. Patients without a history of thyroid disease who had a thyroid function test at admission, before starting any treatment, were enrolled.

Results
The mean age of the patients was 75.2 ± 11.6 years. The mean MPV was 9.03 ± 1.36 fl. The mean levels of TSH, FT3 and FT4 were, respectively 1.69 ± 1.14 μU/ml, 2.48 ± 0.64 pg/ml, 1.43 ± 0.53 mg/ml. FT3 showed a trend of negative correlation with MPV (r = -1.195P = 0.351), not statistically significant. FT4 was positively correlated with MPV (r = 0.291, P = 0.019). Both TSH and FT3/FT4 ratio had a statistically significant inverse correlation with MPV (respectively, r = -0.384, P < 0.001 for TSH, r = 0.2437, P = 0.05 for FT3/FT4). All the linear regression were adjusted for age, sex and BMI.

Discussion
In this cohort of COVID-19 patients the relationship between TSH and MPV showed an opposite behavior with respect to that reported in non-sick subjects, suggesting that different mechanisms of interaction of TH with PLT may exist in the setting of acute COVID-19 infection that may be protective against platelet activation.

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Correlation between painful subacute thyroiditis and COVID-19
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Background
Subacute thyroiditis is an inflammatory condition of the thyroid with characteristic presentations and clinical course. Patients with the classic, painful (DeQuervain’s; Granulomatous) thyroiditis, (PFSAT) typically present with painful swelling of the thyroid. At times, the pain begins and may be confined to the one lobe, but usually spreads rapidly to involve the rest of the gland. Pain may radiate to the jaw or the ears. Malaise, fatigue, myalgia and arthralgia are common. A mild to moderate fever is expected, and at times a high fever of 104°F (40.0°C) may occur. It is suggested that the etiology of the disease is mainly viral, in addition, subacute thyroiditis often develops after infection of the upper respiratory tract, influenza, measles. COVID 19 is a potentially severe, primarily respiratory illness caused by a coronavirus and characterized by fever, coughing, and shortness of breath. In some people, the disease also damages major organs. Aim
This study attempts to review the correlation of PFSAT and COVID 19

Method
Within months after the onset of the Covid pandemic, the number of patients referring to the National Center for Diabetes Research and diagnosed with of PFSAT has increased dramatically. Anamnesis showed that the vast majority had suffered "flu-like" symptoms. Observations were made on 120 patients (8 females/males, mean age 22–52 years) who had a history of Covid-19 within past 2-3 months.

Discussion
The following studies were performed: test for Covid 19 antibodies and thyroid function tests (TSH and elevation of total T4 and T3 levels consistent with the thyrotoxic state). T3 (ng/dl) to T4 (mg/dl) ratio was less than 20. ESR (≤ 80), CRP and thyroglobulin were all elevated; TPO-ab, Tg-ab and TSHR-ab were negative; RAIU/Scan-thyroid gland was "low or not" visible; ultrasound echogeneity was hypoechogenic and vascularization was decreased. Classical treatment of subacute thyroiditis was started initially with non-steroidal anti-inflammatory agents, but the majority of patients (91%) required treatment with prednisone (20-40 mg daily). Beta blocking agents were prescribed in the majority of patients (76%). Most patients recovered in 6-8 weeks.

Conclusions
Data of our small research have shown that Covid 19 can cause sub acute thyroiditis, though its course does not differ from the classical sub acute thyroiditis. Data of new large-scale studies are needed. We plan to continue our observations and increase the number of patients involved.

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Predictors of associated autoimmune diseases in patients with Hashimoto’s thyroiditis.
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Background
Increased rates of autoimmune diseases (ADs) have been reported in association with Hashimoto’s thyroiditis (HT); however, the risk factors for coexisting ADs in HT patients have been poorly investigated.

Objective
To evaluate the prevalence and factors associated with AD comorbidities in patients with HT.

Materials and Methods
We recruited 687 patients (626 F and 61 M, mean age at diagnosis 39 ± 14.0 yr, F: M = 10.2: 1) diagnosed with HT in 2019-2021. Clinical, biochemical and demographic data of subjects with and without concomitant ADs were statistically compared.

Results
Among the 687 patients with TH, comorbid ADs were found in 322 (47% n = 292 F, mean age 39.5 ± 14.8 yr), of whom 86 (12.5%) suffered from more than one associated ADs. Rheumatic diseases exhibited the highest frequency (n = 226, 33%, including in order of frequency fibromyalgia, rheumatoid arthritis, Siogren syndrome, to mention a few.), followed by cutaneous (n = 71, 10%, including vitiligo, psoriasis, alopecia, …) and gastroenteric (n = 62, 9% coeliac disease, atrophic gastritis, IBD, …) disorders. HT patients with and without comorbidities did not differ in gender and age at diagnosis (P > 0.005). However, stratifying patients by age, the prevalence of comorbidities increased with increasing age. The two groups did not differ regarding exposure to the main environmental factors (including cigarette smoking), residence in urban areas with high industrial density compared to small towns/countryside, eating habits, iodine nutrition and vitamin D). However, a family history of either thyroid or non-thyroid autoimmune diseases was significantly more frequent (P < 0.0001) in patients with associated comorbidities than in those without. Logistic regression analyses revealed that female sex (odds ratio [OR] = 2.45, 95% confidence interval [CI] = 1.14-4.82, P = 0.011), age (OR = 1.61, 95% CI = 1.18-4.27, P = 0.04) and family history of ADs (OR = 5.18, IC 95% = 2.55-12.105, P = 0.001) were predictors of associated ADs.

Conclusions
Female HT patients with increasing age and a family history of ADs have increased rates of AD comorbidities. These data suggest a preponderant role of genetic background, of which familiarity can be considered a surrogate marker, in determining the risk of developing autoimmune comorbidities in HT patients.

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The impact of insulin resistance on thyroid function in pregnancy
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Background
The influence of hyperinsulinemia and insulin resistance on thyroid function is debatable. Insulin, as an anabolic hormone, may also play a role in thyroid hypothyrosis and nodular goitre development. Some recent reports focus on the possible interplay between thyroid function and glucose status in pregnancy, including gestational diabetes mellitus.

Aim
The study aimed to assess the relationship between insulin resistance indices and thyroid function in pregnancy.

Material and methods
The study included 1069 pregnant women (median age 29 years, IQR 6 years). Serum TSH, FT4, FT3, and aTPO were measured in each patient. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index was assessed based on fasting glucose and insulin concentrations. In each pregnant woman, a thyroid ultrasound was also performed.

Results
The study participants were stratified into three groups based on HOMA-IR. Group 1 included 324 women with HOMA-IR <1; group 2 – 570 women with HOMA-IR between 1 and < 2.5, and group 3 – 175 women with HOMA-IR ≥ 2.5. Group 1 and 2 differed significantly in TSH (1.66 mIU/L vs. 1.84 mIU/L, P = 0.0205), and FT3 concentrations (5.12 mIU/L vs. 4.76 mIU/L, P = 0.002). There was no difference was found in FT4 concentrations (12.91 pmol/l vs. 12.65 pmol/l, P = 0.1153). Group 1 and 3 differed significantly in TSH (1.66 mIU/L vs. 1.96 mIU/L, P = 0.0023), FT4 (12.91 pmol/l vs. 11.47 pmol/l, P = 0.0000), and FT3 concentrations (5.12 pmol/l vs. 4.66 pmol/l, P = 0.0000). The significant difference between group 2 and 3 was only found for FT4 concentrations (P = 0.0000) (P values for difference in TSH and FT3 concentrations were 0.1958 and 0.2593 respectively). The groups did not differ in aTPO concentrations. aTPO-positivity was not related to HOMA-IR values (mean HOMA-IR in aTPO-positive and aTPO-negative women was 1.63 and 1.80 respectively, P = 0.32).

Fasting insulin > 10 mIU/ml was found in 27.53% of pregnant women (286 out of 1039) with thyroid volume < 25 mL, in contrast to 36.67% women (11 out of 30) with thyroid volume < 25 mL.

Conclusions
Our results indicate that insulin resistance may impact thyroid function in pregnancy independently of thyroid autoimmunity, with higher TSH and lower thyroid free hormone concentrations in pregnant women with higher HOMA-IR indices.

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P740 Sub acute thyroiditis following COVID-19 vaccination – case report and International survey

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Case report
A 52-year-old woman developed painful anterior neck swelling seven days after receiving the first COVID-19 vaccine AstraZeneca (AZ). Investigations showed TSH 0.14 mIU/l, CRP 34 mg/l and TRAB 0.3 IU/l. A neck Doppler ultrasound scan on day 15 showed features of thyroiditis, and one occurred after Moderna mRNA vaccine. Nine cases developed after the first dose of vaccine and eight after a second dose, with symptom onset a mean of 14.5 days after vaccination, ranging from self-limiting to a more severe illness requiring glucocorticoid therapy.

Survey results
In light of this case report, we conducted an email survey via the Society for Endocrinology UK, about subacute thyroiditis arising within 28 days of administration of a COVID-19 vaccine. Seventeen cases were reported to us: seven were from the UK, 14 were from physicians, and three were from patients. Eleven cases followed Pfizer/BioNTech mRNA vaccine, five followed AZ ChAdOx1 S recombinant vaccine, and one occurred after Moderna mRNA vaccine. Nine cases developed after the first dose of vaccine and eight after a second dose, with symptom onset a mean of 14.5 days after vaccination, ranging from self-limiting to a more severe illness requiring glucocorticoid therapy.

Discussion
There was a temporal association between COVID-19 vaccination and the onset of subacute thyroiditis. It appears likely that COVID-19 vaccines can trigger subacute thyroiditis due to an autoimmune/inflammatory (ASIA) syndrome. Case reports and small case series of subacute thyroiditis following COVID-19 vaccination have recently been described. Endocrinologists should be aware of potential vaccine sequelae when managing thyrotoxic patients, including the heightened risk that thyrotoxicosis following COVID-19 vaccination will result from a potentially self-limiting subacute thyroiditis. It has also been reported that Graves’ disease can develop shortly following COVID-19 vaccination. With over 7 billion COVID-19 vaccine doses administered to date, and a background subacute thyroiditis incidence of 4.9 per 100,000, there remains a caveat that the cases reported here may have arisen by chance.

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P742 Curcumin attenuates the pro-inflammatory response induced by hyaluronan oligosaccharides in human thyroid fibroblasts and thyrocytes

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Background
Lymphocytic infiltration and inflammation in autoimmune thyroid diseases (AITDs) results in accumulation of HA, contributing to the pathogenesis of both thyroidal and extra-thyroidal (ophthalmopathy, pretibial dermopathy and mixedema) manifestations of AITDs. HA fragments, originating from native HA during tissue inflammation and injury, in turn promote the expression of different mediators of oxidative stress and inflammation, by interacting with the Toll-like receptor 2 (TLR-2) and 4 (TLR-4) and CD44, via nuclear factor kappa-B (NF-kB). Curcumin (diferuloylmethane) is a phytochemical with anti-inflammatory properties. It has been reported to have suppressive effect on NF-kB signaling pathway in various cell types. This study was aimed at investigating the effects of curcumin treatment in cultured primary human thyrocytes and fibroblasts after exposure to 6-mer HA oligosaccharides (6-mer HA).

Methods
 Cultured cells were treated with increasing concentrations of curcumin (5 and 10 μg/ml), with and without 6-mer HA (50 μg/ml). mRNA and proteins expression for TLR-2, TLR-4, inducible nitric oxide synthases (iNOS), interleukin-1β (IL-1β), IL-6, matrix metalloproteinase 9 (MMP-9), and thyroid-specific genes [thyroglobulin (Tg) and sodium iodide symporter (NIS)] were evaluated by real-time PCR and Western Blot, respectively. Protein quantification was assessed by densitometry analysis. NF-kB (p65) activation was determined in nuclear extracts by DNA binding activity assay. The pro-inflammatory cytokines IL-1β and IL-6 levels were measured by ELISA. Levels of NO were measured in culture medium by a fluorometric assay.

Results
In both cell lines 6-mer HA treatment induced the increase in mRNA and protein of TLR-2, TLR-4, CD44, as well as the activation of NF-kB, that in turn increased iNOS, IL-1β, IL-6 and MMP-9 expression and NO levels. The addition of curcumin at increasing concentrations (5 and 10 μg/ml) decreased NF-kB activation and significantly reduced, iNOS, IL-1β, IL-6, MMP-9, and NO levels in a dose-dependent manner (P<0.01 and P<0.001) respectively. Furthermore, in thyrocytes curcumin significantly restored the mRNA expression of Tg and NIS, decreased after exposure to 6-mer HA. Curcumin only slightly reduced CD44 expression (P<0.05) and did not change TLRs levels, suggesting that its anti-inflammatory effect mainly depends on the inhibitory effect on NF-kB activation.

Conclusions
Curcumin attenuates the pro-inflammatory effects of HA oligosaccharides in both thyrocytes and fibroblasts. Since HA fragments might contribute to inflammation in both thyroidal and extra-thyroidal (i.e. dermal and orbital) tissues in the course of AITDs, curcumin could be beneficial in these disorders as a suitable adjunct to conventional pharmaceutical therapy.

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P743
Concomitant Graves' disease with COVID-19 infection
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Background
Subacute thyroiditis, autoimmune thyroiditis and an atypical form of thyroiditis due to primary injury of the thyroid gland by SARS-CoV2 itself are complications of COVID-19. Antigen-converting enzyme 2 is also expressed in the thyroid gland. On the other hand, both untreated thyrotoxicosis and COVID-19 affects heart, generating cardiac complications.

Case report
A 36-year-old woman resident in an iodine sufficient area, heavy smoker, presented for palpitations, resting dyspnea, pedal edema, 40 kg weight loss in the past 2 months, tremor and asthenia. She denies cough, sore throat, rhinorrhea, smell or taste loss, myalgias or diarrhea. Physical examination reveals resting dyspnea, SaO2 95-96%, atrial fibrillation with arrhythmic HR = 200/min, severe heart failure with right pleural effusion and pedal edema, small goiter, tremor, lower fever, agitation. Biochemical assessment revealed autoimmune thyroiditis (TSH = 0.0007 mU/l, FT4 = 40.06 pmol/l, total T3 = 309.88 ng/dl, increased TRAB (160 U/l) and TPO Abs (209.7 U/ml), anemia, leukopenia (5680/mm3) with lymphopenia. ESR, fibrinogen, C-reactive protein, procalcitonin were normal. Liver enzymes are elevated, hyperbilirubinemia was present (total bilirubin = 2.6 mg/dl, direct bilirubin = 1.9 mg/dl), alkaline phosphatase (180 U/l) and GGT were also increased. From cardiac point of view, D-Dimers were increased (403.925 ng/ml), CK MB was slightly increased (32 UI/l), troponin was increased (43 IU/ml). CK MB was low-normal (8.43 pmol/l), NTproBNP significantly decreased (10.1530/endoabs.81.P743)

Concomitant Graves disease and COVID-19 infection may be a cause of atrial rhythm, FT4 was low-normal (8.43 pmol/l), NTproBNP significantly decreased despite having initially an increased score for thyroid storm (85), this patient with triple complication was transferred to our clinic.

Follow-up
Despite having initially an increased score for thyroid storm (85), this patient with concomitant Graves disease and COVID-19 infection had a significant improvement within 4 weeks: weight gain, atrial fibrillation converted to sinus rhythm, FT4 was low-normal (8.43 pmol/l), NTproBNP significantly decreased (1007 pg/ml). No pleural effusion was described on her chest X-Ray; Her RT-PCR test was still positive for SARS-CoV-2 and IgG Abs were increased (434U/ml).

Conclusion
Concomitant Graves disease and COVID-19 infection may be a cause of atrial fibrillation and severe heart failure during SARS CoV-2 pandemic.

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P744
Echocardiogram findings in patients with hyperthyroidism
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Introduction
Thyroid hormones have an impact on the function and structure of the cardiac muscle. Aim
Investigate the prevalence and risk factors of structural and functional cardiac complications in patients with hyperthyroidism.

Methods
We conducted a cross-sectional study on 30 patients with uncontrolled hyperthyroidism. Clinical, biological and therapeutic data were collected. A trans-thoracic echocardiography (TTE) and lung ultrasound has been performed to all patients.

Results
Eight patients presented with left heart failure (HF) signs/symptoms, two presented with right HF signs/symptoms. TTE was abnormal in 12 patients (40%) (Table; all of whom presented pulmonary hypertension (PH). Echocardiographic signs of HF were present in eight patients: seven patients met the definition of HF with preserved ejection fraction and one had HF with reduced ejection fraction. Clinical signs/symptoms of HF, lower TSH levels, elevated LVFP and a higher E/Ed were associated to PH. P = 0.013, P = 0.004, P = 0.003, P = 0.002. HF and PH were associated to the presence of tachycardia in the 24-h Rhythm Holter monitoring.P = 0.039, P = 0.011, they were also associated to a higher number of premature atrial contraction.P = 0.007, P = 0.007.

Conclusion
Hyperthyroidism can modify the cardiovascular hemodynamic leading to congestive heart failure and pulmonary hypertension.

Table 1 Echocardiographic parameters in patients with hyperthyroidism

<table>
<thead>
<tr>
<th>Echocardiographic parameter</th>
<th>Pulmonary hypertension, n (%)</th>
<th>Elevated filling pressure, n (%)</th>
<th>Dilated left atria, n (%)</th>
<th>Dilated right atria, n (%)</th>
<th>Pulmonary B-lines, n (%)</th>
<th>Mitral insufficiency, n (%)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>n( % )</td>
<td>12 (40)</td>
<td>8 (27)</td>
<td>7 (23)</td>
<td>4 (13)</td>
<td>3 (10)</td>
<td>5 (17)</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

LV end-diastolic diameter mm, m ± SD (mm)

LV end-diastolic diameter mm, m ± SD (mm)

LV left ventricle, m mean, SD standard deviation

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P745
Myxedema coma of both primary and secondary origin, with non-classic presentation and elevated creatine kinase
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Introduction
Myxedema coma is the end stage of untreated or inadequately treated hypothyroidism. It has an estimated incidence of 0.22 per million per year. The clinical picture is often that of an elderly obese female, presenting in midwinter with increased lethargy, somnolence and confusion. The presentation is one of severe hypothyroidism, with or without coma. Such cases are predominantly based on a primary thyroid disorder such as Hashimoto's thyroiditis. However, the underlying cause in approximately 5% of myxedema cases is hypothalamic or pituitary disease, where the patient usually lacks multiple anterior pituitary hormones, including thyroid-stimulating hormones (TSH). Case study
A 69 years old male presents to the ER with dizziness, headache, postural instability, bradylalia and bradypsychia symptoms that appeared 1 week prior. A stroke diagnosis was suspected and a cerebral CT scan was made showing a 22/2138 mm pituitary adenoma with suprasellar extension. Laboratory tests showed high creatine kinase (4459 U/l) and LDH (591 U/l) and low natrium (122 mmol/l). He was then transferred to our clinic.

General examination revealed bradylalia, bradypsychia, dry, coarse skin, hoarse voice, thin scalp and eyebrow hair with little to no body hair. Laboratory tests showed low FT4 (<0.3 ng/dl), TT3 (<40 ng/dl) low values for IGF1 (43.92 ng/ml), FSH (0.683 mU/ml), LH (<0.1 mU/ml), morning cortisol (1.06 mcg/dl), ACTH

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Lenvatinib-induced hypocalcaemia due to transient hypoparathyroidism: a case-report
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Radioiodine refractory differentiated thyroid cancer can be effectively treated with multi-tyrosine-kinase inhibitors (mTKI). Due to their pleiotropic mechanism of action, these drugs may cause different side effects. Hypocalcaemia has been reported in up to 35% of patients treated with mTKI, but little is known about its pathophysiology and clinical relevance. We report the case of a 78 years old woman treated for a multifocal papillary thyroid cancer, infiltrating perithyroidal tissues, striated muscles, oesophagus, blood and lymphatic vessels. Due to the tumour extension and infiltration to contiguous structures, the extent of surgery was limited to hemithyroidectomy and radioactive-iodine treatment could not be performed. The patient was therefore started on lenvatinib 10 mg per day. During the first months of treatment, the patient experienced grade III anorexia, fatigue, diarrhoea, nausea and hypertension, according to CTC AE, with no significant alteration at blood exams. Serum thyroglobulin (Tg) decreased from 6825 µg/l to a minimum of 49.6 µg/l, with negative anti-Tg antibodies. After four months of therapy, the patient accessed the E.R. for sudden dyspnoea, muscular cramps and spasms in the upper and lower limbs. Blood exams revealed a grade III hypocalcaemia (corrected serum calcium: 6.6 mg/dl), due to primary hypoparathyroidism (serum PTH: 12.6 pg/ml; serum phosphorus: 4.7 mg/dl). The patient was treated with intravenous calcium infusions and oral vitamin D supplementation. After discharge, the oral dose of carbonate calcium was of 6 g per day. Lenvatinib was restarted three days after discharge, when serum calcium levels were effectively stabilized by oral supplementation (corrected serum calcium: 8.8 mg/dl). Calcium intake was titrated according to blood exams performed every 3-5 days. Two weeks after discharge, while taking calcium 3 g per day, the patient complained worsening of anorexia and stupor. Grade II hypercalcemia (serum calcium: 11.7 mg/dl) was demonstrated. She was treated with an intravenous infusion of 7 physiological solution and calcium supplementation was interrupted. During the following follow up, the patient remained and still is eucalcemic without calcium supplementation. Though hypocalcaemia has already been described as potential side effect, this is the first report of a lenvatinib-induced primary hypoparathyroidism. This case is of particular interest since the patient was submitted to parathyroid localization imaging. Our study showed 11% that required further investigations with incidental diagnosis of thyroid cancer.

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Oncocytic carcinoma of the thyroid: epidemiological, clinical and anatomopathological characteristics
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Introduction
Oncocytic thyroid carcinoma is rare. It is an aggressive tumor, with high nodal and distant metastatic potential. Purpose of the study: to describe the epidemiological, clinical and anatomopathological particularities of oncocytic carcinomas of the thyroid.

Method
Descriptive retrospective study, including patients followed in thyroid carcinoma consultation at the Endocrinology Department of the CHU Ibn Rochd in Casablanca from 1986 to 2021. Results: we collected 12 cases of oncocytic carcinomas of the thyroid. The average age of the patients was 53.4 years with a female predominance (11women/1 man). The circumstance of discovery was a multiheteronodular goiter in 67% of the cases, a thyroid nodule in 25% and a toxic multinodular goiter in 8% of the cases. In our series, the majority of patients (67%) had nodules on ultrasound classified EU-TIRADS4. Treatment consisted of total thyroidectomy in 100% of patients, associated with cervical lymph node dissection in 17% of patients. The average size on the anatomopathological examination of these carcinomas was 4.4 cm; the multinodular character was objectified in 25% of the cases with an extrathyroid microscopic extension in 41.6% of the cases. All our patients subsequently benefited from radioactive iodine therapy.

Conclusion
Oncocytic carcinomas of the thyroid constitute a particular anatomo-clinical entity. The diagnosis is based on a range of clinical (size of the nodule, age over
50 years) and histological (capsular rupture, multifocality, angioinvasion) arguments. The surgery must be wide in front of the resistance to radioactive iodine therapy.

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**P749**
Sonographic and cytological characteristics of non invasive thyroid follicular neoplasm with papillary nuclear features vs papillary carcinomas

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli

**Introduction**
NIFTP (non invasive follicular neoplasm of the thyroid with papillary-like nuclear features, formerly noninvasive encapsulated follicular variant of papillary thyroid carcinoma) has been removed from the carcinoma category due to its indolent nature and its good prognosis. The purpose of our study was to identify preoperative ultrasound and cytological differences between NIFTP and papillary thyroid carcinoma (PTC).

**Materials and methods**
A retrospective study including patients followed in the endocrinology department of the CHU Ibn Rochd in Casablanca, from 2017 to 2021, with histological diagnosis of PTC or NIFTP.

**Results**
A total of 113 cases, including 27 NIFTPs, 86 papillary carcinomas, were observed. The 14 NIFTPs involved 24 women and 3 men, with an average age of 51.9 years, 2 patients had a history of familial thyroid carcinoma. The majority of patients (n=24) were euthyroid, 3 were hyperthyroid. Preoperative cytological data were available for 11 cases. Compared to papillary carcinomas, nodules corresponding to NIFTPs are more isochromatic (59.3% vs. 81.1%; P ≤ 0.001), have regular contours (85.2% vs. 52.3%; P ≤ 0.01) and have a TIRADS score 3 (48.1% vs. 81.1%; P ≤ 0.01), TIRADS 4 (40.7% vs 43%) or TIRADS 5 (7.4% vs 48.8%). Cytologically, NIFTPs are preferentially distributed in categories III (18% vs. 3.8%), IV (9% vs. 11.5%) and V (36.3% vs. 38.4%) of the Bethesda classification with significant difference compared to papillary carcinoma (P ≤ 0.9).

**Conclusion**
NIFTPs appear mostly non-suspicious on preoperative ultrasound and of indeterminate significance on cytology. These differences compared to papillary carcinomas can make it possible to suspect the diagnosis preoperatively and to better adapt the surgical management.

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**P750**
BRAFV600E, NRAS, TERT promoter mutations and correlations with clinicopathological features and distant metastasis in Turkish patients with papillary thyroid carcinoma

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**Background**
Various molecular mechanisms play a role in the pathogenesis of papillary thyroid cancer (PTC). Understanding the underlying pathogenesis and genetic changes is needed to improve clinical outcomes in PTC. In this study, it was aimed to determine the frequency of BRAF V600E, TERT promoter and NRAS mutations in Turkish patients with papillary thyroid cancer, the relationship of mutations between clinicopathological features and distant metastasis and the prognostic and predictive value of mutations.

**Methods**
In the study, mutations were detected by PCR and direct sequencing method from the paraffin-embedded tumor tissues of 42 PTC patients over 18 years of age who were followed up in Hacettepe University Hospital and archived in the Department of Pathology between 2004-2021, with 16 distant metastasis and 26 without distant metastasis patients and their relationship with clinicopathological features was determined. Pearson’s, chi-square and Mann-Whitney U tests were used for statistical analysis. A value of P < 0.005 was considered statistically significant.

**Results**
The overall frequency of BRAF V600E mutation was 64.3% (27/42), BRAF positivity was found in 22.2% (6/27) of patients with distant metastasis and 77.8% (21/25) in those without (P = 0.006). There was no statistically significant difference between BRAF V600E mutation and age at diagnosis, gender, tumor size, histological variant, extrathyroidal invasion, multifocality, lymphovascular invasion, capsule invasion, lymph node metastasis, recurrences and distant metastasis. The survival rate was found to be lower in BRAR TERT promoter mutation and age at diagnosis, gender, tumor size, histological variant, extrathyroidal invasion, multifocality, lymphovascular invasion, capsule invasion, lymph node metastasis, recurrences and distant metastasis. There was no statistically significant difference for clinicopathological features and distant metastasis in cases with BRAF V600E and TERT promoter mutations and in cases with both.

**Conclusions**
In contrast with the observations in other populations, BRAF V600E was found to be higher in Turkish PTC cases without distant metastasis compared to ones with distant metastasis. The combination of BRAF V600E and TERT promoter mutations in PTC is not prognostic or predictive for distant metastasis.

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**P751**
Postoperative thyroglobulin (Tg) as a predictor of long-term recurrence in differentiated thyroid carcinoma (DTC)

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**Introduction**
To determine the risk of recurrence in DTC, different clinical factors have been used (presence of adenopathies, extrathyroid extension, histology...). The objective was to examine whether the value of early postoperative Tg concentration may also predict long-term recurrence of DTC.

**Material and Methods**
The study included 249 consecutive patients (78.3% women, mean age 50.72 ± 14.26 years) with DTC who were initially treated by total thyroidectomy ± lymphadenectomy between 2000 and 2016. Serum Tg level was measured 6–8 weeks after surgery using the Immulite 2000 Siemens method, with a sensitivity of 0.5 ng/ml. The patients have been followed-up for a minimum of 3 years (mean 7.27 ± 2.7 years) until recurrence was detected. At the end of follow-up, their clinical situation was analyzed according to dynamic risk stratification. Patients with positive anti-Tg antibodies were excluded.

**Results**
The results obtained are shown in Table 1.

<table>
<thead>
<tr>
<th>Tg</th>
<th>n=249</th>
<th>Disease recurrence</th>
<th>Excellent response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5 ng/ml</td>
<td>175</td>
<td>6 (3.4%)</td>
<td>152 (68.9%)</td>
</tr>
<tr>
<td>0.5-2 ng/ml</td>
<td>41</td>
<td>6 (14.6%)</td>
<td>25 (61%)</td>
</tr>
<tr>
<td>&gt;2 ng/ml</td>
<td>33</td>
<td>17 (51.5%)</td>
<td>12 (36.4%)</td>
</tr>
</tbody>
</table>

*Excellent response was defined as Tg <0.2 ng/ml and no structural disease in neck sonogram. The mean time to recurrence was 35.9 months in patients with Tg <2 ng/ml and 26.4 months in those with Tg ≥2 ng/ml (P= ns).*

**Conclusions**
Postoperative Tg helps to predict the risk of DTC recurrence, so it should be used routinely in the postoperative evaluation of these patients. 2. In our series, Tg >2 ng/ml predicts a high risk of long-term recurrence, so therapeutic measures and surveillance should be intensified.

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P752
Thyroid Cystic Papillary Carcinomas - What’s visible is not always seen
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The vast majority of thyroid cancers are solid. Predominantly cystic tumors occur in <3% cases. Guidelines report as US characteristics consistently associated with a higher risk of malignancy eccentric position of the solid component, acute angle interface and microcalcifications and as less robustly associated lobulated margins and increased vascularity of the solid portion. We reviewed the US characteristics of predominantly cystic papillary carcinomas confirmed on histological analysis diagnosed at our institution in 2021. The patients had no identifiable clinical risk factor for malignancy. Ultrasound evaluation: Patient 1, 49 y.o. female; predominantly cystic 15 mm nodule with a 5 mm eccentric mixed isoechoic and hypoechogenic solid component with irregular margins and hyperhogenic foci, on the isthmus. Histology confirmed 12 mm PTC, pT1b(N)xMx. Patient 2, 30 y.o. male: predominantly cystic nodule with 61 mm on the right lobe, with an isoechoic solid component with irregular margins and an area of thick wall with hyperechoic foci. Histology confirmed the rare macrofolicular encapsulated variant of the PTC with 50 mm, pt3 NxMx. Patient 3, 42 y.o. male: A solid hypoechoic nodule with lobulated margins and hyperechoic foci with 29 mm on the isthmus and a predominantly cystic nodule with a solid lobulated hypoechogenic component with hyperechogenic foci that showed increased sign on color-doppler on left lobe. Histology confirmed as a 25 mm PTC, pT2(N)xN1R2. All patients had a single mixed supra-centimetric nodule. Margin irregularity or lobulation, microcalcifications and eccentric position of the solid component were present in all three. In all cases the nodules had more than one suspicious feature on US, but not all were described in the US report. US image review is crucial in thyroid nodule evaluation as it alerts the clinician and enables identification of at risk patients to be selected for timely and proper treatments.

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P753
Somatostatin analog therapy in advanced sporadic medullary thyroid carcinoma: a case report
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Introduction
Medullary thyroid carcinoma (MTC) is an aggressive neuroendocrine tumor derived from C cells that is responsible for approximately 5% of the gland malignancies, most of them occurring sporadically. Lymph node metastasis may occur early in disease pathogenesis and is one of the most important negative prognostic factor. Surgery is the only curative therapy while other chemotherapeutic options are limited. Neuroendocrine differentiated C cells may express somatostatin receptors (SSTR) and somatostatin analogs have been used with variable therapeutic success in cases of advanced MTC.

Case description
We present the case of a 56-year-old male patient who underwent total thyroidectomy for MTC. He was admitted in our clinic for an anterior neck mass. Thyroid ultrasonographic examination demonstrated a hypoechogenic 25/23/37.5 mm sized nodule invading the left thyroid lobe with microcalcifications. Laboratory work-up revealed an elevated calcitonin, greater than 2000 pg/ml (normal range <14.3), carcinoembryonic antigen (CEA) of 139.79 ng/ml (normal range: 0-2.5) and normal thyroid function. Our patient underwent a total thyroidectomy with total neck dissection. Histological and immunohistochemical studies diagnosed the presence of multifocal MTC (pT2 mN1b) and papillary thyroid microcarcinoma (pT1aN0). The lymph nodes specimen showed metastases from the first lesion (six lymph nodes). The Ki-67 index was <1% and at the investigation for multiple endocrine neoplasia (MEN), RET protooncogene mutation was negative. Since CEA and calcitonin levels were high during follow-up period, neck ultrasonography was performed, with no evidence of pathologic lymphadenopathy, Cervical CT scan revealed a paratracheal left mass. Immunohistochemistry showed positive expression of somatostatin receptors (SSTR) 2 and 5 and the therapy with Octreotide LAR 30 mg every 4 weeks was initiated. An octreotide scan was performed with no detection of metastatic lesions. Six months later, under therapy with octreotide, calcitonin, CEA, serotonin, neuron specific enolase were within the normal range. The therapy was well tolerated with no side-effects recorded.

Conclusions
MTC can be a rare source of carcinoid syndrome. Some studies have shown that long-term octreotide and octreotide-LAR treatment offer a subjective and biological partial remission in one third and in one fourth of the MTC patients, respectively, but it does not improve the natural course of the tumor.


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P754
Graves’ disease and neutropenia: Diagnostic trap
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Introduction
Hematologic abnormalities are frequently observed during hyperthyroidism and are related to complex multifactorial pathogenic mechanisms that are still poorly understood and may affect the three hematopoesic lineages in isolation or in combination. These abnormalities are exceptionally revealing and are usually subclinical. For the endocrinologist, they raise the problem of their aggravation under the hematotoxic effect of synthetic antithyroid drugs (AT1S). However, certain abnormalities such as leuko-neutropenia are sometimes simply the expression of a physiological phenomenon of margination of white blood cells which falsely underestimates the count of this lineage and which must be detected.

Observation
Patient aged 45 years, followed for hyperthyroidism on Graves’ disease initially put on CTC 60 mg with adjuvant treatment, presented a cardiac complication such as an AFib put on Sintrom and b-blockers, with a past history of angina put, diabetic since 5 years on insulin, at the clinical examination, patient in good general condition, FC: 89 bpm, homogeneous grade 2 goiter without palpable nodul with bilateral inactive exophthalmos, the biological test objectified a TSH: 0. 001 mU/ml, T4L: 48.4 pg/ml (6-12), T3L: 13.2 pg/ml (2.6-5.7), TRAK: 19. 8 IU/L, associated with haematological disturbances such as neutropenia controlled on several occasions: WBC: 5320/mm3, PNN: 850/mm3, before the start of the antithyroid treatment, a control of the blood count formula after 2 h of physical activity, objectified a re-ascension to normal PNN levels at 2780/mm3. This was in fact a physiological margination of the PNN on the blood vessel wall, which was unmasked by the effort, a situation aggravated by the hyperthyroidism but which did not contraindicate the introduction of synthetic antithyroid.

Conclusion
Faced with the coexistence of hyperthyroidism and leukocyte lineage disturbances, a simple stress test should be rapidly performed to unmask false neutropenia, thus avoiding unnecessary transfer to the hospital.

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P755
Graves’ disease and unilateral gynecomastia - An uncommon initial presentation of a common disease
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Most cases of gynecomastia are idiopathic. Among the most frequently identified etiologies are: persistent pubertal gynecomastia, hypogonadism, anabolic steroids and other pharmaceutical drugs use. In the literature, gynecomastia is a well-recognized manifestation of thyrotoxicosis in male patients (in the range of 10% to 40%). However, it is extremely rare in clinical practice as the initial presentation of thyrotoxicosis. The two main factors that contribute to gynecomastia in thyrotoxicosis are: increase of SHBG production in the liver

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(which leads to a reduction in free testosterone); and increased peripheral aromatization of androgens. We report a case of a 41-year-old white male who applied to our clinic with a 2 weeks history of right-sided breast enlargement. He did not report reduced libido. No past medical history or drug intake were reported. On examination he was normotensive and had normal-weight. Glandular tissue could be palpated on the right breast, underneath the nipple area. Galactorrhea was not observed. Cervical palpation was normal. The testicles had a normal size and no palpable abnormalities were found. Laboratory data showed testosterone level of 1116 ng/dl (241-827), free testosterone level of 24 pg/ml (8.69-54.69), estradiol level of 51 pg/ml (<32), SHBG of 107 nmol/l (10-57), LH 7.46 mUI/ml (1.5-9.3), FSH 7.68 mUI/ml (1.4-18), TSH <0.01 mUIU (0.35-5.5), free T4 (FT4) 2.16 ng/dl (0.8-1.76) and free T3 (FT3) 7.52 pg/ml (2.3-4.2). Anti-TSH receptor antibodies values were 2.47 U/l (<1). Levels of prolactin, alpha-fetoprotein, human chorionic gonadotropin, dehydroepiandrosterone sulfate were normal. An ultrasound examination revealed a thyroid gland diffusely heterogeneous, without nodularity. The diagnosis of Graves’ disease was made. He was treated with thiamazole 15 mg daily. After 1 month from the start of treatment, gynecomaestia had resolved. The monthly follow-up laboratory findings showed normalization of FT3 and FT4. SHBG and total testosterone levels decreased significantly after 2 months and free testosterone increased. GD may present with atypical symptoms and the classic symptoms of thyrotoxicosis may not always be in the foreground. In case of gynecomaestia, thyrotoxicosis should be kept in mind. An attentive diagnosis may identify a potentially treatable cause of gynecomaestia.

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P756

Radiofrequency and ethanol ablation for benign thyroid nodules: case series
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Introduction
Thyroid nodule is a frequent condition, being diagnosed in up to 70% of subjects who had undergone thyroid ultrasound. Around 90-95% of them became benign and, if the do not cause compressive symptoms or esthetical problems, they do not need specific therapy, only clinical follow up. Traditionally, thyroidectomy has been the main therapeutic option in these cases. Radiofrequency and ethanol ablations are recently introduced non-invasive therapies that permit avoid surgery and its related complications. Many studies have already evaluated the effectiveness of radiofrequency and ethanol ablation therapies in the reduction of benign thyroid nodule volume. The aim of this study has been to evaluate its efficacy in reducing the volume of benign thyroid nodules.

Material and Methods
This study is a series of 5 patients with a benign thyroid nodule, verified by FNA. All of them were woman between x and y years old, three radiofrequency ablation and two ethanol ablations. We have determinate the hormonal levels and the measures of the nodule before the ablation, 1 month, 2 months and 6 months after of the intervention. We also asked patients about their initial symptoms and the degree of satisfaction with this procedure.

Results
5 subjects (100% woman) were analysed with an average age of 53.2 ± 12 years old with diagnosis of benign thyroid nodule. Initially, measures average was 20.4 x 24.20 x 33 cm (APxTxS), thyroid function was normal in all the patients, and 80% of the cases noticed compressive symptoms. One month after the intervention, nodules size decreased to 14x19x27 cm on average and compressive symptomatology disappeared total or partially. Even six months later nodules continued decreasing to 11.2 x 11.7 x 20.6 cm. Along this time, thyroid hormones were at range. All the patients are so satisfied and would repeat it if were necessary.

Conclusions
As we have found (and many other studies), radiofrequency and ethanol ablations permit reduce nodules size and solve compressive symptoms caused by them. Both techniques have few complications and patients feel so satisfied. Considering all this points, they are demonstrating being excellent alternatives to hemithyroidectomy in the treatment of benign thyroid nodules.

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P757

Clinical presentation of patients with primary hypothyroidism in rural India
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Background
Hypothyroidism is a clinical state resulting from underproduction of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). Most cases are due to primary hypothyroidism, a failure of the thyroid gland to produce thyroid hormones. Primary hypothyroidism is defined as thyroid-stimulating hormone (TSH) concentrations above the reference range and free thyroxine concentrations below the reference range. Patients with hypothyroidism usually present with puffy eyes, cold intolerance, coarse hair, constipation, poor memory, slow thinking, muscle cramps, weak muscles, depression, dry skin, and hypersomnolence.

Aim
To study the clinical presentation of patients with primary hypothyroidism in rural India.

Materials and methods
This cross-sectional study was conducted in a hospital in rural India from March 2021 to December 2021. TSH, free T3 and free T4 levels were measured using venous blood in all patients with presented with signs-symptoms of hypothyroidism. Patients having biochemically confirmed primary hypothyroidism (elevated TSH, low free T3 and low free T4) were selected for the study. Proper history was taken from patients and their relatives to obtain the demographic and clinical data including hypothyroidism symptoms.

Results
87 patients with primary hypothyroidism were included in the study among whom 75% were female, 45% aged between 25 to 50 years, 90% lived in rural and suburban areas. Hypertension was the most common (45%) co-morbid condition followed by obesity (29%), diabetes (23%), obstructive sleep apnoea (19%) and ischemic heart disease (15%). 31% patients presented with TSH more than 100. Puffiness of face was most common (65%) symptom followed by dry skin (52%), cold intolerance (42%), constipation (29%), muscle cramps (23%) and hypersomnolence (19%).

Conclusions
Primary hypothyroidism is one of most common and easily treatable endocrine disorder. Despite being potentially manageable, primary hypothyroidism is often undiagnosed and untreated. Timely diagnosis of primary hypothyroidism is utmost important. The medical and family history can be very helpful in identifying patients in whom thyroid dysfunction should be assessed. Gender, age, family or personal history of thyroid diseases, recent pregnancy, presence of autoimmune diseases, medications and radiation history should all be noted. Hypothyroidism is far more common in women, and the prevalence of mild hypothyroidism increases in the elderly. Patient education regarding signs and symptoms of hypothyroidism, regular screening with TSH, free T3 and free T4 are very crucial to diagnose this easily manageable endocrine disorder.

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P758

Prevalence and factors associated with arrhythmia in patients with hyperthyroidism
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Introduction
Thyroid hormones represent a biomarker of heart rhythm disorders and pathophysiological origins remain unknown. Some of these disorders like atrial fibrillation (AF) are major issues particularly in asymptomatic patients with hyperthyroidism and cause of thromboembolic complications. Aim
Taking into account the uncertainty of prevalence of cardiac rhythm disorders, we aimed to investigate the prevalence of rhythm cardiac complications and its risk factors in patients with hyperthyroidism.

Methods
We conducted a cross-sectional study on 30 patients with uncontrolled hyperthyroidism. Clinical, biological and therapeutic data were collected. A 24-h Rhythmic Holter monitoring has been performed to all patients.

Results
The patients were seven male and 23 female, mean age was 44.8 ± 14.4 years. Twenty three patients (77%) had palpitation. The mean heart rate was 95 ± 14
(66 – 124) and 16 patients (53%) had tachycardia. Electrocardiogram showed ventricular premature complexes in one patient (3%). Atrial fibrillation was present in two patients (7%). The 24-h Rhythm Holter monitoring revealed tachycardia in 16 patients (53%), supra-ventricular premature contraction in 16 patients (53%). Thirteen patients (43%) had ventricular premature complexes. Atrial fibrillation was present in three patients (10%), it was permanent in one patient (3%) and paroxysmal in two (7%). The study of risk factors showed that age > 50 years, the presence of nodules (palpable and on ultrasound) and negativity of TSH receptor antibodies were associated to atrial fibrillation. \( P = 0.041, P = 0.020, P = 0.029, P = 0.008 \). Toxic nodular goiter was associated to atrial fibrillation. 

Conclusion

Hyperthyroidism increases heart rate and may cause arrhythmia, mainly atrial fibrillation. This complication is more frequent in older patients with toxic nodular goiter.

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P759

Autoimmune polyglandular syndrome Type 2 presenting with autoimmune thyroid disease, diabetes mellitus Type 1 and Addison’s disease

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A. Background/Significance

Autoimmune polyglandular syndrome Type II (APS-II) is a rare polyendocrinopathy with a prevalence of 1 in 2 in 100,000, instigated by immune-mediated destruction of several organs. Knowledge of APS-II is crucial, especially in the early detection of polyglandular disorder among patients with endocrine autoimmunity.

B. Case

This case is of a 40-year-old male who initially presented with Grave’s disease after showing signs and symptoms of hyperthyroidism, as supported by low thyrotropin (0.05 uIU/ml; nv: 0.35-4.94) and high free thyroxine levels (2.05 ng/dl, nv: 0.71-1.85).

Hyperthyroidism increases heart rate and may cause arrhythmia, mainly atrial fibrillation. This complication is more frequent in older patients with toxic nodular goiter.

Table 1

<table>
<thead>
<tr>
<th>Age (years old)</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Female</td>
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<td>Female</td>
<td>Male</td>
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<tr>
<td>Nationality</td>
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<td>Portugal</td>
<td>Portugal</td>
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<tr>
<td>GD diagnosis</td>
<td>2012</td>
<td>2016</td>
<td>2016</td>
<td>2018</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>(Clinical/Biochemical)</td>
<td></td>
<td>Activity Severity</td>
<td></td>
<td>Activity Severity</td>
</tr>
<tr>
<td>Initial TRAb (positive &gt; 1.5)</td>
<td>2.8 U/l</td>
<td>Moderate/Severe</td>
<td>40 U/l</td>
<td>Active</td>
</tr>
<tr>
<td>GO:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>GD Medical therapy</td>
<td>Treatment</td>
<td>Thiamazole (Evacuated to Portugal in 2017 without therapy)</td>
<td>Thiamazole (Evacuated to Portugal in 2016 under thiamazole)</td>
<td>Thiamazole</td>
</tr>
<tr>
<td>Maximum dose</td>
<td>20 mg/day</td>
<td>45 mg/day</td>
<td>60 mg/day</td>
<td>300 mg/day</td>
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<tr>
<td>Duration</td>
<td>2.5 years</td>
<td>3 years</td>
<td>1 year and 4 months</td>
<td>3.5 years</td>
</tr>
<tr>
<td>Total thyroidectomy (histology)</td>
<td>Yes (9 mm papillary microcarcinoma)</td>
<td>Yes (8 mm medullary carcinoma)*</td>
<td>Yes (Follicular hyperplasia)</td>
<td>Waiting</td>
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<td>OG Medical therapy</td>
<td>Treatment</td>
<td>Local treatment (artificial tears)</td>
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<td>Treatment (artificial tears)</td>
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<td>MPDN (4.5 g)</td>
<td>MPDN (8 g)</td>
<td>MPDN (8 g)</td>
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</table>

* negative for RET mutations, maintained cure criteria

Endocrine Abstracts (2022) Vol 81
P761
Role of corticosteroids in the treatment of refractory hypothyroidism: a case report
Yousra Settai, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI

Introduction
Refractory hypothyroidism is known as the persistence of clinical and biological signs of hypothyroidism after 6 weeks of treatment or therapeutic adjustment, despite a dose exceeding 1.9mg/Kg/d of Levothyroxine. Several etiologies may be incriminated.

Observation
A 36-year-old patient, followed for Gougerot-Sjögren syndrome, having benefited from a thyroidectomy in 2015 in a context of biological hyperthyroidism, on Levothyroxine (LT4) 200mg/d and Liothyronine Sodium (LT3) 25mg/d with persistence of refractory hypothyroidism. The clinical examination revealed a slightly slowed down patient, presenting a mucocutaneous infiltration, a hoarse voice, a bilateral galactorrhea evolving since 1 year, and a chronic constipation. All this in a context of generalized asthenia. At the workup, TSHus was 500 mUI/l, free T4 <0.4 ng/dl (0.7-1.5), hypertriglyceridemia at 12.9g/l put on fenofibrate 160 mg/d. Brain MRI showed a pituitary bulge with no other detectable abnormality. After elimination of poor compliance and possible drug interactions, the diagnosis of refractory hypothyroidism was retained. Parasitological examinations of the stools showed Giardiasis and the patient was put on metronidazole. The Helicobacter Pylori serology came back positive with a pangastritis aspect at the stools showed Giardiasis and the patient was put on metronidazole. The Helicobacter Pylori serology came back positive with a pangastritis aspect at the stools showed Giardiasis and the patient was put on metronidazole.

Conclusion
High-dose glucocorticoids may be considered in some cases of hypothyroidism, especially in patients requiring high doses of thyroid hormones when even the LT4 + LT3 combination is insufficient to achieve euthyroidism.

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P245
Recalculating renin and aldosterone to improve specificity in the diagnosis of primary aldosteronism
Luc Doyle1, Julie Okiro1, Aysha Sarwani1, Michael Troy2, Youssef Ansari3, Darragh O' Donoghue1, David Lappin3, John Mcevoy4, Paula O'Shea2,5, Darragh O'Neill1,2

Background
The diagnosis of hypocortisolism is challenging in hemodialysis (HD) patients due to shared clinical features between renal failure and cortisol deficiency. We hypothesize that in a significant percentage of HD patients we miss cortisol deficiency.

Methods
A prospective cohort of 56 end stage kidney disease patients on maintenance HD treatment (mean age 65.3 ± 13.1, females 80 %) was studied. Low dose (1 mg) adrenocorticotropic hormone (ACTH) test was performed on all patients and blood tests for cortisol, ACTH, insulin like growth factor 1 (IGF-1), triiodothyronine (T3), free thyroxine (FT4), renin and aldosterone, were investigated. Logistic Regression was used to estimate the relationships between renin, aldosterone, ACTH, cortisol variables and the probability of a diagnosis of PA. Predictive capacity of each model was measured using Area Under the Curve using “leave one out” cross validation to avoid overfitting.

Results
The AUC for the model using ACTH on its own was estimated to be 0.68. The model, excluding ARR, but including renin, aldosterone and their interaction on the log-scale: log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone), improved the AUC to 0.73. Using this log-structure, as opposed to including aldosterone and renin as linear effects in a logistic model, makes sense since the model involving alog(Aldosterone) alone is nested within the log-structure model, which would not be true under the linear model. Covariates including eGFR, serum potassium and the presence of an adrenal nodule were then individually tested for statistical significance, conditional on the choice of this log-scale interactive model. The model Log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone) + Adrenal_Nodule provided the highest performance with an AUC of 0.782. For the ARR and the log-model, at a sensitivity of 80%, specificity was 37.5% and 64% respectively, and for a sensitivity of 98%, specificity was 12.5% and 24% respectively.

Conclusion
This log model incorporating the adrenal nodule as a variable improved the AUC from 0.68 (model with ARR alone) to 0.782. This study highlights the importance of statistically re-visiting well-established calculations to better inform clinical practice. Ongoing validation of our findings is proceeding in other clinical samples.

DOI: 10.1530/endobs.81.P245

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Late Breaking
P246
Pituitary -adrenal axis insufficiency among hemodialysis patients
Anat Bel-Angel1, Daniel Fux1, Dana Zelnik Yovel1, Ronit Koren1, Ilan Beberavishi1, Carlos Benbassat1 & Shlomit Koren1,2

Background
The diagnosis of hypothyroidism is challenging in hemodialysis (HD) patients due to shared clinical features between renal failure and cortisol deficiency. We hypothesize that in a significant percentage of HD patients we miss cortisol deficiency.

Methods
A prospective cohort of 56 end stage kidney disease patients on maintenance HD treatment (mean age 65.3 ± 13.1, females 80 %) was studied. Low dose (1 mg) adrenocorticotropic hormone (ACTH) test was performed on all patients and blood tests for cortisol, ACTH, insulin like growth factor 1 (IGF-1), triiodothyronine (T3), free thyroxine (FT4), renin and aldosterone, were investigated. Logistic Regression was used to estimate the relationships between renin, aldosterone, ACTH, cortisol variables and the probability of a diagnosis of PA. Predictive capacity of each model was measured using Area Under the Curve using “leave one out” cross validation to avoid overfitting.

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The AUC for the model using ACTH on its own was estimated to be 0.68. The model, excluding ARR, but including renin, aldosterone and their interaction on the log-scale: log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone), improved the AUC to 0.73. Using this log-structure, as opposed to including aldosterone and renin as linear effects in a logistic model, makes sense since the model involving alog(Aldosterone) alone is nested within the log-structure model, which would not be true under the linear model. Covariates including eGFR, serum potassium and the presence of an adrenal nodule were then individually tested for statistical significance, conditional on the choice of this log-scale interactive model. The model Log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone) + Adrenal_Nodule provided the highest performance with an AUC of 0.782. For the ARR and the log-model, at a sensitivity of 80%, specificity was 37.5% and 64% respectively, and for a sensitivity of 98%, specificity was 12.5% and 24% respectively.

Conclusion
This log model incorporating the adrenal nodule as a variable improved the AUC from 0.68 (model with ARR alone) to 0.782. This study highlights the importance of statistically re-visiting well-established calculations to better inform clinical practice. Ongoing validation of our findings is proceeding in other clinical samples.

DOI: 10.1530/endobs.81.P245
1.15 (95% CI: 1.03 to 1.29). In addition, IGF-SDS (standard deviation score) higher than -0.04 significantly decreased odds for hypocortisolism (OR 0.14, 95% CI: 0.02 to 0.81) in multivariable logistic regression models.

Conclusions

We offer routine testing of hypophyseal-adrenal axis function to detect adrenal insufficiency in HD patients even in the absence of markers characteristic of hypocortisolism.

DOI: 10.1530/endoabs.81.P246

P247

Long-term mortality and excess mortality after hip fracture in the main urban area of Romania

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Background

Excess mortality after hip fracture remains a problem of public health concern. Until present, for Romania no data is available regarding long term mortality rate and excess mortality after hip fracture. We aimed to evaluate the mortality rate and standardized mortality rates of osteoporotic hip fracture in the capital city of Romania and suburban area.

Methods

we collected data from over 98 % of fractures admitted during 12 months (09/01/2017 - 08/31/2018) in Orthopedic Surgery Departments in the area of interest. Patients were selected using the hip fracture codes (S72.0, 1, 2, 3, 7, 8, 9), age > 40 years old and low-trauma mechanism (fall from a standing height or less). We used the 2018 estimations for stable population in the area selected. We calculated the mortality rate (MR) 3 years after the event and standardized mortality rates (SMR) of hip fracture.

Results

we included a total of 1977 patients with fragility hip fracture (86.5% in the capital city and 13.5 % in the suburban area). MR after 3 years was 46.42% in all patients with a mean age of 81 years old, 69% women. Almost a quarter of patients were not surgically treated. Advanced age, male sex, extracapsular fracture and especially conservative management were associated with increased mortality. SMR after 1st 2nd and 3rd year and cumulative for the whole 3-year period in all patients were 13.69, 5.45, 5.94 and 26.06 respectively. As expected, SMR decreased with advancing age, but remained higher even in patients >85 years old (2.79 for 1st year, 2.34 for 3-year period). Notable differences were observed in SMR between sexes, 29.18 for women and 19.6 for men, 3 years after the fracture.

Conclusion

this is the first study to describe the long-term mortality rate and excess mortality after osteoporotic hip fracture in Romania. Hip fracture has the highest impact on short-time mortality, the risk in the 2nd and 3rd year being significantly smaller compared to 1st year. Even after 3 years, excess mortality for hip fracture patients can be still observed.

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P248

The differences between normocalcemic and hypercalcemic primary hyperparathyroidism: a tertiary center’s experience

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General Hospital Korgialenio-Benakio, Hellenic Red Cross, Department of Endocrinology & Metabolism – Diabetes Center, Athens, Greece

Introduction

Normocalcemic Primary Hyperparathyroidism is today considered a variant of Primary Hyperparathyroidism. It is characterized by persistently normal calcium levels and increased levels of parathyroid hormone, after the exclusion of other causes of secondary hyperparathyroidism. We aimed to compare clinical, biochemical and imaging data from patients with normocalcemic and hypercalcemic primary hyperparathyroidism.

Methods

This is a retrospective study from the archives of our Department that included 161 patients (38 men and 123 women), who were monitored from 2010 to 2021, 68 with Normocalcemic Primary Hyperparathyroidism (NPHPT) and 93 with Hypercalcemic Primary Hyperparathyroidism (HPHT). The biochemical tests included calcium, total and adjusted for albumin, phosphorus, magnesium, parathyroid hormone and 25OHD3 levels and 24-h urine calcium concentration (P>0.05). Patients with HPHPT had significantly higher levels of corrected calcium (11.3±0.57 vs 9.8±0.44 mg/dl, P<0.001) and PTH (219.2±209.8 vs 111.8±35.5 g/ml, P<0.001) and lower phosphorus levels (2.7±0.54 vs 2.9±0.28 mg/dl, P<0.001) compared to patients with NPHPT. No differences were found in the prevalence of osteopenia/osteoporosis, fragility fractures and the need to receive anti-osteoporotic treatment (P>0.05). Patients with HPHPT had significantly higher prevalence of nephrolithiasis clinically (history of renal colic: 40.3% vs 25.8%, P<0.05) and discovered by imaging (renal ultrasound: 54.3% vs 34.7%, P<0.03). Patients with HPHPT more often met the criteria for surgical treatment (54.3% vs 34.7%, P<0.001).

Conclusions

Patients with NPHPT often have disease complications, especially osteoporosis, fragility fractures and nephrolithiasis both clinically and through imaging. Until more data on the pathophysiology and natural course of NPHPT is provided, patients with this form of primary hyperparathyroidism should be managed as patients with HPHPT.

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P249

Glycogen hepatopathy - a case series

Bhavna Sharma, Rohit Baslas, Amir Sharif & Elaine Hui
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Glycogen Hepatopathy (GH) was initially described in 1930 by Pierre Mauriac. 90 years later, GH remains underrecognized in adults. The clinical or radiological characterization of GH is difficult, further compounded by lack of widespread literature. We present two cases of GH characterized by recurrent lactacетemia and transient liver function and radiological abnormalities.

• 19 years old male with Type 1 diabetes admitted with nausea and vomiting. pH 6.9, glucose 33 mmol/l and lactate 7.7 mmol/l (normal 0.5-2 mmol/l). He was started on intravenous (IV) fixed rate insulin. Lactate initially improved however was noted to be rising 8 h into being started on insulin peaking at 9.2 mmol/l. On admission, bilirubin 10 umol/l (normal range 0-21 umol/l), ALP 80 IU/l (normal range 0-190 IU/l) ALT 162 IU/l (normal 0-50 IU/l) Albumin 44 gm/l(normal 35-50 gm/l). ALT worsened during admission peaking at 790 IU/l corresponding to lactate. Liver screen including hepatitis, HIV, EIB, CMV, alpha 1 antitrypsin, caeruloplasmin, anti-smooth muscle antibodies, anti-liver kidney microsomal antibodies and ANA were negative. Liver ultrasound revealed smooth gross hepatomegaly with increased liver reflectivity. Liver function started resolving at Day 5 and ALT came down to 442 IU/l on Day 8. Repeat liver function 2 months later was normal. MRI liver three months later revealed normal sized liver with no abnormal enhancement with a smooth surface and no fatty infiltration or cirrhosis.

• 21 years old female, first presentation of Type 1 diabetes with diabetic ketoacidosis (DKA). pH 7.2 on admission, glucose 20 mmol/l and lactate 7 mmol/l. Lactate initially improved with fluids however at 24 h peaked at 8.6 mmol/l. Liver ultrasound showed echogenic enlarged liver. Liver function on admission was normal (ALT 31 IU/l) but worsened after starting IV insulin to 578 IU/l and peaked to 752 IU/l at Day 4. Liver function normalized after 3 months. GH was first reported when short acting insulin was introduced. Supraphysiologic rapid acting insulin dosages during DKA management may be a potential cause to drive glycogen storage in rapid hypo- and hyperglycemia cycle. A dual peak of lactate may signify a change from Type 1 (impaired perfusion) to Type 2 lactatemia (impaired gluconeogenesis). Further work is needed to characterize patients at risk of GH in re-attendances and potential plans to give lower dose of rapid acting and higher dose of long-acting insulin in acute phase may be explored.

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P250

Metabolic parameters in type 2 diabetic patients with positive Candida cultures

Daniela Radiojkovic1, Saša Radenkovic1, Vojislav Ćirić1, Milan Radiojkovic1, Jana Pesic Stankovic2, Sanja Curkovic2 & Sonja Kostic1

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Polyglandular autoimmune syndrome in the elderly: a case report

Sindhuja Suresh, Felicity Kaplan & Alastair Cruickshank

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Introduction

Polyglandular autoimmune syndrome (PAS) is characterised by the coexistence of two or more autoimmune mediated disorders. While the pathophysiology remains poorly understood, environmental triggers and genetic susceptibility are thought to contribute to the dysregulated immune response. PAS has been classified into three main subgroups: Type 1 is seen in the paediatric population while types 2 and 3 are found in adults with autoimmune thyroid disease and insulin-requiring diabetes, are differentiated by the presence or absence of Addison’s disease, and most commonly present in the third decade. There are very few studies looking at the presentation of type 3 PAS in the elderly. Thyroid dysfunction commonly presents in the elderly, but newly diagnosed antibody positive type 1 diabetes is rare in this group. Coeliac disease is prevalent in nearly a quarter of patients with thyroid disease and 10% of those with type 1 diabetes but also rarely presents late in life. We present a rare case of a 76 year old female with features of type 3 PAS. She had a history of hypertension and dyslipidaemia but no personal or family history of autoimmune conditions. The patient was referred to the endocrinology department for further investigation of diabetes and mild hypercalcaemia in the context of weight loss and thirst. Given her age and mildly elevated HbA1c, she had been diagnosed with type 2 diabetes but on further investigation, it was found to be GAD and IA-2 antibody positive and started on treatment for type 1 diabetes. Further evaluation also identified TPO antibody positive hypothyroidism and anti-TTG positive coeliac disease. She had normal vitamin B12 levels showing no evidence of pernicious anaemia, no history of vitiligo and normal cortisol, antinuclear antibody and serum angiotensin converting enzyme levels. She is currently under investigation for probable hyperparathyroidism. This is a unique case of type 3 PAS presenting atypically in an elderly patient. Not only is the age of presentation unexpected, but the lack of pernicious anaemia and other autoimmune features typically seen in type 3 PAS make this very distinctive. It highlights the need for further epidemiological research into this presentation, particularly in the elderly, to allow for early detection of a possible autoimmune syndrome. With an ageing population, further understanding is needed on how to manage these complex autoimmune conditions in this vulnerable group.

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P252

Immuno therapy induced hypopituitarism including hypogonadism in patient with previous PCOS: call for early detection and endocrine work-up

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Northwick Park Hospital, United Kingdom

Background

Immune checkpoint inhibitors are now commonly used in melanoma, renal cell carcinoma and non-small cell lung cancers. Patients on immune check point inhibitors experience at least one type of immune related adverse event(irAEs) which can occur even after discontinuation of therapy. Endocrine toxicities are commonly reported irAEs and tend to be irreversible. The most frequently recognized endocrine complications include thyroid dysfunction (30%) hypophysitis (5.6-11%), type-1diabetes (0.2-2%) and adrenal insufficiency (0.7%) Literature is limited on potential impact on gonadal axis.

Case presentation

We report a 50-year-old Caucasian female with metastatic renal cell carcinoma, who was treated with a nephrectomy followed by immune checkpoint blockade with ipilimumab plus nivolumab. After 4 months of treatment she presented with fatigue, generalized pains and being emotional. She switched to single agent nivolumab, however her symptoms persisted. Investigations revealed hypocortisolism [cortisol 50 mmol/l [range 160-550 mmol/l], hypogonadism [testosterone <0.7 mmol/l [range 0.2-8 mmol/l], estradiol 280 pmol/l [range 45-1461 pmol/l], FSH10.9 IU/l [normal 25.8-134.8 IU/l] and hypothyroidism (TSH 0.15 mIU/l [0.27-4.2 mIU/l], T4 10.4 vs. 10.4, T3 1.89 vs 1.13 vs 1.80 vs 0.83) and HDL (1.63 ± 0.25 vs 1.08 ± 0.44) were verified in study group, compared to the control group, but without statistical significance. HbA1C values were significantly higher in study group patients (9.8 ± 1.74 vs 6.99 ± 1.89; P<0.05) as well as FPG (10.87 ± 1.35 vs 7.47 ± 1.03; P<0.01).

Conclusion

Type 2DM patients with positive Candida sp. have higher FPG, HbA1C and BMI. Uncontrolled glycoregulation is one of the host condition which favors candida colonization and subsequent infection. This may be related to the decrease in commensal bacteria-probably the result of yeast-bacterial competition. On the other hand, we have to keep in mind, that a significantly increased number of commensal bacteria—probably the result of yeast-bacterial competition. On the other hand, we have to keep in mind, that a significantly increased number of Commensal bacteria—probably the result of yeast-bacterial competition.

DOI: 10.1530/endoabs.81.P252

P253

Central diabetes insipidus from a patients’ perspective – from management to psychological co-morbidities and re-naming of the condition

Cihan Atiya, Ben Loughrey, Aofie Garrah, Bettina Winze1, Julie Keaford, Patricia Gildroy, Aparna Pal, Malak Hamza, Chris Thompson, Joseph Verbalis, Steven Hunter, Mark Sherlock

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Central diabetes insipidus from a patient's perspective – from management to psychological co-morbidities and re-naming of the condition
Methods
A web-based anonymous survey was developed by an international team of endocrinologists and patient representatives covering issues from management of their cDI. In total, 85% (n = 615) of participants had received cDI treatment for at least 5 years, with 81% (n = 506) suffering from chronic diabetes insipidus (CDI). Additionally, 90% (n = 551) of participants self-reported that they misheard the diagnosis and its aetiologies were idiopathic 30% (n = 184), diabetes mellitus 19% (n = 115), pituitary and hypothalamic dysfunction 19% (n = 114), and other causes 6% (n = 36) of participants. Participants were provided with the link to the online survey either via their physician during routine check-ups or the homepages of the UK Pituitary Foundation, Pituitary World News, Facebook group Got Diabetes Insipidus?, and Pituitary Society.

Results
Worldwide, 1034 participants with CDI, 47% (n = 488) with isolated posterior and 53% (n = 546) with combined anterior/posterior pituitary dysfunction, participated. Median [IQR] age was 42 (32, 53), 77% (n = 794) were female. Duration of CDI was 9.0 (3.0, 19.0) years and its aetiologies were idiopathic 30% (n = 315), pituitary tumours/cysts (pre-surgical 21% (n = 217), post-surgical 25% (n = 254)), inflammatory/autoimmune 6% (n = 61), infiltrative diseases 6% (n = 59), genetic/familial 4% (n = 44), head trauma 3% (n = 34), and other causes 5% (n = 50). Ninety-six percent (n = 994) were on desmopressin therapy - oral tablets 56% (n = 575), nasal spray 23% (n = 233), and sub-lingual tablets 12% (n = 126). Among these patients, 26% (n = 273) experienced hyponatremia (self-reported) at least once whilst on desmopressin. Patients who routinely omitted desmopressin (up to several times a week) to allow aquaresis had significantly lower risk of hyponatremia compared to those who did not follow this approach (OR 0.4, 95%CI 0.3-0.7, P < 0.01). Sixty-four percent (n = 660) reported low quality of life indicated with JQR 4-7) out of 10 points. Thirty-six percent (n = 369, equally prevalent in isolated posterior and combined pituitary dysfunction) experienced psychological problems after the diagnosis, of whom 70% (n = 258) reported higher anxiety levels, 71% (n = 263) sleep disturbances, and 65% (n = 239) depressed mood. Eighty percent (n = 823) indicated that this confusion affected the management of their CDI. In total, 85% (n = 884) would prefer a re-naming of the condition; amongst those, the most common suggestion was “vasopressin deficiency.”

Conclusion
This is the so far largest survey conducted in patients with CDI using a web-based method and patient involvement in the survey development. We show a high percentage of treatment-related hyponatremia, a high prevalence of psychological comorbidities and a clear need for re-naming of the condition from patients’ perspective.

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P255
Cushing syndrome in older women: age-related differences in disease origin and clinical manifestations

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Background
Adrenocorticotropic hormone (ACTH)-producing pituitary adenoma is the most common cause of endogenous Cushing syndrome (CS), but the relative proportion of adrenal causes of CS is rising. Limited data are available on the clinical manifestations and cause of CS in older women.

Objective
Determine the clinical presentation, biochemical profile, and cause of CS in women 65 years of age and older, compared with younger patients with CS.

Methods
Retrospective charts review of women with pituitary or adrenal CS, treated at Rathvon Medical Center between 2000 and 2017, or at Maccabi Healthcare Services in Israel between 2005 and 2017. Patients were classified into 3 groups, according to age at diagnosis: ≤ 45 (young), 46-64 (middle-age), or ≥ 65 (elderly) years.

Results
The cohort included 142 women (mean age, 46.0 ± 15.1 years), including 81 (57.0%) with ACTH-producing pituitary adenoma, and 61 patients (43.0%) with adrenal CS: 68 young, 55 middle-aged, and 19 elderly women. Pituitary source for CS was more common among young patients (48 patients, 70.6%), compared with middle-aged (27 patients, 49.1%) or elderly women (6 patients, 31.6%) (P < 0.05). Weight gain was evident in 57.4% of young women (60.0% pituitary, 56.3% adrenal), compared with 15.8% of elderly women (50% pituitary, 0% adrenal) (P = 0.011). Cushingoid features were more common among young vs. elderly patients, but the difference was not significant (40.0% vs. 22.1%, respectively; P = 0.15). Among patients with adrenal CS, diagnosis of hypercortisolism was established following an incidental finding of an adrenal mass in 3 of 20 (15.0%) young women vs. 7 of 13 (53.8%) elderly women (P < 0.001). Mean urinary free cortisol levels were highest for young women (5.03 ± 3.6xULN) followed by middle-aged (4.80 ± 6.0xULN) and elderly (3.5 ± 2.6xULN) women (P < 0.001), while no difference was recorded for serum cortisol levels following low-dose dexamethasone. Adrenal or pituitary tumor size was not different between groups. While in young patients with CS, urinary free cortisol levels were higher for those with adrenal vs. pituitary CS (6.61 ± 3.2xULN vs. 4.36 ± 3.6xULN), in middle aged (3.42 ± 3.4xULN vs. 6.24 ± 7.7xULN) and elderly (2.62 ± 1.9xULN vs. 5.33 ± 2.9xULN) patients, pituitary CS was associated with higher urinary free cortisol levels than adrenal CS.

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Conclusions
Older patients with CS have distinct disease cause and presentation, as pituitary source is less common than adrenal CS, the latter is associated with milder hypercortisoluria and is frequently diagnosed incidentally. Weight gain was prevalent in young women, and uncommon in older women.

DOI: 10.1530/endoabs.81.P255

**P256**

Hobnail variant of papillary thyroid carcinoma, a systematic review and meta-analysis

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Background
Although papillary thyroid carcinoma (PTC) is considered to have an excellent prognosis, some more aggressive variants have been identified that show reduced overall survival rates. Besides from the diffuse sclerosing, tall cell, columnar cell and solid variant, the hobnail variant was newly recognized as one of these aggressive forms, affecting recurrence, metastasis, and overall survival rates.

Methods
We performed a systematic review and meta-analysis of studies including cases or case series with patients with hobnail variant of PTC. Furthermore, we included our own case series consisting of six patients.

Results
Twice-fold mortality rate in the cohort consisting of 191 patients was 3.43 (95% CI 1.72-6.82) per 1000 person/months. No sex differences could be observed concerning mortality (P = 0.52) but older age and tumor size significantly affected mortality (P = 0.03 and P = 0.02, respectively). The percentage of hobnail variant did not affect mortality (P = 0.29), neither did the presence of BRAF mutations. Classical characteristics as the presence of extrathyroidal extension (P = 0.001), distant metastases (P < 0.001) and lymph node metastases (P < 0.001) all had a significant impact on mortality.

Conclusions
Hobnail variant correlates with worse overall survival and all PTC cases should be carefully assessed for this variant.

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**P257**

Retrospective assessment of malignant thyroid nodules in a group of children and adolescents according to BTA U classification and ACR TI-RADS ultrasound-based risk stratification system in combination with elastography

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The risk of malignancy in thyroid nodules correlates with the presence of ultrasound features. In adults, ultrasound risk-classification systems have been proposed to indicate the need for further invasive diagnosis. Furthermore, elastography has been shown to support differential diagnosis of thyroid nodules. The purpose of our study was to assess the application of the American Thyroid Association (ATA) and British Thyroid Association (BTA) ultrasound risk-classification systems as well as strain elastography in the management of thyroid nodules in children and adolescents.

Seventeen nodules with Bethesda III, IV, V and VI were selected from 165 focal lesions in children. All patients underwent ultrasonography and elastography followed by fine needle aspiration biopsy. Ultrasound the ATA and BTA stratification systems were assessed retrospectively. The strain ratio in the group of thyroid nodules diagnosed as malignant was significantly higher than in benign nodules (6.07 vs. 3.09, P = 0.036). According to the ATA guidelines, 100% of malignant nodules were classified as high suspicion and 73% of benign nodules were assessed as low suspicion.

Using the BTA U-score classification, 80% of malignant nodules were classified as cancerous (U5) and 20% as suspicious for malignancy (U4). Among benign nodules, 82% were classified as indeterminate or equivocal (U3) and 9% as benign (U2). Our results suggest that application of the ATA or BTA stratification system together with elastography may improve differential diagnosis and help make a clinical decision about the need for further invasive diagnosis of thyroid nodules in children.

DOI: 10.1530/endoabs.81.P257

**P258**

Discordant thyroid function tests following Ibrutinib therapy

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Background
Tyrosine kinase inhibitors (TKI) are a chemotherapeutic group which include drugs known to cause thyroid dysfunction such as axitinib, imatinib, pazopanib, sorafenib, and sunitinib. However, reports of TKI-Ibrutinib causing thyroid dysfunction are scarce. Although several hypotheses have been proposed to explain TKI-associated thyroid dysfunction there is no clear guidance on how to manage this situation.

Case
86-year-old lady was referred to the endocrinology clinic for evaluation of abnormal thyroid function tests. Her recent medical histories included stage IV mantle cell lymphoma, hypothyroidism, stage III chronic kidney disease, hypertension, and diverticular disease. She was diagnosed with hypothyroidism in 2003 and has been on Levothyroxine dose of 100 mg and 75 mg on alternate days for many years. She was diagnosed with stage IV mantle cell lymphoma and was commenced on Ibrutinib in June 2020. Her first recorded thyroid function test in 2012 showed hypothyroidism, following that remained relatively stable with the same dose of Levothyroxine. Following introduction of Ibrutinib in June 2020, there was a concurrent rise in thyroid-stimulating hormone (TSH) and free thyroxine (FT4) with mildly decreased free triiodothyronine (FT3). She was fully compliant with Levothyroxine and confirmed taking the tablet well apart from her meals and other tablets. Other relevant blood tests showed stable chronic kidney disease, normal liver function test. Assay interference results were unremarkable. Serial thyroid functions showed rise in TSH (9.4;11.4;8.34;4.39;5.91;11.1) with concurrent rise in FT4 (19.5;23;26;26.9;23;23.1) and low FT3 levels (2.4;2.2;2.5;2.6) following Ibrutinib. Thyroxine dose was increased to 100 mg daily as TSH had risen to 11.1 and she complained of excessive tiredness.

Discussion
Suggested mechanism for this pattern is the induction of type 3 deiodinase (D3) pathway which converts FT4 to rT3 and inhibition of type 2 deiodinase (D2) which converts FT4 to FT3, with the balance towards D2 inhibition. Thyroid-binding globulin was not elevated hence it could not account for the raised FT4. Induction of uridine diphosphate-glucuronosyltransferases is a plausible cause, which enhances clearance of T4 and T3 (as suggested for another TKI-Imatinib) resulting in hypothyroidism in patients receiving Levothyroxine replacement, however T4 levels were not reduced.

Conclusion
This case highlights the importance of thyroid function testing prior to starting Ibrutinib and the value of close monitoring of thyroid status throughout. Clinicians who prescribe Ibrutinib should be aware of this potential thyroid function dysfunction, and to seek endocrinology advice as appropriate.

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**P503**

Salivary free cortisol and serum DHEA-sulfate measurements with cosyntropin stimulation improve accuracy of secondary adrenal insufficiency diagnosis in pregnancy

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Background
Diagnosis of secondary adrenal insufficiency (SAI) during pregnancy is challenging due to physiological adaptations and progressive increase of cortisol level throughout the pregnancy (1). The 250-mg standard ACTH stimulation test

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Adrenal incidentaloma, single center clinical experience
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Background
Adrenal incidentalomas (AI) are lesions discovered incidentally on imaging without clinical symptoms or examination findings. AI can produce hormones in 5-30% of cases. Autonomic cortisol secretion (ACS) is the most common of these. Although ACS is asymptomatic, it increases the risk of metabolic disorders.

Methods
Patients aged <18 years with adrenal adenoma and upper abdominal MRI who were presented and examined in the endocrinology outpatient clinic, had their data retrospectively documented. Comorbidities, examinations and hormonal tests and results of these patients were evaluated. Those who failed dexamethasone suppression tests (cortisol >1.8 g/dl) and did not have Cushing’s syndrome were classified as ACS.

Results
Among the 223 patients, 138 (61.9%) were women with a median age of 56 (18-80). Of the patients, 26.9% had diabetes mellitus (DM), 54.3% had hypertension (HT), 17.9% had hyperlipidemia, 12.1% had coronary artery disease (CAD), 1.3% had heart failure (HF), 7.9% had osteoporosis or osteopenia, and so 4-gland exploration was undertaken with the removal of three glands, and so 4-gland exploration was undertaken with the removal of three glands, and so 4-gland exploration was undertaken with the removal of three glands.

Table 1 Comparison of patient characteristics with and without autonomous cortisol secretion

<table>
<thead>
<tr>
<th>Autonomic cortisol secretion</th>
<th>Yes</th>
<th>No</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, Woman/Man</td>
<td>2.18</td>
<td>1.54</td>
<td>0.45</td>
</tr>
<tr>
<td>Age (years), median (min-max)</td>
<td>59 (36-80)</td>
<td>55 (18-74)</td>
<td>0.071</td>
</tr>
<tr>
<td>Size of adenoma (mm)</td>
<td>25 (10-54)</td>
<td>18 (10-60)</td>
<td>0.001</td>
</tr>
<tr>
<td>T2DM</td>
<td>17 (48.6%)</td>
<td>43 (22.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>HT</td>
<td>25 (71.4%)</td>
<td>96 (51.1%)</td>
<td>0.028</td>
</tr>
<tr>
<td>HL</td>
<td>13 (37.1%)</td>
<td>27 (14.4%)</td>
<td>0.003</td>
</tr>
<tr>
<td>CAD</td>
<td>7 (20%)</td>
<td>20 (10.6%)</td>
<td>0.154</td>
</tr>
<tr>
<td>HF</td>
<td>1 (2.9%)</td>
<td>2 (1.1%)</td>
<td>0.402</td>
</tr>
<tr>
<td>Osteoporosis or osteopenia</td>
<td>6 (30%)</td>
<td>13 (56.5%)</td>
<td>0.125</td>
</tr>
</tbody>
</table>

Introduction
Primary hyperparathyroidism (PHPT) is an endocrine condition in which autonomous excessive secretion of parathyroid hormone (PTH) results in hypercalcaemia. In approximately 80% of cases the aetiology is due to a single parathyroid adenoma, the remainder are due to hyperplasia of more than one gland. Familial Hypocalciuric Hypercalcaemia (FHH) is an autosomal dominant, inactivating mutation of the calcium-sensing receptor, causing a right-shift in the concentration-response curve, and producing biochemical similar to PHPT. Although usually benign, it can cause pancreatitis. More than 75% of cases are due to the following genotypes, in descending order of incidence, CASR, AP2S1, GNAS.

References

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**P506**

Initial results and patient satisfaction with the new oral formulation of semaglutide

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Introduction

Oral semaglutide has been available in the Spanish market since November 2021. This new formulation has broken the self-injection barrier, and may enhance patient satisfaction.

Methods

Retrospective review of the patients’ records and personal or telephonic interviews. All patients expressed their consent for the anonymous processing of their data. Numeric data are given as mean ± s.d., paired t-test was used for comparison. Satisfaction was categorically expressed as very poor, poor, fair, good or very good.

Results

36 obese patients with type 2 diabetes who had taken at least one pill of oral semaglutide were included. Their age was 56 ± 12 years; 58% were female; diabetes duration was 6 ± 2 years. Of them 34 remain on treatment, 1 withdrew due to gastric intolerance and 1 due to difficulty to schedule the medication intake. 9 are still on the lowest dose (3 mg/day), 11 on the medium dose (7 mg/day) and 14 on the full dose (14 mg/day). 5 of which started on this dose because they were transferred from previous parenteral GLP-1RA therapy. 24 patients have a 14 on the full dose (14 mg/day), 5 of which started on this dose because they were transferred from previous parenteral GLP-1RA therapy. 24 patients have a high prevalence of obesity and other co-morbidities, a varied treatment history, and improved glycemic control following therapy initiation. The relatively high number of patients allocated 3 mg as their maximum dose shows that, in patients who tolerate oral semaglutide well, dose escalation to 7 and 14 mg, as indicated, may result in even more significant glycemic control improvements. These findings emphasize the critical nature of bridging existing treatment and knowledge gaps in order to maximize the potential of oral GLP-1 RA therapy. Further examination of real-world data will give more information on the translation, uptake, and impact of such breakthroughs in standard treatment.

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**P508**

In Individuals with obesity, resting energy expenditure does not decrease after weight loss with GLP-1 agonist liraglutide

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Background

Obesity (BMI <30 kg/m²) is a chronic and progressive disease, that is associated with many co-morbidities such as cardiovascular and psychiatric diseases, cancer, and arthritis. Lifestyle interventions are the cornerstone of obesity treatment, but when ineffective, anti-obesity pharmacotherapy could be added. In recent years, several anti-obesity agents have been approved, such as the glucagon-like peptide-1 (GLP-1) analogue liraglutide. Liraglutide induces weight loss, presumably by suppressing appetite and improving satiety. It is however unclear whether liraglutide also induces weight loss by alterations of the resting energy expenditure (REE).

Methods

In this observational longitudinal study, we evaluated individuals with obesity who were treated with liraglutide 3.0 mg at the Obesity Center CGG, Erasmus MC, Rotterdam, The Netherlands. We included 24 individuals (18 women), of whom four had a confirmed genetic obesity, thirteen had clinical features suggestive of genetic obesity, and seven had common obesity. At baseline and after 16 weeks of treatment, which included dose escalation over a period of 4 weeks, we measured anthropometric parameters, body composition using bio-electrical impedance (Inbody S10, BioSpace, Seoul, Korea), and REE using indirect calorimetry (Quark P, Cosmed, Roma, Italy). Predicted REE was calculated using the Harris-Benedict formula.

Results

At baseline, mean weight and BMI were 124.1 kg (± 24.1) and 42.7 kg/m² (± 7.5), respectively. Their weight decreased significantly (-5.7%, n = 23) after 12 weeks of treatment. Fat mass and fat-free mass (FFM) decreased significantly (-5.2 kg and -2.7 kg, respectively; n = 18) and percentage of fat mass decreased from 47.6% to 46.5% (P = 0.096).REE increased from 1879 kcal/day to 1956 kcal/day (P = 0.150), and REE per kg FFM increased from 29.7 kcal/kg/day to 32.3 kcal/kg/day (P = 0.023). Lastly, REE as a percentage of predicted REE increased from 94% to 98% (P = 0.204).

Conclusion

In patients with obesity, treatment with GLP-1 analogue liraglutide effectively induces weight loss, with improved body composition. Furthermore, despite decreases in fat free mass, of which muscle mass is a major component, resting energy expenditure did not decrease. Our findings suggest that weight loss induced

**P507**

Insights into the early use of oral semaglutide in routine clinical practice

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Introduction

Oral semaglutide (Rybelsus; Novo Nordisk) is the first glucagon-like peptide-1 receptor agonist (GLP-1 RA) developed for oral administration for the treatment of type 2 diabetes (T2D), and it has been approved by the US Food and Drug Administration and the European Medicines Agency. The efficacy and safety of oral semaglutide were assessed in the (PIONEER) program.

Aim

The purpose of this study was to investigate the patterns of routine clinical use of oral semaglutide, as well as the clinical features and glycemic control, and weight of patients.

Method

A retrospective, observational cohort study utilizing retrieved electronic medical records involved database search of 28 patients for the demographic parameters at the index date, as well as baseline co-morbidities, antidiabetic drugs, and HbA1c. Baseline and after 1-month, weight and FBS levels were determined for patients with relevant data. For inclusion, adult patients (aged <18 years) required a diagnosis of T2D and at least one prescription for oral semaglutide. Patients with type 1 diabetes or gestational diabetes were excluded. The results were analyzed using MS Excel.

Result

Although the medical instructions recommend raising the dose to 7 mg after 30 days, 64.3 percent of patients obtained a prescription solely for the initial 3 mg dose. The mean body mass index was 36.2 kg/m², and the mean HbA1c level was 9.1%. The mean change in FBS from baseline to about one month after initiating oral semaglutide was 6.3%, with more significant reductions in those with higher baseline FBS. The average weight loss was 2.3 kg, significantly more significant in patients with a higher baseline BMI.

Discussion

Our data demonstrates early trends in the use of oral semaglutide in routine clinical practice. Oral semaglutide initiators have a high prevalence of obesity and other co-morbidities, a varied treatment history, and improved glycemic control following therapy initiation. The relatively high number of patients allocated 3 mg as their maximum dose shows that, in patients who tolerate oral semaglutide well, dose escalation to 7 and 14 mg, as indicated, may result in even more significant glycemic control improvements. These findings emphasize the critical nature of bridging existing treatment and knowledge gaps in order to maximize the potential of oral GLP-1 RA therapy. Further examination of real-world data will give more information on the translation, uptake, and impact of such breakthroughs in standard treatment.

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by liraglutide may not only be facilitated by decreases in caloric intake through the anorexigenic effects of GLP-1 analogues, but also by increasing the resting energy expenditure per kg fat-free mass.

Finding
EFCvR is funded by a Vidi grant from the Netherlands Organization of Scientific Research NWO/ZONMW (grant number: 91716453). EFCvR is financially supported by the Elisabeth Foundation.

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P509
Neuroprotective properties of GLP-1 receptor agonists and SGLT-2 inhibitors in experimental stroke
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Background and aims
The most outstanding cardioprotective potential has been demonstrated for GLP-1 receptor agonists (GLP-1RA) and SGLT-2 inhibitors (SGLT-2). But only long-acting GLP-1RA dulaglutide (DULA) and semaglutide decrease stroke incidence, while data concerning the influence of any drug on stroke severity are lack. At the same time, ischemic stroke remains one of the leading causes of death in type 2 diabetes mellitus (DM2). The aim of our study was to investigate neuroprotective actions of liraglutide (LIRA), DULA and empagliflozin (EMPA), in comparison with metformin (MET).

Methods and materials
Male Wistar rats 200-255 g were treated for 7 days with LIRA 1 mg/kg s.c. once daily (“LIRA”, n=12), DULA 0.12 mg/kg s.c. every 2 h (“DULA”, n=10), EMPA 2 mg/kg per os once daily (“EMPA”, n=9), MET 200 mg/kg per os once daily (“MET”, n=8) or 0.9% NaCl s.c. once daily (“Control”, n=12). Then all animals were subjected to 30-min filament middle cerebral artery occlusion (MCAO). 48 h after MCAO neurological deficit was evaluated by Garcia scores — healthy animals have 18 points, maximal neurological deficit is characterized by 3 points. Then rats were euthanized, brain slices were incubated with 1% 2,3,5-triphenyltetrazolium chloride for necrosis measurement. Blood glucose level (BGL) was studied every second day.

Results
Brain infarct volume was significantly smaller in “LIRA” and “DULA” (5.50(3.97;5.50)% and 6.65(4.1;11.0)% comparing with “Control” (12.9(6.5;14.0)%), with no difference between LIRA and DULA. EMPA had less prominent neurological deficit and more points according to Garcia score among “LIRA”, “DULA” and “EMPA” groups. Treatment with MET also led to brain damage volume decrease (8.67(5.39;30.07)%), controlling with control, but it was larger than in other treatment groups. Rats in groups “LIRA” and “DULA” had less prominent neurological deficit and more points according to Garcia score (10.9(6.5;15.5) and 13.9(5.8;15.0)%) comparing with “Control” (12.9(6.5;14.0)%), with no difference between LIRA and DULA. Neither EMPA (12.0(9.5;14.0)%) nor MET (12.0(6.5;12.5) points) diminished neurological deficit, controlling with “Control”. BGL was normal in all groups.

Conclusions
GLP-1RA, SGLT-2 and MET are neuroprotective in rat transient brain ischemia and this effect is not connected with glucose metabolism. Infarct-limiting effect of LIRA, DULA and EMPA is similar and is more prominent than that of MET. Only GLP-1RA diminish neurological deficit. Neuroprotective property of GLP-1RA with different action duration is similar, being most probably a class-effect.

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P510
Suppressor of cytokine signalling-3 in pregnant females with or without hypertension: a case control study
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Background
Mammamomatotroph cell adenoma is rare, accounting for fewer than 2% of all pituitary adenomas and about 8% of tumors associated with acromegaly. A variety of adenomas may present with clinical signs and symptoms of GH hypersecretion including pure GH cell adenomas, mixed GH and prolactin cell adenomas, and monomorphous adenomas with primitive cells able to secrete GH and prolactin including the acidophilic stem cell adenoma and the mamo-matotroph cell adenoma. Here we present a patient with pituitary macroadenoma discovered three years ago with elevated Insulin Growth Factor-1 (IGF-1) but no clinical features of acromegaly.

Clinical presentation
A 35-year-old Caucasian nulliparous woman, known case of pituitary macroadenoma with a recent onset of hypertension presented to the clinic for routine check-up. Her initial presentation was of irregular menstruation, labs revealed high HPL and MRI confirmed pituitary macroadenoma in the year 2019. MRI’s at the time of diagnosis and further follow-ups were compared, despite the use of cabergoline the tumor size did not reduce; Hence she was evaluated for NPPA. Endocrinological workup for our patient revealed FSH 1.10(1-2 ng/dl), prolactin 186 (29.9 ng/ml), cortisol 10.3(3.7-19.4 mg/dl), OGTT values were 114/144, Hba1c 5.5, serum IGF-1 levels of 721(63.4-223.0 ng/ml), Growth hormone suppression test revealed 1 h GH of 12 ng/ml. Over the three years pituitary MRI’s were done each year and size in first, second and third MRI are 1.2X1.3X1.2 cm,1.2X1.3X 1.1 cm and 1.2X1.1X0.95 cm respectively. There was no reduction in tumor size over the past 3 years. Her serum IGF-1 levels were 3 times the normal upper limit. GH suppression test confirmed somatotroph adenoma with no symptoms of acromegaly. With these results, cabergoline was stopped, patient was advised for pituitary surgery.

Conclusion
In conclusion, the clinical spectrum of acromegaly varies from florid to subtle/no features and the diagnosis may be missed in some patients who are presumed to have clinically nonfunctioning pituitary tumors or no pituitary disorder. IGF-1 and GH should be checked in all patients of pituitary macroadenomas irrespective of initial symptoms as clinical features may take time to evolve. This recognition expands the therapeutic options to include pharmacological treatment and also provides a tumor marker to monitor the efficacy of treatment.

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Changes in acromegaly presentation and treatment over a three-decade period

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Objective
To study time-dependent changes in the prevalence and patient characteristics of acromegaly, as well as to access the impact of changes in treatment on disease control.

Methods
A total of 107 patients with acromegaly were identified by healthcare registries and subsequently validated by patient chart review over a three-decade period (1992–2021).

Results
The prevalence of acromegaly significantly increased throughout the study period (R² = 0.94, P < 0.001) and was 122 cases/10⁵ in 2021 whereas the annual incidence was constant 4.6 cases/10⁵. The age at the first sign of acromegaly and the age at diagnosis significantly increased during the study period, whereas GH and IGF-1 decreased. Incidentalomas constituted 32% of all cases diagnosed with acromegaly in the last decade. Primary surgery was used in 93% of all cases, and reoperations decreased from 24% to 10% during the three decades. The use of somatostatin analogues (SSA, 21%-48%) and second-line medical treatment (4%-20%) increased with a concomitant improvement of biochemical disease control (5%-91%).

Conclusion
The prevalence of acromegaly is higher than previously reported and the clinical presentation has shifted towards a milder phenotype. Modern treatment of acromegaly enables individualized treatment and disease control in the majority of patients.

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The first reported pregnancy and birth by a patient affected by Alström Syndrome: a case report

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Background
Alström Syndrome (ALMS, OMIM 203800) is an ultra-rare disease caused by autosomal recessive mutations of the ALMS1 gene (2p13). ALMS is characterized by double sensory impairment and systemic comorbidities, including hyperandrogenism in female patients. Fertility issue and conception have not been systematically studied.

Case
This case report describes the pregnancy and birth by an ALMS patient with mild phenotype, characterized by late onset visual impairment, hypertension and mild cardiac fibrosis at MRI. Patient had no history of hyperglycaemia, metabolic, hepatic, nephological comorbidities and auditory disorders. From a gynaecological point of view, menarche occurred at the age of twelve years and the following menses was regular, she had a Tanner stage of 5 for breast development and 3 for pubic hair representation. The year before her pregnancy her hormonal evaluation on follicular phase showed normal levels of gonadotropin, prolactin, oestradiol, progesterone, testosterone, dehydroepiandrosterone-sulfate, SHBG, TSH, insulin, fasting glucose and increased levels of Dihydrotestosterone (1.33 nmol/l normal values 0.08-1.26) and androstenediol glucuronide (7.70 mg/l normal values 0.34-7.53). She had conceived spontaneously in January 2020. A rigorous clinical follow-up of maternal and fetal conditions was carried out. A weight gain of 10 kg during pregnancy was registered. A Tanner stage of 5 for breast development and 3 for pubic hair representation. The year before her pregnancy her hormonal evaluation on follicular phase showed normal levels of gonadotropin, prolactin, oestradiol, progesterone, testosterone, dehydroepiandrosterone-sulfate, SHBG, TSH, insulin, fasting glucose and increased levels of Dihydrotestosterone (1.33 nmol/l normal values 0.08-1.26) and androstenediol glucuronide (7.70 mg/l normal values 0.34-7.53). She had conceived spontaneously in January 2020. A rigorous clinical follow-up of maternal and fetal conditions was carried out. A weight gain of 10 kg during pregnancy was registered. A Tanner stage of 5 for breast development and 3 for pubic hair representation. The year before her pregnancy her hormonal evaluation on follicular phase showed normal levels of gonadotropin, prolactin, oestradiol, progesterone, testosterone, dehydroepiandrosterone-sulfate, SHBG, TSH, insulin, fasting glucose and increased levels of Dihydrotestosterone (1.33 nmol/l normal values 0.08-1.26) and androstenediol glucuronide (7.70 mg/l normal values 0.34-7.53). She had conceived spontaneously in January 2020. A rigorou...

Conclusion
The pregnancy and delivery by an ALMS patient with mild phenotype, characterized by late onset visual impairment, hypertension and mild cardiac fibrosis at MRI, was normal. Hyperandrogenism was an initial feature of the disease.

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Superior vena cava syndrome associated with Graves’ disease
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Introduction
Goiter means that the thyroid gland is larger than the normal size for the patient’s age and gender. Some of the causes of goiter are iodine deficiency, thyroid nodules, Graves’ disease(GD). Goiter, hyperthyroidism, ophthalmopathy and dermopathy can be seen in GD. Compression symptoms due to goiter (dyspnea, dysphagia, superior vena cava syndrome) are also seen. Here, we will present a case of GD with superior vena cava syndrome.

Case
A 50-year-old male patient, who had been using methimazole for 6 years due to hyperthyroidism, applied to our outpatient clinic with swelling in the neck. The patient was taking methimazole 10 mg/day. On physical examination, he had goiter, bilateral venous collaterals in the neck, and inactive Graves’. ophthalmopathy. Pemberton’s sign was positive. In laboratory tests, TSH, fT4, fT3, antiTPO, antiTG, TSH receptor antibody were: < 0.008 mU/l, 1.01 ng/dl, 10.6 ng/l, > 13000 UI/l (< 60 negative), 724 IU/ml (< 1.3 negative), 34.3 UI/l (≤ 1 negative). In the thyroid ultrasound, the dimensions of the right lobe were 33 x 33 x 43.74 mm, the dimensions of the left lobe were 35 x 35 x 50.78.5 mm, the dimension of the isthmus was 20 mm, no thyroid nodule was observed. The thyroid gland showed retrosternal extension. Thyroid scintigraphy was consistent with GD. Computed tomography of the neck and thorax was performed to evaluate the differential diagnosis and cervical region: the dimensions of both thyroid lobes had increased considerably, extending to the paraesophageal, paratracheal, and intrathoracic retrosternal areas, and significant extrinsic compression of the larynx and esophagus was observed. In addition, bilateral subclavian veins were pressed by the thyroid gland, and diffuse dilated venous structures were observed in the skin-subcutaneous part of the anterior of the thyroid. Varicos dilated veins were observed in the anterior mediastinum. (Secondary to subclavian vein compression?). No pathological finding was detected in the lung parenchyma. Bilateral total thyroidectomy was performed. Its pathology was reported as diffuse toxic hyperplastic thyroid gland. Venous collaterals in the neck of the patient disappeared in the postoperative period. Clinical improvement was observed.

Conclusion
The most common cause of hyperthyroidism is GD. Compression symptoms due to diffuse hyperplasia of the thyroid gland may be seen. In particular, the retrosternal extension goiter may cause superior vena cava syndrome by compressing the vascular structures. The most common cause of superior vena cava syndrome is malignancy. GD should also be considered in the differential diagnosis of superior vena cava syndrome. Improvement in this situation is expected with thyroidectomy.

DOI: 10.1530/endoabs.81.P514

Parathormone washout in cytology of Suspicious for Follicular Neoplasm
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Introduction
The risk of malignancy in thyroid nodules is reported by the Bethesda system by performing fine needle aspiration biopsy (FNAB). Atypia of undetermined significance(AUS) or follicular lesion of undetermined significance(FLUS) is suspicious for a follicular neoplasm (Bethesda 3) and suspicious for a follicular neoplasm (Bethesda 4) create uncertainty about treatment and follow-up. Molecular tests, ultrasonographic features of the nodules, and calcitonin level help us for this uncertainty. Here, we will present a patient whose FNAB cytology was Bethesda 3 and Bethesda 4.
Case
A 53-year-old female patient was admitted to our outpatient clinic after detecting a thyroid nodule in neck ultrasound. She had familial Mediterranean fever, osteoporosis, and renal transplantation (5 years ago). In addition, the patient stated that she had been operated on the parathyroid gland while she was receiving dialysis treatment. There was no document related to parathyroid surgery. In laboratory tests, thyroid function tests, calcitonin, calcium levels were normal. 25-OH vitamin D, parathormone level, creatinine, eGFR were 14 ng/ml, 152 pg/ml, 1.51 mg/dl, 39 ml/minute respectively. Secondary hyperparathyroidism due to vitamin D deficiency was considered. On thyroid ultrasound, a hypoechoic nodule containing cystic degeneration areas was observed adjacent to inferior carotid artery in the right lobe. The dimensions of nodule were 9.7x11.4x13.7 mm. FNAB was reported as Bethesda 3. The second FNAB cytology was also reported as Bethesda 4. Molecular testing could not be performed in our hospital. The microscopy of FNAB revealed "some of the cells were small, round, monotonous nuclei with pale cytoplasmic cytoplasm with unclear borders". No uptake suggestive of parathyroid lesion was observed in parathyroid scintigraphy. Third FNAB cytology was ondiagnostic; Parathormone washout was 525 pg/ml. Due to the high suspicion of parathyroid lesion, fourth FNAB and diuted PTH washout were performed. Fourth FNAB cytology was Bethesda 3, diuted parathormone level was 103871 pg/ml. The lesion was evaluated as intrathyroidal lesion (adenoma or parathyroid seeding due to surgery). Follow-up was planned for the patient.

Conclusion
In parathyroid lesions evaluated as thyroid nodules, FNAB cytology and microscopy give an idea in terms of intrathyroidal parathyroid lesion. Parathyroid scintigraphy also does not always show uptake. In this situation, PTH washout can be done. If the ultraos features, FNAB microscopy and PTH washout are inconsistent, diuted PTH washout may provide accurate results due to possible hook effect. In addition, intrathyroidal parathyroid seeding should also be kept in mind in patients who have undergone parathyroid surgery for tertiary hyperparathyroidism.

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P762
Do polymorphisms of the glucocorticoid and mineralocorticoid receptors play a role in adrenal crises?
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Introduction
Polymorphisms of the glucocorticoid (NR3C1) and mineralocorticoid receptor (NR3C2) have been linked to the regulation of HPA-axis and to glucocorticoid sensitivity. We investigated whether NR3C1 and NR3C2 polymorphisms correlate with the occurrence of adrenal crises (AC) in patients with primary adrenal insufficiency (PAI).

Material and methods
We investigated 100 patients with PAI (70% women, mean age 51 ±15 years). DNA was extracted from whole-blood and NR3C1 and NR3C2 polymorphisms were genotyped by PCR and MALDI-TOFF mass spectrometry. Results were correlated with history of AC (number of events since first diagnosis and number of events per patient years), replacement therapy, HbA1c and 24-h blood pressure profile.

Results
Three NR3C1 polymorphisms (rs6198, rs1700289, rs4912911) and one NR3C2 (rs5522) polymorphism were significantly associated with a higher prevalence of AC. For NR3C1 rs6198, AC occurred more often in C allele carriers (66% CC/CT vs 44% TT, P = 0.04, OR 2.5 95% CI 1.0-6.0). For NR3C1 rs1700289, patients with AA genotype experienced more frequent AC (61% AA vs 40% TT/TA, P = 0.03, OR 2.4 95% CI 1.0-5.5) and exhibited lower HbA1c levels (5.3 (4.8-8.2) AA vs 5.7 (4.8-8.1) TT/TA, P = 0.03) and higher degrees of nocturnal blood pressure dipping (-14% (26, -5) AA vs -8% (19, 7) TT/TA, P = 0.02). For NR3C1 rs4912911, AC occurred more often within AA genotype (61% AA vs 38% GA/GG, P = 0.021, OR 2.6 95% CI 1.1-5.8). For NR3C2 rs5522, AC occurred more often in C allele carriers (74% TC/CC vs 44% TT, P = 0.02, OR 3.5 95%CI 1.2-10.6).

Conclusion
We identified several NR3C1 and NR3C2 polymorphisms that are associated with a higher incidence of AC. The identified NR3C1 polymorphisms have been shown to decrease glucocorticoid sensitivity, whereas NR3C2 rs5522 seems to interfere with the glucocorticoid stress response. Our preliminary data suggests that inter-individual differences in glucocorticoid sensitivity may contribute to increased susceptibility to AC.

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P763
Actions taken for prevention of adrenal insufficiency in adult patients who are at risk - audit report
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Background
Adrenal insufficiency (AI) is can be often under recognised condition in the clinical practise which can potentially result in adrenal crisis or even death if not treated properly. Identification of patients who are at risk of developing AI is important in order to take appropriate steps in minimising unwanted incidents. Objectives
Study aims to assess whether we identify patients who are at risk of AI and take recommended precautions.

Method
We performed a single centred retrospective audit at West Suffolk hospital in the United Kingdom using electronic health records to identify 57 adult patients who were on long term steroid therapy. This included oral, inhaled or injected steroids

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for a period exceeding 4 weeks, being prescribed by different specialties (respiratory, rheumatology, haematology, renal gastroenterology) and patients who already had the diagnosis of hypopituitarism and Addison’s disease. The records were then searched from 2016 to 2022 and data was collected on demographics, whether appropriate advice had been given and whether they were managed appropriately during inpatient stays.

Results
Over two thirds (64.3%) of patients had no alert on their record to state they were at risk of AI. Only one patient had documentation of having received a steroid emergency card. Just 22.8% of patients were documented as having an emergency intramuscular hydrocortisone pen. Documented ‘sick day rules’ advice was not given to almost two thirds of patients (67.9%). In contrast we noted 100% of patients who had the diagnosis of hypopituitarism and being followed up at endocrine clinics had been given sick day rules. Nearly one fifth of our study population comprised patients with a former diagnosis of hypopituitarism and Addison’s disease. Just less than a half of patients who had surgery or invasive procedure had been appropriately managed with pre-operative steroids. Finally, 17.5% of patients had been admitted to hospital in adrenal crisis at least once.

Conclusion
This audit report highlights the importance of raising awareness of AI among clinicians across different sub-specialties and making relevant recommendations to prevent any undesired events.

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P764
Hypertension in Pheochromocytoma and paraganglioma: Characteristics, treatment and outcomes
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Introduction
Pheochromocytomas and paragangliomas are neuroendocrine tumors that arise from the chromaffin cells of the adrenal medulla or originate from the autonomic nerve ganglia. Hypertension in patients with PPGL is the most frequent symptom and can be responsible of lethal cardiovascular complications. The aim of our work is to describe the clinical characteristics of hypertension in PPGL, the treatment and the outcomes after surgical treatment.

Materials and methods
Our study is retrospective descriptive, involving 34 patients (29 patients with pheochromocytoma and 5 patients with functional paraganglioma) followed in our Endocrinology-Diabetology and Nutrition Department of Mohammed VI University Hospital Center in Oujda, Morocco.

Results
The mean age of our patients was 47 ± 17.9 years (15-81) with a sex ratio H/F of 0.4. History of hypertension was present in 58.8% of cases of which (55%) had uncontrolled treated hypertension, and (45%) had well controlled hypertension under antihypertensive medication. Hypertension was diagnosed at the same time as the tumor in 14.3% of cases. Half of our patients (47%) had permanent hypertension, 11.7% had paroxysmal hypertension and 11.7% experienced orthostatic hypertension. 24-h urinary metanephrine level was elevated in 76% of the cases, and 24-h urinary normetanephrine level was elevated in 84% of the cases. Imaging revealed unilateral abdominal PPGL in 73% of cases, bilateral pheochromocytoma in 11.7% of cases and cervical PGL in 6% of cases. The mean size of the tumor was 51.4 mm ± 29.4. Before surgery, all of our hypertensive patients received β-blockers preparation 15 days before surgery. Peroperatively, only 12% of patients presented hypertensive peaks without further complications. Good blood pressure control was achieved postoperatively and antihypertensive medication was reduced in all of our hypertensive patients with good clinical and biological outcomes.

Discussion-Conclusion
Although rare, PPGL can be dangerous due to the excess of catecholamines and cardiovascular complications. Treatment of hypertension before, during and after the removal of the tumor is mandatory to avoid complications. The preoperative management of hypertension usually includes treatment with β-blockers at least 10 to 14 days before surgery, with the addition of alpha blockers when necessary. Surgical removal of functional PPGL is the main treatment.

PPGL: Pheochromocytoma and paraganglioma

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P765
Multiple vertebral fractures following ibrutinib therapy in a patient with B-cell chronic lymphocytic leukemia
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Some hematologic malignancies might increase the risk of fractures due to intrinsic factors of the disease but also because of the treatment with steroids or chemotherapy. The direct impact of novel targeted agents on the development of osteoporosis in these patients has not been recognized yet. A 64-years old female patient with B-cell chronic lymphocytic leukemia (B-CLL) has been followed for four years with no other comorbidities. In order to measure the burden of the disease consecutive CT scans were performed. Two years ago, she underwent endocrinological evaluation because of incidental adrenal adenoma. Hypercortisolism and other endocrine disorders were excluded. She has never experienced a bone fracture before and no radiographic vertebral fractures were present. According to Fracture Risk Assessment Tool her 10 years probability of fractures with bone mineral density and adjusted for trapecular bone score was 5.2% for major osteoporotic fracture and 0.7% for hip fracture. Her B-CLL progressed with lymph nodes enlargement and first line therapy with ibrutinib – bruton tyrosine kinase (Btk) inhibitor was started. Three months later the patient presented with severe lumbar pain that occurred suddenly without clear precipitating factor. Radiographic examinations were performed and multiple osteoporotic lumbar vertebral fractures were found (Genant’s grade 2 in L2 vertebra and grade 1 in L1, L3 and L4 vertebrae). We repeated endocrinological investigation. Vitamin D was reduced (44 nmol/l) but no evident secondary causes of osteoporosis were revealed. Her bone mineral density was significantly deteriorated. We deferred vertebroplasty and the treatment with teriparatide and cholecalciferol was introduced. Increased risk of axial fractures was already observed in B-CLL patients and infiltration of bone marrow with leukemic cells has been recently shown to impair osteosteatogenics and promote osteosteatogenies. Ibrutinib up to now has not been labeled as a drug that could significantly impair bone health. Early experimental studies suggested that it could even inhibit osteosclerotic differentiation and function. However, recent observations recorded signals of potential increase of fractures with ibrutinib therapy. Although no cause and effect could be claimed, the occurrence of multiple osteoporotic vertebral fractures shortly after the ibrutinib therapy was introduced, suggests that this might play a role in bone damage and warrants further studies.

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P766
Diagnostic process in a lipodystrophic syndrome suspicion, a clinical case
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The lipodystrophic syndromes are a heterogeneous group of congenital or acquired disorders characterized by either complete or partial lack of adipose tissue with the apparent accumulation of fat in other regions of the body. Their prevalence is low and ranges from 1:200000/500000 and they usually suffer metabolic abnormalities associated with the abnormal distribution of fat such as severe insulin resistance with acanthosis and diabetes, progressive liver disease along with muscle hypertrophy, internal megalia, hirsutism, developmental delay or proteinuric renal damage. The diagnosis of these syndromes is thus very complex and demand multiple studies. We report a case of suspected lipodystrophy that we follow in our center in Alcorcón (Madrid) in the year 2022.

Case Report
36 year old woman, born in Colombia, with unique background of diabetes mellitus cataloged as type 2, diagnosed at age 18 with no familiar history and...
treated with insulin along with severe acantosis nigricans and PCOS. Admitted under episode of hyperemostatic hyperglycemic syndrome secondary to poor access to treatment, extended folliculitis and urinary infection due to K. pneumoniae. Good progress under emergent insulin and antibiotic treatment. We detect a particular phenotype consisting of prominent muscularity and low peripheral adipose tissue, severe acantosis nigricans plates, rough facial traits and hirsutism. There was therefore a suspicion of a syndrome that could include all the manifestations detected, specifically lipodystrophic syndrome. We deepened in the study of diabetes with a 12% HbA1c determination but normal C-Peptide, pancreatic autonimmunity and pancreatic imaging with abdominal tomography that on the other hand revealed several dermic thickening, low subcutaneous cellular tissue, gastric and renal lypomas. Greater find of difuse adenopathies in all the abdominal cavity though normal proteinogram without monoclonal pike and normal urine immunofixation. 24-h urinanalysis demonstrated nefrotic proteinuria in context of diabetic nephropathy in a renal biopsy. Negative HIV study. Due to clinical stability the patient is discharged, with presumptive diagnosis of acquired generalized vs partial congenital lipodystrophy, only remaining the leptin determination.

Conclusion

The lipodystrophic syndromes though rare entities, must be suspected when several metabolic disorders combine with phenotypic features i.e lack of peripheral adipose tissue. The proper study of the endology and the secondary alterations is crucial to assure the good treatment and prognosis of these patients.

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P767

Correlation of adiponectin and resistin with atherogenic markers in insulin resistant and non-insulin resistant adolescent women with polycystic ovary syndrome

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Aim

To evaluate adiponectin and resistin levels and their relationship with various biochemical and metabolic and atherogenic parameters markers, as well as their correlation, and to investigate its contribution in pathogenesis of insulin resistance in cohort women with PCOS and of insulin resistance as well as in non-insulin resistant women with PCOS. Methods: This study was designed as a cross-sectional and involves 80 premenopausal women. Of these patients, 63 females have met the criteria for PCOS (59 insulin resistant, 28 non-insulin resistant). We assessed anthropometric indices of obesity –waist and hip circumference, waist to hip ratio, serum glucose, insulin, total cholesterol, HDL-cholesterol, triglycerides, FSH, LH, E2, testosterone, adiponectin and resistin. Body mass index, waist to hip ratio, HOMA-IR, LDL-cholesterol, and adiponectin to resistin ratio were calculated. Results: Insulin resistant PCOS woman had significantly lower levels of adiponectin compared to non-insulin resistant PCOS women, and controls. Resistin levels were higher in IR-PCOS, but without statistical significance. Adiponectin showed significant positive correlation with LH, HDL-C, and negative correlation with BMI, insulin, HOMA-IR and triglycerides. Resistin correlated positively with BMI and WC. A/R was significantly higher in insulin resistant PCOS women compared to non-insulin resistant and control women. Conclusions: These results suggest that PCOS women were at higher metabolic and atherogenic risk as compared to the healthy women, and also more pronounced in the insulin-resistant group. Correlations of adipokines with insulin resistance suggest their involvement of adipokines in modulation of insulin action in PCOS women.

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P768

Insulin-Like Growth Factor-I might be a predictor for severe nonalcoholic fatty liver disease in morbidly obese patients

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Aim

To compare the IGF-1, metabolic and clinical parameters among the ultrasonographically classified NAFLD groups, to examine the effect of weight loss on metabolic parameters and determine the factors that may predict the NAFLD severity in morbidly obese patients who underwent bariatric surgery.

Method

This descriptive cross-sectional study was conducted in 316 morbidly obese patients (150 females, 66 males). The data of patients before and 1 year after bariatric surgery were included in the study. According to the NAFLD assessment, patients were classified as normal (Group 1, n=57), mild and moderate (Group 2, n=219), or severe (Group 3, n=40). IGF-1 standard deviation score (SDS) levels were calculated according to age and gender. Preoperative and postop 1st-year clinical and metabolic parameters and factors that could predict the presence and severity of NAFLD were evaluated in all groups.

Results

IGF-1 levels were significantly associated with severe NAFLD compared with the normal group, and the significance remained between the same groups when IGF-1 levels were standardized as SDSIGF1. Moreover, liver diameter explained 50% of severe NAFLD than the normal group and %13 of severe NFLAD compared to mild-moderate NAFLD. FFG, ALT, AST, and GGT were also significant predictors for severe NAFLD compared to the normal and mild-moderate NAFLD groups.

Conclusion

Together with liver diameter, FFG, AST, ALT, and GGT, IGF-1 is among important predictors of NAFLD in bariatric surgery candidate morbidly obese patients. Further studies are needed to validate the clinical utility of IGF-1 in the presence and staging in NAFLD patients.

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P769

Coexistence of hypopituitarism caused by Sheehan’s syndrome and Hashimoto’s thyroiditis. A case report, review of literature.

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Introduction

Hypopituitarism due to Sheehan’s syndrome is a rare complication and its diagnosis is often overlooked. The vast majority of people with hypothyroidism have primary hypothyroidism, often due to Hashimoto’s thyroiditis. Coexistence of hypopituitarism and primary hypothyroidism, may accelerate clinical manifestations, mainly those associated with hypothyroidism. Hashimoto’s Thyroiditis with concomitant hypopituitarism is rare but has been described previously, but there are no reports of Hashimoto’s Thyroiditis occurring with Sheehan’s syndrome.

Case report

In this case study, we report a patient with Hashimoto’s Thyroiditis associated with Sheehan’s syndrome. Our case is a 38-year-old female patient, presented with generalized fatigue, weakness, pain in the muscles of the lower extremities and other nonspecific complaints which were aggravated in recent months. She was consulted with various doctors but with the medication she received, there was no improvement until she presented in poor condition in emergency unit. She gave birth 7 years ago; after delivery she had a history of prolonged bleeding, amenorexia and inability to lactate. Her physical examination revealed pale, dry, cold, rough skin, sluggish speech and thick voice, decreased body hair. Her laboratory evaluation showed, low levels of free thyroxin (FT4) and free triiodothyronine (FT3), high normal level of thyrotropin stimulating hormone (TSH). Thyroid antibodies were high level. She had hypogonadotropic hypogonadism, hypoprolactinemia, hypocortisolism with low level of adrenocorticotropin hormone and growth hormone deficiency, normochronic normocytic anemia, high level of LDL-cholesterol. Her magnetic resonance imaging was empty sella. Her thyroid ultrasonography revealed aspect of chronic thyroiditis.

Our diagnosis was Hypopituitarism due to Sheehan’s syndrome co-existing with Hashimoto’s Thyroiditis. She was treated with hormone replacement and she was in a good condition 2 months later.

Conclusion

A high index of suspicion is crucial for the early diagnosis of the coexistence of hypopituitarism due to Sheehan’s syndrome and Hashimoto’s thyroiditis that is a rare condition in clinical practice, to prevent long-term morbidity.

DOE: 10.1530/endoabs.81.P769
A patient with acromegalic heart disease

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A 36 years old patient was admitted to the intensive care unit of cardiology when he experienced palpitations and orthopnea. The patient’s complaints started about 2 years ago as syncope and sudden shortness of breath. Thorax CT showed pleural effusion and increased cardiothoracic index. Findings on ECHO were: Ejection fraction 35%, severe mitral regurgitation and global hypokinesia. Coronary angiogram showed a fibrocalcific plaque noted in the distal LAD. The pathophysiology most likely was dilated cardiomyopathy. The patient was started on Furosemide, spironolactone, isoribidine mononitrate. Despite the treatment, the patient’s complaints gradually increased and over the course of the next 24 months, the patient was repeatedly hospitalised due to heart failure, and his medication was adjusted several times. Two years later, the patient was admitted to our center with the diagnosis of acute heart failure. A decrease in ejection fraction was detected in the new echocardiography (%10), and no further clinical improvement was seen, the decision was then taken to initiate treatment with levosimendan and noradrenaline. Dilated cardiomyopathy was observed with cardiac MRI. He was consulted to the endocrine department because of suspected acromegaly. When he was evaluated, he complained of shortness of breath, arthralgia and increasing shoe size. Physical examination was positive for acral growth, nose widening, and prognathism. GH and IGF-1 levels were increased at diagnosis (table 1), the baseline and peak GH concentrations were 8.74 and 34.4 ng/ml during 75-g OGTT, showing paradoxical increases in GH

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A decrease in ejection fraction was detected in the new echocardiography (%10), and no further clinical improvement was seen, the decision was then taken to initiate treatment with levosimendan and noradrenaline. Dilated cardiomyopathy was observed with cardiac MRI. He was consulted to the endocrine department because of suspected acromegaly. When he was evaluated, he complained of shortness of breath, arthralgia and increasing shoe size. Physical examination was positive for acral growth, nose widening, and prognathism. GH and IGF-1 levels were increased at diagnosis (table 1), the baseline and peak GH concentrations were 8.74 and 34.4 ng/ml during 75-g OGTT, showing paradoxical increases in GH.
Thyronamides-induced agranulocytosis in a patient with previous hematological disease; a case report
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Introduction
The treatment of thyroid diseases with thionamides can cause agranulocytosis a potentially fatal side effect. The manifestations resulting from such a condition include, in most cases, infections that, if not treated immediately, have a high risk of septicemia. Therefore, the clinical presentation includes fever of unknown origin and infections such as pneumonia, tonsillitis, and abscesses. Most patients who do not receive immediate medical intervention progress to septicemia, a fact that shows the relevance of early diagnosis and adequate management.

Case report
A 38-year-old female patient had Chronic Myeloid Leukemia without follow-up and treatment. She developed severe neutropenia induced by thionamide used to control hyperthyroidism. Laboratory tests performed on admission at the Hospital showed Hb 8.6 g/dl, pancytopenia with worsening leucopenia: leukocytes 720/mm3, absolute segmented count 9 mm3, 0/mm3 (zero) basophils, 0/mm3 (zero) lymphocytes, TSH 0.029 mU/l (normal 0.4-4.5 mU/l) and free T4 4.93 ng/dl (normal 0.7-1.8 ng/dl). Autoantibodies against TSH receptor (TRAb) were negative. The absence of evidence of transformation into accelerated and blastic phases of Chronic Myeloid Leukemia, positive clinical response, resolution of neutropenia 8 days after the suspension of thionamides, and the presence of a 5/1 Myeloid: Erythroid ratio in bone marrow biopsy, suggested the previous destruction of neutrophils, with recovery after drug discontinuation.

Conclusion
The state of severe neutropenia is attributable to drugs in 70 to 90% of cases. The absence of evidence of transformation for the accelerated and blastic phases of Chronic Myeloid Leukemia, positive clinical response, resolution of neutropenia 8 days after the suspension of thionamides, and the presence of a 5/1 Myeloid: Erythroid ratio in bone marrow biopsy, suggested the previous destruction of neutrophils, with recovery after drug discontinuation.

Regulatory B cells involvement in autoimmune phenomena occurring in pediatric graves' disease patients.
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Graves’s disease is the most common type of autoimmune hyperthyroidism. Numerous studies indicate different factors contributing to the onset of the disease. Despite years of research, the exact pathomechanism of Graves’ disease still remains unresolved, especially in the context of immune response. B cells can play a dual role in autoimmune reactions, on the one hand, as a source of autoantibody mainly targeted in the thyroid hormone receptor (TSHR) and, on the other, by suppressing the activity of proinflammatory cells (as regulatory B cells). To date, data on the contribution of Bregs in Graves' disease mechanism, especially in children, are scarce. Here, we investigated the frequencies of Bregs before and during a methimazole therapy approach. We reported higher Foxp3+ and IL-10+ Breg levels with CD38+ phenotype and reduced numbers of CD38+ Foxp3+ IL-10+ in pediatric Graves' patients. In addition, selected Breg subsets were found to correlate with TSH and TRAb levels significantly. Noteworthy, certain subpopulations of Bregs were demonstrated as prognostic factors for methimazole therapy outcome. Our data demonstrate the crucial role of Bregs and their potential use as a biomarker in Graves’ disease management.
**EP1**

**Fatty acid binding protein 4 mediates atherosclerosis by disrupting gut microbiota and immunity**

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**Introduction**

Atherosclerosis is a chronic inflammatory arterial disease and is currently one of the most common causes of cardiovascular morbidity and mortality worldwide. Therefore, there is an urgent need to discover new therapeutic targets for treatment of this fatal chronic disease. Fatty acid binding protein 4 (FABP4), a pro-inflammatory adipokine that links obesity with its related metabolic diseases, has been implicated in the development of atherosclerosis. This study aims to investigate whether FABP4 potentiates atherosclerosis by mediating the crosstalk between gut microbiota and immunity and to explore whether targeting FABP4 is therapeutically effective for treatment of this disease.

**Method**

FABP4+/− ApoE−/− and FABP4−/−/− ApoE−/−/− mice were generated for the study and fed with high fat and high cholesterol diet (HFHC) for 12 weeks. Biochemical, immunological, flow cytometry and denaturing gradient gel electrophoresis (DGGE) analysis were conducted to determine the pathophysiological roles of FABP4 in potentiating diet-induced atherosclerosis by altering gut microbiota and immunity. Fecal microbiota transplantation (FMT) was performed to further investigate the role of FABP4 in atherosclerosis mediated through microbiota. The FABP4 chemical inhibitor BMS309403 was used to evaluate the effects of FABP4 inhibition in alleviating atherosclerosis.

**Result**

The aortic tissues stained with Oil Red showed significantly reduced atherosclerosis in FABP4−/−/− ApoE−/−/− mice comparing to FABP4+/−/− ApoE−/−/− littermates. Likewise, FMT of FABP4−/−/− mice significantly attenuated the development of atherosclerosis. DGGE analysis of fecal DNA showed that the pattern of bacterial phyla was obviously changed in FABP4−/−/− mice comparing to FABP4+/−/− littermates. These changes in FABP4−/−/− mice were accompanied by significantly increased expression of zona occludens protein-1 (ZO-1) and occludin in intestinal villi, suggesting that FABP4 may enhance the intestinal permeability in mice in response to HFHC diet. Furthermore, FABP4 promoted macrophage infiltration and the polarization of macrophage from M0 to pro-inflammatory M1 subtype in the intestine of mice. Treatment with the FABP4 inhibitor BMS309403 dramatically alleviated the inflammatory response in the gut and atherosclerotic plaque formation, and elevated the intestinal expression of ZO1 and occludin in FABP4−/−/− mice.

**Conclusion**

FABP4, which is elevated during obesity, alters the composition of gut microbiota and intestinal permeability by creating a pro-inflammatory microenvironment, leading to endotoxinemia and subsequently contributing to the development of atherosclerosis. Targeting FABP4 with small-molecule inhibitors such as BMS309409 is a promising therapeutic strategy for treatment and prevention of atherosclerosis by modulating gut microbiota and intestinal immunity. Acknowledgement

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**EP3**

**Impact of adrenocortical carcinoma and associated adrenal insufficiency on patient wellbeing – a systematic review**

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**Context**

Adrenocortical carcinoma is a rare cancer with an annual incidence of 0.7-2 cases per million population and 5-year survival of 31.2%. Adrenal insufficiency is a common and life shortening complication of ACC and little is understood about how it impacts on patients.

**Objective**

To understand patients’ experience of the condition, its treatment, care process, impact of AI on ACC wellbeing, self-care needs and support.

**Design**

Systematic review of MEDLINE, EMBASES, CINAHL, PsyCINFO and Open Grey for studies published until February 2021. All research designs were included. The findings underwent a thematic analysis and narrative synthesis. Studies quality was assessed using mixed method assessment tools.

**Results**

A total of 2837 citations were identified; 15 titles with cohort, cross sectional, case series and case report study designs met the inclusion criteria involving 479 participants with adrenal insufficiency secondary to adrenocortical carcinoma. Quantitative research identified impacts of disease and treatment on survivorship, the burden of living with AI/ACC, toxicity of therapies, supporting self-care and AI management. These impact factors included adjuvant therapies involved and their toxicities, caregivers/family supports, healthcare and structure support in place, specialist skill and knowledge provided by healthcare professional on ACC management, No qualitative patient experiences evidence was identified.

**Conclusion**

ACC appears to have high impact on patients’ wellbeing including the challenges with self-care and managing AI. Evidence is needed to understand patient experience from a qualitative perspective.

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**EP4**

**Clinical-laboratory and morphological predictors of pheochromocytoma progression**

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According to the 4th edition of the WHO classification of endocrine organ tumors (2017), all pheochromocytomas are classified as malignant tumors (ICD-O code 8700/3). However, in the literature there are no unambiguous data on the significance of clinical and laboratory predictors of the aggressiveness of pheochromocytoma. The aim of the study was to verify possible predictors of pheo-progression using clinical data, the results of laboratory and instrumental
examination (including PASS and GAPP scales) of patients with a verified diagnosis of pheochromocytoma.

Material and methods
According to the data of this pilot retrospective study, data were analyzed from 27 patients with pheochromocytoma (16 women, 11 men) aged 22–73 years (median 51 years), who were operated on for the period from 2016 to 2021. 24-hour urine analysis for free metanephrines was determined by high performance liquid chromatography with tandem mass spectrometry with the addition of a preservative. The location and size of the pheochromocytoma was assessed by CT data with the determination of the native HU density. An immunohistochemical study was performed with antibodies to chromogranin A, synaptophysin, Ki-67, followed by an assessment of the potential for malignancy using the PASS and GAPP scales.

Results
There was a strong positive correlation between the PASS and GAPP scales ($r = 0.725$), which is statistically significant ($P < 0.01$). Both scales have a statistically significant positive correlation of mean strength with tumor size (PASS: $r = 0.382$, $P = 0.049$; GAPP: $r = 0.403$, $P = 0.037$). Correlation of these scales with the gender and age of patients, as well as the secretory activity of the tumor, was not revealed. A direct correlation was established between the PASS and GAPP scales and the size of the tumor.

Conclusion
According to our data, tumor size should be considered as a clinical predictor of metastatic potential of pheo, however gender, age, and functional activity of the tumor were not useful.

Keywords: pheochromocytoma; immunohistochemistry; PASS; GAPP.

DOI: 10.1530/endoabs.81.EP5

EP5
Adrenal incidentalomas in geriatric patients: Prevalence, radiological features, and hormonal profile
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Background and Aims
The incidence of adrenal incidentaloma (AI) has been rising sharply due to the increased use of radiologic imaging. It shows evident variation with age, with the majority of the cases presenting in the 5th to 7th decade of life. This study aims to assess the prevalence of AI and its radiological features and hormonal profiles in the geriatric population.

Patients and Method
We conducted a retrospective descriptive study including 177 patients diagnosed with AI referred to the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia during 2011–2020. All patients have undergone clinical examination, adrenal CT, and biochemical workup for hormonal secretion.

Results
Among the 177 patients diagnosed with AI, 38.9% were 65 years and older. We focused our investigation on the geriatric population sample ($n = 69$). The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance (57.5%). At the time of diagnosis, older adults reported various unspecified “aging-related symptoms” such as asthenia (50%), weight loss (40%), and paresis (37.5%), Hypertension (67.5%), diabetes (42.5%), and dyslipidemia (30%) were the leading comorbidities in geriatric patients bearing AI. Ninety-five percent of AI were detected on CT scans performed mainly for nephritic colitis (42.5%) or abdominal pain (17.5%). Complementary centered adrenal CT featured adrenal adenomas in 90%, less frequently adrenal incidentaloma (7.5%), and macronodular adrenal hyperplasia (7.5%), and macronodular adrenal hyperplasia (7.5%). AI was unilateral in 61%, mainly left-sided (54.5%), and bilateral in 39%. The mean size of AI was 24.1 ± 12.8 mm. 10% of aged patients were harboring AI larger than 40 mm. Non-contrast CT density was < 100HU in 82.5%. As for the remaining patients (17.5%), enhanced CT showed an absolute washout > 60% in 42.9% of cases. Based on the hormonal workup, 70% of elderly patients had non-secreting lesions. The functioning incidentalomas displayed autonomous cortisol secretion (32.5%), primary hyperaldosteronism (25%), or secondary hyperaldosteronism (21.8%). Only one senior had a secreting pheochromocytoma. AI with mixed hormonal secretion was recorded in 12.5%.

Conclusion
AI often affects the geriatric population, with an incidence reaching 10% after 70 years compared to 1–4% in younger adults. The vast majority of the AIs are non-functioning adenomas. Less common, some hormonal secretions, especially autonomous cortisol secretion and primary hyperaldosteronism, may be individualized in elderly patients bearing AI, although the hormonal excess often remains subclinical. Due to frailty and comorbidities frequently associated with advanced age, surgical management should be discussed on a case by case basis and proposed for seniors harboring lesions suspected of malignancy or overt hormonal secreting tumors: pheochromocytoma, cortisol secreting adenoma, etc.

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EP6
Application of machine learning techniques in a qualification for a surgical treatment of adrenal tumors
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Background
The gradual increase in the detection rate of adrenal incidentalomas makes them a common clinical problem. The vast majority of them are benign adrenocortical adenomas. Nevertheless, every patient with adrenal incidentaloma requires performing number of tests to exclude pheochromocytoma, autonomous cortisol secretion, adrenal carcinoma and primary hyperaldosteronism. Evaluation of whether adrenal incidentalomas are malignant or functional and continuing patient follow-up to assess the necessity for surgery assumed important place in endocrinology practice.

Objective
The aim of the study was to compare several machine learning techniques in a qualification for a surgical treatment of adrenal tumors and choose the most accurate algorithm as a valuable adjunct tool for decision-making.

Methods
A retrospective, single-center study was performed on hospitalized patients with adrenal incidentaloma between 2017 and 2019. From a database comprising 264 patients with adrenal incidentaloma, clinical data for 30 patients who underwent adrenalectomy due to suspicion of primary aldosteronism, pheochromocytoma, Cushing’s syndrome, or adrenal cancer were extracted. All included patients underwent the endocrine work-up aimed to study the hormonal status of adrenal incidentalomas and every adrenal lesion was assessed with CT scan. On the basis of the comparative histopathological examinations, primary qualifications, were confirmed in 20 out of 30 selected patients. Several machine learning algorithms, including Support Vector Machine, Multilayer Neural Network, C4.5 Decision Tree, Random Forest, k-Nearest Neighbours, Naïve Bayes, Zero R, One Rule, Logistic Regression, were trained to qualify the patients for an adrenalectomy. Finally, attribute selection technique was used to assess their usefulness in classification.

Results
The highest average accuracy was obtained for Support Vector Machine with linear kernel and soft margin – 90% of properly classified subjects. The Neural Network gave the second best result and was able to classify with an accuracy of 86%. Statistical evaluation using Pair T Student modified for dependent samples was significantly better in comparison to baseline approach Zero R ($P < 0.05$). The most commonly selected by classifiers attributes were tumor homogeneity (100%), maximum diameter of the tumor (100%) and obesity (98%). Nevertheless prior attribute selection did not improve accuracy of trained algorithms.

Conclusions
Presented results show that application of machine learning methods in qualifying patients for an adrenalectomy may improve the decision process. The new training machine learning-based methods might be used to simplify making therapeutic decisions in adrenal incidentalomas patients and reduce the time from the initial identification of adrenal incidentaloma to the final decision about surgery.

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A phase III trial of recombinant human growth hormone in pediatric patients with growth failure caused by chronic kidney disease

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Background and objective

Children with chronic kidney disease (CKD) have impaired growth that leads to short stature in adulthood and treatment with recombinant human growth hormone (rhGH) is associated with improved growth. This study aimed to evaluate the efficacy and safety of daily rhGH (Intropin®) in children in China with growth failure caused by CKD prior to transplantation.

Methods

Prepubertal patients (2–13 years old) with CKD-related short stature were enrolled in this multicenter, randomized, open-label, negative-controlled study (NCT03535415). Eligible patients were randomized 1:1 to receive daily rhGH 0.05 mg/kg/day administered subcutaneously or control (no rhGH given, only placebos). The primary endpoint was improvement in height standard deviation score (HT SDS). Secondary endpoints included improvements in height velocity (HV), bone maturation (bone age [BA]/chronological age [CA]), insulin-like growth factor 1 standard deviation score (IGF-1 SDS), IGF-1/IGFBP-3 molar ratio, and safety.

Results

A total of 68 patients were randomized to either treatment or control; 11 patients (treatment: 7; control: 4) dropped out, 8 (treatment: 5; control: 3) of whom due to treatment discontinuation. At week 52, ΔHT SDS from baseline was 0.747±0.579 (P<0.001) and 0.173±0.470 (P=0.039) in the treatment and control groups, respectively (intergroup P<0.001). Least-squares mean difference between both groups was 0.582 (95% confidence interval 0.323–0.842). Statistically significant improvements were also observed in those who received treatment compared with those in the control group for ΔHV (7.021±3.795 cm/year vs 2.566±3.577 cm/year; intergroup P<0.001), ΔIGF-1 SDS (1.697±0.989 vs −0.171±1.506; intergroup P<0.001), ΔIGF-1/IGFBP-3 molar ratio (0.046±0.073 vs 0.001±0.034; intergroup P=0.001), and Δheight (0.987±2.89 cm vs 0.647±2.72 cm; intergroup P<0.001). Δ(BA/CA) was 0.041±0.074 and 0.008±0.079 in the treatment and control groups, respectively (intergroup P=0.118). Most treatment-emergent adverse events (TEAEs) were mild to moderate; 19 patients (treatment: 10; control: 9) experienced serious adverse events, and 5 in the treatment group temporarily discontinued rhGH due to TEAEs. 7 reported drug-related TEAEs, which included elevated blood insulin, scoliosis, glycosuria, musculoskeletal discomfort, hyperinsulinemia, and abnormal liver function.

Conclusion

Daily rhGH 0.05 mg/kg per day for 52 weeks was effective and well tolerated in children with short stature caused by CKD. At the end of the study, significant improvements in ΔHT SDS, ΔHV, ΔIGF-1 SDS, ΔIGF-1/IGFBP-3 molar ratio, and Δheight were observed with treatment.

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The spectrum of CYP21A2 copy number variations and gene mutations by MLPA in a pediatric Romanian population with 21-hydroxylase deficiency

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Objective

The analysis of the copy number variation of CYP21A2 gene in a cohort of 21-hydroxylase deficiency (21-OHD) pediatric patients in a tertiary referral center from Romania.

Methods

A total of 24 patients (21 female and 3 male, 7:1 female to male sex ratio) with previously biochemically and clinically diagnosed 21-OHD were enrolled in this study from October 2020 to October 2021. The age at the diagnosis was 4.6±4.8 years (mean±s.d.). All clinical and biochemical data were collected. Genomic DNA was extracted from peripheral blood leukocytes, and copy number variations along with several point mutations of CYP21A2 gene were detected by multiple ligation-dependent probe amplification (MLPA) using MRC-Holland SALSA MLPA P050-C1 kit and Coffalyser.net software. The study has been approved by Ethical Committee of the Institute.

Results

Clinical and biochemical phenotype revealed 13 patients (54.17%) with classic and 11 patients (45.83%) with non-classic form of 21-OHD. Salt-wasting phenotype was diagnosed in 8 patients in whom MLPA analysis results were: large deletion/rearrangement in CYP21A2 (2 patients with homozygous CYP21A2 deletion and 2 patients with fused CYP21A1P/CYP21A2 gene (chimeras)); 2 patients with heterozygous g.655AC>G (IG2) mutation, 1 patient compound heterozygous for p31L/h72N and one patient heterozygous for h71N mutation. In 5 patients with classic simple virilizing 21-OHD MLPA analysis showed: CYP21A1P deletion (2 patients), CYP21A1P duplication (1 patient), E2G/h71N (2 patients). The MLPA analysis in the remaining 11 patients with non-classic form of 21-OHD indicated: heterozygous gene deletion and h71N mutation (2 patients), partial CYP21A1P deletion (1 patient), CYP21A2 duplication (1 patient), homozygous mutation h71N and a heterozygous p31L mutation (1 patient), with a normal profile in 5 patients.

Conclusions

Copy number variation analysis is a very useful tool in 21-OHD molecular diagnosis, especially in classic salt-wasting patients but a complete precise diagnosis should be complemented by CYP21A2 sequencing analysis.

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Phaeochromocytoma during pregnancy: diagnosis and treatment challenges

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Introduction

Phaeochromocytoma in pregnancy is rare with an incidence of 0.007%. A timely diagnosis is essential since fetal and maternal mortality depends on the early treatment. Our object is to report a phaeochromocytoma diagnosed in a patient at the beginning of the pregnancy and to highlight the particularity in the therapeutic care.

Case presentation

A 32-year-old female patient was admitted to our endocrinology department for exploration of palpitation associated with headache and sweats. She had a family history of diabetes and hypertension and no history of pituitary adenoma or hyperparathyroidism. The symptoms were concomitant to food intake, and evolving for 02 years. The patient decreased her diet to avoid the symptoms, therefore, losing 09 kg. Clinically, her systolic blood pressure was ranging between 140 and 170, and diastolic between 80–90 mmHg. Pheochromocytoma was suspected and confirmed with increased plasma normetanephrine and metanephrine levels (104 the normal range). Abdominal CT scan showed a heterogenous mass of the left adrenal gland (5*4 cm) with spontaneous density of 40/4H. Shortly after, the patient discovered she was 9 weeks pregnant. We started
treatment with doxazosin, and blood pressure values were normalized. At 18 weeks of menstrual age, laparoscopic adrenalectomy of the left adrenal gland was performed without any complications during or after surgery. The tumor was confirmed to be a 7-cm pheochromocytoma in histological exam. After surgery, blood pressure was normal without treatment and post-operative measurements of serum normetanephrines and metanephrines were normal. At 30 weeks of menstrual age, the fetus was healthy.

Conclusion
Maternal and fetal mortality due to pheochromocytoma decreases to less than 15% if the diagnosis was made antepartum. Symptoms in pregnant patients do not differ from symptoms in non-pregnant patients. However, they may worsen with advancing pregnancy due to an increased pressure on the tumor by the abdominal dimension, fetal movements and uterine contractions. When the diagnosis is made within the first 24 weeks of pregnancy and adequate α-blockade can be established, tumor removal is recommended in the second trimester via laparoscopic surgery. Decisions for those patients should be made by an experienced multidisciplinary team.

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EP11
The concentration of metanephrine and normetanephrine in the most common indications for biochemical monitoring
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Objectives
Pheochromocytomas are rare neuroendocrine tumors that originate in chromaffin cells of the adrenal medulla and excessively secrete catecholamines, which leads to a multitude of different symptoms. The most common symptoms include headaches, palpitations and sweating. Because of a diverse clinical picture, they pose a major challenge in diagnostics and often go unidentified. The diagnosis is confirmed by measuring plasma and 24-hour urinary metanephrine and normetanephrine. The aim is to determine the most common indications for biochemical testing by sex and age and the association between the concentrations of metanephrine and normetanephrine and indications, sex, and age.

Study design
Cross-sectional study with historical data. Participants and methods
The study was conducted on subjects in whom the concentration of metanephrine and normetanephrine in plasma was determined in 2019. A list of patients was collected from the Clinical Institute for Laboratory Diagnostics at the Osijek Clinical Hospital by accessing the laboratory information system. Data (indications for biochemical testing, sex, age) was collected from the Department of Nephrology for each patient by accessing the hospital information system.

Results
The study was conducted on 224 respondents (42.9% men and 57.1% women). The most common indication for biochemical testing is adrenalin incidentaloma (61.6%) and symptoms of pheochromocytoma (18.3%). There is no significant difference in the distribution of patients according to gender. The median age of participants with adrenal incidentaloma and participants with previously treated pheochromocytoma is higher compared to subjects with hereditary risk for pheochromocytoma and hypertension before they turned 20 years old. There is no significant association between the values of metanephrine and normetanephrine and the indication for biochemical testing. Metanephrine values are significantly lower in women. There is no significant association between age and metanephrine values, while the association between age and normetanephrine values is positive and significant, but very weak.

Conclusion
Higher values of metanephrine are associated with males and higher values of normetanephrine are associated with older age. Adrenal incidentalomas and pheochromocytoma-indicating symptoms are very common in the general population, while the incidence of pheochromocytoma is extremely rare. Given the risk of missing a diagnosis, it is important to know the indications for biochemical testing to make a timely diagnosis and prevent complications.

Keywords: adrenal gland; catecholamines; hypertension; paraganglioma; pheochromocytoma

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EP12
QTE interval in patients with pheochromocytoma and paraganglioma
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Objectives
Prolonged QTE interval is a known risk factor for developing ventricular tachycard/arrhythmias. QTE prolongation is often reported in patients with pheochromocytoma, however the literature data on this issue are rather heterogeneous. Here we report the results of QTE measurement in patients with pheochromocytoma and paraganglioma (PPGL) in comparison to hormonally inactive benign adrenal tumors.

Introduction
Prolonged QTE interval is a known risk factor for developing ventricular tachycardia/arrhythmias. QTE prolongation is often reported in patients with pheochromocytoma, however the literature data on this issue are rather heterogeneous. Here we report the results of QTE measurement in patients with pheochromocytoma and paraganglioma (PPGL) in comparison to hormonally inactive benign adrenal tumors.

EP10
A case of ChAdOx1 vaccine-induced thrombocytopaenia and thrombosis syndrome leading to bilateral adenal haemorrhage and adrenal insufficiency
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Introduction
Vaccine-induced thrombosis and thrombocytopenia (VITT) after vaccination against SARS-CoV-2 with the adenoviral vector-based vaccines ChAdOx1 and Ad26.COV2.S has been associated with adrenal pathology, such as bilateral adrenal vein thrombosis, adrenal cortex haemorrhage and adrenal insufficiency in six percent of patients1. Case report
We report the case of a 23-year-old healthy woman who presented at eight days after ChAdOx1 vaccination with a low platelet count of 43×109/l, raised D Dimer >100 000 ng/ml and multiple lobar and segmental pulmonary emboli, Anti-platelet factor 4 antibodies were detected confirming definite VITT in accordance with the UK diagnostic criteria. At sixteen days post-vaccine, further imaging showed bilateral adenal haemorrhage, non-occlusive splenic vein thrombosis and right ventricular thrombosis. Her cortisol level was <25 nmol/l. She was treated with anticoagulation, plasmaexpansion, immunosuppression and steroid replacement. She had high anti-spike titre and positive anti-nucleocapsid titres for SARS-CoV-2. She developed seizures secondary to posterior reversible encephalopathy, requiring intensive care. After 4 weeks in hospital, she was discharged on warfarin, hydrocortisone and fludrocortisone replacement. Short synacthen tests three and nine months later showed no recovery of adrenal function, although magnetic-resonance-imaging of the adrenal glands showed resolving adrenal haemorrhage. Discussion and conclusions
Adrenal insufficiency secondary to bilateral adrenal vein thrombosis and adrenal cortex haemorrhage should be suspected in patients with vaccine-induced thrombosis and thrombocytopenia (VITT) and treated promptly. Adrenal haemorrhage can occur as the initial presentation of VITT or days to weeks after the development of thrombosis in other sites. Completion of vaccination schedule against SARS-CoV-2 post VITT using an mRNA-based vaccine should be recommended to patients post-VITT, as mRNA-based vaccines have not been associated with VITT. There is paucity of data regarding the potential recovery of adrenal function after bilateral adrenal haemorrhage in the context of VITT and thus more studies are needed to inform clinical practice. The need for disease registries for rare conditions, such as VITT, is crucial as direct communication and sharing of information by clinicians might enable quicker identification of disease patterns than would have been possible via established reporting tools of adverse events. Reference

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EP12
QTE interval in patients with pheochromocytoma and paraganglioma
Dina Rebrova1, Elisey Fedorov1, Igor Chinchuk1, Vladimir Rusakov1, Leonid Kraštov1, Ilya Sleptsov1, Roman Chernikov1, Ilya Sablin1, Natalya Vorokhobina1, Sergej Fug1, Ilya Shcherbaykov1, Shamil Shihmagomedov1, Ekaterina Zgoda1 & Arseny Semenov1,2
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Objectives
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Introduction
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EP13

A challenging case of hypertension: an ACTH-secreting pheochromocytoma

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Pheochromocytoma is a rare catecholamine-secreting tumour arising from chromaffin cells in the adrenal medulla and one of the main causes of endocrine hypertension. We here report the case of a 48-year-old man admitted to the Internal Medicine Department for evaluation of resistant hypertension. The patient presented with headache, sweating, palpitations, pitting edema, hypertension and hypokalemia both resistant to conventional polytherapy. He was therefore investigated for endocrine causes of hypertension with evidence of urinary metanephrines above the upper reference limit. Besides, an abdominal CT scan showed a left adrenal mass highly suspicious for pheochromocytoma. Calcium and PTH levels were within the normal range. Further investigations showed high ACTH and blood cortisol levels. The latter remained unsuppressed after low-dose and high-dose dexamethasone suppression tests (1289 μg/l and 1302 μg/l, respectively). To rule out Cushing’s disease, a pituitary MRI was performed, without evidence of sellar abnormalities. All other anterior pituitary hormone levels were within the normal range, except for biochemical central hypothyroidism. The severe Cushing syndrome associated with hypokalemia along with the very high ACTH level (319 ng/ml, normal values 7–63 ng/ml) supported an ectopic source of ACTH. A total body CT scan confirmed only the adrenal mass. The patient was referred to the Endocrine Unit, where the diagnosis of an ACTH-secreting pheochromocytoma was confirmed by imaging and biochemical findings. The patient was treated with metyrapone 250 mg every six hours and thyroxine replacement were initiated to control hypercortisolism and hypothyroidism. The patient is now asymptomatic, with no evidence of recurrence.

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EP14

Adrenal sarcomas – Exceptionally rare or more common than thought?

Prevalence in adrenocortical specimens over 12 months period and presenting features.

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Adrenal/periadrenal sarcomas are very rare entity of adrenal tumours. An epidemiological study of primary adrenal cancers found prevalence of adrenal sarcoma of 1.3% compared to adrenocortical carcinoma (ACC) 43.8%, neuroblastoma 39.7%, pheochromocytoma 10.9% and non-Hodgkin’s lymphoma 4.3% (1). In 2021, 26 adrenocortical cancers were performed in our institution. 12/26 had malignant histology, 9/26 lesions were > 6 cm, 7/9 lesions > 6 cm were malignant (2 adrenal sarcomas, 2 ACC, 2 infiltrative renal cancer, 1 metastatic melanoma). Adrenal sarcoma was detected in 2/26 adrenocortical specimens. We present two cases of adrenal sarcoma detected over 12-month period in University Hospital Southampton, United Kingdom. Case 1: 35-year-old woman presented with right abdominal pain for over one year. Ultrasound showed right suprarenal mass. CT CAP and adrenal MRI confirmed large tumour 4.9×6.1×5.7 cm adjacent to or arising from right adrenal gland and invaded IVC. Patient underwent open adrenalectomy and post-operatively her pain resolved. Histology revealed high grade leiomyosarcoma (pT2 N0 G3) adjacent to adrenal with narrow excision margin. Patient opted against adjuvant chemotherapy and remains under surveillance. Imaging 8 months post-op showed no evidence of recurrence. Case 2: 70-year-old man presented with two months history of left flank and back pain, weight loss, and elevated CRP (159 mg/l). CT detected suspicious 7.8 cm heterogeneous left adrenal mass extending to splenic hilum. Metanephrines, lymphoma screen, normal, 1 mg ODST-raised (72 nmol/l). Patient underwent open adrenalectomy, splenectomy and wedge excision of the liver due to intraoperative findings of liver metastases. Histology confirmed high grade epitheloid angiosarcoma. Restaging CT post-op showed lung, liver metastases and local recurrence in resection bed. He commenced palliative pacitaxel chemotherapy, with good radiological response. Adrenal sarcomas should be considered in any age in differential diagnosis of indeterminate adrenal masses especially when > 6 cm, associated with ipsilateral pain and raised CRP. 1 mg ODST can be raised due to raised metabolic rate associated with high-grade malignancy. The duration of symptoms could range from few weeks to 12 months. In our second case with metastatic disease, surgical debulking of primary tumour provided significant pain relief and increased patient’s quality of live and prognosis. Both patients are alive at the time of writing.

Reference

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EP15

Don’t break my heart: sparing the knife in SDHB mutated cardiac paraganglioma treated with cabozantinib

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Introduction
Cardiac paragangliomas are rare endocrine neoplasms. Surgical resection is first line treatment. Here, we describe a case of cardiac paraganglioma where surgical resection was aborted due to involvement of important cardiac structures. Systemic therapy was instead pursued with tyrosine kinase inhibitor cabozantinib.

Case
A 64-year-old man with a past medical history significant for tobacco use and poorly controlled type 2 diabetes mellitus presented with chest pain, several months of progressive fatigue and 15 pound unintentional weight loss. Echocardiogram revealed a 6.9 × 5.8 × 4.9 cm right-sided cardiac mass. Biopsy was performed demonstrating cytology consistent with paraganglioma. Laboratory studies revealed chromogranin A 1.038 mg/ml (normal <0.93 mg/ml), plasma normetanephrine 1.87 nmol/l (0.80-8.99 nmol/l) and plasma metanephrine 0.14 nmol/l (0.0-0.49 nmol/l). Ga-68 DOTATATE Positron Emission Tomography/Computed Tomography (PET/CT) scan revealed DOTATATE avidity within the region of the cardiac mass. No additional lesions or metastatic foci were identified. Next-generation sequencing performed on the tissue biopsy demonstrated a SDHB mutation (H244D) at a variant allele frequency of 62.2%. Surgical resection was attempted and aborted due to the paraganglioma encasing the right coronary artery and the tricuspid valve. Systemic therapy was initiated with tyrosine kinase inhibitor cabozantinib. Dose reduction was required due to development of palmar-plantar erythrodysesthesia. Subsequent surveillance Ga-68 DOTATATE PET/CT scan revealed partial response to treatment at two months with increasing central photopenia of the cardiac mass from 94 standardized uptake value (SUV) to 54 SUV. The patient had biochemical response with decreasing chromogranin A and norepinephrine levels.

Conclusion
Treatment of cardiac paraganglioma ideally consists of local resection, however this is not always possible due to involvement of critical structures of the heart. Systemic therapy for paragangliomas is largely based on small, retrospective studies. Our case illustrates an unresectable cardiac paraganglioma with response to cabozantinib as evidenced by radiologic and biochemical data.

EP17
Associated factors with metabolic syndrome in elderly patients harboring adrenal incidentaloma: A comparative study
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Background and Aims
Numerous studies have suggested that metabolic syndrome (MetS) is related to adrenal incidentaloma (AI) in young adults. Limited data about MetS in geriatric patients diagnosed with AI are available, despite the high incidence of this adrenal disease in the elderly. This study aims to assess the prevalence of MetS and its associated factors in aged patients harboring AI. Patients and Methods
We conducted a retrospective, comparative, and analytical study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from 2011 to 2020. MetS was diagnosed based on the National Cholesterol Education Program’s Adult Treatment Panel III (ATP III) criteria. We compared two groups: [MetS+]: elderly subjects with MetS (n=17) vs [MetS−]: elderly subjects without MetS (n=52).

Results
There was no significant age difference between both groups ([MetS+]:72.1 vs [MetS−]:71.0 years old; P=0.82). Female gender was significantly associated with MetS ([MetS+] 82.4% vs [MetS−] 39.1%; P=0.006). Patients bearing bilateral AI were significantly more affected by MetS ([MetS+] 58.8% vs [MetS−]: 45.3%; P=0.000) compared to those having unilateral AI. Smaller incidentaloma size seems to aggravate substantially the risk of developing MetS in the elderly (incidentaloma size in [MetS+]:21.0 vs [MetS−]:26.7 mm; P=0.009). Both groups had similar electrolyte profile except higher phosphatemia which was statistically linked to the presence of MetS ([MetS+] 1.30 vs [MetS−]:1.096 mmol/l; P=0.018). We noted no significant correlation between hormonal hypersecretion and MetS in older adults, since there was a comparable distribution of functioning (MetS+[+46.7% vs [MetS−]:40.0%) and nonfunctioning AI([MetS+]:53.3% vs [MetS−] 60%; P=0.693) in the two groups. Conclusion
AI is associated with a higher cardiometabolic risk. This risk seems to increase in advanced age. Metabolic abnormalities are classically attributed to hormonal hypersecretion, especially in Cushing’s syndrome. However, several studies have recently proven that insulin resistance and metabolic dysregulation also occur in nonfunctioning AI. Our results suggest that bilateral and smaller AI may worsen the risk of metabolic disturbances in geriatric patients, regardless of their secreting profile. Further research is needed to elucidate this hypothesis.

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EP16 Optimization of familial hypercholesterolemia diagnosis through LDL cholesterol correction formula for lipoprotein(a) levels
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Introduction
For the clinical diagnosis of heterozygous familial hypercholesterolemia (HeFH) validated algorithms are used, with the Dutch Lipid Clinic Network (DLCN) Criteria being the most recommended in our environment. One of the items that scores for the system proposed by the DLCN is the value of LDL cholesterol. However, LDLc levels can be distorted by lipoprotein a (Lp(a)) levels. Criteria being the most recommended in our environment. One of the items that scores for the system proposed by the DLCN is the value of LDL cholesterol.

Methods
Observational, retrospective, cross-sectional, and analytical study in a cohort of 91 patients with clinical diagnostic criteria for probable or defined familial hypercholesterolemia according to the DLCN criteria, followed in our Lipid Unit at Lozano Blesa University Clinical Hospital, from 1 May 2019 to 31 December 2020. The DLCN criteria have been calculated based on LDLc values, and LDLc corrected for Lp(a) [according to the corrected LDLc formula = LDLc – 0.30*Lp(a)] in all the statistical test performed, significant values of P<0.05 were considered. Several ROC (Receiver Operating Characteristic) curves have been generated between the initial LDLc and that LDLc corrected by Lp(a) values to predict the presence of genetic mutation. Corresponding cross tables have been made between LDLc (initial and corrected) and genetic mutation; as well as between the DLCN score (obtained with uncorrected LDLc) and genetic mutation.

Results
We included 91 patients (51.65% women, mean age at diagnosis 48.80±12.96 years, 43.95% of them did not present mutation in the genetic study for HeFH). Lp(a) in subjects with no known mutation was 24.70 ± 86.10 mg/dl compared to 22.50 ± 60.35 mg/dl in patients with known mutation. The area under the ROC curve of the LDLc variable and the presence of mutation in the genetic test was higher in the case of LDLc corrected by Lp(a) (AUC=0.639, P=0.038) than in the uncorrected LDLc (AUC=0.623, P=0.065). This improves the specificity of the LDLc variable to predict genetic mutation if used corrected by Lp(a): 70% versus 62.74% if used uncorrected. When using the LDLc corrected by Lp(a) for the calculation of the DLCN score, 66.66% of the patients were reclassified from probable diagnostic group to a possible diagnosis, without presenting 56.26% of them a known genetic mutation.

Conclusions
The use of adjustment of LDL cholesterol levels according to Lp(a) levels in the diagnosis of HeFH facilitates a more specific diagnosis than with the use of unadjusted LDLc.

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EP18 Cardiovascular risk factors in mild adrenal autonomous cortisol secretion in a Caucasian population
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**Background**

Cardiovascular (CVS) risk factors could be present in patients with mild adrenal autonomous cortisol secretion (MACS), which could account for up to 50% of patients with adrenal adenomas. However, the most frequent CVS risk factors in MACS have not been established.

**Objective**

The aim of the present study was to analyse the difference in CVS risk factors in patients with MACS in comparison to those with non-functioning adrenal tumour (NFAT).

**Materials and Methods**

A total of 295 patients with adrenal incidentaloma who were hospitalised in the single-center between 2017 and 2019 were included in this retrospective study. All patients underwent a 1 mg overnight dexamethasone suppression test (DST). We divided our group into those who showed suppression in the DST (NFAT) and those who did not show suppression in the DST (MACS). In the studied groups, we analysed the presence of CVS risk factors, such as obesity, prediabetes (PD), type 2 diabetes mellitus (T2DM), hypertension, hyperlipidaemia, and chronic kidney disease.

**Results**

In our study, 18.9% of patients were defined as MACS, and the remaining 80.1% of patients were defined as NFAT. In the group with MACS, we observed obesity in 33.9%, whereas in NFAT, the prevalence of obesity was 34.7% (P = 0.9). Hypertension was diagnosed in 78.5% of MACS vs. 69.5% of NFAT (P = 0.2), whereas chronic kidney disease was observed in 32.1% of MACS vs. 28.5% of NFAT (P = 0.7). Accordingly, we did not find differences in the diagnosis of prediabetes in MACS vs. NFAT (26.8% vs. 34.3% (P = 0.35)). Importantly, T2DM was diagnosed in 41% of MACS vs. 23% of NFAT (P < 0.01). Interestingly, we observed a higher frequency of occurrence of hyperlipidaemia in NFAT (72.4%) vs. MACS (53.6%) (P = 0.01). Accordingly, in patients without T2DM, MACS was observed in 15.2%, in comparison to 29.5% in patients with T2DM (P < 0.01).

**Conclusions**

In our retrospective analyses, we found that T2DM is more prevalent in MACS than in NFAT, whereas hyperlipidaemia is more prevalent in NFAT. Accordingly, no differences were observed in the incidence of obesity, hypertension, prediabetes, or kidney damage in NFAT and MACS patients. This could suggest that mild hypercortisoilaemia is not associated with a higher CVS risk in comparison to NFAT.

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**EP20**

**Adrenal hemangiom with subclinical cushing's syndrome**

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**Introduction**

Adrenal cavernous hemangiomia is a rare tumor with few cases reported in the world. Usually this adrenal masses are incidentally discovered and non functional.

**Case report**

We describe the case of a 63 year old male patient with a history of hypertension and treated prostate. He was referred to our endocrinology department with complaints of his left lower back. At the admission the BMI was 21 kg/m², his blood pressure was 160/90 mmHg and the heart rate was 84 beats /min. In the clinical examination there were no clinical signs of hypercortisolism or catecholamine or mineralocorticoid excess. The abdominal enhanced C T showed a left large heterogeneous adrenal tumor of 50 mm with hemorrhage, necrosis and calcification, the C T value of solid part was 30 UH. The laboratory evaluation revealed a morning cortisol level of 179 µmol/l after a 1 mg overnight dexamethasone suppression test and a low ACTH concentration. The plasma metanephrine, normetanephrine, aldosterone level and renine activity were normal. All these features make it difficult to distinguish from a primary adrenal cortical carcinoma and then required operative management. An adrenalectomy was performed and the tumor was safely completely resected with no evidence for local invasion. The results of pathological examinations were in favor of a cavernous hemangiomia of the left adrenal gland.

**Conclusion**

Adrenal cavernous hemangioma is a rare tumor that can have a very large size, and it is difficult to differentiate from adrenal cortical carcinoma clinically or radiologically.

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**EP21**

**Metabolic and cardiovascular consequences of hormone replacement by hydrocortisone in adrenal insufficiency**

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**Introduction**

During adrenal insufficiency (AI), glucocorticoid treatment is supposed to be neutral on the metabolic parameters of patients. However, recent data from the literature report that this corticosteroid replacement therapy increases the metabolic risk. The aim of our work was to determine the metabolic and cardiovascular impact of hydrocortisone (HC) replacement therapy during peripheral AI.

**Patients and methods**

This was a descriptive and analytical study involving 77 patients with peripheral AI (66 women and 11 men), all treated with HC. For each patient, we determined the length of the disease, the duration of the follow-up, the daily and cumulative dose of HC, the evolution of metabolic parameters (weight, blood pressure, glycemia, lipid parameters), and the Framingham score under HC.

**Results**

The mean age was 40.5 years (range: 22-63 years). The mean duration of evolution was 7.7 years. The study of metabolic and cardiovascular parameters after treatment with hydrocortisone showed weight gain in 96.1% of patients (overweight: 46.73% and obese: 40.25%). We noted that 41.5% of patients had developed hypertension, 54.54% had pre-diabetes, 37.66% had diabetes mellitus, 52% had dyslipidemia. We noted a significant positive relationship between daily HC dose and the development of obesity (P < 10^-4), hypertension (P = 0.003), diabetes mellitus (PP = 0.025) and dyslipidemia (P = 0.004), respectively. We found a significantly positive relationship between, on the one hand, disease duration, cumulative HC dose and, on the other hand, obesity (P = 0.05), hypertension (P = 10^-4), and glycemic homeostasis disorders.

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Introduction

Aldosterone synthase participates in the key reactions of aldosterone synthesis – 11-hydroxylation, 18-hydroxylation and, finally, 18-oxidation. In recent works devoted to evaluating the effectiveness of hybrid steroids in the differential diagnosis of subtypes of primary aldosteronism (PA), it is worth emphasizing the experience of using high-performance liquid chromatography – tandem mass spectrometry (HPLC-MS/MS), which allows detecting even very low concentrations in peripheral plasma (the lower limit for 18-oxocortisol is 0.25 ng/dl).

Objective

To evaluate differences in the synthesis of steroid end products by HPLC-MS/MS in the differential diagnosis of various forms of PA has been proved.

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EP24

Complex adjuvant treatment of patients with two-component adrenocortical cancer (clinical case)

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Adrenocortical cancer (ACC) is a tumor of the adrenal cortex, clinical manifestations, recurrence, and progression potential are determined by its biological characteristics. Morphological diagnosis of tumors of the adrenal glands in some cases presents significant difficulties. According to the WHO classification of tumors of the endocrine organs (4th revision, 2017), in addition to the classical one, myxoid, sarcomatoid and oncocytic histological variants of ACC are distinguished. According to a number of studies, the oncocytic variant is characterized by a less aggressive clinical course. In our work, we present a clinical case of combined treatment of two-component hormonally active (hypercorticism and virilization) adrenocortical carcinoma. After radical surgical treatment, pathological examination was verified a polyclonal adrenocortical carcinoma, represented by two components different in cellular composition and architecture. Most of the tumor is of classical structure (Weiss score 4), the second component is an oncocytic variant of ACC (2 major and 2 minor Lin-Weiss-Bisciglia criteria). An immunohistochemical (IHC) study of the oncocytic component of tumor revealed expression of subtype somatostatin 2 receptors (SSTR2), Ki67 index was 21%. There was no expression SSTR2 in classical component, the Ki67 proliferation index was 10%. Chromogranin A expression was absent in both tumor components. Invasion of periadrenal adipose tissue, Ki67 10% or more in both tumor components, positive expression of SSTR2 served as the basis for starting adjuvant drug treatment with mitotane in combination with long-acting somatostatin analogs. There was no progression of
the disease during 30 months of patient monitoring. To date, mitotane remains the only drug for the treatment of ACC with proven efficacy. A number of targeted drugs interacting with specific tumor receptors have been proposed, but their use is limited by low efficiency. Recently, reports have been published on the expression of SSTR in tumor tissue, as well as on the effect of synthetic somatostatin analogs on the growth of ACC cell lines. A feature of this clinical case is the development of polycythaemia vera with different functional activity, histostucture, proliferation index and receptor status of its components, which suggests a different malignant potential of tumor components and emphasizes the need for accurate morphological verification of adrenocortical tumors for individualization of treatment. The progression-free period more than 30 months after radical surgical treatment gives grounds for the use of somatostatin analogs in the drug treatment of ACC, but its effectiveness requires further study and evaluation.

EP25

Acute adrenal crisis following COVID-19 in a patient with 11β-hydroxylase deficiency
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Introduction
11-Beta-hydroxylase deficiency (11β-OHD) is the second most common cause of congenital adrenal hyperplasia. It leads to the accumulation of steroidal precursors prior to the enzyme defect, notably 11-deoxycorticosterone (DOC), leading therefore to low renin hypertension and hypokalemia. Hence, patients with 11β-OHD are reportedly protected from adrenal crisis. Here, we report a case of a male with 11β-OHD presenting with acute adrenal insufficiency.

Observation
A 40-year-old male, following in our department for congenital adrenal hyperplasia due to 11β-OHD, was admitted for abdominal pain and vomiting. He had also headaches, chills without shortness of breath, that started one day before his admission leading to the diagnosis of Covid-19 infection. The patient was receiving glucocorticoid replacement therapy (hydrocortisone 30 mg b.i.d.) with good compliance. On examination, he had a blood pressure of 120/70 mmHg despite discontinuation of antihypertensive treatments (Calcium channel blocker, Beta-blocker and spironolactone). His heart rate was 114 bpm and his blood oxygen saturation rate was 95%. Laboratory analysis showed normal serum potassium level of 4.2 mmol/l, functional acute kidney failure and elevated C-reactive protein of 49 mg/l. The patient received hydrocortisone hemisuccinate 200 mg the first day with an improvement of his symptoms.

Discussion
Acute adrenal crisis is exceptional in patients with 11β-OHD. The diagnosis in our case was based on abdominal pain, vomiting, the abnormally normal blood pressure and serum potassium level, and the favorable progression after hydrocortisone hemisuccinate. It was hypothesized that regular treatment with hydrocortisone in these patients will suppress ACTH secretion and leads to a reduced accumulation of steroids precursors that may expose them to the risk of developing acute adrenal crisis in case of hydrocortisone therapy interruption or in the absence of doses adjustment in stressful conditions.

Conclusion
Myxoid adrenocortical adenoma with pseudo glandular pattern may suggest adrenocortical metastasis or pheochromistoma by adrenal imaging method. Immunohistochemical markers are very useful in differential diagnosis. References

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EP26

A rare cause of a surrenal mass
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Introduction
Malignant adrenocortical adenoma was described by Brown et al. in 2000 (1). Myxoid adrenal cortical adenoma with pseudo glandular structure is a particular histological variant and is extremely rare. Accurate diagnosis is based on the combined evaluation of clinical features, adrenal imaging, and pathological features. Immunohistochemical studies (cytokeratin, melan-A, USP10, chromogranin, vimentin) can distinguish adrenocortical adenoma from other retroperitoneal myxoid tumors (2).

Case
A 43-year-old male patient uses a bi-level positive airway pressure device for known obstructive sleep apnea syndrome. The patient described occasional high blood pressure had left flank pain in the last 15 days. No pathology was detected in the urinalysis performed by the urology and in the abdominal X-ray. Contrast-enhanced upper abdomen computed tomography was then performed on the patient. In his report, it was seen that there was a 29 x 27 mm mass lesion in the left adrenal gland with intense contrast enhancement in the arterial and venous phases. In the 1 mg dexamethasone suppression test performed by us, aldosterone, renin, adrenaline, noradrenaline, dopamine, metanephrine and normetanephrine levels were within the normal range. Dexamethasone treatment was given to the patient who described occasional blood pressure attacks. The patient underwent laparoscopic left adrenalectomy two weeks later. No complications developed. Histopathological study showed that the mass was a myxoid adrenocortical adenoma with a pseudo glandular pattern. Immunochemical, vimentin, CD56, melan-A, CK8 were diffusely positive, while inhibin was focally positive. No immunoreactivity was found in cytokeratin 7, S-100, calretinin, synaptophysin, chromogranin A, TTF1, CK7, napsin, mesothelin, WT-1, PanCK, CD99. The patient has been followed for 15 months after laparoscopic adrenalectomy. No pathology was detected in the control adrenal hormone profile and control computed tomography. Blood pressure is regulated.

Conclusion
Myxoid adrenocortical adenoma with pseudo glandular pattern may suggest adrenocortical metastasis or pheochromistoma by adrenal imaging method. Immunohistochemical markers are very useful in differential diagnosis. References

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EP28
Addison disease masquerading as hyperemesis gravidarum and good fetal outcome.
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Here we report the case of a woman with first presentation of Addison disease in pregnancy that went undiagnosed until postpartum period. She gave birth to a healthy child by vaginal delivery at 40 weeks of pregnancy. Our patient is a 31 years pregnant woman with unremarkable medical or familiar history. At 8 weeks of pregnancy she was complaining of nausea, vomiting, loss of appetite and fatigue, leading to hospitalization. The physical examination revealed a blood pressure of 80/50 mmHg, a check-up that included blood and urine analyses did not reveal any abnormalities. She received treatment with saline and glucose perfusion, vitamin B and was discharged after one week, with persistent symptoms attributed to hyperemesis gravidarum. At 16 weeks of gestation the patient noticed a bronze appearance of the skin. Her condition was deteriorating, with accentuation of fatigue and 9 kg weight loss, leading to another 2 hospitalizations due to presumed hyperemesis gravidum. Nevertheless at 40 weeks of gestation she gave birth to a healthy child by vaginal delivery; 2 months later she was hospitalized in the endocrinology department due to extreme fatigue and persistent gastrointestinal symptoms. At admission the patient’s blood pressure was 85/55 mmHg, pulse – 88 beats/minute and respiratory rate – 20 breaths/minute. She had tanned skin and hyperpigmented spots on gums, tongue and along the crease of cheeks. Laboratory data showed: ACTH 1006 (0-46 nmol/l), cortisol 2.41 (69-690 nmol/l). A diagnosis of primary adrenal insufficiency was established and intravenous hydrocortisone hemisuccinate was initiated. Thereafter, the patient was transferred to oral cortisol, and discharged on the 5th day. Currently the patient is in good condition, taking tablets of Cortisone 25 mg at 0800 h and 12.5 mg at 1200 h, and is breastfeeding.

Discussion
Addison disease (AD) is a rare condition, usually due to autoimmune destruction of the adrenal cortex. Addison disease complicating pregnancy is even rarer, about 100 pregnancies being reported worldwide. Untreated Addison disease during pregnancy leads to increased maternal mortality and fetal growth retardation. Nausea and vomiting due to adrenal insufficiency may be confused with typical symptoms of pregnancy. Generalized hyperpigmentation – a hallmark of Addison disease may be seen in normal pregnancy, but dark spots on lips and mouth mucosa should prompt adrenal insufficiency evaluation.

Conclusion
First diagnosis of Addison disease during pregnancy may be challenging due to misleading symptoms attributed to normal pregnancy. Differential diagnosis of severe and prolonged hyperemesis gravidarum should include adrenal insufficiency.

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EP30
Rare case of SIADH related hyponatremia in sarcoidosis
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Disorders of sodium metabolism in sarcoidosis are predominated by diabetes insipidus; SIADH is extremely rare, restricted to sporadic case reports. We present the case of a 68 year old South Asian female presenting with a 3 year history of chronic, mild hyponatraemia, which was asymptomatic apart from mild lethargic Presentation. She had a history of stable sarcoidosis that was not requiring treatment, based on lung pathology. Despite fluid restriction, serum sodium remained around 128 mmol/l; serum osmolality was 263 mOsm/kg, urine osmolality 296 mOsm/kg, and urine sodium 76 mmol/l. TSH was normal, 3.52 mIU/l. A Short synacthen test was normal: baseline serum cortisol of 497 mmol/l, rising at 30 mins to 809 and at 60 mins to 1002. IGF-1 and HbA1c were normal. Serum ACE was raised, 82 U/L. CT Chest/Abdomen/Pelvis revealed two calcified paratracheal lymph nodes and stable apical thickening in both lungs, with slightly more marked subpleural reticulation in right upper lobe of lung. An MRI scan of the brain showed no gross pituitary pathology. The patient was managed with oral slow-sodium 2 tabs bd and furosemide 20 mg od. In light of the hyponatraemia, active management of the sarcoidosis was reconsidered in case of neurosarcoidosis and for this, an MRI scan of the brain with the use of gadolinium needs to be undertaken first.

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EP31
Spontaneous haemorrhage of an adrenal angiomylipoma: case report
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Introduction
Angiomyolipomas are rare mesenchymal tumours arising from the perivascular epithelioid cells. They are benign endocrinologically inactive tumours with a histological structure consisting of variable amounts of adipose, thick-walled blood vessels and smooth muscle cells. Commonly, angiomyolipomas occur in the kidney with few extra renal case reports in adrenals.

Case Report
We report the case of a 76-year-old-man with personal history of hypertension and hypercholesterolemia, who presents as an incidental finding on ultrasound performed by urology due to an episode of acute urine retention, a 91 mm right kidney with few extra renal case reports in adrenals.

Case presentation
An 85 years-old female patient was admitted to our endocrinology department for exploration of adrenal incidentaloma. She was followed for hypothyroidism and hypertension for 10 years now. The mass was discovered at an abdominal CT scan when the patient developed vomiting and abdominal pain. The mass was a heterogeneous 65 mm tumor of the left adrenal gland, with a spontaneous density of 55 UH and was in contact to the left renal vein. Biological explorations confirmed the presence of a pheochromocytoma with an elevated level of metanephrines and normetanephrines (5-fold the normal range). Treatment with doxazosin was administered for 2 weeks in preparation for surgery. A left adrenalectomy was performed without incidents. Histologically, the tumor was confirmed to be a benign pheochromocytoma. The follow-up showed a complete remission with a normal blood pressure and a normal level of plasma metanephrine.

Conclusion
Management of pheochromocytoma is delicate in the elderly population, giving the comorbidities associated. Thus, surgical removal should be made by an experienced multidisciplinary team to avoid post-operative complications. Multicentric preparation for surgery should be made with a particular attention on maintaining balance between the adrenal disease and comorbidities.

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EP29
Pheochromocytoma in the elderly: treatment challenges
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Introduction
Pheochromocytoma is a rare neuroendocrine tumor with a prevalence ranging from 0.05% to 0.1%. Those tumors are usually diagnosed in young adults. However, they can also affect children and the elderly, with sporadic cases being more common in older patients. Giving the recent increases in life expectancy and improvements in imaging techniques, there has been an increase in the number of pheochromocytoma in the elderly.

Case presentation
An 85 years-old female patient was admitted to our endocrinology department for exploration of adrenal incidentaloma. She was followed for hypothyroidism and hypertension for 10 years now. The mass was discovered at an abdominal CT scan when the patient developed vomiting and abdominal pain. The mass was a heterogeneous 65 mm tumor of the left adrenal gland, with a spontaneous density of 55 UH and was in contact to the left renal vein. Biological explorations confirmed the presence of a pheochromocytoma with an elevated level of metanephrines and normetanephrines (5-fold the normal range). Treatment with doxazosin was administered for 2 weeks in preparation for surgery. A left adrenalectomy was performed without incidents. Histologically, the tumor was confirmed to be a benign pheochromocytoma. The follow-up showed a complete remission with a normal blood pressure and a normal level of plasma metanephrine.

Conclusion
Management of pheochromocytoma is delicate in the elderly population, giving the comorbidities associated. Thus, surgical removal should be made by an experienced multidisciplinary team to avoid post-operative complications. Multicentric preparation for surgery should be made with a particular attention on maintaining balance between the adrenal disease and comorbidities.

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previously reported cases of adrenal angiomylipoma. Of these, 15 were sporadic and 3 were reported in patients with tuberous sclerosis or lymphangiomyomatosis. There were 2 reported cases of spontaneous haemorrhage. Management of spontaneous haemorrhage in an adrenal angiomylipoma was guided by the limited number of case reports in the literature. It is general consensus that smaller lesions detected incidentally should be managed non-surgically and their size should be kept under surveillance. Surgical management has been proposed for lesions which are either symptomatic and/or greater than 5 cm. Laparoscopic adrenalectomy has successfully been used, but larger lesions are best removed using open adrenalectomy. Conclusion Adrenal angiomylipomas are rare benign tumours that have the ability to reach a large size and potential to bleed. Here we report the 3rd case reported on literature of spontaneous haemorrhage in an adrenal angiomylipoma, which was successfully treated with open adrenalectomy.

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EP32
Interference in aldosterone assay revealed by hemolysis.
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We report an interference in an immunoassay for aldosterone, which potentially could have led to a wrongful diagnosis and unnecessary surgery. The interference was serendipitously recognized due to a preanalytical error. A 59-year-old female patient with hypertension was referred to the department of endocrinology after an adrenal incidentaloma was detected. Because of her hypertensive history, screening for primary hyperaldosteronism was performed. An elevated aldosterone and a raised aldosterone/renin ratio was measured. To confirm the diagnosis of primary hyperaldosteronism a saline infusion test was performed. However, Aldosterone could not be reliably measured by our own immunoassay (Liaison XL) due to hemolysis in the sample. After 24 h saline infusion this sample, together with the sample before infusion, was sent to our referral laboratory, where aldosterone was measured by LC–MS/MS. Low concentrations of aldosterone were measured by LC–MS/MS in both samples, rejecting the diagnosis hyperaldosteronism. Strikingly, the basal aldosterone concentration as measured by LC–MS/MS was much lower compared to the concentration as measured by the Liaison XL immunoassay, raising suspicion of an assay interference. Confirmative testing with a repeat sample, using an additional immunoassay (Lumipulse 2100) and a dilution experiment all pointed towards a method specific interference in our own immunoassay. These results showed that the patient did not have primary hyperaldosteronism and that her incidentaloma was hormonally inactive. In retrospect, based on these results dynamic testing was not performed and the patient was treated with antihypertensive drugs. Since in most laboratories aldosteron results from both screening and confirmative tests are derived from the same method, analytical interference in an immunoassay is difficult to detect. This especially holds true if there is a high clinical probability for primary hyperaldosteronism as in this case due to presence of hypertension and the finding of an adrenal incidentaloma. This may also explain the low number of publications on this type of interference in the literature.

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EP33
Large adrenal tumor in paucisymptomatic ACTH – independent Cushing syndrome’s patient – a clinical case
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Background Cushing’s syndrome is represented by the cumulation of signs and symptoms of excess glucocorticoids and has many potential causes. Approximately 20 percent of all cases are represented by ACTH-independent adrenal tumors – with a majority of these being represented by cortisol secreting adrenal adenomas. Generally, a large adrenal tumor has over 5 cm in diameter and the risk of it being malignant raises proportionately with the dimensions. Large adrenal tumors are rare and the management and surgical indication is patient-specific. Case report A 20 years old female presented for weight gain (30 kg in the last 3 years), bradimenorrhea, hirsutism and treatment-resistant acne, referred by a dermatologist. Clinical exam revealed general obesity with little central redistribution, facial and shoulders postural acne, vessel fragility (bruises and hematomas), purple axillary striae and hirsutism (Ferriman score=29). Blood pressure was normal upon multiple examinations. The patient had upper-normal 8000 h cortisol values (19.19 μg/dl) with suppressed 8000 h plasma ACTH (1.05 pg/ml), with low of circadian secretion rhythm (late-night serum cortisol – 15.8 μg/dl) and lack of cortisol suppression both after 1 mg overnight dexamethasone (17.8 μg/dl) and after 2 mg×2 days dexamethasone suppression test (19.7 μg/dl). She also had increased free urinary cortisol levels (324 μg/24 h) and late-night salivary cortisol (19.1 nmol/l). She also had increased androgens (testosterone and androstenedione), with a FAI of 14, with upper-normal values of DHEA-S, without suppression after the dexamethasone dynamic tests. Glucose metabolism was normal, with normal HOMA-IR score. Abdominal MRI was performed, revealing a large left adrenal tumor 6.75/5.6/3 cm and a hypo-plastic right adrenal gland. The diagnosis was ACTH-independent Cushing syndrome due to adrenal tumor secreting cortisol and androgens, with radical-surgery indication. Treatment Taking into account the potential malignancy, the patient underwent open surgery. The histopathological examination revealed an 87/77 cm cortical adrenal adenoma, without any malignancy characteristics. The immunohistochemistry analysis is pending. Follow-up Postoperatively, the patient showed adrenal insufficiency. Five months later, the basal cortisol value was low (0.97 μg/dl) with a slightly raised value of ACTH (56.64 pg/ml). The MRI confirmed total removal of the left adrenal tumor and a slightly smaller right adrenal gland. Conclusion Despite having a large adrenal tumor, our young patient had a paucisymptomatic ACTH – independent Cushing syndrome. Morning cortisol values aren’t enough to exclude hypercortisolism especially in young patients.

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EP34
Single centre experience of assessment of adrenal incidentalomas – it’s time for a change
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Background Adrenal incidentalomas (AIs) refer to adrenal masses discovered on imaging performed for conditions unrelated to suspected adrenal diseases. In an ageing population with improving radiological modalities, the detection of AIs has increased. While most are benign, non-functioning adenomas, some may represent functioning and/or malignant disease including adrenal carcinoma. Investigating AIs can be time-consuming and anxiety-inducing for patients, while under-investigation can result in missing life-threatening diagnoses. Thus, AI investigation pathways should be streamlined to achieve both efficiency and cost-effectiveness. Method A review of management of AIs was conducted in a large, tertiary centre within the United Kingdom. The size and laterality of lesions including attenuation, functional status and multidisciplinary team (MDT) meeting outcomes were assessed. This is an ongoing audit and the full data analysis will be available at the time of presentation. Results A total of 182 patients with AIs were referred between 2019 and 2022. 91 patients were seen in 2021, the data for which is presented below. Discussion Under current hospital guidelines, (based on the European Society of Endocrinology’s 2016 recommendations), all patients with AIs undergo biochemical testing and clinical assessment followed by discussion at the adrenal MDT meeting. Similar to published evidence, our data demonstrates that the majority of AIs are benign and under-investigated (80%). Thus, an investigation pathway should be remodelled to avoid unnecessary clinic appointments. For those with benign, non-functional adenomas, a nurse-led or virtual consultation could be offered. Face-to-face appointments for further examination and treatment should be reserved for those with functioning and/or malignant lesions.
Given the low risk of malignancy or functional lesions amongst AIs and the expected rise in incidence of reported AIs, it’s imperative to optimise current practice and avoid further strain on clinical services.

<table>
<thead>
<tr>
<th>Total patients (2021)</th>
<th>Biochemistry completed and discussed in MDT</th>
<th>Awaiting results and/or MDT outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>91</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td></td>
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Laterality of lesions

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Unilateral</td>
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</tr>
<tr>
<td>Bilateral</td>
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</table>

Diagnosis

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<tr>
<th>Number of patients</th>
<th>Average size of adenoma (mm) %</th>
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<tbody>
<tr>
<td>Non-functioning adenoma</td>
<td>45</td>
</tr>
<tr>
<td>Autonomous adenoma</td>
<td>8</td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>0</td>
</tr>
<tr>
<td>Primary adrenocortical malignancy</td>
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</tr>
<tr>
<td>Metastases</td>
<td>0</td>
</tr>
</tbody>
</table>

Initial imaging modality

<table>
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<tr>
<th>Number of patients</th>
<th>%</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>CT without contrast</td>
<td>5</td>
</tr>
<tr>
<td>MRI</td>
<td>5</td>
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Radiology MDT outcome

<table>
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<th>Number of patients</th>
<th>%</th>
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<tbody>
<tr>
<td>Benign</td>
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<tr>
<td>Indeterminate</td>
<td>6</td>
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<tr>
<td>Malignancy</td>
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</table>

Clinic outcome

<table>
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<th>Number of patients</th>
<th>%</th>
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</thead>
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<td>Discharge</td>
<td>45</td>
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<tr>
<td>Monitor</td>
<td>8</td>
</tr>
<tr>
<td>Treat</td>
<td>0</td>
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</tbody>
</table>


EP36

Evaluation of the efficacy of osilodrostat in five patients with Cushing’s syndrome: A single-center study

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Context
Osilodrostat (Osi), a potent inhibitor of 11b-hydroxylase, blocks the conversion of 11-deoxycortisol to cortisol and improves hypercortisolism in patients with Cushing’s syndrome (CS). Here, we report a study evaluating the efficacy of Osi in five non-Cushing’s disease (CD) CS patients treated with Osi in Japan.

Subjects and Results
Five patients with non-CD CS were treated with Osi at Chiba University [primary disease breakdown: 4/5 patients with adrenal Cushing’s syndrome (cortisol-producing adenoma (CPA): 3, primary macronodular adrenal hyperplasia (PMAH): 1) and 1 with an adrenocorticotropic hormone (ACTH)-producing tumor originating from the thymus]. The mean age was 38.4 years, the male to female ratio was 1:4, and the mean duration of treatment was 3.4 months for the 3 patients who underwent CPA surgery after receiving Osi, 15 months for the patient with an ACTH-producing tumor and 18 months for the patient with PMAH. The maximum dose of Osi ranged from 4 mg/day to 10 mg/day. Three patients had been treated with metyrapone before Osi was administered. The maximum dose of metyrapone ranged from 1000 mg/day to 5000 mg/day. Osi efficiently normalized symptoms and rapidly and persistently lowered urinary 11-deoxycortisol levels in patients with CS due to adrenal or ectopic ACTH. Our findings show that Osi is an effective treatment option and contributes to safely undergoing surgery for CPA patients.


EP35

Carbohydrate metabolism disorders in patients with Addison’s disease

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Introduction
In adults with Addison disease, over glucocorticoid replacement therapy is associated with an increased morbidity and decreased life expectancy, related to low bone mineral density and cardiometabolic outcomes. The aim of our study was to assess the prevalence of carbohydrate metabolism disorders in patients with Addison disease and identify its predictive factors.

Patients and methods
A cross sectional study including 50 patients diagnosed with Addison disease with a mean duration of glucocorticoid replacement of 13.9 years. Biochemical markers of glucose metabolism were evaluated. The prevalence of type 2 diabetes and its complications were analyzed. Patients presenting type 1 diabetes were excluded from our study.

Results
The mean age of patients was 49.5 ± 13.9 years (18–78 years) with significant female predominance and a sex ratio of 0.25. High blood pressure (52%) and diabetes mellitus (52%) were the most common family histories. Mean fasting blood glucose at the diagnosis of Addison disease was 4.6 ± 0.6 mmol/l (3.6–5.4 mmol/l). Mean glycated hemoglobin (HbA1c) was 4.6 ± 0.7% (3.8–5.5%). No patient had prediabetes nor diabetes at the diagnosis. At the time of our study, disorder of carbohydrate metabolism was found in over a third of patients (38%) after a mean duration of Addison disease of 17.5 ± 5.4 years (4–35 years). Among those patients, 31.6% had type 2 diabetes. Diabetic retinopathy occurred in 2 patients and one patient complained of diabetic neuropathy. Daily and cumulative dose were higher in patients with diabetes compared to those with normal blood sugar level (27.5 ± 5 mg/day versus 25.6 ± 6.9 mg/day; 506.2 ± 277.2 mg versus 355.4 ± 282.9 mg) without significant difference. As well, longer Addison disease duration was found in patients presenting diabetes compared to those with a normal glucose tolerance (19.8 ± 9 versus 13.2 ± 8.4 years; P = 0.1).

Conclusion
At the present time, despite of the worldwide availability of replacement therapy in Addison disease, exposure to supraphysiological dose of corticosteroids leads to altered insulin secretion and decreased hepatic and muscular insulin sensitivity, that result in risk exacerbation of carbohydrate metabolism disorders.
**EP37**

Clinical sexual dimorphism in patients with nonfunctioning adrenal incidentaloma

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Introduction

The incidence of adrenal incidentaloma (AI) increases with age. According to epidemiological studies they are more frequent in women than in men.

Aim

The aim was to determine the possible clinical sexual dimorphism in patients with nonfunctional adrenal incidentaloma (NAI).

Patients and methods

This was an observational, cross-sectional study of 381 patients with AI that were functionally assessed in our Clinic. After exclusion of patients with overt adrenal hyperfunction, malignancy, cysts and patients with (possible) autonomous cortisol secretion the studied group consisted of 195 patients with NAI: 129 female and 66 males. Based on average menopause age of 51, we stratified women in two groups: < 51 and ≥ 51. For the sake of comparison, we age-matched the male group, and evaluated differences in body mass index (BMI), adrenal tumor size (ATS), localization, ACTH, 24 h cortisol, 1 mg dexamethasone suppression test cortisol (1 mg DST), and prevalence of hypertension (HTA) and type 2 diabetes mellitus (T2DM).

Results

Female sex was predominant in the whole NAI cohort (F:M%: 66.1/33.8) as well as in both age groups (< 51, 44 patients – F:M%: 61.3/38.7 and ≥ 51, 51 patients – F:M%: 67.5/32.4) with no difference in gender frequency between younger and older patients. There was no difference in age, BMI, ATS, localization, ACTH, 24 h cortisol, 1 mg DST cortisol, HTA and T2DM prevalence between female and male patients. Upon stratification by age, older female patients had significantly higher BMI (P = 0.002), higher 24 h cortisol (P = 0.017) and more prevalent T2DM (P = 0.003) than younger female patients, while HTA was equally prevalent in both female groups. In a linear regression, BMI was the most significant predictor of HTA in premenopausal female patients (β = 0.552, 95%CI R = 0.006–0.102, P = 0.028).

Conclusion

Despite younger age and significantly lower BMI in premenopausal women with NAI, the frequency of HTA was the same as in the menopausal group with BMI being the most significant predictor. Our results add to the body of evidence that female gender plays a role as a cardiometabolic risk factor in NAI patients indicating the existence of clinical sexual dimorphism in patients with NAI.

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**EP39**

Hypertension during pregnancy: A diagnosis that should not be overlooked.

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Farhat Hached University Hospital, Endocrinology, Sousse, Tunisia.

Introduction

Hypertension disorders during pregnancy constitute a significant cause of maternal and perinatal mortality worldwide. Paragangliomas represent a rare cause of hypertension in gestation. The management of these endocrine tumors can be challenging, especially when diagnosed during pregnancy. We describe a case of a paraganglioma discovered in a pregnant woman.

Case report

We report the case of a twenty-seven-year-old female patient who presented to our endocrinology department with gestational diabetes when she was 27 weeks pregnant. At 20 weeks of gestation, she was explored for high blood pressure, and the diagnosis of gestational hypertension was retained and treated with calcium inhibitors. The patient continued to have elevated blood pressure with typical signs of the Menard triad. A pheochromocytoma was then suspected. Plasma metanephrine levels were twelve times above the normal range. Since the patient was pregnant, MIBG scintigraphy could not be practiced. Thoracic and abdominal MRI showed a retroperitoneal and right latero-aortic mass of 3.5 cm. The diagnosis of paraganglioma was established, we treated the patient with alpha-blockers. For her diabetes, she required insulin therapy. Surgical treatment was postponed. She had regular control of her hypertension and diabetes. The obstetrical ultrasound did not show any abnormalities during control. The patient had cesarean delivery at 38 weeks of gestation with a positive outcome.

Conclusion

Paraganglioma represents a rare cause of hypertension during pregnancy. The association between hypertension and diabetes should be alarming, especially during the first weeks of gestation. The early diagnosis of this situation can make its management less complicated.

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**EP40**

Pheochromocytoma with subclinical and adrenocorticotropic hormone-independent Cushing Syndrome

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Introduction

Adrenal incidentaloma prevalence is rising with the advancement of imaging techniques. The hormonal work-up should always include free metanephrines for the diagnosis of a pheochromocytoma and 1 mg overnight dexamethasone suppression test for the diagnosis of autonomous cortisol secretion. These tumors have two distinct embryologic origin and don’t usually coexist, and when they do, it occurs in case of a eutopic adrenocorticotropic hormone (ACTH) production by the pheochromocytoma. We herein describe a pheochromocytoma with an ACTH-independent possible autonomous secretion of cortisol.

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Observation
We report the case of a 57 years old woman, with a history of an insulin-treated type 2 diabetes mellitus, high blood pressure treated with captopril and amlodipine, atrial fibrillation treated with beta-blockers and vitamin K antagonists, referred to our department for an adrenal incidentaloma. It was a left adrenal mass measuring 28*23*32 mm with a spontaneous density of 28HU, an absolute washout of 71% and relative washout of 40%. She didn’t have any clinical sign of pheochromocytoma or Cushing syndrome. On laboratory investigation, she had a glycated hemoglobin of 8.7%, a low potassium level at 3.4 mmol/l and TSH levels at 1.38 µIU/ml. Adrenal hormonal work-up found urinary fractionated metanephrines levels at 364 nmol/creatinine (3*normal) and urinary fractionated normetanephrines levels at 463 nmol/creatinine (1.65*normal) confirming the diagnosis of pheochromocytoma. Cortisol levels after 1 mg overnight dexamethasone suppression test were at 87 nmol/l, confirming a possible autonomous secretion of cortisol with ACTH levels inferior to 5 pg/ml excluding an ectopic secretion of ACTH. Aldosterone and renin levels were assessed and a secondary hyperaldosteronism was discovered with aldosterone levels at 740 pmol/l, renin levels at 53 pg/ml and aldosterone/renin ratio at eight. Sex hormones and steroid precursors were normal. The diagnosis of a corticomedullary mixed tumor of the adrenal gland is suspected in our patient. Complementary work up didn’t find osteoporosis, calcitonin and calcium levels were normal, transthoracic echocardiography concluded to a concentric hypertrophy of the left ventricle. The patient was put under alpha blockers and was referred to surgery.

Conclusion
This case illustrates the presentation of a corticomedullary mixed tumor, which is a rare adrenal tumor presenting as a pheochromocytoma with an ACTH-independent cortisol production. The pre and peri operative management includes the management of a pheochromocytoma and an autonomous cortisol secretion. Confirmation of this diagnosis relies on histology and immunohistochemistry.

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EP41
Papillary stasis edema revealing arterial hypertension in the context of an 11beta-hydroxylase deficiency
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Introduction
11-Hydroxylase deficiency is a rare form of congenital adrenal hyperplasia characterized by glucocorticoid deficiency, hypertension, hypokaliemia and virilization in females. We report a case of congenital adrenal hyperplasia due to 11beta-hydroxylase deficiency revealed by bilateral papilledema in the context of arterial hypertension.

Case report
A 13-year-old patient, with no medical history, presented with complaints of headache, vomiting and bilateral visual blurring. Visual acuity was 10/10 in both eyes. The fundus examination showed bilateral papilledema. Brain magnetic resonance imaging was normal. The blood pressure was at 17/10. Holter monitoring of blood pressure revealed high blood pressure levels. The patient also presented with hirsutism. The etiological assessments concluded with an adrenal enzymatic block caused by 11-hydroxylase deficiency. The patient was successfully treated with glucocorticoids.

Discussion
11beta-hydroxylase deficiency is the second cause after 21-hydroxylase deficiency of congenital adrenal hyperplasia, and accounts for about 5 to 8% of cases. 11beta-hydroxylase deficiency is clinically manifested by a syndrome of hyperandrogenism associated with arterial hypertension found in two out of three patients with this anomaly. In this case, the condition was revealed by bilateral stasis papilledema associated with arterial hypertension. Indeed, papilledema is the clinical expression of various conditions in children. Its management is urgent because vital and visual prognoses can be engaged. Stasis edemas are caused by general conditions, the leader of which is intracranial hypertension, whatever its etiology. A second cause that should not be overlooked is represented by malignant hypertension.

Conclusion
Papilledema in children poses many problems, including diagnostic ones. Its management is urgent because vital and visual prognoses can be engaged. The diagnosis and the treatment can be multidisciplinary involving ophthalmologist, radiologist and neuropediatrician and endocrinologist.

DOI: 10.1530/endoabs.81.EP41

EP42
Giant non-functioning adrenocortical carcinoma – the elephant in the room
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Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence of 0.7–2.0 cases/million habitants/year, often with a dismal prognosis. Patients present with abdominal symptoms or symptoms of hormone excess. However, 15% are diagnosed incidentally. (1) A 59y male was referred with progressive lethargy, weight loss, dyspepsia and abdominal distension over the past 2 years. He was dismissive of ‘the elephant in the room’ and in denial. He was pushed to seek medical attention by his family when abdominal mass and cachexia could no longer be ignored. His weight was 63 kg, BMI 20.2 kg/m². He looked emaciated with no Cushing’s stigmata. There was a large firm mass on the entire left half of his abdomen extending midline. CT chest/abdomen/pelvis showed 23 cm mass arising from the left adrenal gland, heterogeneous with punctate calcification and central necrosis. Mass was hormonally non-functional apart from incomplete cortisol suppression on 1 mg overnight dexamethasone suppression test – 86 nmol/l (< 50).

Results
Normetanephrine 1.67 µmol/24 h (0–3), Urine metanephrine 0.49 µmol/24 h (0–1.40), Urine 3-methoxytyramine 0.75 µmol/24 h (0.57–2.39), DHEA 12.9 µmol/l (1.3–9.8), testosterone 4.8 µmol/l, androstenedione 12.2 µmol/l (2.8–10.5), SHBG 30.9 nmol/l (15–48), TAI 13.9 (34–100), 170HP 2.2 µmol/l, aldosterone/renin ratio 30 pmol/mU.

FDG PET CT showed a large avid necrotic left upper abdominal mass with SUV max 7 inseparable from the left adrenal gland. He underwent an open adrenalectomy. 6.4 kg organised mass with central necrosis was fully excised measuring 37×21×21 cm. Post-operative period was complicated by hypoaemia despite Hydrocortisone cover. Histology showed positive staining for calretinin, inhibin and melan-A. Staining for PAX8, S100, chromogranin was negative. The appearances were consistent with ACC, Weiss Score 5 and ki-67 5.9%. T1, N0, M0, R0. Post-operatively he was very well, off steroids and back at work part-time. He was offered adjuvant mitotane but decided not to receive it. His circumstances were borderline—he did not meet ESMO guidelines for mitotane, although the ESE guidelines would suggest, that it could be considered ‘on a case-by-case basis’.

Conclusion
To our knowledge, this is the largest and the second heaviest ACC ever reported. This case highlights a very wide heterogenicity in ACC behaviour from a very poor prognosis, to a long survival of 20 years. ACC generally has a poor prognosis with a 5-year survival rate of 20–25%.

References

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EP43
Clinical case: adrenal cortical carcinoma
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Introduction
Adrenal cortical carcinoma (ACC) is a rare and aggressive malignancy. Most patients (80%) are asymptomatic at the time of diagnosis. ACC generally has a poor prognosis with a 5-year survival rate of 20–25%.

Case
A 37-year-old man came to the Hospital of Lithuanian University of Health Sciences Kaunas Clinics for general weakness, fatigue, intermittent abdominal pain, and weight loss (~ 10 kg in 9 months). During the abdominal US, the mass in the right adrenal gland was found. Physical examination: no clinical signs of hypercortisolism and no changes in other endocrine systems were observed.
Lipid profile in patients with Addison disease

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Introduction

Long-term glucocorticoid replacement therapy in patients with Addison disease has been linked to an increased cardiovascular risk and consequent mortality. Our objective was to determine the frequency of dyslipidemia in patients with Addison disease and its potential predictive factors.

Patients and methods

This was a cross-sectional study, performed in the department of endocrinology in Hedi Chaker hospital –Sfax–Tunisia. Fifty patients with Addison disease were recruited between March 2020 and July 2021. Lipid profile at time of disease diagnosis and after glucocorticoid replacement was analyzed.

Results

The mean age of our patients was 49.5 ± 13.9 years (18–78 years). The female sex was the most affected with a sex ratio of 4. The disease duration was 13.9 ± 8.7 years on average with extremes between 5 and 35 years. Lipid profile at time of Addison disease diagnosis was normal in 81.5% of patients. For those presenting disturbed lipid balance, there were isolated hypercholesterolemia in two patients, hypertriglyceridemia in one patient and mixed dyslipidemia in 2 patients. At the time of our study, the prevalence of hyperlipidemia was 16% (8 patients), occurring after a mean duration of glucocorticoid replacement therapy of 13.6 years. The alterations in the lipid balance observed were mixed dyslipidemia in 5 patients, isolated hypercholesterolemia in one patient, hypertriglyceridemia in 2 patients and low HDL-cholesterol level in 5 patients. Among those patients, five patients were treated with statins and 2 patients with fibrates. One patient was on hydrocortisone replacement, taking daily 27.4 mg/d replacement therapy. Renin, aldosterone, cortisol (in the background of cortical adenoma pT1 N0 Mx LVI R0. Chest and abdominal CT Osteopenia. MEN1, Beckwith-Wiedemann, and Lynch syndromes were ruled out by genetic tests. Post-operative treatment included Hydrocortisone 20–30 mg/d replacement therapy, and the changes were controlled. At the follow-up, the lipids were within the normal range. The levels of marker CA-125, occasionally controlled, remained normal. The cyst spontaneously disappeared 6 months after having stopped the treatment, and the patient became spontaneously pregnant having an uncomplicated delivery 2 years later.

Conclusion

Our findings highlight the importance of controlling lipid status in patients with Addison disease. Identifying patients at risk of lipid metabolism disorders at the preclinical phase seems imperative to reduce cardiovascular complications of long-term glucocorticoid replacement therapy.

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Ovarian cyst in woman treated with mitotane, side effects not to be ignored

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Introduction

Mitotane is an adrenolytic drug that is used as an adjuvant to treat adrenocortical carcinoma. The side effects of lysodren® are numerous, but some of them are less well known. We report a case of ovarian cyst in a woman of childbearing age. It is a 26-year-old patient treated with Lysodren® for a locoregional recurrence of an adrenal carcinoma stage II of the ENSAT. After 9 months of treatment, the patient presented an amenorrhea, with the appearance of a large ovarian cyst of 50 mm, detected on the follow-up CT scan, which initially led to the suggestion of a recurrence. At presentation, FSH, lutetizing hormone (LH), were within the normal range. The levels of marker CA-125, occasionally controlled, remained normal. The cyst spontaneously disappeared 6 months after having stopped the treatment, and the patient became spontaneously pregnant having an uncomplicated delivery 2 years later.

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Background
Cortisol is an essential steroid hormone released from the adrenal gland. Plasma cortisol levels follow a circadian rhythm under the control of the Hypothalamic–Pituitary–Adrenal axis, reaching peak levels in the morning. Cortisol has long been known to exert immunosuppressive effects and accordingly, glucocorticoids are central in treating inflammatory disease. Cortisol’s propensity to down-regulate certain pro-inflammatory cytokines and upregulate other anti-inflammatory cytokines is well-established. However, there remain gaps in our mechanistic understanding of how cortisol modulates various cytokines. Historically, studies have focussed on a small number of relatively well-established cytokines yet the different contribution of IGF1R and IR in mediating insulin-like growth factor 2 (IGF2) effects in adrenocortical carcinomas

Methods
The patients were recruited at the university hospital of Ludwig-Maximilians-Universität München (Germany) and the Department of Hypertension, Institute of Cardiology, Warsaw (Poland). We analyzed 31 patients (mean age: 42.9 ± 13.2 years, 25 females, 86% HT) with active CS (n = 25) and subclinical CS (n = 6). They were compared with 31 age, sex and BMI matched patients with EHT (mean age: 44.3 ± 12.7 years, 25 females) and 31 age and sex matched HC (mean age: 43.8 ± 12.8 years, 25 females). The following variables were assessed: plasma fibrinogen, permeability (Darcy’s constant, K0), clot lysis time (CLT) and a kinetics profile of thrombin generation i.e. the endogenous thrombin potential (ETP) with the use of a calibrated automated thrombogram. Immunoenzymatic and chromogenic assays were used to determine plasminogen activator inhibitor-1 (PAI-1) and plasma-activated thrombin-activatable fibrinolysis inhibitor (tAFII).

Results
Fibrin clot structure in patients with CS is less dense in comparison to EHT, but comparable to HC (median CLT CS 6.98 [5.53–8.91] vs. EHT 4.68 [3.96–6.11] 10–3 cm3, P = 0.001; CS 6.98 [5.53–8.91] vs. HC 7.89 [7.19–8.36] 10–3 cm3, P = 0.09). Higher density is generally found in patients with higher cardiovascular risk. Fibrin clot structure was most resistant to lysis in EHT (median CLT CS 97.10 [90.0–113.6] vs. EHT 110.5 [95.8–126.3] vs. HC 93.8 [79.2–104.0] min, CS vs. EHT P < 0.0039). Furthermore, CS patients present with a higher ETP as compared to healthy controls, but in EHT this is even more pronounced (median ETP in CS 1753.3 [1370.2–1881.4] vs. EHT 2087.6 [1946.0–2394.4], nM*min, P < 0.001; CS 6.98 [5.53–8.91] vs. HC 7.89 [7.19–8.36] 10–3 cm3, P = 0.09). Proteins inhibiting fibrinolysis such as PAI-I and tAFII are significantly higher in CS than in EHT (mean PAI-1: CS 49.22 ± 26.43 vs. EHT 24.44 ± 23.79 ng/ml, P < 0.001; mean tAFII: CS 131.25 ± 18.66 vs. EHT 95.03 ± 26.59 AG %, P < 0.001).

Conclusion
Despite an overlap of hypertension in CS and EHT, we observe significant differences in fibrin clot structure and fibrinolysis in both entities. Fibrin clot density, CLT and ETP are more altered in EHT than in CS, whereas proteins inhibiting fibrinolysis are higher in CS.

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IR to the biological effects of IGF2 in ACC is still unknown. Aim of this study was to investigate the specific roles of IGF1R and IR in mediating IGF2 tumorigenic effects in ACC. To this purpose we performed genetic silencing of both IGF1R and IR by transfecting H295R, MUC1 and primary ACC cells with specific siRNAs directed against IGF1R and IR. We found that the IGF2 anti-apoptotic effects were enhanced in H295R and ACC primary cultured cells silenced for both IGF1R (−15.16±3.27%, P<0.01 and −4.5%, P<0.05, of control 3/7 activity, respectively) and IR (−2.8±1.63%, P<0.05 and −32.4%, P<0.01, respectively). In addition, we demonstrated that IGF2 was still able to promote ERK and AKT phosphorylation after IGF1R and IR silencing in H295R and ACC primary cultured cells. Moreover, both IGF1R and IR silencing did not affect the IGF2-mediated proliferation in H295R. In MUC1 cells, IGF1R silencing did not alter IGF2-induced cell apoptosis and proliferation. Heterogeneous results were obtained in primary cultured cells obtained from 2 different ACC. In one of them IGF1R silencing decreased IGF2-induced cell proliferation, underlining the importance of this receptor in mediating IGF2-mitogenic effects. In the other one IGF2-mediated cell proliferation was reduced after IR, but not IGF1R, silencing. IGF1R, but not IR, knockdown reduced the antiproliferative effects of IGF1R/IR inhibitor Linsitinib in H295R and ACC primary cultured cells (−32.76±20.81% in control cells, P<0.05 and −18.36±11% in IGF1R silenced H295R cells, P<0.05), suggesting a main role of IGF1R in the response to Linsitinib. In conclusion, our data demonstrated a differential involvement of IGF1R and IR in mediating IGF2 tumorigenic effects in adrenocortical cancer cells.

Conclusion Urine steroid profiling is a promising tool for the evaluation of treatment efficacy in ACC patients.

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**EP50**

Urine steroid profiling as a tool for the treatment evaluation assessment in patients with adrenocortical carcinoma

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Background The aim of the study was to evaluate urine steroid profiles by gas chromatography–mass spectrometry (GC–MS) in patients with adrenocortical carcinoma (ACC) to assess therapy efficacy. Patients and Methods 39 ACC patients were examined before and after treatment. The median age was 47 years (41–60). The Weiss score was no less than 4 points. 10 patients were disease-free in the early postoperative period (up to 12 months after surgery). Metastases were detected 1–5 years after the surgery in 29 patients. The control group consisted of 25 patients with adrenocortical adenoma (ACA) without malignant features defined by the histologic analysis. The median age was 52 (47–61) years. We evaluated the urine steroid profile using gas chromatography–mass spectrometer SHIMADzu GCMS – TQ 8050. Statistical data was processed with software STATISTICA for WINDOWS (Version 10). Results comparison was made using Mann–Whitney test.

Results ACC’s main biomarkers urinary excretion rates [dehydroyepiandrosterone (DHEA), etiocholololone (Et), pregnanediol (P2), pregnanetriol (P3)] did not differ between the disease-free postoperative ACC patients and the control group (P>0.05). The 3α,16α,20-DP urinary excretion rate and the 3α,16β,20-DP/3α,16,20-DP ratio were identified as the most discriminating markers in differentiating disease-free postoperative patients from preoperative ACC patients (receiver-operator characteristics (ROC) analysis revealed specificity=96%, sensitivity=96%, AUC=0.92, cut-off < 194 μg/24 h and sensitivity=85.7%, specificity=92%, AUC=0.87, cut-off > 3.4, respectively). Patients after surgery and chemotherapy had decreased urinary excretion rates of 3β,16α,20-DP (cut-off < 100 μg/24 h sensitivity=specificity=100%, AUC=1.0) and the increase of 3α,16α,20-DP/3β,16,20-DP ratio (cut-off < 2.7 sensitivity=75%, specificity=88%, AUC=0.81) in comparison with the same patients’ preoperative steroid profiles. Patients with recurrent ACC (in the postoperative period before the chemotherapy initiation or with the relapse occurrence after the completion of chemotherapy) had the similar excretion rates of ACC biomarkers as in the preoperative period.

Conclusion Urine steroid profiling is a promising tool for the evaluation of treatment efficacy in ACC patients.

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**EP52**

Incidence and clinical manifestations of neurogenic bladder dysfunction in type 2 diabetes: a population-based survey

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Background and aims Lower urinary tract (LUT) symptoms are one of the most common complications related to autonomous diabetic neuropathy. It is responsible for several dysfunctions due to distended bladder with a high risk of contracting retention.
The current survey aims to assess the clinical manifestations of neurogenic bladder dysfunction (NBD) and determine its prevalence in patients with type 2 diabetes (T2DM).

Patients and method
We conducted a cross-sectional descriptive study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administered the Urinary Symptom Profile (USP) questionnaire to all patients to assess clinical manifestations of NBD.

Results
The mean age was 59.3 ± 10.6 years, with a female predominance (55.5%). Dyslipidemia (57%) and hypertension (49.7%) were the most common comorbidities. The duration of the evolution of diabetes was 11.0 ± 7.9 years. Oral antidiabetic agents (OAD) and insulin therapy were prescribed in 40% and 13.6%, respectively. Most of the patients were receiving a mixed insulin-OAD treatment (44.2%). A glycemic imbalance was noted in 79.7%. Stress urinary incontinence prevailed in 22.5%: the discomfort linked to this dysfunction was mild or moderate in 53.3% and 42.2%, respectively. An overactive bladder was recorded in 70.5% and caused severe or extreme discomfort in 24.1% and 16.3% of patients, respectively. Near one-half of investigated patients (51.5%) reported dysuria. The latter disorder was responsible for serious distress for 26.2% of patients. In total, the prevalence of LUT dysfunction was as high as 79.5% of patients with T2DM.

Conclusion
NBD is a cluster of lower urinary tract disorders such as stress urinary incontinence, dysuria, and overactive bladder. NBD is considered a chronic diabetic complication [1]. The prevalence of NBD varies from 25% to 87% in different studies. Urodynamic studies remain the gold standard diagnostic tool. However, the USP questionnaire represents a simple and very sensitive questionnaire for screening of NBD in patients with diabetes in clinical practice [2]. Due to its frequency, NBD should be screened for in patients with diabetes suffering from LUT dysfunctions.

References

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EP54
False positive metanephrines secondary to sinemet-diagnostic dilemmas in interpretation
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A 50-year-old lady was referred to the endocrine service for evaluation of significantly elevated 3-methoxytyramine (3-MT) levels. Past medical history included well controlled HIV and hypertension controlled by a single agent only (amlodipine). On one occasion, she was noted to have an elevated systolic blood pressure of 189 mmHg in clinic and therefore 24 h urinary metanephrines were requested. She did not have any other symptoms to suggest excess catecholamines. Systems review was unremarkable. There was no family history of endocrinopathies. She had recently been diagnosed with multiple system atrophy. A Dopamine Active Transporter scan revealed reduced uptake at the basal ganglia. She had been started on Sinemet 125 mg TDS by the neurologist and her symptoms, which include postural hypotension, greatly improved. In the endocrine clinic, her systolic blood pressure was 128 mmHg. The history was revisited and it transpired that on one day her blood pressure had been elevated, she had omitted her amlodipine. Physical examination did not reveal any obvious stigmata of an endocrinopathy. Blood tests showed normal electrolyte, renal function, bone profile and thyroid function. However, repeat 24 h urinary metanephrines were a follows: Metanephrine 488 nmol/24 h (NR 0-2000), normetanephrines 1139 nmol/24 h (NR 0-4400) and 3-MT 20 424 nmol/24 h (NR 0-2500). This confirmed a previous 24 urine collection result. It was thought that the isolated markedly raised 3-MT, a dopamine metabolite, was secondary to Sinemet which is a combination of carbidopa and levodopa. Sinemet could not be discontinued as it significantly improved her symptoms. A differential diagnosis of a dopamine secreting neuroendocrine tumour was a considered. Chromogranin A & B were evaluated and were normal. Her case was discussed at the regional adenal MDT meeting. The MDT concluded that the markedly raised 3-MT were secondary to Sinemet and no further investigations such as functional imaging would be required. Interpreting biochemical markers in the presence of influencing factors and drugs can often be challenging. Abnormal results can trigger unnecessary investigations which can be distressing to the patient. This case highlights the importance of MDT discussions in such scenarios.

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EP55
The asymmetric adrenal in mice and men: Sexual dimorphism and potential hormonal consequences
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Evidence indicates that the adrenals are sexually dimorphic and asymmetric. These differences may have implications for the prevalence and progression of adrenal diseases, which also show asymmetry and sexual dimorphism. The present study aims to characterize the morphological and metabolic differences associated with adrenal sex and asymmetry in mice and humans. Adrenals were compared bilaterally in male and female C57/B6JR mice with regard to

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morphological and hormonal characteristics. Female adrenals were consistently larger than male adrenals (330.2 ± 14.7 vs. 215.4 ± 15.8 μg protein/adrenal, \( P < 0.001 \)). Although males had smaller adrenals, total contents of catecholamines were higher in males than in females (mean both adrenals: 3.8 ± 0.3 vs. 3.5 ± 0.2 μg catecholamines/adrenal). In contrast, adrenal contents of the two main adrenal steroids, corticosterone and aldosterone, were significantly higher in females than in males. In females, the right adrenal was significantly smaller than the left adrenal (293.5 ± 19.0 vs. 365.2 ± 12.9 μg protein/adrenal, \( P = 0.03 \)), whereas no clear differences were observed in males. In both sexes, total tissue catecholamines as well as corticosterone and aldosterone were higher in the left than the right adrenal. We confirmed these findings in three additional mouse strains (C57BL/6J, CD6 and Tcz GFP/PVB). Furthermore, we performed a systematic review of adrenal imaging data in humans. Unlike in mice, women have smaller adrenals than men, but also in humans the left adrenal gland is larger than the right adrenal. Using adrenal vein samples and human adrenal tissue data, we will further characterize hormonal differences in patients. Characterization of differences between sexes and of adrenal asymmetry in mice and humans may have implications for prediction and diagnosis of adrenal disease, and it may also allow improved translation of results from experimental murine models to the clinic.

**EP57**

### Monitoring for the long-term metabolic complications in patients with subclinical Cushing’s syndrome: service evaluation

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**Introduction**

Patients with subclinical Cushing’s syndrome (SCS) are thought to have excess cortisol from an adrenal adenoma, secreting ACTH-independent cortisol that is not fully suppressed by the pituitary feedback system. High cortisol levels may be linked to metabolic complications. There are no specific guidelines on the surgical management of SCS.

**Objective**

To evaluate if patients with SCS are monitored and managed for metabolic complications due to cortisol excess.

**Method**

A retrospective service evaluation study on patients diagnosed with SCS from 2016 to 2019 at the University Hospital of Wales, United Kingdom. We identified 114 patients with a non-suppressed response to the overnight dexamethasone test (ODST), qualified as a 0900 h cortisol > 50 nmol/l. 48/114 were excluded either due to a further negative dexamethasone suppression test or no adrenal adenoma present on imaging. Data of 66 patients were collected on the monitoring and management for metabolic complications in July 2021.

**Results**

66 patients showed a mean age of 66 ± 12.74 s.o., a male to female ratio of 2:1. 89/114 had a single adenoma, 11% (7) had bilateral adrenals, and the mean lesion size was 2.82 cm ± 1.34 s.o. 70% (46) of patients had at least one known metabolic complication present. The four metabolic complications present were hypertension (65%), diabetes mellitus (21%), dyslipidaemia (15%), and osteoporosis/ostestenopasia (27%). 21% (14) of patients had a history of cardiovascular disease (CVD). The majority had one to three metabolic risk factors (RF) screened; four patients had all four RF tests done; positive results for Hba1c (7/22), lipid profile (11/33), blood pressure (24/43), and DEXA scan (18/21). 28 (42%) patients had been discharged, 12 (18%) were deceased. Surgery was discussed in 26 patients (39%); 10/26 were offered and ultimately 8 underwent the surgery. The criteria to be offered surgery were only clear in 4/8 (50.0%) patients, as they had a lesion > 4 cm. 6/8 surgical patients had at least one metabolic complication, and 5/8 had a minimum of one positive RF result. All the adrenal adenomas removed were shown to be benign in the histopathology studies.

**Conclusion**

SCS is linked with other metabolic complications; improvement in monitoring of these complications will help the patient receive the required treatment earlier to reduce their CVD risk. More defined surgical criteria could aid clinicians in decision-making. Non-surgical patients may benefit from continued monitoring of metabolic risk factors/complications even after discharge.

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small size, craniofacial dysmorphism, dysphagia, poor feeding and hepatomegaly. Laboratory data revealed elevated liver functions, abnormal coagulation profile and modified adrenal tests: elevated adrenocorticotrophic hormone (ACTH) with normal morning cortisol level. The diagnosis of subclinical adrenal insufficiency was confirmed by the impaired plasma cortisol response following the Synacthen test. Hydrocortisone supplementation was recommended during stressful situations and intercurrent illness.

Discussion

Our patient’s clinical picture fits with an intermediate PBD-ZSD. Given the complexity of the disease, the management of PBD-ZSD is multidisciplinary and it focuses mostly on symptomatic or supportive treatment. These patients need close monitoring for adrenal insufficiency onset, which may by life-threatening if the diagnosis is delayed. Experts recommend yearly endocrinological check-ups by measuring serum morning cortisol and ACTH. Also, the endocrinological management may include vitamin D supplementation and bisphoshonates treatment, as patients with PBD-ZSD are at risk for osteopenia over time.

Conclusion

Our patient’s clinical picture fits with an intermediate PBD-ZSD. Given the complexity of the disease, the management of PBD-ZSD is multidisciplinary and it focuses mostly on symptomatic or supportive treatment. These patients need close monitoring for adrenal insufficiency onset, which may by life-threatening if the diagnosis is delayed. Experts recommend yearly endocrinological check-ups by measuring serum morning cortisol and ACTH. Also, the endocrinological management may include vitamin D supplementation and bisphoshonates treatment, as patients with PBD-ZSD are at risk for osteopenia over time.

Objective

In this retrospective study we investigated the clinical and radiological characteristics, hormonal status and metabolic components of the patients with adrenal incidentaloma (AI). Additionally, we investigated whether tumor size or hormonal status changes during long-term follow-up and the effect of these on metabolic parameters.

Methods

The data of 384 patients who were followed up with the diagnosis of AI between 2010 and 2020 were retrospectively analyzed. All patients underwent radiological, hormonal and metabolic evaluation and prospective follow-up.

Results

374 patients (248 female (%64)) enrolled to this study. 348 (%90.6) of them were reported as adenomas and 31 (%9.4) of them as non-adenomas and 4 (%1.0) of them were indeterminate. The mean adenoma diameter was approximately 2 centimeters and was mostly detected on the left (%48.9). %13.8 of the subjects (n = 53) were functioning and among functional adenomas 9 subjects (17.0) have primary hyperaldosteronism, 4 subjects (7.6) have pheochromocytomas, and 39 subjects (10.1) have possible autonomous cortisol secretion. In patients with bilateral incidentalomas, the mean diameter of adenomas was higher than unilateral incidentalomas with a diameter of 24.22 mm in comparison to 20.36 mm. Similarly, in patients with bilateral incidentalomas, systolic and diastolic blood pressure was higher than unilateral incidentalomas (135.83 ± 20.27, 130.02 ± 18.84% and 79.25 ± 11.56, 78.32 ± 10.11, respectively). Moreover, our study revealed that the frequency of diabetes, hypertension and hyperlipidemia in patients with possible autonomous cortisol secretion was %37, %63, %22.2, respectively. Of 384 patients, 9.11% (n = 35) underwent surgery. The most common pathological finding was adrenocortical adenoma (n = 19, %5). The median follow-up duration of patients was 48.91 months. Of 384 patients, %44.7 (n = 172) were followed up regularly with CT/MRI. During the follow-ups, the diameter of adenomas (%11.6) has increased by more than 10 mm. Of 384 subjects, %56.7 (n = 218) were followed with hormonal evaluation and 6 patients have developed possible autonomous cortisol secretion and 3 patients have developed autonomous cortisol secretion. Moreover, 1 subject has been developed primary hyperaldosteronism.

Conclusions

The main findings of the present study are that there was no relevant tumor growth after 5 years of follow-up and that the conversion rate to subclinical or clinical hypercortisolism was low and there were no new cases of pheochromocytoma. Only one subject has shown the development of primary hyperaldosteronism. Our study revealed a significantly increased risk of developing DM, HT and HL in patients with possible autonomous cortisol secretion.

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EP60

Adrenal incidentaloma: clinical and metabolic characteristics and follow-up results, a 10-year experience

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Objective

Growing scientific evidence supports the hypothesis of an increased cardiometabolic risk in patients harboring adrenal incidentalomas (AI). This risk would be higher in aging populations and patients with functioning adenomas. The current study aims to determine the clinical and biochemical characteristics of metabolic syndrome (MetS) and assess its prevalence in older patients with AI.

Patients and Method

We conducted a retrospective descriptive study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia; Faculty of Medicine of Sfax, Department of Family Medicine, Tunisia.

Background and Aim

Growing scientific evidence supports the hypothesis of an increased cardiometabolic risk in patients harboring adrenal incidentalomas (AI). This risk would be higher in aging populations and patients with functioning adenomas. The current study aims to determine the clinical and biochemical characteristics of metabolic syndrome (MetS) and assess its prevalence in older patients with AI.

Results

The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance (57.5%). Seventy percent of elderly patients had non-secretory AI. The functioning incidentalomas displayed autonomous cortisol secretion (32.5%), primary hyperaldosteronism (25%), and secondary hyperaldosteronism (21.8%). One subject had a secreting pheochromocytoma. Hypertension was the most

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EP59

Screening of primary aldosteronism among egyptian hypertensive population

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Background

Hypertension is a common condition that affects many people all over the world. It could be associated with several complications especially in cases of resistant hypertension. Many clinical practice guidelines recommend screening for primary aldosteronism especially in persons with resistant hypertension owing to the worse prognosis when compared with blood pressure-matched essential hypertension.

Objective

The study aimed to screen for primary aldosteronism in high-risk hypertensive Egyptian patients, and to determine the challenges faced in the diagnosis.

Material and Methods

50 high-risk hypertensive patients were recruited from the Outpatient Endocrinology Clinic out of 200 hypertensive patients in the period from February 2019 and April 2021. Creatinine, Glycosylated hemoglobin (HbA1c), lipid profile, potassium level, sodium level, plasma aldosterone concentration (PAC), active renin concentration (ARC), and aldosterone/renin ratio (ARR) were assessed in all patients.

Results

A series of 50 hypertensive patients screened for PA (26 females and 24 males) with a mean age of 41.88 ± 11.91 s.d. We found that 41 (82%) patients were receiving antihypertensive medications and 9 (18%) patients didn’t receive treatment for hypertension previously. 9 (18%) patients kept on no treatment, 6 (12%) patients were kept on the same antihypertensive medications, and 35 (70%) of them were shifted to other anti-hypertensive drugs. 4 patients out of total 50 patients had a positive ARR (≥4), while 13 (26%) patients out of total 50 hypertensive patients had low renin levels. There was a statistically significant relation between serum aldosterone/renin ratio (ARR) and serum potassium (K) with P-value = 0.001 (Figure 4), also a statistically significant relation between serum aldosterone/renin ratio (ARR) and (systolic blood pressure, diastolic blood pressure) with P-value = 0.001 was found.

Conclusion

we recommend routine screening for PA in high-risk hypertensive patients that could offer targeted treatment before adverse cardiovascular consequences develop.

Keywords: High-risk hypertensive patients; Primary aldosteronism; Plasma aldosterone concentration; Active renin concentration; Aldosterone/renin ratio.

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common metabolic disorder encountered in 77.5% of aged patients. The mean Body mass index was 28.5±5.4 kg/m². Our elderly population was frequently overweight (32.5%) or obese (40%). Abdominal obesity affected remarkably the female gender (87% in females versus 35.3% in males) with a mean waist circumference of 106 cm in females and 99 cm in males. We noticed a glucose metabolism disorder in 70%: mainly diabetes mellitus in 60%, impaired fasting glucose in 7.5%, and impaired glucose tolerance in 2.5%. Most senior patients had disturbed lipid profiles. HyperHDLemia prevailed in 45.7%, with hypertriglycerideremia and hypercholesterolemia were found in 17.5% and 28.2%, respectively. The prevalence of MetS in our sample of geriatric patients carrying AI was 24.6%

Conclusion
Recent scientific data has concluded that AI defines a novel risk factor for MetS [11]. We could hypothesize that AI (despite its hormonal profile) may be associated with a subtle excessive cortisol secretion, hardly labeled clinically and biochemically, which could cause an acquired condition of insulin resistance [2]. Along with multiple age-related mechanisms, this condition would be clinically manifest and result in overt MetS in the geriatric population.

References

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EP62
Synchronous adrenal gland masses in a patient: clinical case
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We describe the case of a 69-year-old woman with bilateral adrenal incidentalomas identified in CT-scan; on the right, a 57 mm heterogeneous mass with <10 Hounsfield units(HU) with absolute washout of 16%; on the left a 13 mm mass with 35HU, intense contrast enhancement but washout of 66%. She had a recent onset of diabetes, hypertension, androgenic alopecia and facial hair. The systolic blood pressure remained persistently >160 mmHg despite receiving four antihypertensive drugs. She referred multiple episodes of syncope in the orthostatic position without palpitations, facial flushing or diaphoresis. She had no malignancy history nor had any apparent syndromic physical features. Her BMI was 32.3 kg/m², waist circumference of 110 cm with thin members and she presented with androgenic alopecia, submental hair lacking other Cushing features. Hormonal tests showed elevation of plasmatic metanephrines: metanephrine 79.9 pg/ml (<60), normetanephrine 214.6 pg/ml (<120); 3-methoxytyramin of 12.7 pg/ml (<60), DHEA-SO4 1.54 μg/ml (<0.9), androstenedione 6.7 ng/ml (<0.5–3.4). 17-hydroxyprogesterone: 0.67 ng/ml (<0.1–2.3). 18 F-FDOPA PET confirmed a pheochromocytoma on the left adrenal gland without metastatic lesions. She began treatment with phenoxybenzamine. Gadolium MRI suggested an adrenocortical carcinoma on the right. Urology proposed right adrenalectomy and total adrenalectomy of the left adrenal gland, then converted to total adrenalectomy of the right gland and partial adrenalectomy of the left because the pheochromocytoma was macroscopically hard to find even with patient mobilization. Histopathology was consistent with a pheochromocytoma on the left adrenal gland (PASS-score 4/20) and adenoma on the right. After surgery there was normalization of the levels of metanephrines and androgens. Synacthen showed a 60 minute cortisol of 10 μg/dl. She was discharged with 10 mg hydrocortisone once a day. The genetic study is in process.

Discussion
There are few reports on bilateral adrenal masses since they are uncommon, especially if from different etiologies. This patient had simultaneously a pheochromocytoma and a cortisol producing adenoma confirmed by normalization of hormones after its resection – androgen-hypersecretion by benign tumors is also unusual since is more typical of carcinomas. The surgeon was faced with the need to decide the type of surgical approach at the last minute: there are few recommendations on adrenal surgery but there is general consensus to perform total adrenalectomy on pheochromocytoma-affected glands. However, complete normalization of metanephrines and eventual future adrenocortical-hormone sufficiency are good outcome predictors.

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EP63
Malignant pheochromocytoma with bone, pulmonary and brain metastases
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Introduction
Pheochromocytomas are rare neuroendocrine tumors whose malignancy is defined by the presence of metastases that may appear several years later. The appropriate follow-up time remains uncertain.

Clinical Case
We present the case of a woman with a history of pheochromocytoma who underwent complete resection at 48 years old. The genetic evaluation was negative for mutations on RET, VHL, SDHB or SDHD genes. At 66 years old, a thoracic vertebral metastasis appeared on MIIBG-I123 scintigraphy. The biopsy of the lesion was consistent with neuroendocrine tumor metastasis. The patient was submitted to radiotherapy, radioisotope therapy and kyphoplasty. The radioisotope therapy with MIIBG-I123 proved to be ineffective. Therapy with an antagonist of the alpha-adrenergic receptors (phenoxybenzamine) was initiated. In the next eleven years, the MIIBG-I123 scans and lombar CT showed progression of bone metastases and doubt about the possibility of liver lesions. Over these years, plasma metanephrine and 3-methoxytyramine remained normal but normetanephrine showed marginal and progressive elevations. At 77 years, the patient underwent a second radioisotope treatment with MIIBG-I123, once again ineffective. 3 months later, the patient was admitted with fatigue, respiratory failure and gait imbalance. Chest CT showed miliary pulmonary spread. Bronchoalveolar lavage immunochemistry was compatible with NET metastases. 18F-DOPA PET/CT confirmed pulmonary and massive liver metastases and new bone lesions. Cranial CT scan showed cerebellar, lenticular, frontal and hypothalamic-pituitary involvement suggestive of secondary lesions. Despite the pituitary involvement, there was no hormonal deficiency. Plasma noradrenaline increased. The clinical condition worsened and the patient ended up dying 2 months later.

Conclusions
Metastases typically involve bone, liver and lung – cerebral metastases are rare. MIIBG-I123 scintigraphy can detect metastases susceptible to radioisotope therapy, but about a third of patients do not respond. Even in the absence of obvious high-risk characteristics, malignancy can occur and it is not easy to predict. This case illustrates the importance of life-long follow-up in these tumors and the unpredictability of occurrence of metastatic lesions.

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EP64
Pheochromocytoma experience
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Aim
This study aims to evaluate patients with a diagnosis of pheochromocytoma.

Method
This retrospective case-control study includes data from a tertiary endocrine center from January 1, 2010, to December 31, 2020. Demographic, laboratory, operation/pathology data of patients with pheochromocytoma were recorded.

Results
A total of 38 patients (20 patients (52.6%) were male) were included in the study. Median age 48 years (17–81) IQR:18. Tumor localization (right/left/bilateral: 23/9/6) was most common on the right at a rate of 60.5%. Six patients had bilateral tumors. Five patients (three from the same family) had MEN 2A syndrome, and one patient had MEN 2B syndrome. All MEN syndromes had medullary thyroid cancer. One patient had pheochromocytoma, medullary thyroid cancer, and parathyroid adenoma. Neurofibromatosis was detected in one patient. Median tumor size was 6.5 cm (1.6-24) IQR: 3.3 Metanephrine level median: 6696(18-23115) IQR:2793(52–341 μg/dl) Normetanephrine level median: 3342(187-18900) IQR: 3378(88–444 μg/dl) All patients had a normal aldosterone/renin ratio. There was no response to dexamethasone suppression in 10.5 percent of the patients. Mean calcitonin level in patients with medullary thyroid cancer: 2306.5. Normetanephrine was elevated in 92% of patients. Metanephrine elevated in 65% of patients. Noradrenaline and metanephrine were found to be elevated at the same time in 80% of those with bilateral masses.

Conclusion
Pheochromocytoma is seen equally in both gender. It is mainly localized in the right adrenal. It often secretes noradrenaline. Epinephrine/norepinephrine is
often increased in bilateral disease. MEN syndrome is common in bilateral disease.

Keywords: Pheochromocytoma, adrenal mass, endocrine hypertension

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**EP65**

**False positive metanephrines in high risk patient for pheochromocytoma**

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Background
False positive results are common in the screening of pheochromocytoma. Even in high risk patients with disorders related to multiple endocrine neoplasia it’s crucial to exclude possible interferences with analytical methods.

Clinical case
A 69 year-old man was submitted to total thyroidectomy, due to a 11 mm hypoechogenic nodule suspicious of papillary carcinoma (FNA). Histology confirmed medullary carcinoma pT1b. The surgery ordered the screening for primary hyperparathyroidism and pheochromocytoma and sent the case to Endocrinology. Initial 24 h urinary metanephrines (HPLC) were increased [861 μg/24 h (≥302)], but urine was collected shortly after surgery. The patient didn’t have paroxistic symptoms and the abdominal CT showed normal adrenal glands. The results were normal.

Discussion
There are many interferences with normetanephrine tests. Anesthesiologists and some analogies are known interferences, but there is a comprehensive list of possible medications associated with false positive results. In this case, the first metanephrines were interpreted as interference caused by surgery and anesthetics given that metanephrine levels normalized later. The study of the patient’s medical record shows that the patient was prescribed tamsulosin, atorvastatin, omeprazole and levothyroxine: metanephrines didn’t have paroxistic symptoms and the abdominal CT showed normal adrenal glands. The patient was discharged.

**Results**

The patient had normal urinary metanephrines [200 μg/24 h (≤302)], but the urinary normetanephrines were elevated 4 fold [2005 μg/24 h (≥527)] while plasma remained normal [110 pg/ml (<196)]. RET gene study didn’t show mutations. Given the discrepancy of the results, the metanephrines and normetanephrines were repeated after tamsulosin withdrawal for 15 days, which resulted in normal plasmatic and urinary levels (24 h urinary metanephrines 158 μg/24 h (≤302), normetanephrines 213 μg/24 h (≤527); plasmatic metanephrines 45 μg/ml (≤65), normetanephrines 35 μg/ml (≤196)]

Conclusions
While the cumulative dose of corticosteroids equal to < 65 mg of prednisolone is associated with increased SpO2 and decreased CRP in COVID-19 patients, it leads to prolonged hospital stay compared to the ≤ 65 mg dose of corticosteroids.

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**EP66**

**Effects of cumulative doses of corticosteroids on the recovery of patients with COVID-19**

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Background
Corticosteroids suppress the immune system and have been proposed as a treatment for the severe form of COVID-19 due to their potential ability to inhibit the COVID-19-induced cytokine storm. We aimed to evaluate the effects of cumulative doses of corticosteroids on the recovery of COVID-19 patients.

Methods
In this descriptive cross-sectional study, we retrospectively evaluated patients with COVID-19 (confirmed by [PCR]) receiving corticosteroids at Shahid Mohammadi Hospital, Bandar Abbas, Iran during June-October 2020. All patients had been admitted to the general wards and not the intensive care unit. COVID-19 was not severe in any of the patients. Beside corticosteroids, all patients had received similar standard COVID-19 treatment according to the National COVID-19 Committee protocols. In addition to the demographic features of the patients including age and gender, COVID-19 symptoms, respiratory rate (RR), lactate dehydrogenase (LDH) level, C-reactive protein (CRP) level, oxygen saturation (SpO2), lymphocyte percentage and count on admission and at the last evaluation before discharge were extracted from the patients’ medical files.

Results
A total of 200 patients with confirmed COVID-19 were included in this study. The mean age of the patients was 51.65 ± 9.35 years and 117 (58.5%) were male. The administered corticosteroid was dexamethasone in 55%, methylprednisolone in 32.5%, and prednisolone in 12.5%. The non-administered cumulative corticosteroid dose was equal to 82.69 ± 59.40 mg prednisolone. All COVID-19 symptoms, including fever, cough, dyspnea, headache, body ache, and anosmia decreased in the patients. However, there was no significant difference between patients using < 65 mg of corticosteroids and those using ≥ 65 mg of the medicine regarding the final status of symptoms. The increase in SpO2 was significantly higher in patients using < 65 mg of corticosteroids (P = 0.008). Moreover, the proportion of patients with negative final CRP was significantly higher in this group (P < 0.001). On the contrary, hospital length of stay was significantly shorter in patients using ≥ 65 mg of corticosteroids (P = 0.034). The two groups had no significant differences in terms of LDH levels, lymphocyte percentage and count, RR, and the final status of lung infiltration (P > 0.05).

Conclusions
Arterial hypertension in elderly patients is one of the most common comorbidities in the elderly. The association of arterial incidentoma (AI) with AH in older patients may influence the clinical and therapeutic outcomes of the latter condition. In the current study, we aimed to assess the prevalence of AH and its clinical and therapeutic features in geriatric patients bearing AI.

Patients and Method
We conducted a retrospective descriptive study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia; Faculty of Medicine of Sfax, Department of Family Medicine, Tunisia.

Background and Aims
Arterial hypertension (AH) is one of the most common comorbidities in the elderly. The prevalence of AH in elderly patients (≥ 65 years) varies between 30% and 45%, and up to 50% in those aged 80 years and above. AH is a common form in 70% of cases. Secondary AH was diagnosed in 30% of aged patients and was associated with cardiovascular disease (29.4%) and neurological (22.2%) complications. Primary hypertension was the most common form in 70% of cases. Secondary AH was diagnosed in 30% of aged patients having AI due to autonomous cortisol secretion (52.5%), primary hyperaldosteronism (21.8%), or secondary hyperaldosteronism (21.8%). One senior had a secreting pheochromocytoma. Bilateral AI (92.3%) is subsequently more associated with AH than unilateral AI (57.7%) (Z = 0.027). We did not establish any significant correlation between the AI size and the severity of AH.

Results
The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance (57.5%). Hypertension was the most common metabolic disorder encountered in 77.5% of aged patients carrying AI. The mean systolic blood pressure was 132 mmHg (extremes = 100–180). The mean diastolic blood pressure was 75 mmHg (extremes = 50–120). AH was newly diagnosed in 10% of cases thanks to a 24-hour ambulatory blood pressure monitoring during the AI clinical assessment. For the patients already diagnosed with AH, the average duration of hypertension was 8.7 ± 7.2 years. Most elderly patients with AI had stage I high blood pressure (87.1%) at diagnosis. Stage II (9.7%) and stage III (3.2%) AH were less frequently encountered. Antihypertensive monotherapy was proposed for 51.9% of patients. Antihypertensive thitherapy (29.6%) or thitherapy (11.1%), quaditherapy (3.7%) were less prescribed. Target organ damage related to AH was observed in 37%, mainly renal (29.4%) and neurological (22.2%) complications. Primary hypertension was the most common form in 70% of cases. Secondary AH was diagnosed in 30% of aged patients having AI due to autonomous cortisol secretion (52.5%), primary hyperaldosteronism (21.8%), or secondary hyperaldosteronism (21.8%). One senior had a secreting pheochromocytoma. Bilateral AI (92.3%) is subsequently more associated with AH in aged patients than unilateral AI (57.7%) (Z = 0.027). We did not establish any significant correlation between the AI size and the severity of AH.
EP68  Clinical sexual dimorphism in patients with adrenal incidentaloma and (possible) autonomous cortisol secretion

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Introduction

Many diseases of the adrenal cortex show a higher prevalence in women than men with incidence increasing with age in both genders.

Aim

The aim was to determine the possible sexual dimorphism in patients with adrenal incidentaloma (AI) and (possible) autonomous cortisol secretion (PACS).

Methods

This was an observational, cross-sectional study of 381 patients with AI that were functionally assessed in our Clinic. After exclusion of patients with overt adrenal hyperfunction, malignancy, cysts and nonfunctional AI, the studied group consisted of 186 patients with (P)ACS: 138 female and 48 males. Based on average menopause age of 51, we stratified women in two groups: < 51 and ≥ 51. For the sake of comparison, we age-matched the male group, and evaluated differences in body mass index (BMI), adrenal tumor size (ATS), localization, ACTH, 24 h cortisol, 1 mg dexamethasone suppression cortisol (1 mg DST), and prevalence of hypertension (HTA) and type 2 diabetes mellitus (T2DM).

Results

Female sex was predominant in the whole cohort (F/M % 74.2/25.8) and in both age groups (< 51 years, 35 patients – F/M % 87.8/12.2 and ≥ 51 years, 153 patients – F/M % 71.2/28.8), with a higher frequency in younger group when compared to males (P = 0.048). There was no difference in age, BMI, ATS, localization, ACTH, 24 h cortisol, 1 mg DST cortisol, HTA and T2DM prevalence between female and male patients. Older male patients had a higher prevalence of T2DM (P = 0.013) than younger males with 24 h cortisol level being the most significant predictor of T2DM (P = 0.047). There was no difference in prevalence of HTA, nor other significant differences between younger and older male patients. In the female group, there was no difference in HTA and T2DM prevalence between younger and older patients. In older female patients ATS was the most significant predictor of T2DM (β = 0.247, 95% CI β = 0.002–0.018, P = 0.011) while BMI was the most significant predictor of HTA (β = 0.301, 95% CI β = 0.009–0.031, P = 0.002), whereas there were no detectable significant predictors in younger females for both T2DM and HTA.

Conclusion

Female gender is a predisposing factor for subtle cortisol hypersecretion in patients with AI, while also being a predisposing factor for cardiometabolic comorbidities in women younger than 51 years of age, thus pointing to a relevant clinical sexual dimorphism that could aid in providing a decision-making process and tailored treatment.

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EP69  Epidemiological and clinical data and factors of poor blood pressure control in known hypertensive patients in the Sfax region

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Introduction

Hypertension is a very common chronic disease worldwide. Its imbalance is one of the main causes of cardiovascular and neurodegenerative complications.

Patients and Methods

We collected data from hypertensive patients who voluntarily presented for screening on both diabetes and hypertension screening days. Poor blood pressure control was defined as systolic blood pressure (SBP) greater than or equal to 140 mmHg and/or diastolic blood pressure (DBP) greater than or equal to 90 mmHg. The Student t test and the Chi-squared test were used. A threshold of statistical significance was set at 5% for the different tests used.

Results

There were 389 patients who were known to be hypertensive among 2012 patients who were collected at the diabetes and hypertension screening days (19.3%). The median age of the known hypertensives was higher than that of the nonknown (60 years versus 50 years). Men were significantly more affected by hypertension than women (46.7% versus 39.3%) (P = 0.001). Among the known hypertensives had a family history of hypertension with a frequency of 64.5% (P < 0.001). One hundred and fifty known hypertensive patients were diabetic (38.6%) versus 238 who were diabetic without associated hypertension (15.2%) with P < 0.001. Smoking was found in 23.1% of known hypertensive patients versus 28.3% of those without hypertension (P = 0.02). Alcohol consumption was found in 8.2% of the known hypertensive subjects versus 11.7% of the non-known hypertensive subjects (P = 0.05). A minority was on diet (11.2%). The majority were on monotherapy (58.4%). The use of two hypotensive drugs was for 58 subjects (17.6%). The remaining 42 subjects were on triple therapy (12.8%). The mean SBP was 138.2 mmHg with extremes ranging from 98 mmHg to 215 mmHg and the mean DBP was 82.5 mmHg with extremes ranging from 50 mmHg to 120 mmHg. It was noted that 58.6% of hypertensive patients were poorly balanced. Almost half of the women were well balanced (50.3%) whereas only 35.6% of the men had a good balance of their BP (P = 0.004). For both subjects with a family history of hypertension and those without, the frequency of well-controlled BP was almost the same (41%). Known diabetics had a balanced BP in 44.3% of cases, whereas this balance was achieved in only 39.6% of the non-diabetics (P = 0.35).

Conclusion

The management of hypertension is part of the management of all cardiovascular risk factors, which also indicate the therapeutic attitude and target blood pressure values.

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EP70  Adverse events associated with supraphysiological glucocorticoid dosing in congenital adrenal hyperplasia (CAH): results of a structured literature review

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Objectives

Congenital adrenal hyperplasia (CAH) is a rare condition caused by enzyme deficiency in cortisol biosynthesis. Patients with CAH require lifelong therapy, with the aim of replacing deficient hormones (cortisol +1/− aldosterone) and reducing excess androgen production. Guidelines state that the lowest effective glucocorticoid (GC dose) should be used; however, current GC therapy is suboptimal, and supraphysiological GC doses are used to reduce excess androgens. This study aimed to evaluate the published evidence on long-term adverse events (AEs) associated with GC dosing in CAH.

Methods

A structured, comprehensive literature review was conducted to identify evidence for the link between supraphysiological GC levels and long-term AEs of interest to the CAH population: such as cardiovascular disease (CVD), osteoporosis/bone health, obesity, diabetes, reduced growth, and poor fertility.

Results

In total, 4,874 records were identified, and 53 studies were included. There is a lack of prospective randomised controlled trials comparing standard GC regimens. Available literature report heterogeneity of patient populations, treatment regimens and study duration. Studies show that complex and multiple dose GC regimens are used in CAH, and both over- and underdosing are associated with AEs. The relationship between GC dosing and bone health was most widely reported with 17 papers reporting a link between excess GC dosing and poor bone health. Fracture risk was shown to increase in older patients. Sixteen articles reported a link between GC dosing and obesity and associated metabolic syndrome including fat mass and lean body weight. These studies reported that higher GC dosing was associated with higher BMI. Thirteen articles reported a link between GC dosing and height growth in CAH patients providing evidence for an important link between GC dosing and growth period, with high doses of GC during adolescence being associated with lower final height. Four articles linked diabetes markers, such as HbA1c levels, glucose metabolism, and insulin resistance, with GC dosing. Other relationships supported by the literature were the links between GC dosing and patients’ health related quality of life, and CVD-associated risk factors.
Conclusion
This literature review identified a wealth of evidence to support relationships between supraphysiologic GCs dosing and long-term AEIs in CAH. There is an unmet need for a treatment for CAH that provides optimal cortisol replacement at a physiological dose, thereby reducing AEIs associated with excess GC dosing.
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**EP71**
Adrenal incidentaloma rate during coronavirus disease 2019 (COVID-19) pandemic
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Background
Adrenal incidentaloma (AI) is described as an adrenal mass detected on imaging not performed for adrenal disease. In coronavirus disease 2019 (COVID-19) pandemic, chest CT evaluation was performed for all ages in adults. In this study, we aimed to detect adrenal adenoma(s) which were identified with chest CT, during COVID-19 diagnostic work-up to find AI prevalence in our population.

Methods
All patients who underwent chest CT examination for COVID-19 at Istanbul University Faculty of Medicine between March 15, 2020 and June 15, 2020, were screened. Patients’ demographic characteristics were recorded from their medical records. Patients with a history of malignancy were excluded. Images were assessed by two radiologists and consulted with an experienced senior radiologist.

Results
A total of 4449 patients’ CT images were screened. There were 4108 patients with no lesion (control group) and 248 (5%) patients with at least one lesion (adrenal group). The mean age of the control group was 64.58 ± 17.07 and the adrenal group was 60.65 ± 16.83 years (P < 0.0001). In 248 patients, there were 134 patients with at least one adrenal nodule (3% among all screened CT images). The mean age of the patients was 58.70 ± 15.09 years. Thirty-four patients had a right nodule, 78 patients had a left nodule and 22 had bilateral nodules. When nodule size and Hounsfield unit (HU) were compared there was no statistically significant difference between the left adrenal gland and right adrenal gland (P = 0.57 and P = 0.97, respectively).

Conclusion
Our data showed an AI rate of 3% and the majority of nodules were in the left adrenal gland.
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**EP72**
Bone impact of hydrocortisone hormone replacement in adrenal insufficiency.
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Introduction
The treatment of adrenal insufficiency (AI) is based on long-term glucocorticoid substitution. Hydrocortisone (HC) is the most commonly used substitution molecule. The aim of our work was to determine the long-term bone impact of patients with peripheral AI.

Patients and methods
This is a descriptive and analytical study involving 77 patients with peripheral IS (66 women and 11 men), all treated with HC. For each patient, we determined the duration of the disease and the daily and cumulative dose of HC, and performed a phosphocalcic assessment, an alkaline phosphatase (ALP) determination, and a bone densitometry (BMD) performed in 30 patients.

Results
The mean age was 40.5 years (range: 22-63 years). The mean duration of the disease was 7.7 years. We found that among the patients who had a BMD, 75% had bone demineralization at the time of the study, which was more marked in the cancellous bone (spinous site). This prevalence was high compared to the Tunisian adult population (75% vs 45.7%). This demineralization was positively correlated with the cumulative dose of HC (mean cumulative dose (g) = 60 ± 80.4 in patients with normal BMD vs 132 ± 86.4 in patients with bone demineralization; P = 0.042), and was more frequent but not significantly so in postmenopausal women. However, we did not find any correlation between bone demineralization and daily HC dose and disease duration, respectively. Biologically, at the time of the study, ALP was elevated and hypocalcemia was present in 15% and 26.7% of patients, respectively. However, we did not find any correlation between these two biological abnormalities and the daily dose of HC, the cumulative dose and the duration of the disease respectively.

Conclusion
Hormone replacement therapy of peripheral AI with HC seems to be a risk factor for bone demineralization, especially with the higher cumulative dose of this corticoid. Further studies needed to better define the cumulative dose threshold at which bone densitometry monitoring is indicated.
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**EP73**
A rare cause of Cushing’s syndrome
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Introduction
Aggressive ACTH-independent Cushing’s syndrome is rare and frequently related to malignant adrenocortical tumor. However, in exceptional situations, ectopic steroids secretion has been described.

Case report
We report the case of an 87 years-old woman referred to our clinic in September 2020 after a low trauma sacral fracture. Her recent medical history revealed the onset, in the previous months, of severe hypokalemia, uncontrolled type 2 diabetes (glycated hemoglobin 9.2%), worsening of arterial hypertension and spontaneous bruising. Because of the medical history, a Cushing’s syndrome (CS) was suspected and after exclusion of exogenous glucocorticoid use, specific tests were carried out. Laboratory findings confirmed the diagnosis of CS: 24-hour urine free cortisol >4×ULN, cortisol after 1 mg overnight dexamethasone suppression test of 58.8 μg/dl, undetectable adrenocorticotropic hormone (ACTH) levels, and hypokalemia. The subsequent abdominal CT scan revealed normal adrenal glands, but showed a suspicious 8-cm pelvic mass, which was suggestive of malignancy. Unfortunately, given the old age and the severe clinical picture, no further investigations were feasible and a medical therapy with metyrapone was initiated. After few weeks of therapy, we observed an improvement of glucose and pressure control and the restoration of normal potassium levels, even though the clinical picture remained severe. After six months a clinical improvement was observed, and the patient could undergo an abdomen MRI for better characterizing the pelvic mass. This second radiologic evaluation showed a significant increase of the pelvic mass diameter, which had doubled, reaching the diameter of 17 centimeters. Because of the rapid tumor growth and the presence of ACTH independent hypercortisolism, the patient could be suspected to be affected by an ectopic cortisol secreting adrenocortical carcinoma. Histological confirmation would be necessary, but surgical options or other invasive procedures are not feasible.

Discussion
Ectopic adrenocortical carcinomas may result from adrenal embryonic remnants. Adrenocortical neoplasms arising in ectopic locations are extremely rare, and cortisol-secreting ones are even rarer, with only a few cases reported in the literature. The treatment of ectopic adrenocortical carcinoma does not differ from that of eutopic tumors. However, ectopic adrenocortical carcinomas are, in general, aggressive and progressively differentiated and they are, therefore, associated with a high mortality rate.

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**EP74**
Magnetic iron oxide nanoparticles for the delivery of thermal therapy for the treatment of primary aldosteronism
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Abstract
Aims: Magnetic iron oxide nanoparticles (MION) are an attractive adjuvant for photothermal therapy (PTT). We aimed to demonstrate the feasibility of using MION as an effective vehicle for the delivery of thermal therapy for the treatment of primary aldosteronism.

Methods: MION were synthesized and characterized. The adjuvant activity of MION was validated in an established murine model of primary aldosteronism. The effect of MION on irradiation-induced temperature elevation, as well as the effect of hyperthermia on ACE inhibition and aldosterone production, was evaluated. Moreover, we investigated the in vivo efficacy of MION-PTT in a new murine model of primary aldosteronism.

Results: MION were successfully synthesized and characterized. In the established murine model, thermal therapy increased the local temperature by 5°C without affecting the core temperature of the mice. MION increased the local temperature by 8°C. Moreover, hyperthermia increased the level of ACE inhibition and aldosterone production, compared to control mice. In the new murine model, MION-PTT decreased the level of aldosterone production and normalized the blood pressure.

Conclusion: MION-PTT is a promising adjuvant for the treatment of primary aldosteronism.

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To minimise damage to surrounding tissues, targeted delivery of therapeutics to the tumour is highly desirable, and the development of nanotechnology has shown promising results. Magnetic iron oxide nanoparticles (MIONPs) have been gaining traction over the years for applications such as drug delivery, molecular imaging and delivering thermotherapy for treatment of various cancers (1). MIONPs have great therapeutic potential as they can be produced in various sizes and shapes, with the ability to modify the surface by coating the nanoparticles. MIONPs have the ability to be activated by external magnetic field to generate heat and to cause hyperthermia (2). Translationally, the delivery of thermal therapy offers an option for minimally invasive definitive treatment of primary aldosteronism, an endocrinopathy of aldosterone excess/dysregulation which represents the commonest secondary form of hypertension. In this study, MIONPs have been used at different concentrations to evaluate nanoparticle uptake and rate of uptake by adrenal cortical and endothelial cells, as well as gain understanding of the location of nanoparticles within the cell. Magnetic iron oxide nanoparticles (MIONPs) were provided by The University of Kansas. Adrenal Cortical cell lines (MUC1, H295R and HAC15) and Endothelial cell-line (HUVEC) were used in this study. MIONPs were added at concentrations of 0.5, 5, 10, 20 and 50 µg/ml to the cells and incubated overnight. MIONP up-take efficiency, rate of uptake and cytoxicity was assessed by Flow Cytometry. Confocal Microscopy was used to image the cells following MIONP incubation. Cellular proliferation was assessed by Xcelligence system and ala-marBlue. Cellular respiration was assessed by “Seahorse” technology. MIONP location within the cells was assessed by transmission electron microscopy (TEM). Following overnight incubation with MIONPs, Flow Cytometry showed significant uptake by MUC1, HAC15 and HUVEC cells at 10 µg/ml MIONP concentration. Confocal and TEM images revealed MIONPs in the cytoplasm and in the vesicles for all cell types (Fig. 1 and 2). Live Confocal imaging showed MIONP phagocytosis specific uptake by the HAC15 cells.

References

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EP76 Pulmonary thromboembolism as the initial presentation of ACTH-independent Cushing’s Syndrome

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Cushing’s syndrome (CS) is associated with a considerable risk of complications including thromboembolic events (TE). They occur mostly within the first 2–3 months postoperatively. When present before surgery, CS has high rates of perioperative mortality and morbidity. The benefit of steroids inhibitors after TE is not fully known. Furthermore, little guidance is available regarding TE assessment/management in CS. We report a case of a 34-year-old male admitted in our emergency department for a presyncope episode during minimum physical activity. He described severe fatigue that had progressively worsened over 3 months. He experienced progressive weight gain of 10 kg and the appearance of extensive purple trunk striae in the last year. His past medical history included hypertension, obesity and obstructive sleep apnea. His blood pressure was 100/78 mmHg, his heart rate 150 bpm and oxygen saturation was 99%. Laboratory tests revealed: hemoglobin 15 g/dl, leukocytosis 13.200/mm³, AST 259 U/L (15–37), ALT 653 U/L (16–63), indirect hyperbilirubinemia 1.20 mg/dl, D-dimer 70.370 ng/ml (< 500), NT-proBNP 125 pg/ml, troponin T 663 ng/l. CT scan pulmonary angiography found extensive pulmonary embolism involving the right and left pulmonary arteries with extension to lobar arteries, also revealed a 35 mm solid tumor on his left adrenal gland. Lower limb color doppler ultrasound demonstrated deep venous thrombosis in the right popliteal vein. Anticoagulant therapy was initiated. The patient was hospitalized for treatment and further investigation. Elevated urinary free-cortisol(UFC) levels were noted (936 µg/24 h; 1389 µg/24 h;26–213), ACTH level was undetectable (<5 pg/ml), salivary cortisol showed loss of circadian rhythm (32.8 nmol/l-0800 h; 32.5 nmol/l-0011 h), and low dose dexamethasone cortisol result was 26.4 µg/dl and low DHEA-S of 76 µg/dl (80–560). These results were compatible with ACTH-independent CS. He started on metyrapone to control the hypercortisolaemia (maximum 1500 mg S-8–9). Ketoconazole was not an option given the elevated liver enzymes. There was an initial reduction in 24 hours UFC within a few weeks of initiation of metyrapone. However, the UFC level failed to normalize, after 7 months of medical therapy alone(UFC 706 µg/24 h).An uneventful laparoscopic left adrenalectomy was subsequently performed, with hydrocortisone started for empiric treatment of secondary adrenal insufficiency. Postoperative histopathology confirmed an adrenal adenoma. He completed 3 months of rivaroxaban. Presently, 5 months after surgery, he remains on hydrocortisone. Studies on medical therapy directed to lower cortisol values and their effects in TE risk are sparse. Additional studies are needed to reinforce well defined guidelines regarding CS and its thrombotic complications.

Results
Non-secreting adenoma represents 48% of all. The mean age of our patients with non-functional adenoma was 62.4±10.5 years with female predominance (70.8%). Among 24 patients, 13 had a BMI>30, a mean waist circumference of 103.8 mm in women and 108.5 mm in men. 11 patients were hypertensive and 6 were diabetic (25%). Fourteen patients had low HDL cholesterol including 5 male and 9 female patients. Moreover, nine patients had elevated triglycerides. Sixty-eight percent of patients satisfied the definition of metabolic syndrome according to the IDF 2005 criteria (International Diabetes Federation), including 10 women and 6 men. Regarding cardiovascular risk, according to the recommendations of the European Society of Cardiology, 70.8% of patients were classified at very high risk and 29.2% at high cardiovascular risk.

Discussion/Conclusion
Non-functional adrenal adenomas are often associated with metabolic syndrome which is a major risk factor for cardiovascular or thromboembolic events, hence the need to consider cardiovascular risk in patients with non-secretory adrenal adenomas for optimal management.

Keywords: adrenal incidentaloma, metabolic profile, cardiovascular risk

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Adrenocortical carcinoma: experience of a tertiary center
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Introduction
Adrenocortical carcinoma (ACC) is a rare endocrine malignancy with poor prognosis. Objective: The aim of this study is to characterize patients with ACC followed at a tertiary center. Material and Methods: Retrospective analysis of clinical records of patients with histopathological diagnosis of ACC followed in our clinic. Results and conclusions: We reviewed 11 patients. The average age at diagnosis was 57.3 ± 15.2 years and 63.6% were females. Seven patients had a functioning adrenal carcinoma. At diagnosis, 72.7% of the patients presented weight loss, 36.4% back pain and 27.3% referred asthenia. Two patients presented Cushing’s syndrome, one hirsutism and three arterial hypertension and hypokalaemia. Regarding imaging data, the tumour was detected almost exclusively through abdominal computed tomography (CT); dimensions ranged from 3.8 to 20 cm with a median size of 10 cm. 54.5% were located on the left adrenal gland; 28.6% had signs of necrosis; 27.3% presented local invasion and 36.4% distant metastasis. Prognostic stratification based on ENSAT tumour stage was used; two (18.2%) patients were in stage I; four (36.4%) in stage II; one (9.1%) in stage III and four (36.4%) in stage IV. Ten patients (90.9%) underwent adrenalectomy, 70% through laparotomy. Presence of residual tumour could not be assessed (Rs) in 50% of the patients; total resection was reported in 10%; microscopic (R1) or macroscopic (R2) resection margins were observed in 30% and 10%, respectively. The Weiss Score ranged from 3 to 6 (median of 3) and the K67 proliferative index ranged from 2 to 20 (median of 7). Postoperatively, 4 (36.3%) patients received only mitotane treatment and 3 (27.3%) patients were given systemic chemotherapy combined treatment with mitotane. Adjuvant radiotherapy was applied in two patients; and other two required palliative radiotherapy. One patient who received mitotane did not report any drug side effects. The symptoms reported were mostly gastrointestinal disturbances (81.4%, n = 5); one patient presented neurotoxicity and other reported skin lesions and mucositis. Two patients even had to discontinue treatment due e to intolerance. Disease specific mortality was 85.7%. The mean overall survival was 62.1 ± 14.7 months for stages I + II (ranging from 33.3 to 90.9 months) and 8.8 ± 2.9 months for stages III + IV (ranging from 3.1 to 14.5 months), P = 0.005. ENSAT staging at diagnosis was the major prognostic factor in our series.

A multidisciplinary team for diagnosis and management of primary hyperaldosteronism
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Background
Primary hyperaldosteronism (PH) is a syndrome caused by excess aldosterone secretion, which leads to hypertension and hypokalaemia and increased risk for target organ damage. The overproduction of aldosterone at the adrenal gland can be unilateral or bilateral. For unilateral disease the best treatment is unilateral adrenalectomy. According to international guidelines, most of the patients should have adrenal venous sampling (AVS) to distinguish between bilateral and unilateral disease. At 2018 we established a multidisciplinary team for diagnosis and management of primary hyperaldosteronism. The aim of this study was to investigate all cases of PH treated in our institute since establishment, including advantages and pitfalls of AVS procedure.

Methods
A retrospective study was performed on a cohort including all patients that were diagnosed and treated at Shaare Zedek Medical Center during 2018–2021. All patients had adrenal imaging (CT or MRI) followed by AVS as needed. Data collection included demographic, clinical and biochemical information, detailed results of AVS procedures and follow up after. AVS protocol and interpretation of the results were done according to International clinical practice guidelines.

Results
During the described period, 22 patients were diagnosed with PH. Mean age 51.6 ± 10, 19/22 (86%) males. All patients had hypertension and 18/22 (82%) had hypokalaemia. 21 of them had an AVS. All AVS procedures were done by one invasive radiology specialist. In 17/21 (81%) the AVS results were fully successful, with improvement during time, from 70% at the first ten patients to 90% at the last ten patients. In 4/21 (19%) there was difficulty to locate the right adrenal vein; even though, in 3/4 patients there was evidence for lateralization according to indirect interpretation of the results, overall 20/21 (95%) had a conclusive lateralization result. In 8/21 (38%) adrenal imaging wasn’t accurate in confirming lateralization side. No significant complications of the AVS were observed. 11/16 patients with unilateral disease had unilateral adrenalectomy, all of them became normotensive with less medications or no medical treatment for hypertension.

Conclusion
Establishment of a multidisciplinary team can improve management and treatment for patients with primary hyperaldosteronism. Learning curve for AVS can be achieved after 10 cases. With the limitation of adrenal imaging to locate the hyperaldosteronism source, AVS is a critical step in the diagnosis of primary hyperaldosteronism, and with a good implementation process it is a safe and efficient procedure.
Introducción

La hipercalemia es desconocida en pacientes con insuficiencia adrenal. Se puede presentar como acidez de la vejiga y hipercalemia. El paciente fue referido con 10 días de historia de vómito, disminución de apetito, anabolia y dolor abdominal. Después de la adrenalectomía, se desarrolló el cuadro clínico con mejoría. La revisión de cortisol libre y electrolitos mostró mejoría. Los estudios de seguimiento a largo plazo mostraron estabilidad en el tamaño del quiste.

Conclusión

Este caso muestra que la insuficiencia adrenal puede presentarse con hipercalemia y acidez de la vejiga. Se debe considerar la evaluación de su hipercalemia en pacientes con insuficiencia adrenal, especialmente si se investigan etiologías comunes.

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EP82

Glucocorticoids and androgen secreting adrenocortical adenoma: A case report and literature review
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Introducción

La presencia de Adrenocorticotropic hormone (ACTH)-independent Cushing syndrome asociada con androgena exceso es extremadamente rara en los pacientes con adenomas de la glándula suprarrenal. La identificación y el manejo de este subgrupo de pacientes son fundamentales.

Casos

Presentamos el caso de una paciente de 35 años que presentó un incremento súbito de peso y dolor abdominal durante la segunda etapa de su embarazo. Los análisis de laboratorio mostraron una presencia de ACTH-independiente Cushing syndrome, con niveles elevados de 17-OHCS y metanephrinas.

El caso fue discutido con el comité de endocrinología, y se presentó al paciente las dos opciones disponibles: adrenalectomía o ablation con etanol. Después de discutir las opciones con el paciente, optó por la ablation con etanol debido a su preferencia hacia el procedimiento menos invasivo.

La paciente recibió una inyección de 1 mg de dexametasona por vía oral y 36 horas después de la intervención, se realizó una reevaluación de la presencia de ACTH-independiente Cushing syndrome. Los resultados mostraron una mejoría significativa en los niveles de cortisol libre y electrolitos. El examen físico y los análisis de laboratorio mostraron una mejora clínica y pronóstica.

Conclusion

Este caso representa una rara asociación entre glucocorticoides y androgénos, lo que resalta la importancia de un enfoque multidisciplinario para el manejo de este tipo de pacientes. Es crucial que los clínicos estén conscientes de esta asociación para proporcionar el mejor tratamiento para los pacientes.

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EP83

Giant pheochromocytoma: which management?
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Introducción

Los pheochromocytomas gigantes presentan un reto real para los practicantes. Esta enfermedad es rara, con compleja caracterización, y heterogeneidad en su evolución y pronóstico. Dado el raro de este tipo de tumor, es necesario un nuevo tratamiento. El manejo debe estar en un marco multidisciplinario. A través de este caso ilustrativo, proponemos un recuento de algunos de los tratamientos diferentes en el manejo de esta situación.

Observación

Un paciente de 23 años con antecedentes de diabetes gestacional (DG) fue consultado por hipertensión arterial (HTA) persistente. Los exámenes de laboratorio mostraron niveles de cortisol libre y electrodo muy altos. La resonancia magnética (RM) del abdomen reveló un quiste adrenal gigante. La paciente fue sometida a una adrenalectomía derecha complicada por una necrosis en el hígado. El análisis histopatológico de los tejidos mostró un tumor maligno en la región vascularizada.

Discusión

Los quistes adrenales son lesiones que a veces pueden ser de consideración. Pueden resultar en complicaciones como infecciones, hemorragia, ruptura o compresión de estructuras adyacentes. La ablación con etanol puede ser una alternativa viable para el manejo de quistes adrenales en pacientes con grandes o recurrentes quistes.

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EP81

Percutaneous ethanol ablation of large adrenal tumor
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Introducción

La ablación percutánea con etanol ha sido usada en los pacientes que presentan antecedentes de tratamiento invasivo para el manejo del hérnula adrenal, riñón y adrenal, de la frecuencia adrenal. Describe el caso de una paciente con una hipercalemia secundaria a un quiste adrenal gigante que optó por la ablación percutánea como alternativa.

Caso

Se presenta el caso de una paciente de 32 años que fue referida por una masa adrenomedular de 10 cm de diámetro. Después de la ablación percutánea con etanol, se observó una mejora clínica notable en la presencia de hipercalemia.

Conclusión

Este caso muestra que la ablación percutánea con etanol puede ser una alternativa viable para el manejo de quistes adrenales en pacientes con grandes o recurrentes quistes. Es importante informar a los pacientes de las diferentes opciones disponibles para el manejo de estas lesiones.

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Cytoreductive surgery should reduce symptoms and improve response to other treatments. For slowly progressive metastatic pheochromocytomas, treatment with 131I-MIBG has been recommended as first-line treatment, with 177Lu-DOTATOC being a potential alternative for those with positive somatostatin receptor metastases; chemotherapy combining Dacarbazine, Vincristine and Cyclophosphamide, may be considered for progressive disease. Prospective trials, in terms of targeted therapies, are necessary for a better characterization of these tumors in order to identify the appropriate treatment. The prognosis of these tumors remains unfortunate.

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EP84

The primary aldosteronism rollercoaster: hypoadosteronism as a potential postoperative complication

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Introduction

Primary aldosteronism (PA) is a common and potentially reversible cause of secondary hypertension, characterised by resistance to standard antihypertensive therapy and possible hypokalaemia. Lateralisation investigations, including adrenal vein sampling (AVS), are required to distinguish between unilateral or bilateral disease, with unilateral disease representing a potentially surgically curable form of PA. The majority of patients proceeding to adrenalectomy remain well postoperatively, with complete resolution of hypokalaemia. Rarely, patients can develop hypoadosteronism postoperatively, due to prolonged suppression of the contralateral zona glomerulosa. There remains a lack of guidance on how to predict and monitor hypoadosteronism in PA patients undergoing adrenalectomy. We will illustrate these challenges within two cases.

Case

Case 1: A 58-year-old fit and otherwise healthy female was referred with a 20-year history of hypertension (on three antihypertensive agents) and unprovoked hypokalaemia (K+ 2.9 mmol/l). Following diagnosis of PA, lateralisation studies confirmed unilateral left adrenal disease. She underwent an uncomplicated left adrenalectomy. At her 1-month postoperative review, she reported symptoms of postural hypotension with fatigue. A short synacthen test (SST) was normal. However, serum electrolytes revealed hyperkalaemia (K+ 6.1 mmol/l); hypona-træmia (Na+ 129 mmol/l) and renal impairment (creatinine = 129 μmol/l). Additional biochemical testing revealed plasma renin concentration (PRC) 62 mU/l and plasma aldosterone concentration (PAC) 104 pmol/l. Following commencement of fludrocortisone, there was significant clinical and biochemical improvement (serum K+ 4.9 mmol/l; Na+ 135 mmol/l, creatinine = 84 μmol/l). A subsequent attempt to withdraw fludrocortisone therapy was associated with recurrence of hypoadosteronism. Case 2: A 55-year-old male was referred with a 10-year history of hypokalaemia and resistant hypertension (average BP 170/11 mmHg on four antihypertensive agents). He had a history of mild renal impairment (baseline creatinine 107 μmol/l). Following diagnosis of PA, he was commenced on Eplerenone which successfully achieved a normotenive state. Lateralisation studies confirmed unilateral left adrenal disease, and the patient proceeded to left adrenalectomy without complication. At his 1-month postoperative review, he was found to be hyperkalaemic with renal impairment (creatinine 176 μmol/l). His PAC was undetectable (<70 pmol/l); SST was normal. Following commencement of fludrocortisone, there was a rapid improvement in his biochemistry (K+ 5.1 mmol/l, Na+ 141 mmol/l, creatinine 113 μmol/l).

Conclusion

Although considered to be a relatively rare (~5%) complication in patients with PA undergoing unilateral adrenalectomy, hypoadosteronism is a potentially serious manifestation. Factors that may predict its development include severity of PA (e.g. presence of hypokalaemia). Our cases highlight the importance of attempting to identify those patients who are at higher risk of postoperative hypoadosteronism, ensuring that there is a strategy for close biochemical surveillance postoperatively in these patients.

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EP85

Assessment of glucolipid metabolism in patients with Cushing’s syndrome caused by adrenal adenoma

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Backgrounds

Based on anthropometry and blood biochemical tests, this study aims to analyze the variation of glucose and lipid metabolism in Cushing’s syndrome (CS) patients caused by adrenal adenoma combining with flash glucose monitoring system (FGMS) and dual-energy X-ray absorptiometry (DEXA).

Methods

According to the strict diagnostic and exclusion criteria, seven healthy controls (HCs) and seven CS patients were collected in this study. First, the anthropometric parameters and blood biochemical indexes of all subjects were collected. Subsequently, their body composition of the whole body were measured by DEXA. Finally, all were equipped with a sensor of FGMS, and the blood glucose levels were recorded. According to the data of FGMS, the related indexes of blood glucose variation were calculated. The data between HCs and the CS group were analyzed by T-test or Mann–Whitney test.

Results

(1) Anthropometric parameters: compared with HCs, the CS group showed the higher waist circumference and waist-to-hip ratio (all P < 0.005); (2) Blood biochemical indexes: the levels of HbA1c, TG, TC and LDL-C in the CS group were higher than those in HCs (all P < 0.005), while FBG and FINS were generally unaffected in the CS group than in HCs; (3) Data related FGMS: compared with HCs, the changes of general blood glucose alterations, within-day and day-to-day glucose variability, and the percentage of blood glucose above the standard range (PT3) were significantly higher, and the percentage of blood glucose within the standard range (PT2) was significantly lower (all P < 0.005); (4) Data related DEXA: a significantly increased fat ratio in Android area (represent for midsection fat) was found in the CS group (all P < 0.005), but no increase or decrease in fat or lean tissue of other areas were observed; (5) Fast insulin, HOMA-β index and HOMA-IR index of CS group tend to be higher than HCs, but there are no significant difference.

Conclusion

The homeostasis of glucolipid metabolism in the CS group was significantly destroyed, but impaired islet β-cell function and IR were not observed. A limitation of our study is its relatively small sample size due to the rare occurrence of CS.

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EP86

Head and neck paraganglioma: exploring the metastasizing potential.

Case report

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Introduction

Paragangliomas (PGLs) are tumors originating from neural crest-derived cells situated in the region of the autonomic nervous system ganglia. Head-and-neck PGLs (HNPGLs) originate from the sympathetic and parasympathetic para-ganglia, most frequently from the carotid bodies and jugular, tympanic and vagal paraganglia, and are usually non-catecholamine secreting.

Case report

We present the case of a 60 years old male patient, which was admitted at Endocrinology Department for differential diagnosis of bilateral cervical lymph nodes, which occurred over past 10 years, with a clinical exacerbation in the last year. His thyroid ultrasound results were suggestive only for a Hashimoto’s thyroiditis, with hormonal tests implying hypothyroid status. In the context of bilateral lymph nodes, with MRI that indicated a potential haemagological malignancy, the left lateral cervical formation has been biopsied and the histopathological result concluded: head and neck paraganglioma. Immunohis-tochemical result indicates that our HNPGL might have malignancy potential: increased tumor dimensions (over 10 cm identified on MRI exam), Ki 67 positive

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in 3% of the tumor cells, sustentacular cells and low expression of S100 in those cells. Other immunohistochemical staining highlighted positive synaptophysin, chromogranin and GATA3. Our patient was not expressing catecholamine secretion clinical features but we recommend complete hormonal exploration: normetanephrine, 3-methoxytyramine and neuron-specific enolase (NSE); tests in working progress. We will recommend full exploration of adrenal glands also, to exclude synchronous affection.

Conclusion
His case will be reviewed by multidisciplinary committee to conclude proper therapeutic management: surgery, radiotherapy or somatostatin analogs and potential PRRT after specific functional imaging. With integral neuroendocrine tumor markers and functional imaging results we’ll be able to determine if this paraganglioma is malignant or not.

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EP87
Managing Immune checkpoint inhibitors and adrenal insufficiency in acute setting
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The introduction of immune checkpoint inhibitors (ICIs) in clinical management of cancer has had an undeniable impact in management of cancer patients. Currently there are several ICIs are used across Europe including but not limited to, pembrolizumab, atezolizumab, and ipilimumab. Even though their clinical efficacy is reputable, they have the potential of causing serious immunotherapy-related adverse events’ (irADRs) in several organ systems including endocrine organs. With the ever-growing use of ICIs, case reports are emerging with increasing frequency of rare yet life-threatening endocrine dysfunctions, particularly involving the pituitary, thyroid and less frequently adrenals.

Case presentations
Case 1 A 64 y/o patient was admitted under medical team with features of adrenal insufficiency. He had background of metastatic poorly differentiated adenocarcinoma of lung(T4N3M1c), for which he was treated with pembrolizumab (from October 2019 – May 2020), cisplatin, pemetrexed, simvastatin 20 mg OD, ezetimibe 10 mg OD and analgesia. She presented with general fatigue, loss of appetite and mouth ulcers since ICI therapy. He was given iv hydrocortisone and the patient improved clinically. On physical examination, the patient’s looked tired and his HR was 116 bpm. Blood test showed his cortisol to be 8 nmol/l.

Discussion/ conclusion
Adrenal insufficiency (AI) is a rare irADR of ICI therapy. If left untreated AI is life-threatening and unlike other autoimmune complication of ICI use AI is not mandatory characteristics of PA but were present in 97% and 57%, respectively. The number of PA referred for AVS was not increased in the last 10 years. We did not find any significant correlation between the number of PA referred for AVS and the number of subjects who underwent unilateral adrenalectomy. The number of PA referred for AVS and the number of subjects who underwent unilateral adrenalectomy was in line with the literature. The number of PA referred for AVS and the number of subjects who underwent unilateral adrenalectomy was in line with the literature.

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EP89
Alternative treatment in Bilateral Macronodular Adrenal Hyperplasia with possible adrenal hypersensitivity to Angiotensin II
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Bilateral Macronodular Adrenal Hyperplasia (BMAH) is an uncommon cause (< 2%) of endogenous Cushing’s syndrome, characterized by enlarged adrenal glands. Although the exact pathogenetic mechanism remains unclear, recently, it has been reported that aberrant expression of ectopic receptors, such as AVP, GIP, angiotensin II (AT1 receptor) catecholamine, LH, ACTH and leptin, evoked cortisol secretion, which escapes from cortisol-mediated feedback in BMAH. Here we report a case of BMAH that suggested an aberrant response to angiotensin II via AT1 receptor in cortisol hypersecretion. A 66-yr-old man was admitted to a hospital for stroke, medically treated since beyond the established thrombolytic window. On admission he presented severe hypertension (BP 230/140 mmHg). On the hypothesis of secondary hypertension we performed an in-depth analysis. Laboratory test documented undetectable plasma ACTH level (1.6 pg/ml) and high level of 24-h urinary free cortisol (983 mg/die). Plasma cortisol was not suppressed (12.8 µg/dl) after the administration of 1 mg dexamethasone overnight. Abdominal Magnetic Resonance Imaging demonstrated nodular enlargement of bilateral adrenal glands. Moreover, renin and aldosterone levels were high (respectively 83 µIU/ml and 74 ng/dl) and Angio-CT revealed right renal artery stenosis. These results indicated a diagnosis of Cushing’s syndrome due to BMAH with suspected adrenal hypersensitivity to angiotensin II. Therefore, Renal Artery Stenosis Angioplasty (PTA) was performed and the patient underwent a revised assessment which revealed
normal level of plasma ACTH, urinary free cortisol and renine and aldosterone. Although it is well known that angiotensin II stimulates aldosterone secretion mainly through angiotensin II receptor (AT1), there has been no evidence, to our knowledge, that angiotensin II affects cortisol secretion in vivo. In our case, PTA blocked the aberrantly increase of plasma cortisol level. Therefore, it is possible that the adrenal hypersensitivity to angiotensin II is involved in the pathogenesis of BMAH and that angiotensin II aberrantly stimulated cortisol secretion via AT1 receptor. A similar case report described a case of BMAH with adrenal hypersensitivity to angiotensin II, treated with bilateral adrenalectomy [1]. In summary, we have reported a case of BMAH with possible hypersensitivity to angiotensin II. Further investigations are required to clarify the significance of abnormal adrenal response to angiotensin II.


EP90

Tumor enlargement in adrenal incidentaloma is related to glaucoma and statin treatment: are there two new prognostic features?

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Aim

The uncertainty on the management of small adrenal incidentalomas (AIs) in guidelines still represents a challenge in real clinical practice. The aim of the study was to identify risk factors for morphological or functional changes during follow-up by using clinical, radiological, and pathological features.

Methods

We retrospectively evaluated demographic (gender and age at diagnosis), clinical (weight, height, body mass index, smoking habit, comorbidities), radiological characteristics (localization, diameter, HU for CT scan; T1 and T2, and the loss of intensity at chemical shift for MRI) and biochemical parameters of adrenal hypersecretion of 177 AIs (2007-2021). To detected risk factors for tumor enlargement or hypersecretion, diseases associated with AIs were included if the prevalence was higher than 2%. Patients were divided into two groups according to dimension during follow-up (group A: radiological stability; group B: tumor enlargement at radiological scans).

Results

90.4% of patients belongs to group A, while 9.6% to group B. Chronic obstructive pulmonary disease (COPD), neoplasms, and glaucoma were the most frequent associated diseases. Group B showed larger diameter at diagnosis (P < 0.09), higher aldosterone (P < 0.001), DHEAS (P = 0.007), ARR (P = 0.01), lower DRC (P < 0.006) levels and higher weight than group A. Open laparotomy was chosen most frequently in group B (P < 0.004). AI diameter was negatively correlated with age (r = -0.159, P < 0.04), 17-OHP levels (r = -0.461, P = 0.05), statin treatment inversely to the drug potency (r = -0.193, P < 0.02), and positively with ACTH (r = 0.198, P = 0.06) and urinary normetanephrine levels (r = 0.248, P < 0.01).

Analyzing AIs changing over time, an enlargement occurred within 36 months of follow-up and only glaucoma was an independent predictor of it (b = 3.370, ex = 29.077; P < 0.005). Considering concomitant treatments, at 36 months of follow-up, 100% of subjects showing an enlargement were not taking statins, compared to 45.2% of subjects with stable disease (P = 0.06). Subjects suffering from glaucoma, atrial fibrillation, impaired glucose metabolism (T2DM or IGT), COPD (in males only) had a lower dimensional change-free survival than non-affected.

Conclusions

The presence of glaucoma and treatment with statins seems to be a risk and a protective factor, respectively, for an AI enlargement. Further prospective studies of validation are needed. If subtle undetectable cortisol hypersecretion and proliferation cellular mechanisms have a role are two topics for further research.

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EP91

Silent clinical presentation of a rare genetic disorder

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Introduction

Carney complex is a rare autosomal dominant genetic disorder which develops secondary to mutation in the PRKAR1A gene located in the 17q22-24 region. It is commonly characterised by the association between spotty skin pigmentation, cardiac myxoma and secretory endocrine tumors.

Case presentation

A 15.8-year-old boy known with PRKAR1A mutation diagnosed based on his personal history – cutaneous papilloma of the neck resected at the age of 6 years, bilateral testicular microlithiasis, right testicular teratoma resected at the age of 9 years, and atrial fibrillation. At the age of 5 years he was admitted for abdominal pain and was diagnosed with acute appendicitis. At the age of 6 years he was diagnosed with glaucoma. He was treated with statins for 5 years. His family history is negative. Clinical examination reveals a height of +2.03 s.d. (+1.54 DS compared to his familial target height), a height growth velocity of 6 cm per year (+3.86 s.d.), BMI 19 kg/m2; no other specific findings are met. Thyroid function and neck ultrasound are normal. Prolactin, hypophysal-gonadal axis and androgens are within the normal range. Testicular ultrasound reveals the presence of persistent bilateral bilateral microlithiasis, but tumor markers (β-hCG and alfa-fetoprotein) are negative. IGFB1 (468.5 ng/ml; +1.65 SDS), IGFBP3 (5401 ng/ml) have normal values, with a suppressed hormone of 1.28 ng/ml after oral glucose stimulation test. Bone age is comparable to the chronological age (16.5 years old).

Aims

The main aim of this case report is to present a patient with Carney complex that developed secondary to glaucoma and treatment with statins.

Methods

We conducted a literature review of cases with Carney complex presenting with glaucoma and treatment with statins. The data was presented in a descriptive manner.

Results

A 15.8-year-old boy suffered from Carney complex. He was diagnosed with a cutaneous papilloma of the neck resected at the age of 6 years. At the age of 5 years he was treated with statins. He presented with glaucoma at the age of 6 years and was treated with statins for 5 years. This is the first case report of a patient with Carney complex presenting with glaucoma and treatment with statins.

Discussion

Carney complex is a rare autosomal dominant genetic disorder which develops secondary to mutation in the PRKAR1A gene located in the 17q22-24 region. It is commonly characterised by the association between spotty skin pigmentation, cardiac myxoma and secretory endocrine tumors. Case presentation

A 15.8-year-old boy known with PRKAR1A mutation diagnosed based on his personal history – cutaneous papilloma of the neck resected at the age of 6 years, bilateral testicular microlithiasis, right testicular teratoma resected at the age of 9 years, and atrial fibrillation. At the age of 5 years he was admitted for abdominal pain and was diagnosed with acute appendicitis. At the age of 6 years he was diagnosed with glaucoma. He was treated with statins for 5 years. His family history is negative. Clinical examination reveals a height of +2.03 s.d. (+1.54 DS compared to his familial target height), a height growth velocity of 6 cm per year (+3.86 s.d.), BMI 19 kg/m2; no other specific findings are met. Thyroid function and neck ultrasound are normal. Prolactin, hypophysal-gonadal axis and androgens are within the normal range. Testicular ultrasound reveals the presence of persistent bilateral bilateral microlithiasis, but tumor markers (β-hCG and alfa-fetoprotein) are negative. IGFB1 (468.5 ng/ml; +1.65 SDS), IGFBP3 (5401 ng/ml) have normal values, with a suppressed hormone of 1.28 ng/ml after oral glucose stimulation test. Bone age is comparable to the chronological age (16.5 years old).

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Discussion

Carney complex is a rare autosomal dominant genetic disorder which develops secondary to mutation in the PRKAR1A gene located in the 17q22-24 region. It is commonly characterised by the association between spotty skin pigmentation, cardiac myxoma and secretory endocrine tumors.
discharge. The drugs used by the 3 patients during hospitalization, continued after the first and discontinued before the second out-patient appointments were Isomiazid and Rifampicin, which we suspect to cause this previously undescribed pharmacological interference. Rifampicin has been implicated in false positive dexamethasone suppression tests.

Conclusions

We report the association of very high UFCL in patients without stigmata of Cushing syndrome treated with anti-TB regimens containing Isomiazid and Rifampicin. Hopefully in the future we will confirm the underlying mechanism and appraise the impact of this finding on the exclusion criteria for adrenal insufficiency in these specific group of patients.

EP93

Detection of late-onset adrenal hyperplasia in girls with peripubertal virilisation, a case study

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Introduction

Non-classical congenital adrenal hyperplasia (NCCAH) is considered to be a common monogenic inherited disease, with an incidence range from 1:500 to 1:100 births worldwide. NCCAH is often peri or post pubertal pauci or even asymptomatic. We report the case of a young girl with severe hirsutism and sexual ambiguity, despite late disclosure.

Observation

This is the case of a 16-year-old girl, with a history of menarche at the age of 14, presenting since puberty a spaniomennorhea with rapidly worsening hirsutism. The clinical examination finds a normal height at 160 cm, a BMI at 21 kg/m2, severe hirsutism scored at 33 according to Ferriman and Galway with signs of virilization and defeminization associating alopecia of the frontal guls, muscle hypertrophy, hoarseness tract, significant clitoral hypertrophy and breast atrophy. The biological assessment found elevated testosterone at 2.83 ng/ml, baseline 170REP at 5.98 ng/ml, and 47.6 ng/ml after synacthen, normal plasma cortisol at 543 nmol/l, ACTH at 162 pg/ml. The adrenomedulopelvic ultrasound objectified an aspect of micro polycistic ovaries. CT of the adrenal glands and pelvic MRI are without abnormalities. The diagnosis of NCCAH was retained. The patient was treated with cyproterone acetate and valerate of estradiol.

Discussion

Despite the high incidence, there is a low genotype-phenotype correlation, which explains why NCCAH diagnosis is usually delayed or even never carried out, since many patients remain asymptomatic or are misdiagnosed as suffering from other hyperandrogenodic disorders.

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EP94

The burden of illness associated with adolescent and adult congenital adrenal hyperplasia: results of a structured literature review

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Objectives

Congenital adrenal hyperplasia (CAH) is a rare condition caused by enzyme deficiency in cortisol biosynthesis. The aim of this study was to evaluate the burden of illness associated with child/adolescent and adult CAH.

Methods

A structured, comprehensive literature review was conducted to identify articles describing the burden and treatment landscape of CAH. Literature databases (MEDLINE, Embase, the Cochrane Library and EconLit), websites and conference proceedings were searched. Searches were performed in 2016 and updated in June 2020. Eligible articles presented evidence for child/adolescent (aged <18 years where reported) or adult CAH for at least one topic of interest (natural history; risk factors; epidemiology; clinical characteristics; humanistic, caregiver and economic burden; treatment options; or clinical guidelines). The evidence presented here focuses on the humanistic, caregiver and economic burden of child/adolescent and adult CAH.

Results

A total of 3,711 citations were identified and 338 were included. A total of 89 (adults) and 86 (adolescents) references were identified that reported humanistic, caregiver or economic burden data respectively. Compared to the general population, patients with CAH (irrespective of age) were found to be significantly shorter and experienced poor bone health, increased occurrences of cardiometabolic events (including obesity, hypertension and insulin resistance), were at risk of developing adrenal crises (which contributed to excess mortality), and in adolescent/adult CAH, had impaired male and female fertility (with adolescents commonly experiencing precocious puberty). Both adolescent and adult patients with CAH were also at risk of developing psychosocial health issues compared to the general population, with adult patients experiencing emotional trauma related to their condition and subsequently finding it difficult to speak about their illness. The reported generic HRQL (no CAH specific instruments were identified) in CAH was varied, with increased impairment observed in more severe forms of CAH and in general, HRQL frequently more impaired in women compared with men. Although the literature was sparse, it did indicate that CAH is associated with a substantial caregiver burden; parents of children/adolescents with CAH reported high levels of anxiety, depression and worry for their loved one. Furthermore, CAH was also associated with a notable economic burden, with significantly higher annual healthcare costs compared to matched controls (P = 0.007 for patients aged 18–40 years; P < 0.001 for patients aged ≥40 years).

Conclusions

Our review highlights that CAH is a complex and debilitating disease which is associated with significant humanistic, caregiver and economic burden in both child/adolescent and adult CAH patients.

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EP95

Congenital adrenal hyperplasia due to 21-hydroxylase deficiency and hypertension: a case report

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Introduction

Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is the most common of the CAH, it is also the most common of the autosomal recessive diseases. Hypertension is generally absent, and its presence should lead to an investigation of another cause.

Observation

We report the case of a 26-year-old young man, descendant from a second-degree consanguineous marriage with a family history of the death of a brother at the age of 25 days of severe dehydration, who is followed in our department for HCS with HTA. The diagnosis of CAH was suspected at the age of 9 days due to dehydration with electrolyte disorders. Hormonal assays confirmed the diagnosis in front of a high level of 17-OH progesterone. At the age of 3 years old, he was operated for right testicular ectopia and at the age of 8 years old, we discovered a hypertension. The etiological assessment concluded to a secondary hyperaldosteronism.

Discussion

The 21-hydroxylase deficiency is generally not associated with hypertension, taking into consideration the hypocortisolism and the aldosterone deficiency depending on the level of the block. Hyperaldosteronism associated with 21-hydroxylase deficiency constitutes a new entity recently reported by a few studies, but its pathophysiological mechanism remains unclear.

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EP96

Ectopic Cushing’s syndrome

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Introduction

Ectopic Cushing’s syndrome (ECS) is a condition caused by an ACTH-secreting tumor outside the pituitary or adrenal glands. Most cases are caused by neuroendocrine tumors of the lung, pancreas, thymus or medullary carcinoma of the thyroid. Small-cell carcinomas of the lung are probably the most common cause of biochemical hypercortisolism. About 15% of Cushing’s syndrome cases are due to ECS.

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EP97
Adrenal insufficiency revealed during a septic shock
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Introduction
Acute adrenal insufficiency (AAI) is a rare but life-threatening condition. It may occur in 50 to 60% of septic shocks (SS). Its diagnosis can be difficult as symptoms are sometimes nonspecific. Herein, we report the case of a female patient with an AAI revealed during SS.

Abstract
A 30-year-old woman with a history of celiac disease since the age of 25 on a gluten-free diet, presented to the emergency department with abdominal pain, vomiting, fever and profound asthma evolving for five days. Physical examination revealed an increased pulse rate of 120 beats per minute, a rapid respiratory frequency of 40 cycles per minute, fever (38.8) and low arterial hypotension of 60/40 mmHg. The abdomen was diffusely painful. Blood investigations showed leukocytosis (14000), mildly increased C-reactive protein (CRP) (94 mg/l), hypoglycemia (0.5 g/l), severe hyperkalemia (7.22 mmol/l) and hypernatremia (122 mmol/l). Arterial blood gas test noted a metabolic acidosis. A Computed Tomography (CT) scan of the lungs, abdomen and pelvic was normal. The urine culture was positive. The diagnosis of septic shock due to urinary tract infection was then initially retained. The patient was treated with vasoactive drugs and appropriate antibiotic therapy. The evolution was marked by the persistence of abdominal pain, arterial hypotension, hypoglycemia and hydroelectrolytic disorders. The diagnosis of acute adrenal insufficiency was therefore confirmed and then confirmed by a low serum cortisol level of 1.6 mcg/dl (6.6–18). The patient received intravenous hydrocortisone hemisuccinate and parenteral rehydration. Clinical and biological improvement was noticed in few days.

Conclusion
Our case illustrates the difficulty of the diagnosis of an AAI during SS. Thus, acute adrenal insufficiency must be suspected in the context of SS especially in patients with hyperpigmentation; hypernatremia and/or hyperkalemia, a medical history of autoimmune disease or an increased vasopressor dependency. Parenteral rehydration and intravenous hydrocortisone hemisuccinate should be initiated immediately, even before laboratory confirmation of the diagnosis.

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EP98
Adrenal crisis revealing factitious hypoglycaemia in a pregnant woman
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Introduction
Factitious hypoglycaemia in adults is usually due to exogenous intake of insulin or hypoglycaemia sulfonamides. This occult intake is most often voluntary and the diagnosis is not always obvious.

Observation
We report the case of a 37-year-old pregnant woman at 15 weeks of amenorrhea, followed for addison’s disease since 3 years and not diabetic, was referred to our department for acute adrenal insufficiency following the discontinuation of her replacement therapy for more than 3 months. The main symptoms were asthenia, vomiting, abdominal pain and recurrent hypoglycaemia. She was treated with intravenous high-dose hydrocortisone, with improvement of the symptoms except for randomly scheduled hypoglycaemia resistant to correction. She denied taking any medication other than those given by the nurses and the hypoglycaemia continued. Investigations such as plasma measurements of insulinemia, C-peptide, hypoglycaemia sulfonamides were done concomitantly as a venous glyceria at 0.4 g/l and were respectively 87.81 µU/ml (normal: 2.6–24.9), 8.59 mg/l (normal: 1.1–4.4) and 135 µg/dl. The diagnosis of factitious hypoglycaemia by taking sulfonamides was confirmed. The day before and during hospitalization, the patient had admitted to sneaking glibenclamide tablets and the drug was seized.

Conclusion
Factitious hypoglycaemia represents a challenge for the clinician, on the one hand the patient tries to hide certain proofs on the other hand it remains an elimination diagnosis, especially if an organic cause is preexisting as it is in our observation.

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EP99
Gravit myelolipoma adrenal: report of two cases and literature review
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Introduction
Adrenal myelolipoma is a rare, benign and nonfunctional tumor composed of mature adipose and hematopoietic cells. It is often of incidental finding (8%) and the diagnosis is not always obvious.

Observation
Patient D.K. 40 years old, hospitalized for adrenal mass revealed by right back pain radiating to the right hypochondrium, without signs of endocrine hypersecretion. Clinical examination showed sensitivity of the right lumbar fossa. 24-hours urinary methoxyl derivatives and dexamethasone suppression test were correct. The patient underwent the removal of the abdominal masse and anatomo-pathological examination showed adrenal myelolipoma. Patient A.M., 51 years old, with a personal history of simple mammary and renal cysts, consulted for an adrenal incidentaloma of 6.5 cm discovered on pelvic MRI during exploration of myomatous uterus. Clinically, the patient did not present signs of endocrine hypersecretion or abdominal pain. Hormone levels returned normal. Abdominal scan revealed a large left adrenal mass with spontaneous density of – 45 HU, heterogeneous, 60*18*78 mm, without any sign of vascular invasion or neighbouring organs. The patient underwent a left adrenalectomy. Anatomo-pathological study showed adrenal myelolipoma.

Conclusion
Unlike other adrenal incidentalomas, adrenal myelolipoma is a rare, benign tumor that is often asymptomatic with special radiological features. Management is based on clinical and radiological follow up of asymptomatic forms. Surgical treatment is reserved for large, symptomatic or complicated adrenal myelolipomas.

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Management of pituitary apoplexy
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Introduction
Pituitary apoplexy is a rare clinical emergency with an incidence of 2–7% in pituitary adenomas. There does not exist any evidence-based standards of optimum care for the patients. A key controversy in management is related to the functioning of acute neurosurgical intervention. The nature of clinical presentation precludes robust randomised controlled trials. Practical guidelines are derived from high-quality observational studies. On this background, we report the management of pituitary apoplexy in a large cohort of patients treated at a single tertiary referral centre.

Methods
This retrospective study evaluates the clinical presentation, management and clinical outcomes presenting with pituitary apoplexy during 2020–2021.

Results
80 patients with 34 females were included. Among these patients, 10 patients had been previously diagnosed with a pituitary tumour. The common symptoms were visual disturbance, headache, diplopia and cranial nerve involvement. 32 patients had undergone surgery, while 48 patients were conservatively managed. All 32 patients had visual disturbances, while 59% of them had recovered fully. Among these patients, 76% made full recovery while 33 had visual disturbances. In the surgical group, 84% required hydrocortisone, 15% withdrew treatment, 69% required thyroxine, 34% required sex steroids, 9% started growth hormone. In the conservatively managed patients, 79% started hydrocortisone, 13% stopped doing so, 69% required thyroxine, 46% started sex steroids, 19% started growth hormones.

Conclusion
This data represents the largest case series from a single centre. We propose that patients with acute apoplexy who have mild or stable symptoms/signs can be managed conservatively with careful monitoring; only rarely is there a need to change from conservative to surgical management in these patients.

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Visfatin as a potential serum marker of adrenal gland cancers
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Introduction
There are not many studies specifying the role and contribution of adipokines in biology of adrenal gland cancer. Many research show correlation between increased level of serum visfatin and malignant potential, stage progression and prognosis. Visfatin/NAMPT overexpression has been found in a various type of malignances. So far, to the best of knowledge, this is the first research studying the role of visfatin in diagnosis of adrenal cortical carcinoma.

Patients and methods
This was a prospective observational study with a consecutive enrollment.

Results
Thirty-two patients with adrenal gland cancers and 34 patients with benign adrenal tumors were recruited.

Patients with adrenal gland cancers have higher serum visfatin concentrations as compared to controls (Me 7.7 ng/ml vs 5.9 ng/ml, P = 0.0017). Also, ROC curve analysis detected visfatin concentrations higher than 7.1 ng/ml as a biomarker of adrenal cancers (P = 0.0007; sensitivity 59.1%, specificity 85.3%). Visfatin serum concentrations in patients with adrenal cancers did not differ between men and women. In the whole group, visfatin positively correlated with the tumor size (P = 0.0193, r = 0.318).

Conclusion
Visfatin is a potential serum marker of adrenal gland cancers.

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Factors associated with metabolic syndrome in Tunisian psychiatric patients
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Introduction
Metabolic Syndrome (MetS) is a bunch of metabolic disturbances related to insulin resistance and is considered a global public health problem. The screening and management of MetS is particularly challenging in psychiatric practice.

Objectives
We aim to identify clinical and therapeutic factors associated with MetS in a Tunisian psychiatric population.

Methods
We conducted a descriptive and analytical cross-sectional study involving 126 patients who attended the psychiatry department at Gabes regional hospital, Tunisia, from 2019 to 2020. MetS was diagnosed based on the 2005 IDF criteria. We compared two subgroups:

* [MetS+] Patients with MetS (n = 32)
* [MetS−] Patients without MetS (n = 94)

Results
[MetS+] patients were significantly older ([MetS+] 52.1 ± 10.5 years vs [MetS−] 43.3 ± 12.7 years; P = 0.0017). The onset of psychiatric symptoms was significantly earlier in [MetS+] ([MetS+] 36.0 ± 14.1 years vs [MetS−] 26.8 ± 11.0 years; P = 0.004). No significant gender nor addictive behaviours differences were reported in both subgroups. The two shared an unprivileged educational and socioeconomic backgrounds. Married patients were more affected by MetS ([MetS+] 65.6% vs [MetS−] 43.6%; P = 0.006). Schizophrenia and psychiatric disorders (50%), and mood disorders (18.8%) were more recorded in [MetS+] unlike anxiety disorder (18.1%) which was more prevalent in [MetS−], without any statistic significance. Mental patients are more likely to develop MetS when prescribed antipsychotics (OR = 3.4; P = 0.03; 95% CI[1.7–10.8]) or atypical antipsychotics (OR = 9.3; P = 0.001; 95% CI[2.4–36.2]).

Conclusions
Screening psychiatric patients for comorbid MetS is recommended both before and during treatment. The initial drug selection should take into consideration specific metabolic profiles. The opportune identification of MetS can facilitate early lifestyle interventions and treatment to reduce the cardiometabolic risk in this vulnerable population.

DOI: 10.1530/endoabs.81.EP102

Metastatic adrenal carcinoma? When not everything is what it seems...
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69-year-old male, with a history of bipolar disorder under treatment, smoker and high blood pressure. He is referred for left adrenal injury detected incidentally by secondary hypertension study. Abdominal CT shows a mass of 67.7 × 51.8 × 52.3 mm in the left adrenal area, with radiological characteristics of malignancy and aggressive behavior, contacting the left renal pole and upper splenic pole, compatible with adrenal carcinoma vs. metastasis. The functional study is negative. In the extension study, a 10.2 mm right apical pulmonary nodule with nonspecific characteristics and a high-density lesion in the spinal canal at the level of the 9th costal arch compatible with a tumor lesion were detected. The PET-CT does not rule out the malignancy of both lesions. To differentiate whether the adrenal lesion is a primary or metastatic lesion, it was decided to perform FNAX, which was inconclusive on 2 occasions. Finally, surgical intervention of the mass was chosen, with an initial approach of en bloc removal of the left adrenal gland, spleen and left kidney, although it was finally possible to perform an isolated left adrenalectomy as no invasion of neighboring organs was observed during the surgical act. The definitive pathological anatomy is compatible with anastomosing hemangiomia, an exceptional variant of adrenal tumor, difficult to differentiate radiologically from adrenal carcinoma but that presents benign behavior, which completely changes management and prognosis.

DOI: 10.1530/endoabs.81.EP103
EP104 Establishment of humanized mouse humoral immunity evaluation system using the pregnancy immune system
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(Aims) Regulation of humoral immunity is important to develop vaccines for infectious disease and cancer. However, human and mouse humoral immune systems contain different molecular mechanisms, and the evaluation of efficacy is difficult in the pre-clinical investigation. Humanized mice with reconstructed human immune system are useful for drug discovery of molecular-targeted drugs related to the immune system, and evaluation of antibody production by vaccines. The development of a good model for evaluating the antibody-producing ability has been awaited. However, it was difficult to develop antigen-specific IgGs in the mice, because the maintenance of fully developed T cells and B cells was not successful. We focused on the fact that the mother during pregnancy accepts the other, the foetation, while maintaining the production of specific antibodies, and attempted to produce humanized mice based on the expression of pregnancy-related protein interleukin-4 (IL-4). As we found that the mice can secrete antigen-specific antibodies, futher experiments were performed. (Materials and Methods) We immunized the 20mer HER2 peptide CH401M, which we developed as a breast cancer vaccine model, into NOG-hIL-4-Tg mice transplanted with healthy donor’s peripheral blood mononuclear cells (PBMCs). Then, the subsets and activation level of T cells was confirmed by flow cytometry. Glucocorticoid receptor (GR) was quantified by realtime-RT-PCR. Moreover, the antibody production performance was confirmed by ELISA/LC-MS. (Results and Discussion) As a result, in the presence of high concentration of IL-4, antigen-specific IgB antibody production was detected in the plasma of PBMC-transplanted NOG-hIL-4 mice. Because glucocorticoid suppresses not only humoral immunity but also innate and cellular immunity, we analyzed the relationship among GR expression levels, the profile of human lymphocyte subsets and the humoral immunity status of PBMC-transplanted NOG-hIL-4 mice. The results showed that NOG-hIL-4-Tg splenocytes had significantly lower human GR mRNA levels than conventional NOG splenocytes after immunization. Moreover, B-cell proportion and antigen-specific IgG concentration in plasma showed strong negative correlations with the GR mRNA level. It was considered that IL-4 decreased GR expression to increase the viability of B cells and to induce the proliferation and class switching of clones producing specific antibodies. This system may help mother’s immunity to protect their body from the infectious diseases and cancer. Moreover, it may help producing and sending pathogen-specific IgGs to their fetus.

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EP105 Serum cortisol immunoassay performance in the overnight dexamethasone suppression test.
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Background
The 1 mg overnight dexamethasone suppression test (ONDST) is recommended for the differential diagnosis of Cushing’s syndrome and the investigation of adrenal incidentalomas. However, diagnostic performance of the test relies on accurate methods to quantitate cortisol in serum. Although the variable performance of serum cortisol immunoassays has been well-documented, little has been published on their performance following the ONDST.

Aims
Assess the performance of three common immunoassay platforms (Roche Elecsys II, Abbott Alinity & Siemens Centaur) when compared to a liquid chromatography tandem mass spectrometry (LC-MS/MS) method.

Methods
Samples (n=77) sent to the laboratory as part of an ONDST were retrieved prior to storage and stored at −80°C until commencement of the study. Samples were pseudononymised, aliquoted and frozen prior to distribution to participating laboratories for immunoassay analysis. Samples with cortisol > 250 nmol/l and samples with cortisol lower than the limit of quantitation for each assay were excluded. Immunoassay results were compared to a routine LC-MS/MS serum cortisol method that is metrologically traceable to a candidate reference measurement procedure. Statistical analysis was done, for total results and split into male and female cohorts, through Passing-Bablok regression and Bland-Altman plots.

Results
The Roche gen II compared well, with a mean bias of −2.4 nmol/l and a Passing-Bablok regression fit of y = −1.332 + 0.9857x. This bias was not affected by sex. The worst comparison was observed with the Abbott immunoassay. The mean bias here was −17.7 mmol/l, with a Passing-Bablok regression fit of y = −5.565 + 0.8362x. This negative bias was exacerbated in the samples taken from female patients (−20.9 mmol/l) vs male patients (−15.0 mmol/l). The Siemens assay had a mean bias of 3.2 nmol/l and a Passing-Bablok regression fit of y = 0.9305x + 0.048x. This positive bias was worse in male patients (6.7 mmol/l) vs female patients (0.01 mmol/l).

Conclusions
Method-dependent variation exists in the analysis of serum cortisol as a part of ONDSTs. Of the immunoassays, Roche gen II and Siemens more closely aligned with LC-MS/MS. Use of the Abbott immunoassays may result in the underestimation of cortisol and a reduction in ONDST diagnostic sensitivity, particularly in female patients. Clinicians should be aware of the performance of their local assay and on the basis of this data there is evidence to support assay-specific cut-offs for the ONDST.

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EP106 11-deoxycortisosterone producing adrenal hyperplasia as a very unusual cause of endocrine hypertension: case report and systematic review of the literature
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11-deoxycortisosterone (DOC) is an aldosterone precursor synthesized from progesterone and converted to corticosterone in the adrenal cortex. DOC overproduction due to an adrenal lesion is a very rare cause of mineralocorticoid-induced hypertension. The objective of this study is to provide the most relevant clinical features that clinicians dealing with patients presenting with the hallmark of hypertension due to DOC-producing adrenal lesions should be aware of. We report a case of a patient with a DOC producing adrenal hyperplasia and provide a systematic review of all published cases (PubMed, Web of Science) until 2021. A 53-year-old woman without any previous history of hypertension consulted to the Emergency Department for high blood pressure (BP), muscle aches and stiffness. Blood test showed serum potassium of 1.73 mmol/l. After being admitted to the Intensive Care Unit and the hospitalization ward, she was diagnosed of a left functional adrenal mass due to non-aldosterone dependent mineralocorticoid secretion (aldosterone: 81.94 nmol/l; reference range 187–930 and plasma renin activity: undetectable), namely excessive DOC production (35.8 ng/dl; reference range 2–15). A left adrenalectomy was performed. Macroscopy revealed a cortical adenomatous hyperplasia and microscopy excluded atypia, mitosis or necrosis, with a Kt67 index positive in <1% of cells. After surgery, her potassium levels normalized and BP and DOC levels significantly improved. The systematic review of the literature identified 44 cases (including ours). Most cases (30, 68%) affected women with a mean age of 42.8 ± 15.6 years and presented with high BP and hypokalaemia (average: 2.65 ± 0.61 mmol/l). Median (interquartile range) time from onset of first suggestive symptoms to diagnosis was 24 (56) months. DOC levels were a median of 15.8 (18.9) times above the upper limit of the normal reference range reported in each article and overproduction of more than one hormone was seen in 29 (66%) cases. Carcinoma was the most common histological type (48.8%). Median tumour size was 64 (67.5) mm. Reduced 11β-hydroxylase and 17α-hydroxylase enzyme activities were the most frequent immunohistochemical findings. Malignant compared to benign lesions were

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Primary bilateral bilateral macronodular adrenal hyperplasia is a cause of Cushing's syndrome. It is characterised by a large enlargement of the adrenal glands at the expense of multiple non-pigmented nodules. There is inefficient steroidogenesis.

Summary of the case
A 58-year-old woman with a history of extreme obesity, type 2 diabetes mellitus, hypertension and dyslipidemia was admitted to our hospital for cellulitis and metabolic alkalosis, recurrent spontaneous hematomas and depressive syndrome. Surgical treatment was proposed, but was ruled out due to the maximum surgical risk due to her comorbidities. We therefore started medical treatment with ketoconazole, titrating the dose up to 800 mg per day, achieving disease control, after normalisation of hypercortisolism. During admission, functional limitation of the lower limbs was added, and an X-ray of the lumbar spine was performed, awaiting bone densitometry, which revealed vertebral crushing, and zolendronic acid was started. At present, our patient has been hospitalised for a year as a social problem. She remains functionally and cognitively limited due to persistent depression.

Conclusion
Primary bilateral macronodular adrenal hyperplasia as a cause of Cushing's syndrome is rare. The initial management of this pathology is surgical, but there are patients with extensive comorbidity in whom this is not possible, and we have to opt for medical treatment. It is important to discuss all associated comorbidity as it is a pathology with a slow clinical course, but which greatly impairs the quality of life of patients.
EP10

Tertiary adrenal insufficiency revealing Gayet-Wernicke encephalopathy
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Introduction
Gayet-Wernicke encephalopathy (WE) is a rare neurological disorder, caused by thiamine (vitamin B1) deficiency. We report a case of tertiary adrenal insufficiency revealing Gayet-Wernicke encephalopathy.

Case presentation
A 45-year-old woman was admitted with abdominal pain, vomiting and weakness. Her medical history was significant for a long-term self-medication of corticosteroids and chronic vomiting. Clinical examination revealed a cushingoid appearance (discrete facial erythrosis, protuberant abdomen, skin fragility). The Laboratory results revealed a nataremia of 136 mmol/l, a kalaemia of 4 mmol/l, and an 0800 h serum cortisol level of 50 ng/ml. The diagnosis of tertiary adrenal insufficiency was made and treatment with parenteral hydrocortisone hemisuccinate was started. The evolution was characterized by the development of nystagmus, confusional state and flaccid tetraparesis. Brain MRI revealed hyperintense signaling in the periventricular thalamus, mammillary bodies and ophthalmoparesis with nystagmus, ataxia and confusion.

Discussion
The development of nystagmus, confusional state and flaccid tetraparesis. Brain MRI revealed hyperintense signaling in the periventricular thalamus, mammillary bodies and ophthalmoparesis with nystagmus, ataxia and confusion. Early and adequate treatment with thiamine is necessary to avoid death or progression to permanent brain damage.

Conclusion
Our case illustrates the seriousness of self-medication with corticosteroids ranging from a simple tertiary adrenal insufficiency to a serious pathology such as Gayet-Wernicke encephalopathy.

References

EP11

The “RESCUE” Trial: 11-[Hydroxysteroid Dehydrogenase Type 1 (HSD-1) Inhibition for ACTH-Dependent Cushing’s Syndrome
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Background
HSD-1, an intracellular enzyme, converts cortisone to cortisol in tissues where cortisol excess is associated with morbidity including liver, adipose, bone, brain, muscle, skin, and eye. SPI-62 is a potent and specific HSD-1 inhibitor in development for treatment of Cushing’s syndrome and autonomous cortisol secretion, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with minimal liver and brain HSD-1 inhibition. Single and multiple SPI-62 doses decreased urinary cortisol metabolites indicating a similar decrease of hepatocellular cortisol in this important target tissue. After a corresponding transient decrease, circulating cortisol homeostasis was restored by ACTH increase which also resulted in a moderate adrenal androgen increase. SPI-62’s effects on androgens did not result in adverse effects. Urinary free cortisol was unaffected. The RESCUE trial will assess SPI-62 safety and efficacy in patients with a dysregulated HPA axis, i.e., ACTH-dependent Cushing’s syndrome.

Methods
This randomized, placebo-controlled, crossover, multinational, Phase 2 clinical trial, adult patients (n = 26) with ACTH-dependent Cushing’s syndrome with active and consistently elevated urinary free cortisol (UFC) will be randomized to receive SPI-62 and placebo for 12 weeks each. A diagnosis of an inadequately treated pituitary adenoma (Cushing’s disease) or ectopic ACTH or CRH producing tumor based on established criteria is required. Evidence of Cushing’s associated morbidities including at least 2 of A) insulin-resistance/type-2 diabetes mellitus, B) dyslipidemia, C) hypertension, or D) osteopoenia is required. Subjects must not have had recent Cushing’s surgical, radiation other approved or experimental medical therapies for cortisol excess. Medical conditions or treatments likely to interfere with study assessments or subject safety are also excluded. The primary outcome is pharmacological suppression of the urinary ratio of hepatic 5- and 3-steroid reductase metabolites of cortisol and cortisone (tetrahydrocortisol + allo-tetrahydrocortisol/tetrahydrocortisone). Safety is assessed by adverse events, vital signs, ECG, and clinical laboratory analyses including effects on HPA/HPG axis biomarkers. Efficacy is assessed by reduction of Cushing’s features and morbidities of hyperglycemia, dyslipidemia, adiposity, hepatic steatosis, hypertension, glaucoma, osteopenia, muscle strength, cognition, sleep, and mood. Assessments include tumor-imaging by MRI, ocular tonometry, timed up-and-go and hand-grip strength tests, dual-energy x-ray absorptiometry, oral glucose tolerance, continuous glucose monitoring, and ambulatory blood pressure monitoring.

Results
This trial is ongoing; results are pending.

Discussion
This Phase 2 explores SPI-62 safety, HSD-1 inhibition, effects on HPA/HPG axes, and clinical effects in patients with ACTH-dependent Cushing’s syndrome.

EP12

The A-SPiRE trial: 11-[Hydroxysteroid dehydrogenase type 1 (HSD-1) inhibition for autonomous cortisol secretion and adrenal cushing’s syndrome
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Background
HSD-1, an intracellular enzyme, converts cortisone to cortisol in tissues where cortisol excess is associated with morbidity including liver, adipose, bone, brain, muscle, skin, and eye. SPI-62 is a potent and specific HSD-1 inhibitor in development for treatment of autonomous cortisol secretion (ACS) and Cushing’s syndrome, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with minimal liver and brain HSD-1 inhibition. Single and multiple SPI-62 doses decreased urinary cortisol metabolites indicating a similar decrease of hepatocellular cortisol in this important target tissue. After a corresponding...
transient decrease, circulating cortisol homeostasis was restored rapidly by ACTH increase which also resulted in a moderate adrenal androgen increase. SPI-62’s effects on ACTH and androgens did not result in adverse effects. Urinary free cortisol was not affected. The ACSPIRE trial will assess SPI-62 safety and efficacy in patients with dysregulated cortisol production due to ACS or adrenal Cushing’s syndrome (aCs) for the first time.

Methods
In this randomized, placebo-controlled, multinational, Phase 2 clinical trial, adult patients with ACS or aCs with otherwise benign adrenal adenomas, persistently elevated morning cortisol after verifiably adequate dexamethasone suppression, and at least two morbidities associated with hypercortisolism (A) insulin-resistance/type-2 diabetes mellitus, B) dyslipidemia, C) hypertension, or D) osteoporosis] will be randomized to receive SPI-62 or placebo for 12 weeks. Subjects must have declined, delayed, or been deemed ineligible for adrenalectomy and not recently taken approved or experimental medical therapies for cortisol excess. Medical conditions or treatments likely to interfere with study assessments or subject safety are also excluded. Efficacy at 12-weeks is assessed by reduction of cortisol-associated morbidities of hyperglycemia and dyslipidemia while also examining, adiposity, hepatic steatosis, hypertension, inflammatory cytokines, osteopenia, muscle strength, cognition, sleep, and mood. Safety is assessed by adverse events, vital signs, ECGs, clinical laboratory analyses. Pharmacology is assessed by effects on HPA/HPG axis biomarkers and suppression of the urinary ratio of hepatic 5- and 3-steroid reductase metabolites of cortisol and cortisone (tetrahydrocortisol + allo-tetrahydrocortisol/tetrahydrocortisone). Assessments include timed up-and-go and hand-grip strength tests, dual-energy x-ray absorptiometry, oral glucose tolerance test, continuous glucone monitoring, and 24-hour ambulatory blood pressure monitoring.

Results
This trial is ongoing; results are pending.

Discussion
This Phase 2 explores SPI-62 safety, HSD-1 inhibition, effects on HPA/HPG axes, and clinical effects in patients with ACS and aCs.

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**EP114**

Late diagnosis of adrenoleukodystrophy in an adult patient with tetraparesis and Addisonian crisis.

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Introduction
Adrenoleukodystrophy (ALD) is a rare, X-linked inherited, genetic disease, characterized by a disorder of peroxisome metabolism, leading to the accumulation of very long-chain fatty acids (VLCFAs) mainly at the central nervous system and the adrenal glands. It usually occurs in childhood, but there are types of the disease that manifest later in life.

Case
A 57-year-old man with a history of progressive spastic paraparesis, starting at the age of 25, was admitted due to weakness and hypotension, nausea, abdominal pain, and blurred vision. Fever and severe hypotension (Na 108 mmol/l) were present. Due to the clinical-laboratory picture and reported episodes of hypoglycemia, basal cortisol and ACTH levels were determined, which were indicative of primary adrenal insufficiency [cortisol 2.5 μg/dl, ACTH 360 pg/ml (7-64)]. The diagnosis was confirmed by a short synacthen test (250 μg tetraacosactide) with a maximum cortisol response of 1.43 μg/dl. The patient was discharged fever-free and electrolytically stable on hydrocortisone and flurohydrocortisone replacement therapy. Considering the neurological history and the newly diagnosed Addison’s disease, the possible diagnosis of adrenoleukodystrophy was suspected. The new MRI imaging of the brain showed no typical focal lesions while cervical spinal cord atrophy was reported, a typical finding of adrenomyeloneuropathy, one of the most common forms of the disease in adult patients. He underwent a long-chain fatty acid test that confirmed the diagnosis.

Conclusion
The patient suffered spastic tetraparesis without an identified neurological diagnosis for many years. The diagnosis of coexisting primary adrenal insufficiency led to the diagnosis of adrenoleukodystrophy. Adrenomyeloneuropathy is a less severe form of adrenoleukodystrophy, with the onset of symptoms in adolescence or adulthood. This form of the disease does not involve brain damage and should be included in the differential diagnosis of men with adrenal insufficiency or neurological motility disorders of unknown causes.

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**EP115**

Paraneoplastic Cushing’s syndrome in metastatic poorly differentiated carcinoma of the kidney

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Introduction
Paraneoplastic Cushing’s syndrome is attributed to ectopic ACTH release from a non-putitary tumor. The lung is frequently the primary site of the underlying neoplasm but sometimes, in cases of advanced metastatic disease, determining the origin may be challenging.

Case presentation
A 70-year-old man was referred to our centre for generalised bone pain, lethargy, and important weight loss in the last six months. Before admission, a contrast-enhanced CT scan of thorax and abdomen revealed multiple lung nodules, mediastinal lymphadenopathy, spinal bone lesions suggestive of metastases (with considerable size and extension in the spinal canal), bilateral adrenal masses (with washout percentage >55%) and a large heterogeneous renal mass. The patient presented poor general condition, immobilisation (mainly due to intense bone pain), pale skin and maleolar petechiae; classical clinical features of hypercortisolism were not present. Moderate hypercalcaemia, high inflammatory markers, severe ACTH dependence Cushing’s syndrome and low PTH level were noticed. Spine MRI confirmed the osteolytic lesions and also the spinal cord

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Metyrapone treatment in bilateral macronodular adrenal hyperplasia: a report of two cases
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Introduction
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is potentially responsible for variable degree of cortisol excess. In patients with PBMAH the complete remission of cortisol hypersecretion can be achieved only by performing bilateral adrenalectomy, leading to a persistent hypocortisolism and to a consequent need of a lifelong glucocorticoid replacement therapy. Therefore, bilateral adrenalectomy is worth doing only in patients with severe hypercortisolism, while a medical treatment could be a valid alternative for patients with mild Cushing’s syndrome (mCS), particularly in the presence of possibly related clinical conditions (i.e. diabetes, hypertension and bone fragility). In this scenario, steroid synthesis inhibitors, such as metyrapone, have been proposed as possible therapeutic options. We report two cases of PBMAH with mCS treated with low doses of metyrapone (mean dose of 500 mg). Before and after 6 months of therapy, an assessment of clinical consequences of mCS was performed with a 24-hour ambulatory blood pressure monitoring (ABPM) and an oral glucose tolerance test (OGTT).

Case reports
Case 1: A 68 years old male with history of scarcely controlled arterial hypertension. The basal OGTT was consistent with a diabetes diagnosis (fasting glucose levels 128 mg/dl, 2-hour OGTT glucose levels 202 mg/dl). After 6 months of treatment, he achieved: i) the remission of diabetes (fasting glucose levels 97 mg/dl, 2-hour OGTT glucose levels 122 mg/dl) with no changes in anti-diabetic therapies; ii) the ABPM documented improvement in mean blood pressure values (147/80 mmHg and 121/63 mmHg, respectively before and 6 months after treatment). Case 2: A 79 years old female with a history of osteoporosis with 4 clinical vertebral fractures, arterial hypertension and depressive disorder. Before starting the therapy, she had an impaired fasting glucose (104 mg/dl) with a normal response to the glucose load (post-OGTT glucose levels 96 mg/dl). After six months of therapy, we observed: i) the normalization of basal glucose levels (90 mg/dl) and the persistence of a normal OGTT response (132 mg/dl); ii) the important reduction of anti-hypertensive medications with ABPM documented stable mean blood pressure values (119/68 mmHg); iii) the striking amelioration of the depressive disorder and cognitive function. In both patients metyrapone was well tolerated without signs or symptoms of hypocortisolism. In the first patient, potassium levels decreased during the treatment period but remained within the normal range.

Discussion
Our observations suggest that low doses of metyrapone are well-tolerated and can improve blood pressure and glycemic control in PBMAH and mCS.

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adrenal insufficiency with autoimmune thyroid disease and/or type 1 diabetes mellitus. We present a case of 46 year old male, with no significant medical history who presented in our clinic with: weakness, fatigue and weight loss for the preceding last 3 months. On the examination he was found to have hypertension, tachycardia, hyper pigmentation of the skin and vitiligo. Based on the lab reports and physical exam findings diagnosis primary adrenal insufficiency, Graves Hypothyroidism and vitiligo was made corresponding with the Autoimmune Polyglandular Syndrome type 2. Treatment with Hydrocortisone, Fluorocortisone and Thiamamides was started in our patient resulting in significant improvement in patient’s symptoms. After achieving euthyroidism, the thiamamide dose was gradually decreased and later discontinued after a year of treatment. Patient remains euthyroid to present day and continues only adrenal hormone replacement therapy with both glucocorticoid and mineralocorticoid. Patient is on regular follow up and is clinically well. He is given the instructions of “sick day rules” to change the hydrocortisone dose appropriately. Patient consent for publication is obtained. The Case report will be accompanied with the corresponding pictures depicting pre and post treatment appearance of the patient. DOI: 10.1530/endoabs.81.EP119

COVID-19 pandemic and alternative options to classical pathways: real life experience

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Introduction

COVID-19 pandemic obliged physicians to find out alternative options to classical pathways, to lower viral spread and related dangers as well as to cope with redeployment of personnel and resources. We describe here two cases in whom surgery for adrenal Cushing’s syndrome (CS) and pheochromocytoma (PHEO) was deferred due to the unavailability of surgical facilities. Case no 1: A 69-yo woman was evaluated for CS. Type 2 diabetes mellitus was diagnosed some years before and a 35-mm right adrenal mass incidentally found at US; no endocrine work-up was performed. Progressively clinical picture worsened and physical examination suggested ACTH-independent hypercortisolism, confirmed by endocrine work-up performed in January 2020. The whole picture was so severe that she was not considered suitable for surgery that became anyway inaccessible due to pandemic. Ketocozazole was given up to 400 mg/day for a progressive reduction in CLU values. Due to the occurrence of symptomatic hypoadrenalism, a block-and-replace therapy with cortisol acetate was started, obtaining a progressive and persistent improvement in clinical bio-chemical picture. Due to the persistence of pandemic and the unavailability of surgical facilities the emergent surgery was still waiting surgery. Case no 2: In an 83-yo woman, abdominal plastic surgery was complicated by hypertensive crisis, acute pulmonary edema, cardiogenic shock, acute renal failure; multiple stenoses were disclosed at coronary-angiography, reverse Takotsubo at ventriculography. Abdominal CT disclosed a 45×31 mm left adrenal lesion consistent with PHEO, confirmed by Endocrine-workup Recovery of systolic function and pressure control were obtained with doxazosin (in addition to ongoing lowering blood pressure treatment. The planning of adrenal resection was postponed due to an adrenal hematoma developed while on LMWE treatment; the subsequent CT showed hematoma reabsorption but in the meanwhile there was the outbreak of the pandemic. The patient was monitored throughout subsequent months with telemedicine controls, confirming optimal pressure control; she underwent laparoscopic-adenalecomy without any peri-operative complications. A post-op CT and hormonal evaluation did not disclose any tumor remnant/relapse and the patient has an optimal pressure without any anti-hypertensive treatment. Conclusion

This change of the mainstay of treatment for adrenal hypersecreting lesions due to pandemic could offer a new therapeutic paradigm of these diseases in cases when surgery is contraindicated for severe comorbidities. DOI: 10.1530/endoabs.81.EP120

Primary hyperaldosteronism and Graves’ disease, a rare combination

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Introduction

Primary hyperaldosteronism is a known cause for secondary hypertension. In addition to its effect on blood pressure, aldosterone exhibits proinflammatory actions and plays a role in immunomodulation of autoimmune. Autoimmune hyperthyroidism (Graves’ disease) and primary hyperaldosteronism rarely coexist but underlying mechanisms associating the two are still unclear. Case report

A 32-year-old female referred to endocrine unit for further evaluation and management of hypertension and hypokalemia. She was on three anti hypertensive medications at the time of presentation but had poor blood pressure control. She also had nonspecific body aches and intermittent muscle cramps palpitation and sweating with associated heat intolerance, recent weight loss, for the past 2 months. She did not have any vitriling features. She was not on diuretics or any long-term medications except three anti hypertensive medications. None of her family had hypertension, strokes, or sudden deaths at younger age. Examination: pulse: 110 /minute, blood pressure: 140/100 mmHg while on anti hypertensive therapy BMI: 23 kg/m2. There was a small diffusely enlarged goiter without any tenderness. Bilateral mild exophthalmos normal eye movements and vision. Investigations: potassium, 2.1 mmol/l (3.5–5) Patient with hypertension, hypokalemia, possibility of primary hyperaldosteronism was considered. Aldosterone: renin ratio (ARR) was measured after correcting the potassium value and adjusting the interfering medications ARR was 198 [ng/dl]/[ng/ml/hr] (r<20) A contrast enhanced computed tomography (CT) of abdomen showed a right-sided homogenously dense (density of 9.5 Hounsfield Units {HU}) adrenal lesion measuring 2.0 × 1.5 × 0.8 cm Evaluation of the thyroid status revealed evidence of hyperthyroidism: TSH < 0.08 μIU/ml (0.27–4.0), free T4—4.60 ng/dl (0.7-1.91) and free T3—7.56 pg/ml (2-4.4). Ultrasound scan of the thyroid showed diffusely enlarged gland with increased echo pattern and vascularity on Doppler studies, compatible with Graves’ disease Thyrotoxicosis was managed with antithyroid drugs (Carbimazole)30 mg/day titration till she was on 10 mg/day and once patient rendered euthyroid, laparoscopic right adrenalectomy was performed. Antithyroid medications were discontinued after 12 months after which patient achieved remission of Graves’ disease. Conclusion

Primary hyperaldosteronism (PA) is a leading endocrine cause for secondary hypertension, particularly in resistant hypertension Recent studies have demonstrated role of aldosterone on immunomodulation together with its effects on adaptive immune system, suggesting the possible rare link with development of autoimmune disorders. DOI: 10.1530/endoabs.81.EP121

Malignant pheochromocytoma: a case report

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Introduction

Pheochromocytoma (PHEO) is an adrenal medulla tumor secreting catecholamines. Malignancy is defined by the presence of metastases in non-chromaffin tissue. Its optimal management requires experienced multidisciplinary teams. We report the case of a patient followed for malignant pheochromocytoma

Case report

A 58-year-old patient operated for a pheochromocytoma in 2016, then lost sight of. The evolution was marked 6 years later by the installation of right lumbar pain associated with a Menard triad evolving in a context of weight loss not figure. Clinical examination found right lumbar contact with tenderness on palpation, associated with swelling next to the left scapula. The dosage of urinary methoxylated derivatives shows a normetanephrine level twice the normal. The adrenal CT shows a right interhepato-renal lesional process invading the hepatic parenchyma measuring: 8.4 × 10.5 cm. As part of the extension assessment, a CTAP CT scan was performed showing an inter hepatorenal tissue mass invading the liver and the thoracic wall in favor of tumor recurrence with secondary pancreatic and bone localizations at the level of the femoral head, and lysis scapular bone. MIBG scintigraphy and PET FDG are not available The file was...
staffed in multidisciplinary meeting, the therapeutic decision was to complete with palliative chemotherapy with VP 16 cisplatin A genetic study is requested in search of a mutation of the SDHIB gene

Discussion
The prevalence of metastatic pheochromocytomas varies between 5 and 26%. Only the presence of lymph node or distant metastases affirms malignancy; histological examination does not provide certain information. Secondary localizations are most often pulmonary, hepatic and bone. The diagnosis of recurrence can be made through MIIBG scintigraphy despite a normal hormonal balance. Surgery is rarely curative, but tumor reduction or resection of metastases particularly reduces cardiovascular risk. Treatment with T311-MIBG is an interesting alternative in the management of malignant pheochromocytomas when chemotherapy is indicated as first-line treatment in the event of an inoperable tumor or failure of metabolic reoxygenation.

Conclusion
Our case illustrates the importance of clinical, biological, and even morphological monitoring of all patients operated for pheochromocytoma, which must be continued for a long time (15 years) given the possibility of late revelation of metastases. In spontaneous evolution, the 5-year survival is generally less than 50%. Due to the current absence of an effective treatment for malignant tumors, several palliative therapies allow tumor reduction and improved survival.

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EP123
The Adrenal that inCYSTS on causing pain
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Adrenal lymphangiomatous cysts are rare, often found incidentally, but can also present in association with abdominal/ loin pain or hypertension. They have occasionally been reported in association with hormone over secretion of either aldosterone, cortisol or catecholamines. We present a case of a 49-year-old serving soldier who was suddenly awaken with severe left sided abdominal and flank pain. Over the course of several months, he was forced to take time off work, required opiate analgesia and experienced significant psychological burden because of the severity of symptoms. His initial work up involved a cystoscopy (due to dipstick haematuria) which was normal and a CT of the abdomen which showed a left sided 3.4 cm cystic, partially calcified adrenal lesion. Full endocrinological workup revealed the lesion to be non-functioning. He was normotensive. The size of the adrenal cyst was not thought to correlate with the severity of his pain (and a follow up CT showed no growth or intracyst haemorrhage), but in the absence of an alternative explanation, the patient chose to proceed to a laparoscopic left adrenalectomy. His pain immediately resolved postoperatively, he discontinued all analgesia and returned to work. Histology showed multicollated cysts lined by flattened endothelial-like cells. Immunohistochemistry confirmed expression of D2-40, CD31 and CD34 consistent with cystic adrenal lymphangioma. Whilst most small adrenal cysts are asymptomatic, adrenal cystic lymphangiomas have been associated with back/abdominal/loin pain in 48% and hypertension in 14% cases.1,2 This suggests that these endothelial cysts are more likely to cause symptoms regardless of their size. The possible mechanisms of pain in relatively small cysts with no evidence of prior bleed could include retroperitoneal irritation, local cytokine release, abnormal lymphatic drainage, but what exactly causes this phenomenon, especially if pain is severe, remains a mystery. Management of the adrenal cyst and decision on whether to proceed to surgery remains dependent on the size and clinical imperative. However, this case provides an example of small adrenal cyst having life changing implications, had it not been removed. Recognition that small adrenal cystic lymphangiomas can cause such symptoms may help inform future clinical decision making.

References

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EP124
A case report of 24 years old female with stage IV adrenocortical carcinoma in vilnius university saratorus clinics.
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Introduction
Adrenocortical carcinomas (ACC) are rare and frequently aggressive tumors that may be functional (hormone-secreting) – causing Cushing’s syndrome and/or virilization, or nonfunctional – presenting as an abdominal mass or as an incidental finding. We describe a rare case of stage IV adrenocortical carcinoma which first manifested as treatment resistant Cushing’s syndrome.

Case report
In September of 2021, a 24-year-old female came with a complaint of acne and weight gain. During the process of anamnesis collection other symptoms characteristic to hypercortisolism were identified – rounding and flushing of the face, widening of the neck, abdominal weight gain, limb weakening and thinning, increase in blood pressure and thirst. In initial blood test results biochemical parameters testosterone and plasma melatonin were within normal limits. Serum cortisol was elevated (1049.9 nmol/l), also secondary hyperthyroidism was found. Low-dose dexamethasone test was performed and no suppression was observed, cortisol after suppression test remained high – 797 nmol/l. We confirmed autonomous cortisol secretion after disturbed circadian cortisol rhythm. High levels of the 24-hour urinary free cortisol, suppressed adrenocorticotrophic hormone were found. Following that, chest, abdominal, pelvis computed tomography (CT) scan was performed and right adrenal mass was identified (90×62×127 mm), with metastases in the liver and in nearby lymph nodes. Interdisciplinary team decided on a treatment plan consisting of radical surgery followed by a postoperative chemotherapy treatment with mitotane. 2021-10-15 radical surgery was performed and she started the rehabilitation process. After surgery she felt better, she lost weight, her blood pressure became normal. 2021-10-28 histological test results came and adrenocortical carcinoma with metastases in liver was confirmed. 2021-11-20 treatment with doxorubicin, cisplatin and etoposide has begun, but after the first 3 days of treatment – chemotherapy induced cardiotoxicity appeared. She was hospitalized 2021-12-02. 2021-12-06 Abdominal CT scan showed tumor recurrence and progression. Due to hypokalemia, hypercortisolism – etomidate therapy was given, starting from 40 mg a day, through 8h intravenously. 2021-12-22 mitotane was given, starting from 2000 mg per day. One more cycle of chemotherapy was tried, but her condition rapidly deteriorated and on 2022-01-05 she died.

Conclusion
Our case showed that despite the rarity of the tumor and young patient’s age it is important to perform further clinical evaluation in any patient with unexplained symptoms characteristic to hypercortisolism.

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EP125
A case of Cushing’s disease caused by pituitary macroadenoma
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Introduction: Cushing’s disease (CD) accounts for approximately 80% of cases of Cushing’s syndrome. Almost all patients with CD have a pituitary adenoma. The tumors are usually microadenomas, only approximately 5 to 10 percent are macroadenomas. Pituitary adenomas arise from epithelial pituitary cells and account for 10–15% of all intracranial tumors. Pituitary imaging is important in confirming the diagnosis of pituitary macroadenomas and also for determining the differential diagnoses of other sellar lesions. Case report: A 27-year-old woman was referred with a 2-week history of headache, blurred vision, edema, amenorrhea, acne and 14 kg weight gain. Three months previously, her gynecologist had diagnosed hyperprolactinemia (PRL-1053 U/ml) and had started treatment with Cabergoline ½ tab. 2 times per week. She stopped the treatment without doctor’s permission. On examination, there was no galactorrhoea and no purple stretch marks, BMI-19 kg/m², BP-110/70 mmHg, P-75, regular. Investigations: MR scan of brain – chiasm-compressing adenaoma with suprasellar extension 1.2×2.0×1.5 cm, CT scan – without adren al hyperplasia, PRL-1053 U/ml (102-496), TSH-0.696 mIU/ml (0.27-4.2), FT4-10.76 pmol/l (12-22), FT3-3.09 pmol/l (3.1-6.8), LH<0.100 mIU/ml (2.4-12.6),
Hormonally active adrenocortical oncocytoma is a very rare neoplasm. Adrenal oncocytomas are mostly considered as non-functioning, benign tumors, with the size of generally > 6 cm and lack of pathognomonic features on radiological examinations.

Case Report
A 41-year-old woman was referred to the endocrinologist in April 2021 due to weight gain, resistant arterial hypertension and menstrual irregularities. She was also referred due to a magenta oncocytic mass located in the right adrenal gland. The mass was first detected on an abdominal CT scan performed for evaluation of an abdominal pain. She had a history of hypertension grade 3, uncontrolled despite treatment with 4 antihypertensive drugs. She was also referred due to a magenta oncocytic mass located in the right adrenal gland. The mass was first detected on an abdominal CT scan performed for evaluation of an abdominal pain. She had a history of hypertension grade 3, uncontrolled despite treatment with 4 antihypertensive drugs.

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Case Report
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EP129
Altered steroid metabolism in patients following severe trauma: the golden hour study

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Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK; 1National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre, Queen Elizabeth Hospital Birmingham, Birmingham, UK; 2School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK; 3Institute of Cancer and Genomic Sciences, Centre for Computational Biology, University of Birmingham, Birmingham, UK; 4Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK; 5Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; 6Royal Centre for Defense Medicine, Birmingham, UK.

Background
Advancements in medical care have significantly improved survival after major traumatic injury and the main risks are now sepsis and multi-organ failure. An understanding of the hormonal, inflammatory and metabolic changes that occur following trauma is still evolving but it is clear that they impact significantly upon patient prognosis. To date, studies that have examined trauma-induced changes in steroid metabolism have analysed samples taken from patients post-hospital admission, culminating in marked variability in the time of first blood sample. Here we investigated the major changes in steroidogenesis following trauma, focusing on the immediate time after injury.

Methods and Results
We recruited 31 male trauma patients (mean age 28.1 years range 19–59) who had an initial blood sample taken within 1-hour of injury, with subsequent samples taken 4–12 and 48–72 h post-injury. Our control cohort was 35 healthy male volunteers (mean 30 years; range 18–50). Sixteen serum steroids were quantified by liquid chromatography tandem mass spectrometry using a Waters Acquity UPLC and a Xevo-XS mass spectrometer:

- precursors: progesterone, 17hydroxyprogesterone
- glucocorticoids: 11-deoxycorticisol, cortisol, cortisone
- mineralocorticoids: 11-deoxycortocosterone, corticosterone
- androgen precursors: DHEAS, DHEA, androstenedione, androgens, testosterone, DHT

Eleven of the sixteen steroids were significantly increased 1 h after injury in comparison to healthy controls. Maximum concentrations of these steroids were observed one hour post injury, concentrations then decreased at 4–12 h and reached levels similar (or lower than) healthy controls 48–72 h after injury. The exceptions were cortisolone, 11-Keto-androstenedione, 11-Keto-testosterone, testosterone and DHT. The concentrations of testosterone and DHT decreased one hour post injury when compared to healthy controls, then decreased further at 4–12 and again at 48–72 h post injury. To estimate when trauma-induced steroid metabolism changes occurred we employed generalised additive models (GAMs) to the samples collected within the first hour of injury. GAMs allowed us to estimate the time excretion of each steroid was altered compared to the baseline.

Conclusions
This data show major changes in steroidogenesis following trauma, for the first time focusing on the immediate time after injury. Whether those patients that have ultra-early changes in steroid metabolism are associated with poor patient outcome warrants further investigation.

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EP130
More than a coincidence? a true risk factor in spontaneous coronary dissection: hypothyroidism

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Introduction
Spontaneous coronary artery dissection (SCAD) is an uncommon cause for acute coronary syndrome (ACS). It has been linked to many conditions such as physical exertion, emotional stress, fibromuscular dysplaia, autoimmune diseases. Recent studies suggest high prevalence of hypothyroidism in unselected consecutive patients with SCAD compared with a control group of ACS patients without SCAD with more distal dissections on curvy vessels.

Case report
A 51 years old woman with no particular medical history except for hyperthyroidism diagnosed 5 months prior and treated with anti-thyroid drugs, presented to the emergency department for sudden constrictive chest pain following an unusual physical exertion. The EKG showed a regular sinus rhythm of 75 bpm and ST segment depression in the apico-lateral and inferior leads. Troponin levels were high (>40.000 ng/l) and the rest of the lab tests were unparticular. The patient received anti-ischemic treatment and was transferred to our department. At the admission to the intensive care unit, the patient was pain-free, and the EKG showed a sinus regular rhythm with complete regression of the previous patterns, she was then promptly transferred to the cath lab where coronary angiography was performed and showed a tubular dissection of a tortuous mid left anterior descending artery without flow limitation, concordant with type 2 SCAD. The decision then was to perform angioplasty with a DES covering the length of the diseased segment. The transthoracic echocardiography showed an akinetic apex, a left ventricle ejection fraction of 40% and an apical thrombus. The thyroid hormones dosage revealed a hypothyroidism, which was most likely iatrogenic due to the anti-thyroid drugs; subsequent dose lowering was put into effect for an eventual interruption. The patient was discharged with uneventful clinical course.

Conclusion
SCAD is still a topic of interest with unresolved pathophysiology and multiple factors that have been linked to it like thyroid disorder. More studies are needed in this context, which could potentially help elucidate the mechanisms involved in this phenomenon.

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EP131
Adrenal insufficiency revealed during a diabetic pregnancy: a case report

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Introduction
Adrenal insufficiency is rarely diagnosed during pregnancy. In the absence of treatment it is associated with high maternal-fetal morbidity and mortality. We report the case of a twenty-one years old female patient, diagnosed with adrenal insufficiency during a diabetic pregnancy of 12 weeks of gestation.

Observation
Twenty-one years old female patient, diagnosed with type 1 diabetes since the age of 15, Referred to our department for the follow-up of her diabetes with an unplanned, evolving pregnancy estimated at 12 weeks of gestation. The patient reported multiple episodes of hypoglycemia reaching 0.42 g/l and persistent asthma. The clinical examination showed a blood pressure of 100/68 mmHg, heart rate of 71 bpm, and BMI of 22.86 kg/m². Suspicion of adrenal insufficiency is confirmed by a low baseline cortisol of 13 μg/dl for an average of 25.1 μg/dl according to the term (12 weeks of gestation). The patient initially received hydrocortisone 30 mg/d reduced after to 20 mg/d with a favorable evolution after the replacement therapy. Adrenal insufficiency of autoimmune cause in the context of autoimmune polyendocrinopathy, is the most likely etiological diagnosis. The results of the etiological investigation are in progress.

Conclusion
Adrenal insufficiency can occur during pregnancy and be life-threatening if not treated appropriately. However with a correctly adapted hormonal substitution during pregnancy the evolution is favorable in most cases. During delivery, the treatment must be increased and administered by injection as during surgery. The diagnosis can sometimes be difficult due to confusion with the signs of pregnancy or in case of association with diabetes which could be responsible for a delayed management.

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EP132
Association of preoperative therapy by native form vitamin D and hypocalcemia after parathyroidectomy in primary hyperparathyroidism patients
Anna Eremkina1, Anna Erenkina2, Olga Rebрова3, Elena Kovalyeva1 & Natalia Mokryshiva2

Background
Primary hyperparathyroidism (PHPT) is a common endocrine disorder resulting from oversecretion of parathyroid hormone (PTH) in parathyroid glands. Hypocalcemia can occur in the postoperative period after parathyroidectomy (PTE) and can be challenging to control and requires varying doses of supplementation. Vitamin D deficiency can worsen the severity of PHPT and promote the development of “hungry bone syndrome” due to increased influx of calcium into bone after PTE.

Aim
To estimate the association of preoperative cholecalciferol therapy and development of hypocalcemia in 1–3 days after PTE in patients with PHPT.

Methods
Patients with PHPT, serum 25-hydroxyvitamin D (25(OH)D) < 20 ng/ml (vitamin D deficiency), and serum total calcium <3 mmol/l were included. Exclusion criteria was the therapy with drugs affecting calcium-phosphorus metabolism - cinacalcet, denosumab or bisphosphonates (either as monotherapy or as a part of combination therapy). All patients underwent selective PTE at the Endocrinology Research Center in 1993–2010 or 2017–2020. PTH, total calcium, phosphorus were measured on 5 days – 4 years before surgery and before therapy (cholecalciferol therapy). For PTE, 25(OH)D, total calcium, phosphate, alkaline phosphatase (AP), osteocalcin, c-terminal telopeptide of type 1 collagen (CTX-1) and dual-energy X-ray absorptiometry were measured on 4–365 days before surgery.

Results
Among 117 included patients, 110 (94%) were female and 7 (6%) male with median age 58 [49; 65] years. 21 patients took cholecalciferol for 2 weeks–2 months at a dose according to the replenishment of vitamin D deficiency and 96 did not. No significant difference was found in demographical (sex, age at surgery), clinical (severity of bone mass density loss) and laboratory parameters (PTH, total calcium, phosphorus, AP, osteocalcin, CTX-1, 25(OH)D) between these groups of patients. Patients with cholecalciferol therapy had significantly less frequent postoperative hypocalcemia (10% vs 63%, P<0.001, χ2). Cholecalciferol intake is negatively associated with hypocalcemia, RR = 0.15, 95% CI: 0.03–0.51.

Conclusions
Taking cholecalciferol before PTE for 2 weeks–2 months reduces the risk of postoperative hypocalcemia by 2–33 times in patients with PHPT.

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EP134
«Hungry bone» syndrome in delay diagnosed primary hyperparathyroidism with fibrocystic osteitis: A case report
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Background
Fibrocystic osteitis is rare PHPT manifestation. Poor management and delay in diagnosis of fibrocystic osteitis may lead to reduced quality of life and also provoke severe postoperative hypocalcemia – «hungry bone» syndrome. Clinical case

We present a case of 66-years-old Caucasian woman, with history of urulithiasis/nephrolithiasis (CKD stage 4), two pathological fractures and fibrocystic osteitis. After multidisciplinary team (MDT) discussion in Jan 2021 MRI was performed due to increasing bone and joint pain, unstable gait and showed multiple vertebral lesions in L3 and L4. Since the diagnosis was not established CT was performed, it revealed bone resorption sites in Th12, L2 – L5, sacrum, and left ileum. These changes were considered to be multiple myeloma signs, but bone marrow trephine biopsy and monoclonal antibody assay did not support this diagnosis. L3 trephine biopsy suggested the giant-cell tumor. Zoledronic acid (4 mg/28 days) therapy was started and undertook within 4 months. Later PTH was suspected. Subsequently iPTH level was 2306.9 pg/ml (15.0–68.3), serum Ca++ level – 2.17 mmol/l (1.11–1.29), serum total Ca – 3.86 mmol/l (2.15–2.25), 25(OH)D – 10.80 ng/ml (9.40–11.90). Within the adenoma localization neck ultrasound was performed, although it didn’t show any lesions. CT and 11C-methionine PET/CT neck and thorax scans revealed two lesions presumed to be ectopic parathyroid adenomas (3.0x2.1x4.8 cm and 0.8x0.5x0.9 cm). Loop diuretics, rehydration, and cholecalciferol (2000 IU/daily) therapy was started. Parathyroidectomy was performed shortly due to increasing hypercalciemia, both lesions were confirmed to be adenomas. From the third day postoperatively low serum Ca++ was detected 0.85 mmol/l in terms of normal iPTH level (45.83 pg/ml), as the patient was having seizures, muscle pain, hallucinations, fatigue, and bradycardia. This condition was evaluated as a «hungry bone» syndrome in terms of prolonged course of fibrocystic osteitis. IV calcium gluconate (16.8 g/daily) and oral calcium carbonate/citrate (5 g/daily), cholecalciferol (4000 IU/daily) and alfacalcidol (4 g/daily) were used to cope with hypocalcemia. Fourteen-day therapy and replacing alfacalcidol with calcitriol (2 g/daily) allowed to withdraw IV calcium and reduce oral calcium supplementation.

Conclusion
Delayed diagnosis of long-term hypercalcemia, high iPTH level, unsubstituted 25(OH)D deficiency, and the use of bisphosphonates in high doses

EP133
Metabolic parameters in patients with primary hyperparathyroidism before and after parathyroidectomy
Ekaterina Bibik1, Ekaterina Dobrova1, Anastasia Miliutina2, Alina Elfimova1, Anna Eremkina1 & Natalia Mokryshiva2

Background
Metabolic syndrome may be the nonclassical feature of primary hyperparathyroidism (PHPT) because an increased incidence of various glucose and lipid disorders is often observed in patients with this disease. Earlier we showed PHPT patients had higher serum triglycerides and higher rate of insulin resistance compared to the control group. Dynamics of metabolic parameters after surgery is ambiguous. The aim of this study was to compare metabolic parameters in patients with PHPT before and after parathyroidectomy.

Material and Methods
24 patients with PHPT (median age 37 years [33; 41]) underwent biochemical and hormone evaluation, standard oral glucose tolerance test, euglycemic hyperinsulinemic and hyperglycemic clamps, bioelectrical impedance analysis of the body composition before and 1 year after surgery. The exclusion criteria were the GFR < 60 ml/min/1.73 m², severe comorbid illness, body mass index (BMI) ≥ 32 kg/m², diabetes mellitus, using drugs affecting glucose, lipid and calcium balance. Control group (n = 20) was sex-, age- and BMI-matched without any endocrine pathology (median serum albumin-adjusted calcium (Ca adj) 2.24 [2.15; 2.28]mmol/l, parathyroid hormone 40.19 [31.10; 51.04]pg/ml).

Results
Except one patient who had glucose intolerance others had normal glucose metabolism according to standard lab tests. 54.2% had normal weight, 41.7% was overweight and just 1 person had obesity 1, hereewith 45.8% of all had over visceral fat. Insulin resistance (by HOMA) was detected in 54.2% cases. PHPT patients had higher serum triglycerides (1.13 [0.94; 1.39] vs 0.79 [0.63; 1.00]mmol/l), lower HOMA index (5.60 [4.25; 7.45] vs 7.9 [7.0; 10.6]mg/dk/g mm) and higher C-peptide and insulin levels in both phases of pancreas secretion compared to the control group (P<0.05 for all). All patients underwent PTE at the Endocrinology Research Center, Moscow, Russian Federation; 2Endocrinology Research Center, Moscow, Russian Federation; 3Pirogov Russian National Research Medical University, Department of Medical Cybernetics and Informatics, Moscow, Russian Federation; 4Endocrinology Research Center, Director, Moscow, Russian Federation.

Conclusions
Remission of the parathyroid pathology is suspected to improve carbohydrate and purine balance but further studies are required to clarify this statement.

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caused development of “hungry bones” syndrome in early postoperative period. Severe hypocalcemia required prescription of active and native forms of vitamin D, oral calcium supplements and IV calcium therapy.

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EP135

Abstract Withdrawn

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EP136

Quality of life improvement as a valuable outcome of parathyroidectomy in patients with symptomatic and asymptomatic primary hyperparathyroidism

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Background

Comprehensive evaluation of the effect of surgery in patients with primary hyperparathyroidism (PHPT) and monitoring of patient’s well-being after treatment including assessment of patient-reported outcomes is worthwhile.

AIM

We aimed to assess changes in quality of life (QoL) and symptoms in patients with symptomatic and asymptomatic PHPT after surgery (parathyroidectomy, PTX).

Materials and methods.

Adult patients with PHPT who were referred for PTX were included in the single-center prospective observational real-world study. Patients filled out generic and specific questionnaires, namely SF-36 and PHPQoL, for QoL assessment and symptom checklist for assessment of presence and severity of their symptoms prior to surgery and 3, 12 months after PTX. Statistical analysis included Student’s t-test or Wilcoxon’s non-parametric test, the generalized estimating equations (GEE) method, correlation analysis, and χ2 test.

Results

In total 72 patients (mean age (SD) – 52 years (10.4), 97% female) with symptomatic and asymptomatic PHPT were included in the study. Moderate/severe hypercalcemia was observed in 34.7% patients. Before PTX patients with PHPT experienced significantly decreased role functioning, physical and social functioning, and vitality as compared to healthy controls (P<0.005).

Mean PHPQoL score was 53.7 (IQR: 42.2 – 64.1). Half of the patients experienced moderate-to-severe symptoms such as weakness, fatigue, cognitive impairment, changes in mood, as well as joint and bone pain. In 3 and 12 months after surgery, improvement in both physical and psychological components of QoL in PHPT patients was shown. Significant changes were observed for the total PHPQoL score as well as for role, physical, emotional and social functioning and vitality by SF-36 (GEE, P<0.005). Positive QoL changes were demonstrated for patients with both symptomatic and asymptomatic PHPT, but they were more pronounced in the first ones. QoL improvement was not associated with baseline Ca level or type of PHPT (γ2, P>0.05), but correlated with baseline QoL; the lower baseline QoL, the higher QoL improvement after PTX (r=-0.376, P<0.005). Significant decrease in PHPT-associated symptoms such as weakness, fatigue, loss of concentration and mood changes was found within 12 months after PTX (GEE, P<0.005); it was more pronounced in symptomatic PHPT. PTX leads to pronounced positive QoL changes in PHPT patients. The results obtained demonstrate that QoL improvement is a valuable outcome of surgery both in patients with symptomatic and asymptomatic PHPT. Positive effect of PTX from patient’s perspective confirms the value of QoL assessment to measure the degree of recovery at long term follow-up.

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EP137

Glomerular filtration rate 12 months after parathyroidectomy in patients with primary hyperparathyroidism

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Background

In some patients with primary hyperparathyroidism (PHPT), glomerular filtration rate (GFR) demonstrate decrease after parathyroidectomy (PTX). GFR may decrease immediately after surgery due to general anesthesia, but after a month not all patients restore kidney function; a decreased GFR is also observed after 1–2 years after surgery.

Aim

To find the pre-surgical factors of GFR decrease after PTX.

Methods

Patients with PHPT who underwent selective PTX in 1993–2010 (50% of the patients) or 2017–2020 at the Endocrinology Research Center were included. Twenty-two variables were analysed. PTH, calcium total, phosphorus were measured prior to surgery (5 days – 4 years before surgery) and administration of drugs affecting calcium-phosphorus metabolism – cinacalcet, denosumab or bisphosphonates (either as monotherapy or as a part of combination therapy).

25(OH)D, alkaline phosphatase (AP), osteocalcin, c-terminal telopeptide of type 1 collagen (CTX-1), GFR, urea, triglycerides, uric acid, dual-energy X-ray absorptiometry and clinical characteristics were measured on 4–365 days before surgery.

Results

206 patients were included, aged 57 [47; 62] years, 19 (9%) male and 187 (91%) female. On 12 months after surgery 56 of them (27%) progressed to more severe stage of CKD (group 1), and 150 remained at the same stage of CKD (group 2). In the group 1 there were 25 (45%) patients with CKD C2; 17 (30%) with CKD C3a, 8 (14%) with CKD C3b, 6 (11%) with CKD C4, in the group 2 there were 65 (43%) patients without CKD, 63 (42%) with CKD C2, 13 (9%) with CKD C3a, 7 (5%) with CKD C3b, and 2 (1%) with CKD C5. There were no differences in sex, age, BMI, frequency of renal colic and stones, initial stages of CKD, initial GFR, frequency of bone fractures and osteoporosis between the groups. There were also no differences in phosphorus–calcium metabolism (total calcium, ionized calcium, and phosphorus), lipid metabolism (total cholesterol, LDL and HDL cholesterol, triglycerides), PTH, uric acid, urea, osteocalcin and CTX-1. AP was higher in group 1 (309.0 vs 190.3 IU/L, P<0.001, U-test).

Conclusions

Groups with decreased and stable GFR significantly differ by bone remodeling marker AP, but not in clinical manifestations of bone disorder. Moreover, groups were comparable in terms of GFR, uric acid and renal complications (renal colic and stones, CKD).

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EP138

A comparison study of sublingual spray versus peroral capsules and oil in vitamin d supplementation

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Background

Vitamin D is a vital hormone for calcium metabolism, bone and muscle health, and immune responses. Vitamin D deficiency affects entire Latvian population. Aim

To compare the effectiveness of different forms of vitamin D.

Materials and methods

In a prospective, open-label, randomized study in the Jaunliepaja Primary Health Care Centre, data from 98 vitamin D deficient volunteers over one month at initiation of substitution with 4000 IU (100 mcg) Colecalciferol was analyzed. The efficacy of the peroral oil, lanolin-derived microemulsion sublingual spray and peroral capsules dissolved in sunflower oil was evaluated by comparing patient data with age, BMI, renal function. Results

Among 98 volunteers with total 25(OH)D vitamin levels below 30 ng/ml, mean 18.30±7.01 ng/ml and BMI below 35 kg/m², mean age 39.34±13.01 years, 60.2% were female. After one month of intervention, the increase in vitamin D in all groups was 13.21±11.82 ng/ml (95% CI, P=5.72×10⁻⁴). In oil group 14.98±13.58, using capsules 11.06±7.13 and in spray group 9.97±7.73 ng/ml accordingly. In the capsule group, an inversely related – slower increase in vitamin D was observed in the elderly (r=0.36, P=4.53×10⁻³) and in participants with a higher body mass index (BMI) (r=0.40, P=2.30×10⁻²)
but the spray group higher increase in vitamin D levels was in participants with a higher glomerular filtration rate (GFR) (0.37, $P=2.93 \times 10^{-5}$).

Conclusions

An increase in vitamin D levels was observed in all groups after one month of supplementation, and the formulation did not statistically significantly affect the overall outcome. There was at least one respondent with negative vitamin D dynamics in each group. In the capsule group, the changes in vitamin D were statistically significantly inversely related to the respondent’s age and BMI – the younger the person, the more pronounced the increase in vitamin D, similarly, the lower the BMI, the higher the increase in vitamin D. In the spray group, a statistically significant correlation was found between the increase in vitamin D and higher GFR.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research project.

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Pharm & med Ltd.

Keywords: Vitamin D, overweight, age, renal function.

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**EP139**

"Physician to physician" telemedicine consultations in parathyroid pathology: experience of quaternary endocrinological medical center

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Introduction

Telemedicine consultations (TMC) are a useful tool for ensuring communication between medical specialists, especially in a large country and in the era of COVID-19. It is important to study the needs and possibilities of TMC for various diseases, in particular, for the pathology of the parathyroid glands.

Materials and methods

TMC between regional health specialists and Endocrinology Research Centre (Moscow, Russian Federation) were conducted in 2019–2021 via All-Russian Center for Disaster Medicine «Zashchita».

Results

In 2019 1221 TMC were held in our center, 859 (70%) – for adult patients. In 2020 there were 1248 TMC, in 2021 – 3005 TMC, among them there were 1077 (86%) and 1622 (54%) TMC for adults, respectively. A high prevalence of parathyroid disorders in TMC was noticed (Table 1).

Table 1 Parathyroid disorders in nosological structure of ‘physician to physician’ (P2P) TMC.

<table>
<thead>
<tr>
<th></th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total TMC count</td>
<td>1221</td>
<td>1248</td>
<td>3005</td>
</tr>
<tr>
<td>Number of TMC for adults</td>
<td>859</td>
<td>1077</td>
<td>1622</td>
</tr>
<tr>
<td>Number of TMC for parathyroid disorders/% regarding the number of consultations for adults Among them (according to ICD-10):</td>
<td>100 (11,6%)</td>
<td>121 (11,2%)</td>
<td>187 (11,5%)</td>
</tr>
<tr>
<td>E89.2 (Postprocedural hypoparathyroidism)</td>
<td>9</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>E21.0 (Primary hyperparathyroidism)</td>
<td>56</td>
<td>75</td>
<td>111</td>
</tr>
<tr>
<td>E21.1 (Secondary hyperparathyroidism)</td>
<td>20</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>E21.2 (Other hyperparathyroidism)</td>
<td>3</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>E21.3 (Hyperparathyroidism, unspecified)</td>
<td>12</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>E21.4 (Other specified ()disorders of parathyroid gland)</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>21.5 (Disorder of parathyroid gland, unspecified)</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hospitalization recommended/% regarding the number of consultations for parathyroid disorders</td>
<td>43 (43%)</td>
<td>61 (50,4%)</td>
<td>121 (64,7%)</td>
</tr>
</tbody>
</table>

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**EP140**

Practical approach for hypocalcemia in infants: earlier diagnosis, earlier management

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Background

Hypocalcemia is a serious condition that occurs at any age with various etiologies according to various age groups. Hypocalcemia in infant is an emergency condition and the exact etiology should be identified as early as possible to ensure early appropriate management.

Methods

We are presenting 3 cases for infants who presented with seizures caused by hypocalcemia.

Case 1: A 3-month-old male infant presented with apnea and up rolling of eyes. He was full term with normal birth weight. He had poor weight gain, deep-seated eyes, long philtrum and small hands.

Case 2: An 11-day-old male neonate, presented with left-sided focal seizure. He was full term with normal birth weight. He was breast-fed with no vitamin D supplementation. Physical exam was unremarkable.

Case 3: A 6-day-old female neonate who presented with bilateral upper and lower limb clonic seizure. She was full term with normal birth weight. Her physical exam was normal.

Critical sample was sent at the time of hypocalcemia for the three patients. They received intravenous calcium gluconate during admission then switched to oral calcium.

Results

Laboratory work up for case 1 showed hypocalcemia, hyperphosphatemia and absent parathyroid hormone level in blood. Based on his dysmorphic features and laboratory work up, Sanjad Sakati syndrome was suspected which was confirmed by genetic testing. He is currently on daily oral calcium supplement and alfalcacidol. For Case 2, patient had hypocalcemia, normal blood phosphorus level and very low vitamin D level. Vitamin D level was done for his mother and it was low. He was discharged on oral calcium and vitamin D. Calcium supplement was stopped after 1 week and he continued on vitamin D till last follow up. Case 3 had hypocalcemia, normal blood phosphorus level, low parathyroid hormone and low magnesium level. She was treated during admission in addition to intravenous calcium gluconate, with intravenous magnesium sulfate. She was discharged on calcium and magnesium supplement which were decreased gradually till stopped after few months. Magnesium deficiency which was the cause of her hypocalcemia was transient with no obvious cause.

Conclusion

Physicians should be aware of the precise approach for investigating the etiology of hypocalcemia in infants, in order to establish an early diagnosis and an early appropriate management, through taking full history and full physical exam and performing the appropriate investigations.

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**EP141**

Mediastinal parathyroid lipoadenoma as a cause of primary hyperparathyroidism

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Introduction

The parathyroid gland is made up of principal cells and oxyphilic cells, surrounded by stroma, whose main component is adipose tissue, which accounts for 25% of the content of the parathyroid in adults. In parathyroid adenomas, prominent parathyroid cellularity can be observed, with a very marked decrease in
the stroma. Parathyroid lipoadenoma is a rare variant of parathyroid adenoma, characterized by hyperfunctioning parathyroid cells in an abundant fatty stroma.

Case reports:

We present a case of a 76-year-old woman with a history of high blood pressure and a previous diagnosis of non-toxic multinodular goiter without follow-up. During an outpatient study due to weakness and incoherent cognitive disorders, severe hypercalcemia of 18.3 mg/dl with creatinine of 2.3 mg/dl was detected, for which she was admitted for treatment and study. In previous tests, a progressive increase in calcium was observed that had not been studied, with at least 6 years of evolution, with levels of 15 mg/dl the previous year. During admission, she showed parathyroid hormone (PTH) figures of 2.310.7 pg/ml (NV: 15–68), 25-OH-vitamin D of 12 ng/ml and TSH 0.12 mU/ml, with normal FT4. Cervical ultrasound revealed a multinodular goiter. In the 99mTc-sestamibi SPECT scintigraphy with a heterogeneous uptake of the radiotracer. Cervicovthoracic CT revealed a right paracardiac mass with well-defined borders, with solid and fat densities, and dimensions of 5 × 5 × 8 cm, with no other lesions. A biopsy of the mass was performed, obtaining a whitish-brown sample consisting of adipose tissue and with benign characteristics, with a low proliferative index (Ki67 of 1%), confirming its parathyroid origin with no other lesions. A biopsy of the mass was performed, obtaining a whitish-brown sample consisting of adipose tissue and with benign characteristics, with a low proliferative index (Ki67 of 1%), confirming its parathyroid origin with no other lesions. A biopsy of the mass was performed, obtaining a whitish-brown sample consisting of adipose tissue and with benign characteristics, with a low proliferative index (Ki67 of 1%), confirming its parathyroid origin with no other lesions.

Endocrine Abstracts


Bilateral neck exploration is comparable to preoperative visualization methods in searching for parathyroid adenomas on the neck

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Background

Undetected multiglandular disease (MGD) is a leading cause of persistent primary hyperparathyroidism after surgical treatment. There is still a number of clinically significant parathyroid adenomas that remain unseen preoperatively.

Materials and methods

A retrospective cohort study was conducted in order to reveal factors associated with risk of MGD. 810 cases of pHPT patients who had received primary surgical treatment at SPBU Hospital in 2017–2018 were included. All the patients had at least one preoperative visualization study (neck ultrasound performed by a surgeon) before the operation. In 537 cases two studies (additional 4D CT or MIBI scan) were performed and 164 cases had all three studies. A surgeon was free to choose whether perform bilateral neck exploration or not. Data analysis was performed in R.

Results.

Number of patients with at least one adenoma that was not localized preoperatively with no less than two studies performed was 46 (26 single adenomas and 20 complementary). In 30 cases BNE was performed resulting in finding an unseen adenoma in 27 cases (90%). US, CT and MIBI sensitivity values were found to be 83.5%, 92.3% and 75.1% respectively. MGD rate accounted for 6.17% (50 cases). 43 cases of persistent disease after surgery were reported, 25 of them were caused by MGD. Negative predictive value of MGD for different combinations of studies with concordant results (US + MIBI, US + CT and US + CT + MIBI) did not differ significantly and was 96.95%, 97.4% and 97.7% respectively. Logistic regression model was performed, showing that independent negative US, negative CT or negative MIBI were not statistically significant in predicting risk of MGD, as well as age and body mass index.

Conclusion. Bilateral neck exploration added to a routine parathyroidectomy is helpful for discovering an unsuspected MGD case.

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EP144

Serum calcium, magnesium and phosphorus levels in patients with coronavirus disease 2019: an analysis of their relationship with poor outcome and mortality

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tion, Majadahonda, Spain; 3Consejería de Sanidad de la Comunidad de Madrid, Madrid, Spain; 4Hospital Universitario Puerta de Hierro Majadahonda, Department of Biochemistry, Majadahonda, Spain.

Purpose

To assess the impact of serum corrected calcium (CorrCa), magnesium (Mg) and phosphorus (P) levels at hospital admission on SARS-CoV-2 infection outcome. Methods

In this retrospective study, all adult patients with laboratory-confirmed COVID-19 hospitalized in Hospital Universitario Puerta de Hierro Majadahonda during 2020 were included. Demographic, clinical and laboratory data were registered and related to the prognosis of the disease. Poor outcome was considered in patients who presented need for mechanical ventilation, intensive care unit (ICU) admission, or in-hospital mortality.

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Results
Of a total of 2,473 patients (956 females) aged (mean ± s.d.) 63.4 ± 15.9 years were studied. Median (IQR) hospitalization time was 7(4–13) days. During admission, 189 patients (6.8%) required mechanical ventilation, 205 (8.3%) were admitted to the ICU, and 270 (10.9%) died. Composite variable of poor outcome, defined as need for mechanical ventilation, ICU admission or death, was present in 434 (17.5%) patients. In univariate analysis, the need for mechanical ventilation was positively related to Mg levels (OR 2.68, 95% CI 1.54–4.68; Z = 0.0001). ICU admission was related to CorrCa (OR 0.49, CI 0.25–0.99) and Mg levels (OR 5.81, CI 2.74–12.35; P = 0.0001). In-hospital mortality was related to CorrCa (OR 1.73, 95% CI 1.14–2.64; P = 0.011) and the composite variable of poor outcome was only related to Mg (OR 2.68, 95% CI 1.54–4.68; P = 0.001). However, in multivariate analysis CorrCa was significantly related to the need for mechanical ventilation (OR 0.19, 95% CI 0.05–0.72; P = 0.014) and ICU admission (OR 0.25; 95% CI 0.09–0.66; P = 0.005), but not with in-hospital mortality or the composite variable of poor outcome. We found no relationship between poor outcome or mortality and serum levels of Mg or P in the multivariate analysis.

Conclusion
These results suggest that CorrCa can be used as a simple and reliable marker of poor outcome in patients with COVID-19, although not to predict the risk of in-hospital mortality.

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EP145
Autosomal dominant hypocalcaemia type 1 with intact PTH and relative hypocalciuria.
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Autosomal Dominant Hypocalcaemia (ADH) type 1 is caused by activating mutations of the calcium-sensing receptor (CaSR) gene. Although a rare condition, the exact prevalence is uncertain as patients are asymptomatic and, historically, were sometimes diagnosed with hypoparathyroidism (HPT) due to insensitivity of earlier PTH assays and failure to check urinary calcium. The consequences of an erroneous diagnosis of HPT in patients with ADH can be profound, as treatment with calcium salts or activated vitamin D characteristically result in more severe hypercalciuria and nephrocalcinosis. A 28-year-old female was referred with hypocalcaemia, extreme tiredness and generalised muscle aches that persisted despite correction of hypovitaminosis D. She had no paresthesia or tetany or muscle spasms, but suffered from intermittent restless legs at night. There was no history of recurrent urinary tract infections or kidney disease. She had a normal childhood with no significant past medical history. There were no significant medical or genetic conditions in the family, except for type II diabetes. She gave birth to a healthy girl 5 years ago with no complications. She had gastric banding for obesity a year ago and recovered well from the surgery with no complications. She is not on regular medications. On examination, she was clinically euthyroid, with positive Chvostek’s but negative Trousseau’s signs. Other systems were unremarkable. Height was 1.69 m. Her kidney ultrasound showed no renal calculi. Genetic analysis of the patient identified a heterozygous autosomal dominant CASR variant: c.2497G>T (p.Val833Phe) diagnosing her with Autosomal Dominant Hypocalcaemia Type 1 (ADH). This gene variant has not been identified in the gnomAD population database yet. In conclusion, hypocalcaemia needs to be investigated as we now have better assays to detect low normal PTH levels. Misdiagnosing ADH type 1 with hypocalcaemia or HPT increases the risk of nephrocalcinosis and hypercalciuria in those patients.

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EP146
Quality of life in chronic hypoparathyroidism on conventional treatment
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Introduction
Reduced health-related quality of life (HRQoL) is common in patients with hypoparathyroidism (HypoPT) treated conventionally with calcium and active vitamin D supplements.

Aim
We studied the HRQoL in patients with chronic HypoPT estimated with the 36-Item Short-Form Health Survey (SF-36) and multidimensional fatigue inventory (MFI-20).

Methods
64 patients with chronic HypoPT (women/men – 57/7, median age 47[36;59] years) participated in the study. The median duration of the disease was 4 years [3;9]. SF-36 is a 36-item QOL questionnaire with response alternative scores 1–6 for each item. A scoring algorithm transforms the raw score to a score from 0 to 100, where a high score indicates better HRQoL. MFI-20 has an even proportion of positively and negatively worded items that are rated on a 5-point Likert scale. Subscale scores are calculated as the sum of item ratings and a total fatigue score – as the sum of subscale scores. Higher scores indicate a higher level of fatigue.

Results
We didn’t find any associations between the SF-36 and MFI-20 scores of and serum calcium levels. However, HypoPT patients with magnesium (Mg) level under 0.7 mmol/l had significantly higher SF-36 scores such as PF (P = 0.0131); BP (P = 0.0034); RE. (P = 0.0376); PH (P = 0.0042). We found a negative correlation between the number of tablets and SF-36 PF score (P = 0.0133; r = −0.31). Median of tablets’ number in patients with Mg < 0.7 mmol/l is 6[5;10] vs median of tablets’ number 7[5;10] in patients with Mg ≥ 0.7 mmol/l. But the difference isn’t significant. During HypoPT had a positive correlation with SF-36 scores VT (P = 0.0038; r = 0.33), MH (P = 0.2594; r = 0.04) and negative correlations with some MFI-20 scores – general fatigue (P = 0.015; r = −0.31), reduced activity (P = 0.0336; r = −0.27) and reduced motivation (P = 0.0088; r = −0.33). These results may be related to the phenomenon of adaptation to chronic diseases such as HypoPT. In general, the presence of HypoPT complications had a positive correlation with SF-36 scores VT (P = 0.0496; r = 0.25), SF (P = 0.0013; r = −0.39) and negative correlation with reduced activity (P = 0.0204; r = −0.29). These results also can be explained by better examination and thus better awareness in patients with chronic HypoPT, especially if they already have at least one complication.

Conclusion
Further studies with better instruments for assessing HRQoL are required. Patients with HypoPT often can use a lot of medications and should follow the strict rules of their taking, which can significantly affect the HRQoL. Of course, doctors want to improve all mineral disturbances, but therapy should be personalized and clearly discussed with the patients.

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EP147
25-hydroxyvitamin D, parathyroid hormone and bone turnover markers in patients with Addison disease
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Introduction
Patients with Addison disease require lifelong glucocorticoid replacement treatment and it is recommended that glucocorticoid therapy should be monitored in these patients to avoid over replacement and minimize long-term consequences of bone loss. The present study was carried out with the aim of evaluating bone turnover markers in patients with Addison disease.

Patients and methods
A cross sectional study including 50 patients who are followed for Addison disease, at the department of Endocrinology at Hedi Chaker hospital, sfax-Tunisia. Biochemical markers of bone metabolism (calcium, phosphorus, alkaline phosphatases, vitamin D and parathyroid hormone (PTH)) were measured and the average values were retrospectively analyzed.

Results
There were 40 females and 10 males. The average age of patients was 49.5 ± 13.9 years (18–78 years). The majority (70%) were aged between 40 and 50 years old. Average duration of the disease was 13.9 ± 8.7 years (5–35 years). Approximately 42.5% of females were menopausal. Two-thirds (66%) of patients were not physically active. All patients took no calcium oral supplementation nor oestrogen replacement. Only four patients received Vitamin D oral supplementation. Mean serum levels of calcium and phosphorus were 2.29 ± 0.13 mmol/l (1.9–2.55 mmol/l) and 1.10 ± 0.18 mmol/l (0.8–1.66 mmol/l), respectively. Hypocalcemia was observed in 9 (18%) patients after a mean duration of Addison disease of 11.9 ± 7.1 years (4–26 years) and a mean cumulative hydrocortisone dose of 317.7 ± 211.7 mg (75–702 mg). No significant statistically differences were found between hypocalcemia with regard to age, duration of glucocorticoid replacement or glucocorticoid dose. Mean alkaline phosphatase was 77.2 ± 28.5 IU/l (15–90 IU/l). Patients presenting an increasing alkaline phosphatase level (18%) received higher cumulative hydrocortisone dose but without statistical difference (413.4 ± 348 mg versus 365.5 ± 271 mg; P = 0.7). Mean vitamin D level was 22.28 ± 14.14 ng/ml (5.6–78.6 ng/ml). Hypovitaminosis D was observed in 33 (66%) patients. Mean PTH level was 51.79 ± 53.84 pg/ml (16.36–139 pg/ml). An elevated PTH level was observed in 10 (20%) patients who had all vitamin D deficiency.

Conclusion
Long-term glucocorticoid replacement therapy in patients with Addison disease is associated with an increased risk of fractures and osteoporosis, which is not only identified by bone mineral density. Other markers as bone turnover markers may be useful. Markers of bone resorption seem to be higher in patients with Addison disease, particularly those who present hypovitaminosis D.

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EP148
Pregnancy and lactation induced osteoporosis – a social media based survey
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Background
Pregnancy and lactation induced osteoporosis (PLO) presenting as spinal fractures in late pregnancy or early postpartum period is a rare condition. The risk factors and pathophysiology are still incompletely understood. The impact of the disorder on the young mother’s quality of life can be profound, further aggravated by a delay in diagnosis and treatment that often occurs.

Aim
To delineate clinical parameters related to fractures in a group of women with PLO, and to compare risk factors and osteoporosis-related quality of life with a control group.

Methods
Participants of a social media (WhatsApp) group for women with PLO and secondary causes of osteoporosis.

Results
Twenty-four patients with PLO and 43 healthy controls (36.2 ± 4.8 vs 38.8 ± 4.3 y.o, P = 0.11) were included in the study. Fifty percent of patients suffered from fractures of more than 5 vertebrae, 25% of 4 and 25% had 3 or less vertebrae involved. 85.7% of the fractures were a-traumatic. Nineteen percent of the fractures occurred during pregnancy and others, during early postpartum period. Diagnosis was delayed for more than 16 weeks in 41.8% of women. Bone mineral density test was performed in all participants in the PLO group and 62.5% were treated with teriparatide. A significantly lower proportion of women in the PLO group engaged in physical activity over 2 h/week during pregnancy (37.5 vs. 86.3%, P < 0.05) and more PLO patients were treated with low-molecular-weight-heparin during pregnancy, although the difference was of borderline significance (P = 0.06). No difference was observed in smoking, periods of amenorrhea, lactation, or family history of fractures between the groups. Seventy-one percent of the PLO patients expressed fear of fractures and 58.3% fear of falls compared to none and 2.5%, respectively (P < 0.01) of the controls.

Conclusions
PLO-related spinal fractures involve multiple vertebral in the majority of the affected women, and the diagnosis is delayed in many. Less physical activity might pose a risk. Most of PLO patients in our cohort were treated with teriparatide. PLO patients reported a significant impairment of quality of life. Multidisciplinary effort should be exerted to early identification and treatment of this severe condition.

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EP149
Bone mineral density in patients with addison disease versus congenital adrenal hyperplasia
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Introduction
The treatment of Primary Adrenal Insufficiency involves the chronic use of glucocorticoids. The balance between the dose needed to supply the cortisol deficit and the possible consequences of overtreatment is a challenge. In patients with Addison disease (AD), androgens deficiency is an additional factor for osteoporosis.

Objective
To evaluate if there are differences in bone mineral density (BMD) in patients with Addison’s disease versus congenital adrenal hyperplasia (CAH) – classic form.

Methods
We included patients with a diagnosis of Addison’s disease or CAH, with follow-up in a tertiary center. Patient’s characteristics and cumulative doses of glucocorticoid (in hydrocortisone converted doses) were recorded and calculated by body surface area (HC/BSA). BMD was evaluated by dual-energy X-ray absorptionmetry (DXA), at lumbar spine, femoral neck, and distal radius. Excluded patients with secondary causes of osteoporosis.

Results
27 patients were included: 16 with AD and 11 with CAH. Sex and age distribution were similar between groups. Patients with Addison had a lower BMI (26.34 ± 4.17 vs 31.47 ± 6.4, P = 0.030), and shorter disease duration (17.75 ± 12.27 vs 31.63 ± 11.47, P = 0.007). Daily doses of HC/BSA were similar between groups (15.91 ± 4.48 for AD vs 11.22 ± 4.17, P = 0.061), but cumulative yearly doses of HC/BSA were higher in patients with Addison (5672 ± 1621 vs 3480 ± 1885, P = 0.027). Lumbar T-score was significantly inferior in patients with Addison (−2.00 ± 2.10, vs −0.69 ± 0.93, P = 0.022), with no differences in femoral or radius T-score between groups. There was a non-significant correlation between lumbar T-score and cumulative yearly doses of HC/BSA (r = −0.321, P = 0.208).

Conclusion
The significantly different found in lumbar T-score between AD and CAH may be explained by the higher cumulative yearly dose of HC/BSA of the AD group which is associated to high risk of BMD reduction. Also, the AD group had lower BMI, which is known to be a protective factor against bone mineral loss. Androgen deficiency, typical of Addison disease, is also a reasonable explanation for this discrepancy, since androgens are known to increase bone formation markers.

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EP150
SuperJump training in eumenorrheic women and gut peptides: a randomized controlled study about the mechanism of action on bone and glucose homeostasis

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This study was supported by the Ministry of Health of the Czech Republic (MZ CR – RVO; Endokrinologicky ústav – EU, 00023761).

The role played by physical activity in promoting bone health is now widely recognized. Physical activity limits and slows down the physiological demineralization that occurs over the years and plays an important role in the prevention of osteoporosis. SuperJump, a high-impact training activity performed on a mini-trampoline characterized by alternating between aerobic and anaerobic exercises, has been shown to be able to generate a substantial osteogenic response and increase bone balance and strength in eumenorrheic women. In this study it was analyzed whether gastrointestinal peptides play a role in the regulation of bone metabolism and their impact on glucose homeostasis.

Methods
Using a randomized controlled study design, participants were assigned either to the intervention group performing SuperJump activity for 20 weeks or to the control group, that did not undertake any intervention. Blood samples were collected at baseline and at the end of the study and compared within and between the groups for markers of bone metabolism (CTX, osteocalcin, PTH, Vitamin D, albumin adjusted calcium) gut peptides (GLP-1, GIP, GLP-2, PYY, ghrelin) markers of glucose metabolism (glucose, insulin, insulin resistance, β-cell function, insulin sensitivity).

Results
After 20 weeks of SuperJump activity, CTX and PTH was reduced, GLP-1 and GIP levels were significantly increased while levels of GLP-2, PYY and ghrelin did not change. Moreover, SuperJump activity significantly reduced fasting insulin, glucose, insulin resistance and increased insulin sensitivity but did not affect beta cell function.

Conclusion
The results of the study show that 20 weeks of SuperJump was highly effective in improving bone and glucose homeostasis in eumenorrheic women and suggests that GLP-1, and GIP are involved in the mechanism of action.

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EP151
Sex differences of the reaction of undercarboxylated osteocalcin to hypoglycaemia

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In recent years, there has been increasing evidence for the hypothesis of bones as endocrine organs. Osteocalcin, long considered just a marker of new bone formation, is now seen as the first hormone produced by bones, and seems to be associated with regulating glucose metabolism and reproduction. The aim of this work was to monitor changes of osteocalcin in reaction to hypoglycaemia, and determine if there are differences in such reactions between the sexes. The study included 61 healthy probands with physiological calciophosphate metabolism (30 men and 31 women). We applied to each of them an insulin tolerance test, and then monitored levels of undercarboxylated osteocalcin and reactions to hypoglycaemia at regular time intervals. We found differences in the reaction to hypoglycaemia between the sexes. In men there was a significant decline in undercarboxylated osteocalcin between the 30 and 40 min (P<0.0015), which reflects a reaction to a glycemic decline between 25 and 30 min, followed by reversal. Low undercarboxylated osteocalcin in men lasted up to 90 min, after which they returned to levels before the test. In women we did not find any significant changes in undercarboxylated osteocalcin levels. Changes in undercarboxylated osteocalcin induced by hypoglycaemia indicate a relationship between bones and glucose metabolism. There was an interesting difference between the sexes. However, a definitive conclusion about the role of osteocalcin in human metabolism will require numerous future studies. Acknowledgements: This study was supported by the Ministry of Health of the Czech Republic (MZ CR – RVO; Endokrinologicky ústav – EU, 00023761).

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EP152
Teriparatide for hypoparathyroidism after bariatric surgery

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Background
Hypoparathyroidism is an endocrine disorder characterized by hypocalcaemia due to low levels of parathyroid hormone (PTH). Activated vitamin D (calcitriol) and calcium supplementation may be difficult in patients with malabsorption, as calcium requires an acid environment to dissolve. In this setting, subcutaneous administration of PTH analogues may be effective in reducing the dosage of oral calcium and vitamin D supplementation.

Case report
A 36-year-old woman with a history of sleeve gastrectomy and Single Anastomosis Duodeno-Heal switch was diagnosed with papillary thyroid carcinoma and referred to total thyroidectomy. After surgery, she presented paraparesis, undetectable PTH, calcium 6.5 mg/dl and TSH was normal, so an oral regimen of calcium carbonate 1 gr tid and calcitriol 0.5 mcg tid was started without resolution. She came several times both to our Endocrinology Unit and to the emergency department due to symptomatic hypocalcaemia. Therefore, oral treatment was gradually increased up to calcium carbonate 9 gr and calcitriol 4 mcg per day, and then intravenous calcitriol and calcium gluconate infusion was started. However, this did not allow complete resolution of hypocalcaemia and the patient experienced some discomfort mainly due to gastrointestinal symptoms. Symptoms began to worsen after several weeks. At this moment, in Italy, RDNA PTH (1–84) is not refunded by the national health service. For that, after patient’s consent, treatment with rhPTH (1–34 – teriparatide) analogue 20 mcg/day was started with no adverse reaction. Soon, we were able to significantly reduce the dosage of calcium carbonate to 2 gr and calcitriol 2.5 mcg/day. After fifty days of this treatment calcium was 8.5 mg/dl. Recently the dose of teriparatide was titrated to 40 mcg/day, with further reduction of oral treatment, and the patient has not had any symptoms related to hypocalcaemia.

Conclusion
First-line of treatment in hypoparathyroidism is activated calcitriol and calcium supplementation maintain low-normal calcium levels, to prevent hypocalcaemia and avoid hypercalcemia and renal calcification. Gastric bypass or duodenal resection can increase the risk of hypocalcaemia, as they cause malabsorption. As alternative options intravenous calcium, calcitriol infusion and rhPTH should be considered to maintain normal calcium levels. Even when the patient is stabilized, episodes of hypocalcaemia may occur, so careful monitoring is still required. To date, this is the second reported case of the use of a PTH analogue to treat hypoparathyroidism with good calcium control in a patient who underwent bariatric surgery.

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EP153
The parathyroid carcinoma manifesting during pregnancy

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Background
Parathyroid carcinoma (PC) is a rare cause of primary hyperparathyroidism (PHPT) and extremely rare endocrine malignancy during pregnancy. Different maternal and fetal/neonatal complications of PHPT occur in 67 and 80% of untreated cases respectively, probably more due to severe hypercalcemia. The diagnostic and therapeutic approaches are limited in pregnant women and require individual risk-benefit assessment.

Aim
We present a case of PC manifested during pregnancy when delayed treatment led to severe complications.

Clinical case
Young woman suffered from urolithiasis since the age of 19. Moreover, she had a history of multiple low-energy bone fractures of limbs. At the age of 35 lab tests showed high PTH (55.51 pmol/l (NR 1.6–6.9)) and hypercalcemia (total calcium 3.28 mmol/l), US detected a tumor of the left inferior parathyroid gland.
33x25x18 mm (PG). So, PHPT was diagnosed at 29 week of gestation. Given severe hypercalcaemia and gestational age parathyroidectomy was recommended but the patient refused the surgery as well as cinacalcet therapy. Cesarean section was performed at 38 week of pregnancy without any complications. The woman breastfed for 1.5 years. During this period, the patient had low-energy fractures of left humerus that required ostesynthesis. 2 years after delivery exam showed albumin-adjusted calcium 2.9 mmol/l, PTH 1044 pg/ml (15–65), 24-hours urinary calcium 13.3 mmol. US, CT scan, 99mTc-sestamibi scintigraphy confirmed tumor of the left inferior PG. The patient had bilateral nephrolithiasis, significant BMD reduction (Z-score radius − 5.9 s.d.), also osteitis fibrosa cystica and vertebral fractures (Th9-12) were verified. The parathyroidectomy was carried out, PTH and total calcium decreased to 50.1 pg/ml and 2.18 mmol/l respectively on the fifth day after surgery, oral calcium supplementation and alfalcacidol were prescribed. Morphological examination revealed PC.

Density and 1/7 (13%) had osteogenesis imperfecta. The median age at the time of the COVID-19 infection was 35 (range 16.69). The most prevalent symptoms were cough 6/8 (75%), fever 4/8 (50%), and shortness of breath 2/8 (25%). Two patients were asymptomatic (25%). Comorbidities were reported in 3/8 (38%): obesity 2/7 (25%) and asthma 1/8 (13%). None required hospital admission and complete remission occurred in 100% of cases.

**Conclusion**

The results of this survey suggest good clinical outcomes in patients with rare bone and mineral disorders experiencing a COVID-19 infection.

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**EP154**

**Clinical outcomes of COVID-19 infection in rare bone and mineral disorders**

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**Background**

The European Registries for Rare Endocrine Conditions and the European Registries for Rare Bone and Mineral Conditions were created in collaboration with the European Reference Networks for Rare Endocrine and Bone Disorders (Endo-ERN and ERN BOND). Following the onset of the COVID-19 pandemic in 2020, the registries, together with the ESE RD Committee, have collected the occurrence of confirmed and suspected cases of COVID-19 in patients with rare endocrine and bone conditions via the electronic reporting system (e-REC), a tool that does not collect personal identifiable information.

**Aim**

To collect clinical outcome data of patients with rare bone and mineral disorders affected by COVID-19.

**Methods**

Between May 2020 and May 2021, 11 cases of COVID-19 in patients with a preexisting mineral condition and 8 in patients with a preexisting bone condition were reported. Reporters were invited to complete a secure online questionnaire. The questionnaire was completed in 15/19 cases (79%) from four centres in three countries. Of 19 cases, 18(95%) were confirmed by a test. Vaccination status was reported only for one case of mineral conditions (1/19), who had received the vaccine.

**Results**

Of 7 mineral cases, 3 had hypophosphatemia (42%), 3 hyperparathyroidism (42%) and 1 primary hyperparathyroidism (14%). The median age at the time of infection was 39 (range 4.52). Of 7 cases 6 were confirmed by a test (86%). The most prevalent symptoms were fever 5/7 (71%), cough 3/7 (43%), fatigue 3/7 (43%), loss of taste and smell 3/7 (43%), muscle pain 3/7 (43%), runny nose 2/7 (28%), headache 2/7 (28%) and shortness of breath 2/7 (28%). One patient was asymptomatic. Comorbidities were reported in 4/7 (57%): hypertension 2/7 (28%), obesity 1/7 (14%), asthma 1/7 (14%). None required hospital admission and complete remission occurred in all cases. Of 8 bone cases 5 had fibrous dysplasia of bone (62%), 2/8 (25%) had a bone dysplasia with increased bone density and 1/7 (13%) had osteogenesis imperfecta. The median age at the time of the COVID-19 infection was 35 (range 16.69). The most prevalent symptoms were cough 6/8 (75%), fever 4/8 (50%), and shortness of breath 2/8 (25%). Two patients were asymptomatic (25%). Comorbidities were reported in 3/8 (38%): obesity 2/7 (25%) and asthma 1/8 (13%). None required hospital admission and complete remission occurred in 100% of cases.

**Conclusion**

The combination of primary hyperparathyroidism (PHPT) with anemia was first described in 1931. It remains unclear whether PHPT is the direct cause of anemia, or it develops as a PHPT’s complication. The etiology of anemia in PHPT could be multifactorial, including iron deficiency, renal failure as well as bone marrow fibrosis.

**Aim**

To assess the prevalence of anemia in patients with PHPT admitted to the Department of Parathyroid Glands Pathology of the Endocrinology Research Centre from January 2017 to August 2020.

**Materials and Methods**

The study included patients with PHPT over 18 years old. A single-center observational one-stage one-sample uncontrolled study was carried out. We analyzed laboratory and instrumental data obtained during inpatient examination in accordance with the standards of medical care. Statistical analysis was performed using Statistica 13 (StatSoft, USA) and SPSS (IBM, USA) software.

**Results**

The study included 327 patients with PHPT, 28(9%) men and 299(91%) women. The median age was 59 years [51;66], 26 patients (8%) with anemia were identified. Significant differences between patients with and without anemia were found only in the GFR. Comparison of patients with and without anemia didn’t reveal any significant differences in the incidence of PHPT’s complications. Significant differences in serum hemoglobin concentration and average hemoglobin concentration in erythrocytes were revealed between patients with and without vertebral fractures. In the group of patients without compression fractures these parameters were higher (p < 0.001 for both). In the subgroup of patients with total calcium >3 mmol/l and iPTh > 3 normal values, the incidence of anemia reached 21% (95% CI: 10%;35%). Within this subgroup we revealed tendencies to higher levels of iPTh, ionized calcium and osteocalcin in patients with anemia.

**Conclusion**

We did not find any correlations between hypercalcemia, iPTh levels and the presence of anemia in the general group. However, in the subgroup of patients with severe hypercalcemia, there was a relationship between the iPTh, ionized calcium and the incidence of anemia. In patients with PHPT and vertebral fractures, significantly lower concentrations of blood hemoglobin and hemoglobin in erythrocytes were observed.

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**EP156**

**Late diagnosis of life-threatening hypocalcemia in a patient with hypoparathyroidism after hemithyroidectomy: A case report**

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**Introduction**

Hypocalcemia is defined as a decreased level of calcium in the blood. The presentation of hypocalcemia varies widely, from asymptomatic to life-threatening. The most common cause of chronic hypocalcemia is post surgical hypoparathyroidism. This may occur after removal of all parathyroid tissue...
during thyrotoxicosis and radical neck dissection for malignancies or after inadvertent interruption of the blood supply to the parathyroid glands during head and neck surgery. Here we report the case of an elderly patient with hypoparathyroidism after hemithyroidectomy who developed clinical manifestations of severe hypocalcemia and her life was saved through a tracheostomy.

**Case Presentation**

A 72-year-old woman was admitted to Mikaelyan University hospital with shortness of breath. She spoke with difficulty, in syllables. The patient’s general condition was extremely heavy and she was admitted in ICU department. She had a history of hemithyroidectomy 30 years ago. The patient had a disorder of consciousness, perioral paresthesia and tingling of the fingers during these years. For this, she was started treatment with calcium 1-3 g/daily, vitamin D3 5000 U daily for 10 years and i-thyroxine 25 mcg for 5 years. She had a history of acute respiratory infection 1 month before admission. On admission, examination revealed P=122 bpm, BP=160/85 mmHg, T=36.5°C, SpO2 95% (15 liter/min O2 +), BMI = 27.5 kg/m². Trouseau and Chvostek signs were positive. Electrocardiogram revealed a prolonged QTc interval. The patient received first medical aid with oxygen, dexamethasone, euphyllin. After the results of blood chemistry, which showed low serum corrected calcium level (1.80 mmol/l), calcium gluconate 10% 10 ml IV was added to the treatment. Unfortunately, the patient’s condition didn’t improve on treatment and she even could not be intubated because of laryngospasm, that’s why tracheostomy was performed. Endocrine examinations showed: 25(OH)D-39.66 ng/ml (n 30 – 70), parathormone-6.54 pg/ml (n 15 – 65), TSH-0.939 uIU/ml (n 0.3 – 4.5), FT4-15.07 pg/ml (n 8.9 – 17.2). She was diagnosed with postoperative hypoparathyroidism. She continued treatment with calcium gluconate, dexamethasone, l-thyroxine and started treatment with calcitriol 0.25 mcg. The patient improved on this treatment; the tracheostomy was removed after 2 weeks. She was discharged in good general health condition and was advised to continue l-thyroxine, calcitriol therapy with the same dose, calcium 1 g/daily and check serum corrected calcium level in 1 week.

**Conclusion**

This case report showed that severe hypoparathyroidism can develop even after hemithyroidectomy and lead to life-threatening hypocalcemia requiring emergency procedures. Screening programs for patients with thyrotoxicity could help to prevent these life-threatening complications.

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**EP158**

**Milk-alkali syndrome in a patient with chronic hypoparathyroidism**

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**Introduction**

Milk-alkali syndrome is defined by the triad hypercalcemia, metabolic alkalosis and renal impairment, due to intake of calcium salts and absorbable alkali. It is the 3rd leading cause of hypercalcemia but often underdiagnosed. Patients with chronic hypoparathyroidism after total thyroidectomy have increased risk for this potentially life-threatening complication and its epidemiology is unclear. We present a case of milk-alkali syndrome in a patient with chronic hypoparathyroidism.

**Case report**

Female, 60-years-old. Chronic hypoparathyroidism and hypothyroidism after total thyroidectomy due to non-toxic multinodular goiter 2 years ago. Rheumatoid arthritis, chronic kidney disease and inferior limb deep vein thrombosis. Brown-Sequard syndrome 1 year ago due to cervical spine hematoma and submitted to vertebral laminectomy. Medication: levothyroxine 100 mcg, calcitriol 0.25 mcg id, calcium carbonate/cholecalciferol 1500 mg/400 UI 2id, acenocoumarol, methotrexate, and methylprednisolone 4 mg bid. She presented with nausea, vomiting and polydypsia for 4 days. She was dehydrated, BP 139/77 mmHg, HR 78 bpm, SaO2 99% (room air), temperature 36.4°C. Normal cardiological auscultation. No signs of acute abdomen and no peripheral oedema. Arterial blood gas analysis: pH 7.49, PCO2 59 mmHg, PO2 79 mmHg, HCO3– 38.6 mmol/l, icr 1.70 mmol/l, ECG: 57 bpm. Venous blood analysis: creatinine 2.5 mg/dl, urea 89 mg/dl, sodium 142 mmol/l, potassium 3.1 mmol/l, corrected total calcium 14.4 mg/dl, magnesium 2.3 mg/dl, phosphate 3.7 mg/dl, PTH < 4 pg/ml, 25-hidroxicholecalciferol 5 mmol/l, TSH 0.81 uIU/ml, T4L 1.22 mg/dl, CRP 6 mg/dl, leukocyte count 10690/ul., Kidney ultrasound: non-obstructive bilateral echogenic foci. She was diagnosed with milk-alkali syndrome. Calcium and vitamin D supplements were suspended and started treatment with intravenous isotonic saline and potassium chloride, maintaining a good urine output. Calcium and creatine levels improved progressively. Calcium carbonate/cholecalciferol 1500 mg/400 UI 2id and calcitriol 0.25 ug once every other day were restarted and she was discharged 4 days after. At the follow-up, she was asymptomatic with a corrected total calcium 8.7 mg/dl, phosphate 4.0 mg/dl and creatinine 1.37 mg/dl.

**Discussion**

In people exposed to large doses of calcium and alkali, normal kidney function and calcitriol suppression help maintain calcium and acid–base balance. However, once hypocalcemia develops, it perpetuates metabolic alkalosis, which itself decreases renal calcium excretion. Risk factors are older-age, chronic kidney disease, pregnancy and medication. Potential triggers are dehydration, volume depletion, infection, diets rich in pH-basic foods and altered medication dose. Our patient had chronic kidney disease, so when exposed to volume depletion and dehydration secondary to vomiting, she was unable to excrete excessive calcium. Additionally, the inability to decrease calcium absorption, due to exogenous calcitriol, in response to increased serum calcium levels might have aggravated hypercalcemia.

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**EP159**

**Long term treatment with teriparatide in hypoparathyroidism**

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Hypoparathyroidism is, in Italy, an orphan disease because the hormonal replacement therapy is possible only with teriparatide (fragment 1–34 of human parathyroid hormone). Otherwise the patients use oral calcium and calcitriol. This scheme of therapy obtained correct plasmatic calcium and phosphate levels, correct uric acid, correct serum creatinine, correct bone mineral density at ultrasound and good quality of life – QoL only in a little percentage of patients. Especially kidney stones, intra-renal calcifications, chronic kidney disease are too frequent during this “conventional” therapy. Recently, Italian Agency of drug approved the use of recombinant human parathyroid hormone (rhPTH) for chronic hypoparathyroidism, but only on payment. Long-term studies on rhPTH(1–84) replacement therapy, up to 6 years, demonstrated prolonged efficacy of this drug, with persistent normal plasmatic and urinary levels of calcium and phosphate, reduced renal complications, high QoL. We have given teriparatide at the started dose of 20 mcg twice, to four hypoparathyroid patients (all women, post-surgical, after an unsuccessful period of “conventional” therapy characterized by frequent accesses in emergency for hypocalcemic crisis notwithstanding high levels of oral calcium and calcitriol) for six (one patient) or eight years (three patients), monitoring...
plasmatic and urinary biochemical levels, renal ultrasounds, femoral and lumbar densitometry, questionnaire for QoL. All patients quickly obtained increased plasmatic calcium levels, despite reduction or interruption of calcium and calcitriol supplementation; no one had hypocalcaemic crisis: three of them normalised plasmatic calcium levels and one had to stop teriparatide for hypercalcaemia. One patient had persistent low values of serum calcium (even though higher than in conventional therapy), but without hypocalcaemic crisis and a persistent well-being feeling. Plasmatic phosphate levels decreased up to normal, as urinary excretion of calcium and phosphate. No other biochemical parameter was significantly modified. No patient developed urinary complications. No-one is in therapy with bone active drugs for osteoporosis. We also administered, at baseline, at 6 and 24 months and at the end of study, the RAND 36-Item Short Form (SF-36) Health Survey, covering eight domains of physical and mental health, to evaluate their perception of QoL before and during therapy with teriparatide. Data showed a significant improvement in the mean scores of all eight domains, especially during the first two years of therapy. We can conclude that the treatment with teriparatide in post-surgical hypophosphatidism is effective and safe in improving mental and physical health of patients, also in a prolonged period of therapy.

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**EP160**

Clinical evidence for the benefits of burosumab therapy in two adult cases of X-Linked Hypophosphatemia

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X-linked hypophosphatemia (XLH), representing about 80% of hypophosphatemic rickets, is an X-linked dominant disease due to inactivating mutations in the PHEX gene (located at Xp22.1) resulting in an excessive secretion of the phosphaturic hormone fibroblast growth factor 23 (FGF23). The effects are renal phosphate wasting and reduced active vitamin D synthesis leading to rickets, osteomalacia, bone deformities, odontomalacia, frequent dental abscesses and disproportionate short stature. Conventional therapy, based on phosphate and/or active vitamin D supplementation, heals the active radiologic lesions of rickets and improves statural growth but doesn’t prevent the clinical manifestations of the disease and is associated to potential side effects such as nephrolithiasis, nephrocalcinosis and hyperparathyroidism. Since 2018 burosumab, a fully humanized monoclonal antibody against FGF-23, has been authorized for trials in adults and children. However, all studies include severely affected patients. We present the response to one-year treatment with burosumab injected at each visits showing a great improvement of scores. In fact a persistent well-being feeling. Plasmatic phosphate levels decreased up to normal, as urinary excretion of calcium and phosphate. No other biochemical parameter was significantly modified. No patient developed urinary complications. No-one is in therapy with bone active drugs for osteoporosis. We also administered, at baseline, at 6 and 24 months and at the end of study, the RAND 36-Item Short Form (SF-36) Health Survey, covering eight domains of physical and mental health, to evaluate their perception of QoL before and during therapy with teriparatide. Data showed a significant improvement in the mean scores of all eight domains, especially during the first two years of therapy. We can conclude that the treatment with teriparatide in post-surgical hypophosphatidism is effective and safe in improving mental and physical health of patients, also in a prolonged period of therapy.

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**EP162**

Hypophosphatemia in patients with primary hyperparathyroidism

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Osteoporosis management increased determination of serum calcium (Ca) levels, and detection of hypercalcemia in the set of out patients. Serum phosphate (P) levels are less frequently measured in osteometric patients. Primary hyperparathyroidism (PHPT) is the most common cause of hypophosphatemia. However, hypophosphatemia receives poor attention during the PHPT diagnostic work up, and also data in literature are scanty. We retrospectively reviewed the clinical records from 3 different series of PHPT patients: a first surgical series (group 1; all patients underwent successful parathyroidectomy), a second series from a Hospital setting with Emergency Department (group 2) and a third series of out-patients referred for osteoporosis management (group 3). In group 1, serum P levels were measured in 74 (13%: 13 males, 61 females; 58.0 (49.0, 67.3) years, median (range IQ)) out 567 surgically confirmed PHPT patients, confirming that it is often neglected. Group 2 included 115 PHPT patients. 22 males, 93 females, aged 65.5 (56.0, 74.0) years. Group 3, included 88 PHPT patients; 13 males, 75 females, aged 66.0 (59.0, 75.0) years. Group 1 patients were younger than those in group 2 (P = 0.003) and group 3 (P = 0.005 by ANOVA). Serum phosphate levels were lower in Group 1 patients [2.4 (2.1, 2.8) mg/dl] with respect to levels in group 2 [2.7 (2.3, 3.0) mg/dl, P = 0.016] and group 3 [2.7 (2.4, 3.0) mg/dl, P = 0.009 by ANOVA patients. Considering the whole series of 277 patients, hypophosphatemia (< 3.0 mg/dl) was detected in 209 (75%) patients. Serum P levels were lower in males than females. Hypophosphatemia was mild (2.1–3.0 mg/dl) in 171 patients (62%), moderate (2.0–1.1 mg/dl) in 37 (13%), while severe hypophosphatemia (< 1.0 mg/dl) was not registered in any patients. As expected, hypophosphatemic PHPT patients showed lower serum total calcium, higher PTH levels, than normophosphatemic patients. Any difference in age, serum creatinine levels, ionized calcium levels, serum 25-hydroxyvitamin D (25OH), 24 h urine calcium excretion corrected for body weight, prevalence of kidney stones, bone mineral density at lumbar and femur sites as well as number of fragility fractures could be detected. Indeed, a positive correlation emerged between serum 25OH and P levels (r = 0.176, P = 0.015 by Spearman correlation). In conclusions, our data supported recently published data on hypophosphatemia in PHPT patients, confirming the relationship with a more severe PHPT phenotype. Determination of serum P levels concomitantly with serum calcium, PTH, 25OH and creatinine helps clinicians in the diagnosis of PHPT and in estimation of its severity.

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**EP163**

Primary hyperparathyroidism: what is the impact on bone?

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Key words: Primary hyperparathyroidism-PTH level –osteoporosis-osteolytic bone lesions-brown tumor

Introduction

Primary hyperparathyroidism is a frequent pathology responsible for an alteration of the phosphocalcic metabolism at the origin of numerous complications, in particular osteosclerosis. The objective of this work is to evaluate the bone impact of primary hyperparathyroidism in our series.

Matériel et méthodes

Retrospective descriptive and analytical study, including 44 patients followed for primary hyperparathyroidism over a period spanning 6 years from 2015 to 2021. Data were collected from medical records and analyzed by SPSS-V21 software. Material and methods

The mean age was 55 ± 11 years, with a clear female predominance with a sex ratio M/F = 0.29 which 80% of the women were menopausal. Eighty-one percent of the cases had hypercalcemia with 36% of the cases presenting with malignant hypercalcemia. The assessment of the bone consequences of primary hyperparathyroidism showed osteoporosis in 58.6% of the cases with osteopenia in 24%. A pathological fracture revealed primary hyperparathyroidism in one case or in
EP164
The clinical presentation of primary hyperparathyroidism during the Covid-19 pandemic
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Background
In the last decades, the clinical profile of PHPT in Western Countries has changed from a highly symptomatic to a largely asymptomatic disease. However, a substantial stability in its clinical features has been reported in the last two decades. The usual management, including time to diagnosis and treatment, of PHPT during the Covid-19 pandemic has been changed and likely slowed down.

Whether further changes in the clinical presentation of PHPT have occurred during the Covid-19 pandemic is currently unknown.

Patients
A retrospective survey was conducted in our series of 150 well-characterized consecutive PHPT patients, who were admitted to our Hospital between January 2012 and December 2021. Patients were initially subdivided according to the date of PHPT diagnosis in 2 consecutive 5-year period (n = 79 and 71, respectively). The more recent group was then split into 2 subgroups before and after the Covid-19 Pandemic (i.e. 2017–2019, n = 45; 2020–2021, n = 26).

Results
In the last five-year period an increased rate of post menopausal women (P = 0.011) and of patients with osteoporosis at any site (P = 0.007) was found among PHPT patients compared to those in the previous five-year period. Furthermore a non significant reduction of "mild asymptomatic" patients was observed. After subdividing the last five-year period based on the pandemic, the increased rate of post menopausal women was confirmed in the Covid-19 period compared to the remaining ones (P = 0.022). In addition, the number of criteria for surgery met by asymptomatic PHPT patients has become statistically higher in the pandemic period than in preceding periods (P = 0.017).

Conclusions
During the Covid-19 pandemic, when surgery for benign diseases and hospital visits have been restricted, only minor changes in the PHPT clinical presentation have occurred. An increased rate of postmenopausal women with osteoporosis was diagnosed with PHPT.

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2.3% of cases. The bone CT scan showed osteolytic bone lesions in 51.5% of the cases, the most of them were diffuse, brown tumors in 18.2% of the cases, most often of multiple locations, affecting the maxillomandibular region, pelvis (iliac bone and ischium), scapula and femoral neck respectively. Primary hyperparathyroidism was complicated by fibrocystic osteitis in one case, i.e. 2.3% of our series. Vitamin D deficiency was noted in all patients, with a deficiency in 61.4% of cases. The six point eight percent of cases in our series (n = 3) were complicated by Hungry bone syndrome and 3 cases (6.8%) by defensive hyperparathyroidism.

The relationship between the level of bio-intact PTH 1–84 and the occurrence of bone complications found: a statically significant association with the occurrence of brown tumor and osteolytic bone lesions and with Hungry bone syndrome, while no complications found: a statically significant association with the occurrence of bone syndrome and 3 cases (6.8%) by definitive hypoparathyroidism. The

The effects of long-term replacement therapy of primary adrenal insufficiency
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Objectives
Disorders concerning the endocrine system may be seen in patients with transfusion-dependent thalassemia major. It is thought that iron accumulated in the organs, especially with transfusion, causes this. In our study, we tried to reveal a relationship by comparing the iron parameters of these patients with various endocrine parameters.

Methods
Our study is a retrospective study. The data of 18 thalassemia major patients who applied to Osmangazi University Endocrinology and Hematology departments were collected from medical records. Parameters are sex, age, iron parameters, Hb, Hct, fasting glucose, fructosamine, lipid profile, thyroid function tests, anterior pituitary hormone panel, parathormone (PTH), 25-OH vitamin D level.

Results
18 patients with thalassemia major were analyzed. (8/44.4%) were male and 10 (55.6%) were female. The mean age was 36.94 ± 10.86 years and the age range was between 20 and 54 years. All of the patients received blood transfusion once a month and were followed up with iron chelation therapy. The fructosamine levels of 6 patients were also above the normal value. GH and IGF-1 levels of the patients were in the normal range. The 25 OH vitamin D level of 11 patients was below 30 ng/mL. Osteoporosis was detected in 9 patients. Seven of these patients (70%) were evaluated as secondary osteoporosis. Endocrine parameters of the patients were compared with iron parameters. There was a positive relationship between transferrin saturation and 25 OH vitamin D. A negative relationship between iron and PTH, and a negative relationship between ferritin and FSH/LH. Thyroid function tests were normal in 9 patients (50%), primary hypothyroidism was found in 8 patients (44.4%), and hypothyroidism with graves diagnosis was sometimes difficult. Therefore, some patients are exposed to mild GC excess with potential complications, such as hypertension, diabetes, and skeletal fragility. Data on bone mineral density (BMD) in PAI is still scarce and controversial.

Objective
To evaluate the impact of long-term GC treatment on BMD, in patients with PAI.

Methods
We conducted a retrospective cohort study of patients with a diagnosis of PAI, followed-up between 2011 and 2021. Patients with other causes of osteoporosis were excluded. BMD was evaluated by dual-energy X-ray absorptiometry (DXA). Doses of the various glucocorticoids were converted to hydrocortisone (HC) equivalents. We calculated cumulative doses of HC (annual and lifetime), divided by corresponding body area (mg/m2), until the date of DXA.

Results
47 patients with PAI were included, 29 with autoimmune origin (63%), 11 with congenital adrenal hyperplasia (CAH) (23.9%), 4 from tuberculosis (8.7%), 1 from x-ALD and 1 from spontaneous bilateral bleeding (2%). Mean age 53.8 ± 14.3 years, 57.5% females, disease duration 24.6 ± 15.3 years. Mean daily HC dose was 16.6 ± 4.3 mg²m⁻² and mean cumulative lifetime dose was 154 ± 139 g/m². 43 patients were under mineralocorticoids (91.5%). Osteoporosis was present in 35.5% of patients. There was an inverse correlation between cumulative lifetime GC dose and lumbar (r = -0.435, P = 0.030) or femoral T-scores (r = -0.437, P = 0.030); and between cumulative annual dose and lumbar T-score (r = -0.458, P = 0.025). Patients with osteoporosis (any T-score ≤ -2.5) had a higher cumulative lifetime HC dose (P = 0.027), and a logistic regression model revealed that this association was independent of sex, PAI etiology, and treatment with mineralocorticoids (P = 0.048). There was no association between T-score and type of GC replacement. There was a correlation between lumbar T-score and age (r = -0.460, P = 0.016), but there was no relationship between BMD and disease duration.

Conclusion
In this study, there was an inverse linear relationship between glucocorticoid cumulative dose and bone mineral density at lumbar spine, which is in line with the known preferential action of GC on trabecular bone. Mild GC excess for some periods of life may have a greater impact in BMD reduction than disease duration. Our results reinforce the need for close monitoring of GC replacement therapy in patients with PAI.

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Endocrinopaties in thalassemia patients
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Objectives
Disorders involving the endocrine system may be seen in patients with transfusion-dependent thalassemia major. It is thought that iron accumulated in the organs, especially with transfusion, causes this. In our study, we tried to reveal a relationship by comparing the iron parameters of these patients with various endocrine parameters.

Methods
Our study is a retrospective study. The data of 18 thalassemia major patients who applied to Osmangazi University Endocrinology and Hematology departments were collected from medical records. Parameters are sex, age, iron parameters, Hba1c, fasting glucose, fructosamine, lipid profile, thyroid function tests, anterior pituitary hormone panel, parathormone (PTH), 25-OH vitamin D level.

Results
18 patients with thalassemia major were analyzed. (8/44.4%) were male and 10 (55.6%) were female. The mean age was 36.94 ± 10.86 years and the age range was between 20 and 54 years. All of the patients received blood transfusion once a month and were followed up with iron chelation therapy. The fructosamine levels of 6 patients were also above the normal value. GH and IGF-1 levels of the patients were in the normal range. The 25 OH vitamin D level of 11 patients was below 30 mg/mL. Osteoporosis was detected in 9 patients. Seven of these patients (70%) were evaluated as secondary osteoporosis. Endocrine parameters of the patients were compared with iron parameters. There was a positive relationship between transferrin saturation and 25 OH vitamin D. A negative relationship between iron and PTH, and a negative relationship between ferritin and FSH/LH. Thyroid function tests were normal in 9 patients (50%), primary hypothyroidism was found in 8 patients (44.4%), and hypothyroidism with graves diagnosis was
detected in 1 patient. There was no thymoma in thyroid USG. Autoimmunity was only present in the patient diagnosed with Graves.

Conclusions Evaluation of endocrinopathies in thalassemia patients should be done regularly to detect and treat endocrine complications. It may be appropriate to screen these patients at least once a year in this respect. The role of pituitary hormones in the routine follow-up of thalassemia patients is still controversial. Larger prospective studies are needed. Collaborative multicenter studies should be considered to reach more precise information.

Keywords Thalassemia, endocrinopathy, ferritin, iron, transfusion

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EP167

Classical complications of primary hyperparathyroidism

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Key words Primary hyperparathyroidism-Bone complications-Renal complications and digestive complications.

Introduction Primary hyperparathyroidism is a frequent endocrinopathy whose diagnosis is biological and linked to an inappropriate secretion of parathyroid hormone (PTH), which leads to an altered phosphocalcemic metabolism that can be responsible for numerous complications. The aim of this work is to evaluate the classical complications of primary hyperparathyroidism in our series: bone, digestive and renal.

Material and methodsRetrospective descriptive and analytical study including 44 patients followed for primary hyperparathyroidism between 2015 and 2021. Only classical complications (bone, kidney and digestive) were noticed in this work. Data were collected from medical records and analyzed by SPSS-V21 software.

Results

The mean age was 55 ± 11 years, with a clear predominance of women in 77.3% of whom 80% were postmenopausal. 81% of the cases had hyperparathyroidism, including 36% with malignant hyperparathyroidism (n = 13). The diagnosis of primary hyperparathyroidism was revealed by complications in 25% of cases (n = 11). The impact assessment of hyperparathyroidism showed a remarkable effect on the skeletal system with osteoporosis in 60.7% of the cases, osteolytic bone lesions in 18% (n = 8), the majority of which were of diffuse localization, and brown tumors in 13.6% of the cases (n = 6). Fibrocystic ostensis was observed in 2 cases (4.5% of our series) and a pathological fracture in one patient. On the renal level, renal lithiasis complicating primary hyperparathyroidism in 31.8% (n = 14) which 78.5% of the cases were bilateral (n = 11) and complicated by nephrocalcinosis in 2 cases or 5.7%. Alteration of renal function was noted in 11.6% (n = 5) and GFR 30-60 ml/min. The digestive complications were mainly represented by acute pancreatitis in 3 patients (6.8%) and chronic calcifying pancreatitis in one case. On postoperative, Hungry bone syndrome complicated 6.8% of the cases or 3 cases in our series. On postoperative, Hungry bone syndrome complicated 6.8% of the cases or 3 cases in our series. The relationship between the bio-intact PTH level and the occurrence of complications finds: a statistically significant association with the occurrence of brown tumor as well as a statically significant correlation with osteolytic bone lesions, while no significant correlation with the occurrence of renal lithiasis, osteoporosis and pancreatitis and PTH level.

Discussion

Primary hyperparathyroidism is an endocrinopathy that is usually benign but remains a serious condition because of its bone, kidney and digestive complications.

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EP169

Expanding the phenotype of Familial hypocalciuric hypercalcaemia type 3

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Introduction Familial hypocalciuric hypercalcaemia (FHH) is a rare mostly asymptomatic genetic disorder affecting the calcium sensing receptor (CaSR) and its associated proteins with autosomal dominant inheritance. Mutation in AP2S1 gene is responsible for FHH3.

Aim

Expand the phenotype of FHH type 3.

Methods

Clinical and biochemical characterization of a patient with de-novo FHH3 mutation.

Results

S.Z, A 30-year-old man was hospitalized for recurrent pancreatitis. His medical history included chronic hypercalcaemia in the range of 11.7–13.3 mg/dl attributed to his prior clinical diagnosis of FHH. Abdominal imaging and lipid profile were unremarkable. The working diagnosis was of hypercalcaemia-related acute pancreatitis. He was treated conservatively with resolution of symptoms and normalization of serum amylase and lipase. A multi-gene panel that was performed (INVITAE) revealed a heterozygous mutation in the AP2S1 gene-p.Arg15Leu. His parents and two siblings were normocalcemic. A second genetic panel for pancreatitis related genes was negative. DXA bone mineral density revealed T score of −2.3 at LS and −2.9 at FN and TH – a typical finding in FHH3 patients. Cinacalcet at a dose of 120 mg daily was well tolerated and normalized calcium levels with no episodes of pancreatitis within 26 months of follow-up. His three-year-old son is followed for speech delay and was found to be hypercalcemic; he carries the same AP2S1 mutation.
Conclusions
We describe a family with a de novo mutation in the AP2S1 gene presenting with recurrent pancreatitis, low bone mass and speech delay thus expanding the phenotype of FHH3.

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EP170
Vitamin D levels in relationship to thrombotic markers in severe SARS-CoV-2 infection
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Introduction
Severe infection from the SARS-CoV-2 virus is associated with various manifestations, including hematomelal manifestations. Thrombotic events or a tendency to develop thrombotic events also characterize severe COVID-19 disease and may be related to fatalities. Vitamin D is known to have immunomodulating properties and to enhance the body defense system against invading pathogens and to have immunostimulatory properties as far as the innate immune response is concerned.

Aim
The aim of the study was to measure 25(OH)D3 levels in patients hospitalized for severe COVID-19 infection and to investigate the relationship between 25(OH)D3 levels and ferritin levels and d-dimer levels in this cohort.

Methods
In a cohort of 42 patients hospitalized for severe infection from the SARS-CoV-2 virus 25(OH)D3 levels were measured. In the same cohort ferritin levels and d-dimer levels were also measured. Observations were also performed in a control group.

Results
25(OH)D3 levels were 8.08 ± 1.48 ng/ml (mean ± S.E.M.) and they were inversely related to ferritin levels, correlation coefficient -0.15, P = 0.001, linear regression analysis and to d-dimer levels, correlation coefficient -0.34, P < 0.001, linear regression analysis.

Conclusions
Severe infection from the SARS-CoV-2 virus is related to a tendency for the development of thrombotic events. d-dimer levels are measured and followed in these patients. Ferritin levels are also increased in severe SARS-CoV-2 infection and may be related to adverse outcome. We showed that vitamin D levels are low in hospitalized patients with severe SARS-CoV-2 infection and are inversely related to ferritin and d-dimer levels. It may thus be proposed that vitamin D is an inverse index of severity in the context of SARS-CoV-2 infection.

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EP171
A sporadic case of pseudohypoparathyroidism type Ib and fahr’s syndrome
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Introduction
Pseudohypoparathyroidism is a heterogenous disease characterized by hypocalcemia, hyperphosphatemia and parathyroid hormone resistance. The distinct pseudohypoparathyroidism types are distinguished by physical features, the coexistence of other hormone resistances and genetic defects. Pseudohypoparathyroidism type Ib is more often associated with sporadic cases, unlike others types.

Clinical Case
Male, born in France, diagnosed with pseudohypoparathyroidism during childhood. There was a history of fatigue, gait disorder and delayed eruption of teeth. Laboratory investigation revealed serum hypocalcemia, hyperphosphatemia and elevated serum PTH levels. No family history of phosphocalcium metabolism disorder. He was treated with oral calcium and cholecalciferol. At the age of 9, he starts living in Portugal. Physical examination showed no features of Albright Hereditary Osteodystrophy. Laboratory results showed normal thyroid function and no evidence of other hormone resistances. He started treatment with calcium also in addition to oral calcium and cholecalciferol. Over the years, the goal to an adequate calcium-phosphate level was difficult to obtain in this patient due to poor treatment adherence. At 33 years old, urinary calcii was detected on renal ultrasoundography. 7 years later, he presented with left leg pain with extensive calcifications at the level of the cerebellar hemispheres, lenticular nuclei, corona radiata, central semiovale and subcortical level, suggestive of Fahr’s syndrome. He was started to use a genetist and the molecular genetic result revealed a GNAS gene methylaiton defect specifically in 20q13.13.32 region performed by MS-MLPA analysis. STX16 deletion was not detectable. This result confirms the diagnosis of pseudohypoparathyroidism type Ib caused by a paternal uniparental disomy of the long arm of chromosome 20.

Conclusions
The molecular investigation is not essential for the therapeutic approach. In this patient, the identification of a methylation defect in a region of GNAS gene was useful for the classification of pseudohypoparathyroidism and allowed us to evaluate this case as a sporadic event, therefore without specific risk for the patient’s offspring. The present case also serves to emphasize the importance of treatment adherence that may prevent acute and chronic complications of hypocalcemia.

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EP172
Acute hypercalcemic crisis in an elderly with granulomatous disease
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Background
Tuberculosis rarely leads to clinically significant hypercalcemia. However, elderly patients remain predisposed due to advanced age, multiple comorbidities and polypharmacy.

Clinical Case
An 81-year-old female presented with 1 month history of bilateral weak hand grip and sluggish mastication. She was initially managed as progressive Parkinson’s Disease. After 3 weeks, she was now reported to have episodes of fall from imbalance. After few days, there was noted increased sleeping time, decreased verbal output, response lag and slurred speech. There were no pulmonary symptoms or febrile episodes. Her medical history includes hypertension, Diabetes Mellitus, previous CVD infarct, Chronic Kidney Disease, recovered Moderate COVID-19 infection and pulmonary tuberculosis that was diagnosed 30 years ago. Outpatient evaluation revealed severe hypercalcemia (15.36 mg/dl). Upon admission, Calcium (500 mg/day) and Vitamin D (1500 IU/day) supplements were discontinued. She was started on vigorous intravenous hydration and diuresis with Furosemide. Calcitonin nasal spray was administered for 2 days. Cranial CT scan showed absence of acute infarction or intracranial hemorrhage. On the 3rd hospital stay, serum calcium was still elevated (11.99 mg/dl) but decreased from baseline. Other blood tests results showed elevated 25(OH)D119.72 mg/dl (> 30 ng/ml), normal PTH 15.84 pg/dl (< 67.90 pg/dl), magnesium 2.41 mg/dl (1.6–2.6 mg/dl) and phosphorous 3.6 mg/dl (2.29–4.79 mg/dl). Hence, PTH-independent causes were evaluated with high suspicion of Vitamin D intoxication. Chest imaging showed a thick walled cavitatory mass with adjacent consolidation and surrounding centrilobular nodule in a tree-in-bud configuration in the right upper lobe suggestive of an infectious process. On the 10th hospital stay, CT guided biopsy of the right upper lung mass was done. Histopathology showed lung tissues with fibrosis, focal necrosis, and chronic inflammation. MTB GeneXpert was positive consistent with Tuberculosis for which she was started on Anti-Koch’s medications to be completed for 6 months. An elevated Serum 1.25(OH)D could have supported extrarenal 1α-24 hydroxylation in granulomatous disease but was not readily available. On the 12th hospital stay, due to persistent hypercalcemia (11.72 mg/dl), she was started on Prednisone 10 mg/day which was up titrated to 20 mg/day after 3 days of initiation then down titrated weekly. She was discharged in a stable condition. Normocalcemia was documented upon follow up with subsequent improvement in the patient’s sensorium.

Conclusion
Granulomatos disorders as the etiology of hypercalcemia should be suspected in the setting of hypervitaminosis D and low-normal or low parathyroid hormone level. Hypercalcemic crisis is an infrequent endocrine emergency that portends excellent outcomes with prompt diagnosis and management.

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EP173
Palovarotene for the treatment of fibrodysplasia ossificans progressiva: methodology of the phase III open-label PIVOINE rollover trial
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Objectives
Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disorder characterized by heterotopic ossification (HO) and progressive restriction of mobility. To date, no approved disease-modifying treatments for FOP exist, but interim phase III trial (NCT03312634) results suggest marked efficacy for palovarotene (PVO). Here, we describe methodology of the PIVOINE trial (NCT05027802) designed to allow treatment continuity and further evaluation of PVO safety and efficacy.

Methods
Patients will receive 5 mg PVO daily, or the parent study completion dose, for a maximum of 3 years; during flare-ups, patients will receive 20 mg daily for 4 weeks, then 10 mg daily for 8 weeks. Enrollment criteria: completion of a parent study (end of study/treatment visit of NCT03312634 or NCT02279095/NCT02979769), > 14 years old, full skeletal maturity if aged < 18 years or deemed to be final adult height. PIVOINE aims to enroll 61 patients; recruitment has not begun. Outcomes are presented in Table.

Summary
Results from PIVOINE, estimated to end in November 2024, will allow further evaluation of PVO in FOP.

References

Funding
Sponsored by Ipsen.

Table: Trial outcomes

Primary

<table>
<thead>
<tr>
<th>Incidence of treatment-emergent adverse eventsa</th>
<th>%</th>
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</thead>
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Secondaryb

<table>
<thead>
<tr>
<th>Cumulative Analogue Joint Involvement Scale (CAJIS) total score</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of aids, assistive devices and adaptations</td>
<td>%</td>
</tr>
<tr>
<td>FOP-Physical Function Questionnaire maximum percentage of worst score</td>
<td>%</td>
</tr>
<tr>
<td>Frequency of healthcare utilization</td>
<td>%</td>
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<tr>
<td>Observed/percentage predicted:</td>
<td>%</td>
</tr>
<tr>
<td>Forced vital capacity (FVC)</td>
<td>%</td>
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<tr>
<td>Forced expiratory volume in 1 second (FEV1)</td>
<td>%</td>
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<tr>
<td>Diffusion capacity of the lung for carbon monoxide (DLCO)</td>
<td>%</td>
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<tr>
<td>Absolute/percentage predicted:</td>
<td>%</td>
</tr>
<tr>
<td>FEV1/FVC ratio</td>
<td>%</td>
</tr>
<tr>
<td>Patient Reported Outcomes Measurement Information System (PROMIS) Global Health Scale physical and mental function scores</td>
<td>%</td>
</tr>
<tr>
<td>Number of investigator-reported flare-ups, outcomes and duration</td>
<td>%</td>
</tr>
<tr>
<td>Percentage of patients with new bone growth</td>
<td>%</td>
</tr>
</tbody>
</table>

aCollected continuously over trial period; bCollected every 6 months over trial period; cRaw values and change from inclusion visit.

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EP174
McCune Albright syndrome – a clinician’s challenge and a multi-disciplinary approach: case report
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Introduction
McCune-Albright syndrome is a rare, heterogeneous disorder, consisting of at least two of the following three features: polyostotic fibrous dysplasia, café-au-lait skin pigmentation and autonomous endocrine hyperfunction. We present the case of a patient with an atypical presentation of McCune Albright syndrome (MAS) and severe fibrous dysplasia lesions.

Background
Atypical parathyroid adenoma (APA) is a rare disease that can be challenging to distinguish from benign parathyroid adenoma. APA shows some laboratory and histopathological features with parathyroid cancer. This study attempts to compare clinical, laboratory, radiologic and histopathological characteristics in APA and parathyroid adenoma (PA).

Methods
This was a retrospective study based on the database of eighty-two subjects who underwent surgery for primary hyperparathyroidism at a tertiary referral center between 2010 and 2021. Forty-one patients with APA matched by age and gender to controls with PA. Clinical, laboratory, radiologic and characteristics were obtained from the hospital database.

Results
Forty-five (54.8%) of primary hyperparathyroidism (PHPT) patients were symptomatic, 36 (90%) had nephrolithiasis, 6 (15%) had fracture and 3 (7.5%) had hypercalcaemic crisis. APA patients present with significantly increased serum calcium, parathormone (PTH) and parathyroid hormone levels (P < 0.001, all). No significant difference was observed in the results of bone mineral density (BMD), T-scores and Z-scores. The size of adenoma was significantly greater in APA group (24 (8.8–70) mm vs. 12 (3.8–32) mm, P = 0.005).

Conclusion
Our study revealed that increased preoperative serum calcium, parathormone, alkaline phosphatase concentrations and parathyroid adenoma size on ultrasound may have predicted the atypical parathyroid adenoma.

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EP176

PHT 1–34 delivery via insulin pump in a patient with severe post-operative hypoparathyroidism

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Hypoparathyroidism (HypoPT) is the only hormone deficiency syndrome whose standard treatment is not based on the replacement of the missing hormone. Although most cases of postsurgical PHT can be effectively managed with the conventional use of oral calcium and active vitamin D (SOC therapy), some patients require very high doses and develop complications such as hypercalcemia, renal stones, nephrocalcinosis and ectopic calcifications. In the last few years, recombinant human PTH (rPTH) has become an appealing option for patients affected by chronic HypoPT who are refractory to SOC therapy. Winer et al have adapted an insulin pump delivery system to treat patients with a continuous infusion of rPHT (1–34) (teriparatide). We describe the case of a 33-year-old woman who was referred to our Clinic for severe chronic HypoPT after total thyroidectomy for multinodular goiter. Despite being on therapy with high doses of oral calcium and active vitamin D, she reported muscle spasms, cramps and perioral paresthesia on a daily basis and was frequently admitted to the Emergency Room to be treated with intravenous calcium infusion. At our evaluation, we confirmed a severe hypercalcemia (7.5 mg/dl), hyperphosphatemia (5.2 mg/dl) and hypercalciuria (388 mg/24 h). The abdomen ultrasound showed the presence of medullary nephrocalcinosis and right microcalcifications. After using teriparatide 20 mcg twice-daily injection without success, we decided to treat the patient with a continuous subcutaneous perfusion of rPHT (1–34) by using an insulin pump. rPHT (1–34) (Terressa®, 20 μg/80 mL) was diluted with distilled water and the patient started continuous administration of subcutaneous rPHT (1–34) via a Medtronic® pump with a rate of 0.8 UI/h (equivalent to 11 mcg of teriparatide/day). The patient was monitored by daily clinical evaluation (symptoms and Chvostek and Trousseau signs) and assessment of serum calcium and ionized calcium levels. Moreover, we assessed the patient’s quality of life by using the SF-36 questionnaire at baseline and at 6 months. The daily dose was progressively uptitrated until 22 mcg/day and the SOC therapy was gradually reduced until discontinuation. At the last evaluation (9 months) serum calcium was 9.5 mg/dl, serum phosphate was 3.3 mg/dl and 24 h urine calcium was 100 mg/24 h. Abdomen ultrasound did not show the nephrolithiasis. The SF-36 test showed a significant improvement of the scores. In conclusion, the continuous infusion of rPHT (1–34) in our patient was the only treatment option able to restore long-term calcium homeostasis and improve the quality of life.

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EP177

Identification of GATA3 pathogenic variants in two patients with hypoparathyroidism, deafness and renal dysplasia (HDR) syndrome

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Hypoparathyroidism, deafness and renal dysplasia (HDR) syndrome, also known as Barakat syndrome, is a rare autosomal dominant disease characterized by the triad of hypoparathyroidism (H), deafness (D) and renal abnormalities (R). Its genetic cause is known to be the haploinsufficiency of the zinc finger transcription factor GATA3. This disorder exhibits a great clinical variability and an age-dependent penetrance of each feature. The most frequent manifestation is sensorineural deafness, usually diagnosed during childhood. Symptomatic or asymptomatic hypoparathyroidism affects about 90% of patients. Kidney abnormalities, such as renal cysts, are less common. We report two cases of HDR syndrome due to pathogenic variants in exon 3 of the GATA3 gene. Subject 1 was a 17-years-old boy who was referred to our Department in 2018 for hypocalcemia incidentally detected at routine blood tests. At physical examination Trousseau and Chvostek signs were positive and laboratory evaluation confirmed a severe hypercalcemia (ionized calcium 0.62 mmol/l, n.v. 1.13–1.32), hyperphosphatemia (8.8 mg/dl) with undetectable PTH levels (< 10 pg/ml, n.v. 8–40). At abdomen ultrasound and magnetic resonance multiple renal cysts were detected. Subject 2 was a 16-years-old boy who was referred to our Department in 2005 for hypocalcemia complicated by epileptic seizure. His past clinical history was remarkable for right nephrectomy at 4 months of age for multicystic renal disease. At our first evaluation physical examination was normal and blood tests showed low ionized calcium (0.99 mmol/l, n.v. 1.13–1.32) with undetectable PTH levels (< 10 pg/ml, n.v. 15–75). Computed tomography displayed multiple cerebral calcifications and the audiometric evaluation revealed the presence of bilateral mild sensorineural hearing loss in both patients. On the basis of clinical and biochemical data, HDR syndrome was suspected and genetic analysis of the GATA3 gene revealed the presence of a pathogenetic variant in exon 3, c.404dupC in subject 1, but not in his parents and sister, and c.431dupG in subject 2. These frameshift variants produce a premature stop codon resulting in the synthesis of a non-functional truncated protein (p.Ala136GlyfsTer168 and p.His145ProfsTer159, respectively). A good control of H is achieved in both patient by using rPHT in subject 1 and oral calcium and active vitamin D in subject 2. HDR syndrome, although rare, is one of the genetic causes of H and must be excluded in all patients with idiopathic H, particularly if young. A correct diagnosis is important for the early detection of other features of the syndrome and for genetic counseling.

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EP178

Sickle cell disease and hyperparathyroidism: case report

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Introduction

Primary hyperparathyroidism (pHPT) is a common endocrine disorder usually diagnosed by the presence of elevated serum calcium levels with inappropriate normal or increased parathyroid hormone (PTH) serum levels. This condition has been reported in few cases of patients with sickle cell disease (SCD), a multisystem disorder with acute and chronic complications.

Observation

We report a case of a 63-year-old Tunisian woman with a history of homozygous sickle cell disease (SS phenotype), high blood pressure and atrial fibrillation, referred to the emergency department for hypercalcemia 3.68 mmol/l (n: 2.25–2.6) with electrocardiogram (ECG) abnormalities. After hydration, a decrease of calcium level 2.82 mmol/l and normalized ECG, she was admitted to the endocrinology ward. Physical examination showed a centimetric basal cervical mass. Blood tests showed: hypophosphatemia 0.73 mmol/l (n: 0.78–1.52), an elevated parathyroid hormone level 1479/ps/ml (n: 26.5–96.5) and a moderate decrease in kidney function (creatinine clearance <24 ml/min). A urinary cast showed no hypercalciuria. This case was compatible with pHPT. Hypercalcemia was treated with oral route and intravenous hyper hydration along with phosphate perfusions. Ultrasonography of the neck revealed a mass at the left inferior parathyroid lobe of 17 x 14 mm and the Sestamibi scan showed a 15 mm single left parathyroid adenoma. Renal echography revealed no nephrolithiasis albeit an aspect of chronic renal disease. Bone densitometry revealed osteoporosis (T scores of —3.5, —2.5 in lumbar spine and left hip respectively). Then the patient underwent an excision of the parathyroid adenoma. The histological analysis showed pseudo adenomatous parathyroid hyperplasia.

Discussion

Some explanations for the association of SCD with pHPT have been delineated in the literature, such as vitamin D deficiency, high levels of EPO due to chronic hemolysis which could stimulate the parathyroid glands and increased growth factors and fibroblastic growth factor which seem to promote parathyroid cells proliferation.

Conclusion

If we consider pHPT to be a complication of SCD, calcium levels should be routinely checked, keeping in mind the fatality of hypercalcemia complication adding to that the threatening complications of SCD. Further research is required to underpin the association of SCD with pHPT.

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EP179

Primary hyperparathyroidism revealed by a brown tumor: a case report

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Parathyroid carcinoma (PC) rarely presents with metastasis at diagnosis and usually in patients also having gross local invasion. Case presentation: We report the case of a 51-year-old postmenopausal woman presenting at our institution in June 2019 with symptomatic hypercalcemia (fatigue, polyuria, constipation and bone pain), but with a surprisingly good general condition. She had been treated with bisphosphonates for osteoporosis (DXA: LS T score -4.2 s.d., Z score -3.6 s.d.; FN T score -2.4 s.d., Z score -1.7 s.d.) for 2 years, having a variable hypercalcemia up to 12.6 mg/dL, but undiagnosed for primary hyperparathyroidism (PHPT). She had no family history of parathyroid disease or endocrine neoplasia. Initial laboratory finding revealed marked hypercalcemia (17.5 mg/dL), very high PTH levels (1561 pg/mL) and turnover (CTX 4.58 ng/mL) and normal kidney function, which led to the suspicion of PC. Neck ultrasound showed a hypoechoic tumor with slightly irregular margins, Ø max 1.5 cm, in the position of right superior parathyroid gland. The tumor was surgically removed and three other parathyroids were identified in canonical location and of normal appearance, with no gross invasion. As the preliminary pathology report revealed characteristic features of PC, a total thyroidectomy was performed, and a small normal parathyroid gland was found adjacent to the initial tumor. After tumor removal, her PTH levels decreased by 65%, from 1561 pg/mL to 560 pg/mL (Ca 11.34 mg/dL) and then increased fast, at the the same rate as preoperatively: 39% in 3 weeks preop vs 39% in 1 mo postop; and progressively reached 1084 pg/mL after 3 mo. A MIBI scan including the mediastinum was negative and a FDG–PET CT showed increased metabolic activity in a 10 mm nodule, in the right para aortic mediastinal pleura, the descending colon and skeleton. A bone scan showed homogenous symmetrical uptake throughout the skeleton and X-rays were normal. A CT scan confirmed a mediastinal nodule measuring 11/7/13 mm, tangent to the right antero-lateral face of the ascending aorta and bilateral pulmonary micro-nodules. Total serum Ca was variably controlled (9.1 mg/dL to 15 mg/dL) with pamidronate and then denosumab (60 mg). The surgery performed abroad confirmed that the mediastinal nodule was a metastasis of PC. Eventually, the hypercalcemia became resistant to denosumab (6 mo postop) and the patient died due to a hypercalcemic crisis (20 mg/dL).

Conclusion: This is a rare case of a small and very aggressive parathyroid carcinoma with lung metastasis at diagnosis although with no local invasion.

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EP182

Aberrant promoter methylation, expression and function of RASSF1A gene in a series of Italian parathyroid tumors

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Introduction

Brown tumors are osteolytic lesions rarely revealing hyperparathyroidism. They result from abnormalities of bone metabolism. They usually occur in the terminal stage of hyperparathyroidism. We report the case of a patient with hyperparathyroidism revealed by a brown tumor.

Case

A 39-year-old female patient with no notable medical history who presented for 1 year a mandibular swelling progressively increasing in size after a dental extraction without other associated signs. A phosphocalcic assessment was requested, coming back in favor of a primary hyperparathyroidism: high level of calcemia at 132 mg/dL, a low phosphorhemia at 17 mg/dL and an elevated parathormonemia 9 times above the normal. A biopsy of the mass was performed, which anatomopathological examination was in favor of a reparative giant cell granuloma, hence the diagnosis of brown tumor. Cervical ultrasound revealed a 3–4 cm parathyroid adenoma and scintigraphy confirmed the parathyroid origin. The patient underwent parathyroidectomy and the histological study was in favor of an atypical parathyroid adenoma. The evolution was marked by a normalization of the phosphocalcic balance.

Discussion and conclusion

Brown tumors are rarely revealing bone manifestations of primary PTH. They are very rare and may be identified related to the development of primary or to a failure in the normal reabsorption of bone.

Primary hyperparathyroidism revealed by acute pancreatitis: a case report

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Introduction

Primary hyperparathyroidism (PPH) can be complicated by pancreatitis. The frequency of association of primary hyperparathyroidism with pancreatitis is rare, varying between 1.5% and 7%.

Case

A 78-year-old patient, without any particular history, who consulted the emergency room for an acute digestive picture with abdominal pain and bilious vomiting, an abdominal CT scan was ordered showing stage D pancreatitis. After eliminating other classical causes of pancreatitis with a normal triglyceride level, an emergency room for an acute digestive picture with abdominal pain and bilious vomiting, an abdominal CT scan was ordered showing stage D pancreatitis. After eliminating other classical causes of pancreatitis with a normal triglyceride level, a direct or indirect role of hypercalcemia via activation of pancreatic proteases.

Discussion and conclusion

Primary hyperparathyroidism revealed by acute pancreatitis: a case report

The patient underwent a parathyroidectomy with good clinical and biological evolution. Given a bisphosphonate infusion. After the normalization of the calcemia the patient was discharged with a given furosemide, and when her blood calcium level did not improve, she was given denosumab (6 mo postop) and the patient died due to a hypercalcemic crisis (20 mg/dL).

Conclusion

This is a rare case of a small and very aggressive parathyroid carcinoma with lung metastasis at diagnosis although with no local invasion.

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EP190

Primary hyperparathyroidism revealed by acute pancreatitis: a case report

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Introduction

Primary hyperparathyroidism (PPH) can be complicated by pancreatitis. The frequency of association of primary hyperparathyroidism with pancreatitis is rare, varying between 1.5% and 7%.

Case

A 78-year-old patient, without any particular history, who consulted the emergency room for an acute digestive picture with abdominal pain and bilious vomiting, an abdominal CT scan was ordered showing stage D pancreatitis. After eliminating other classical causes of pancreatitis with a normal triglyceride level, an etiological research revealed a profile of primary hyperparathyroidism: PTH: 392 pg/mL or 9X normal, hypercalcemia: 141 mg/dl (85–105), hyperphosphatemia 19 mg/l (20–45). Cervical ultrasound and cervico-thoracic MRI confirmed the parathyroid localization by showing a paratrachial formation dte in front of the right antero-lateral face of the ascending aorta and bilateral pulmonary micro-nodules. Total serum Ca was variably controlled (9.1 mg/dL to 15 mg/dL) with pamidronate and then denosumab (60 mg). The surgery performed abroad confirmed that the mediastinal nodule was a metastasis of PC. Eventually, the hypercalcemia became resistant to denosumab (6 mo postop) and the patient died due to a hypercalcemic crisis (20 mg/dL).

Conclusion

This is a rare case of a small and very aggressive parathyroid carcinoma with lung metastasis at diagnosis although with no local invasion.

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EP181

Small and foudroyant parathyroid carcinoma with lung metastasis and no local invasion at diagnosis

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Aberrant epigenetic features occurring in parathyroid tumors involve DNA methylation, histone methylation, and non-coding RNAs. RASSF1A and APC were frequently downregulated in human cancers. Here, we investigated RASSF1A and APC methylation status in a series of parathyroid tumors from Italian patients with primary hyperparathyroidism (PAds, n = 80), confirming RASSF1A and APC promoter methylation as a hallmark of sporadic parathyroid adenomas. Moreover, we extended the analysis in parathyroid carcinomas (PCas, n = 9), which displayed RASSF1A promoter methylation, while APC promoter was methylated only in 2 samples. In PAds, RASSF1A promoter methylation levels positively correlated with the methylation levels of APC promoter, suggesting a common methylation process for both genes. We focused the attention on the oncosuppressor RASSF1A. Our results showed that RASSF1A transcripts were significantly reduced in PAds (n = 35) when compared with normal parathyroid glands (PanNs; n = 3), though RASSF1A mRNA levels and levels of RASSF1A promoter methylation did not correlate. At protein level, RASSF1A was detectable by immunohistochemistry in the cytoplasm of cells in PanNs (n = 3) and in the rim of Pan surrounding parathyroid adenomas, while cells in PAds (n = 11) showed weakly positive citoplastic staining. PCas (n = 6) were definitely negative both at cytoplasmic and nuclear levels. Furthermore, we investigated 2 potential epigenetic modifiers involved in RASSF1A promoter methylation: the methyltransferase DNMT1 and the antisense lncRNA RASSF1-ASI. DNMT1 methylates both RASSF1A and APC gene promoters. We found that DNMT activity, investigated in PAds nuclear extracts (n = 16), was inversely correlated with RASSF1A protein levels (r = -0.400, P = 0.009), supporting the involvement of deregulated DNMT activity in the aberrant RASSF1A promoter methylation. RASSF1-ASI (alias ANRASSF1) was implicated in a locus-specific mechanism for the RASSF1A epigenetic repression, mediated by Polycomb Repressive Complex 2 (PRC2), reinforcing RASSF1A long-term epigenetic silencing. In PAds, RASSF1A levels positively correlated with expression levels of RASSF1A (r = 0.788, P = 0.001). Similarly, RASSF1A promoter methylation negatively correlated with ANRASSF1 mRNA levels (r = -0.366, P = 0.031). These findings exclude ANRASSF1 in the methylation process of the RASSF1A promoter in PAds. Finally, using HEK293A cells transiently transfected with human CASR as experimental model (CASR-HEK293A), we investigated the effects of RASSF1A gene silencing on pERK/ERK levels stimulated by the CASR agonist R568. Efficient RASSF1A silencing increased basal pERK/ERK levels and blunted the pERK/ERK increase induced by CASR activation, suggesting that loss of RASSF1A may contribute to the parathyroid cell desensitization towards extracellular calcium concentrations observed in parathyroid tumors. In conclusion, RASSF1A and APC promoter methylation is a hallmark of parathyroid adenomas.

**Results**

153 subjects who meets the inclusion and exclusion criteria were recruited in to the study over a period of one year. The population mean age was 52.1 (s.d. ± 14.385) years and ranged from 18 to 89 years. Out of the whole population 58.8% had vitamin D deficiency while 31.4% suffered from vitamin D insufficiency. Only 9.8% had normal vitamin D levels. ALP level was significantly related to vitamin D deficiency (P < 0.05). At ALP cutoff value of 72.5 U/L the vitamin D deficiency could be predicted with 76% sensitivity and 80% specificity. ALP cutoff 43 U/L predicts vitamin D deficiency at a 100% sensitivity and 20% specificity.

**Conclusions**

The population screening for vitamin D deficiency is not a cost effective intervention. A more cheaper and feasible ALP assessment at a cutoff value of 72.5 U/L can predict vitamin D deficiency at a significantly higher specificity and sensitivity.

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### EP184

**The short test with active metabolites of vitamin D in differential diagnosis between primary normocalcemic and secondary hyperparathyroidism for inpatient treatment**

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**Objective**

Normocalcemic primary hyperparathyroidism (PHPT) is a phenotype of PHPT characterized by normal serum calcium and persistently increased parathyroid hormone (PTH) after exclusion of secondary causes of PTH elevation.

The aim of this study was to investigate the capability of the short test with active metabolites of vitamin D for differential diagnosis between normocalcemic PHPT and secondary hyperparathyroidism (SHPT) for inpatient treatment.

**Material and methods**

We included 90 hospitalized patients with normal albumin-adjusted calcium (Caadj.) and elevated PTH levels (84 women, 6 men, median age 60 years). Caadj, PTH, creatinine, eGFR, daily calciuria were evaluated before and PTH, Caadj., phosphate, eGFR, daily calcium were evaluated after taking 1 mcg of alfalcacidol or calcitriol. Data is presented by medians and interquartile ranges (Median, (25;75)).

**Results**

According to baseline and dynamic biochemical evaluation patients were divided into 3 groups: group 1 (n = 32) – patients with elevated or within the upper limit PTH (n = 4) who reached hypercalcemia (Caadj. > 2.55 mmol/l); group 2 (n = 14) – patients with normalization of PTH and normal Caadj. group 3 (n = 44) patients with elevated PTH and normal Caadj. In group 1, baseline Caadj. was 2.52 mmol/l (2.50; 2.54), PTH 101.1 pg/ml (81.9; 138.0), after short test – 2.61 mmol/l (2.58; 2.64), and 92.3 pg/ml (71.2; 119.5) respectively, regarded as PHPT. Among them 19 patients underwent surgery with histological confirmation of diagnosis, 2 patients are waiting for surgery, 11 patients with asymptomatic form are under dynamic observation. In group 2, baseline Caadj. was 2.34 mmol/l (2.31; 2.44), PTH 81.1 pg/ml (72.9; 95.7) vs 2.40 mmol/l (2.33; 2.51) and 54.53 pg/ml (40.7; 63.6) respectively after short test regarded as SHPT. Groups with PHPT and SHPT significantly differed from each other in Caadj. and daily calciuria (P < 0.05) but not in PTH, eGFR. 44 patients from group 3 did not show significant changes thus differential diagnosis was continued on an outpatient basis.

**Conclusion**

The study showed significant changes in calcium and PTH levels during the short test in 46/90 patients. Stable normocalcemia and normalization of PTH allows confirming SHPT while elevated or within the upper limit PTH levels with hypercalcemia – PHPT.

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### EP185

**Evaluation of response to alendronate treatment on osteoporosis using cathepsin K and other biomarkers**

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**Objective**

Osteoporosis is a disease characterized by low bone mass and microarchitecture deterioration leading to bone fragility and increased fracture risk.

**Background**

In the last years alendronate and other bisphosphonates have been used as a first line treatment in osteoporosis.

**Aim**

To evaluate the response to alendronate treatment on osteoporosis using cathepsin K and other biomarkers.

**Methods**

A retrospective study was conducted from March 2019 to March 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Analytive sampling was done recruiting all patients who have had vitamin D assessment as part of the routine medical care. Interviewer administered questionnaire was used collect data. Vitamin D sufficiency, insufficiency and deficiency was defined on levels of > 50 ng/ml, 20–50 ng/ml, < 20 ng/ml respectively. Pearson correlation analysis was used to determine the effects of vitamin D status on various blood parameters including serum total calcium, serum phosphate, ALP and PTH level. Receiver operating characteristic (ROC) curves were used to determine the optimal ALP level to predict vitamin D deficiency.

**Results**

The current study included 85 patients with osteoporosis (10 men, 75 women, median age 73 years). 50% of patients were postmenopausal. All patients were treated with 70 mg alendronate daily for 1.5 years. The mean percentage of bone mineral density change was 2.5% (range -12.1% to 19.4%). The mean percentage of vitamin D change was 15% (range 28% to 15%). The mean percentage of cathepsin K change was 6.3% (range -24% to 40%). At baseline and after 1.5 years the levels of vitamin D, cathepsin K, ALP, PTH were not significantly different.

**Conclusions**

Our study showed no significant changes in vitamin D, cathepsin K, ALP, PTH levels during the treatment with alendronate. The percentage change in bone mineral density was 2.5% which is consistent with previous studies. Further studies are needed to evaluate the long-term effects of alendronate treatment on osteoporosis.

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Background
Osteoporosis has been an excruciating disease for many years now. Although various treatments are available, there is an unmet need for disease prognosis, early disease diagnosis and prediction of treatment efficacy. New biomarkers are crucial for the diagnosis or prognosis of a disease as well as for monitoring treatment efficacy and improve decision making. Cathepsin K is a cysteine protease that cleaves collagen type I, the major type of collagen found in bone, so it is useful to measure to assess the function and number of osteoclasts. The aim of the current study was to evaluate the fluctuation of cathepsin K, phosphorus, 25 HO vitamin D, alkaline phosphatase and PTH before and after 6 and 12 months of treatment with alendronate.

Methods
We conducted a longitudinal study with a cohort of 28 female patients with osteoporosis and 15 healthy controls. All subjects were menopausal, non-diabetic, non-obese, without secondary osteoporosis. All patients were treated with alendronate and calcium and vitamin D supplements. Serum samples were collected longitudinally before treatment, at 6 and 12 months post treatment initiation and the levels of cathepsin K, phosphorus, 25 HO vitamin D, alkaline phosphatase and PTH were measured. Basal serum cathepsin K levels were also compared to premenopausal women without osteoporosis (n = 15).

Results
We observed that serum cathepsin K levels were higher in premenopausal women with osteoporosis (7747.33 RFU/ml) +/- 2713.23 compared with healthy premenopausal women (7747.33 +/- 762.67 RFU/ml; P < 0.01). Also, serum cathepsin K decreases gradually after alendronate treatment (5.09% at 6 months, and 7.17% at 12 months, P < 0.05). We also found a positive association of cathepsin K and phosphorus and alkaline phosphatase and a negative association with 25 HO vitamin D.

Conclusion
We conclude that serum cathepsin K may serve as an additional biomarker for bone metabolism and alendronate treatment monitoring besides phosphorus and alkaline phosphatase. The role of Cathepsin K as a risk biomarker marker in premenopausal women without osteoporosis is also discussed.

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EP187
A special case of type Ib pseudohypoparathyroidism
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Introduction
Pseudohypoparathyroidism type Ib are genetic diseases with transmission maternal. defined by a resistance to the action of the parathormone without resistance to the TSH. Clinical manifestations are variable and depend on the severity of hypocalcaemia. We report the case of a patient presenting with type Ib pseudohypoparathyroidism.

Observation
This is a 9-year-old child admitted for care and exploration of a severe hypocalcaemia. The patient has been followed for unlabeled laryngeal stridor since birth. We note childhood obesity. He has episodes of spasm repetitive pedal carpe with vomiting. The clinical examination demonstrates a moon faces with macroglossia. The phosphocalcic balance shows a severe hypocalcemia at 56 mg/l with elevated phosphoremia and hypocalciuria. The parathormone dosage was high (160.6 pg/ml) with normal TSH (1.27 uU/ml). Brain CT finds Fehr’s syndrome. X-ray of the hands finds a slight brachymetacarp of the fourth ray. The genetic study highlights evidence of pseudohypoparathyroidism in non-transmissible somatic mosaicism. The patient received vitamin-calcium supplementation with a good clinical and biological evolution.

Discussion
Pseudohypoparathyroidism is a pathology that is sometimes difficult to diagnose, generally evoked in front of any hypocalcaemia with hyperphosphatemia and PTH high. This observation underlines the interest of thinking about pseudohypoparathyroidism in children in front of spasms in order to allow an adapted treatment allowing avoiding the occurrence of severe hypocalcaemia threatening the vital prognosis and the impact on child growth.


EP188
Chronic bone pain revealing a parathyroid adenoma
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Introduction
Primary hyperparathyroidism is an endocrinopathy characterized by the excessive secretion of parathyroid hormone, most commonly associated with parathyroid adenoma. The ostearticular manifestations of hyperparathyroidism are currently exceptional. The diagnosis is most often established at the asymptomatic stage by measuring calcium levels and parathyroid hormone.

Observation
We report the case of a 67-year-old patient with a history of partially calcified right parietal meninges, and who consulted for diffuse mechanical bone pain. A phosphocalcic balance is carried out objectifying a hypercalcemia corrected to 117 mg/l with a normal phosphoremia at 29 mg/l, a normal vitamin D and a parathyroid hormone elevated to 115 g/l. A subtraction parathyroid scintigraphy with MiBi-99mTc/Pertechnetate revealed a right lower polar parathyroid adenoma measuring 5x4x6 mm, oval, regular, hypochoic and heterogeneous. Ablation of the parathyroid adenoma was performed in our patient with simple operative consequences and good progress.
Discussion and conclusion
Bone manifestations have become rare in hyperparathyroidism. They are characterized mainly by mechanical polyarthalgia, bone swelling or even pathological fractures. The positive diagnosis is based biologically on confirmed hypercalcemia with elevated PTH and morphologically on parathyroid scintigraphy at TC 99 m which allows visualization of the parathyroid adenoma. The treatment is surgical.

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EP198
Bilateral pathologic fracture of the femur in brown tumor Induced parathyroid carcinoma
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Introduction
Brown tumor refers to the skeletal change that develops as one of the complications of hyperparathyroidism, in which cystic and fibrous changes occur in the bone. It occurs in approximately 10–20% of patients with primary hyperparathyroidism. Parathyroid cancer is a rare cause of primary hyperparathyroidism and accounts for approximately 1% of cases. In some cases, hyperparathyroidism may be asymptomatic until it becomes a pathological fracture and may be the first sign of a malignant tumor. Here, we report a case of parathyroid carcinoma presenting with bilateral femoral fracture because of its rarity.

Case
A 56-year-old male patient presented with pain and limitation of movement in both thighs after falling in the bathroom. It was learned that he had difficulty in walking and pain in the legs for 6 months in his history, and he did not have an additional disease or medication. X rays showed the fractures in both femurs and left olecranon and findings consistent with multiple (bilateral femur, tibia, fibula and right radius and ulna) Brown tumors were found in the bones. Blood investigations showed raised levels of serum calcium, with highly raised levels of serum parathyroid hormone (PTH). After neck ultrasonography and parathyroid scintigraphy, an appearance compatible with parathyroid adenoma was found in the inferior of the right thyroid lobe, and parathyroidectomied was performed, but postoperative PTH elevations continued. Thereupon, the patient was evaluated with neck tomography and parathyroid scintigraphy for the second time, and he was reoperated when another focus was detected in the upper mediastinum at the level of the angulus venosus in the isthmus inferior of the thyroid gland. The operative pathology resulted as parathyroid carcinoma. The patient who developed postoperative hungry bone syndrome was operated for bilateral femoral fracture after calcium normalization was achieved.

Conclusion
The main treatment for parathyroid carcinoma is surgery. In the presence of fracture, it is recommended to perform parathyroidectomy first and then orthopedic treatment. In the presence of osteolytic lesion and high serum calcium in patients presenting with pathological fracture, Brown tumor related to parathyroid carcinoma should be kept in mind in the differential diagnosis.

Keywords
Hyperparathyroidism, brown tumor, femur, pathological fracture.

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EP199
Giant cells and a hungry bone: a diagnostic and therapeutic challenge. Rashmi Nanjundaswamy1,2, Sunil Navalagund1, Govindarajan Mallarajapatta1, Srimant Srimivas Bindiganavil1 & Hema Venkataraman1
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Introduction
Brown tumours (BT) are a recognised complication of severe prolonged untreated hyperparathyroidism (HPT). BT can mimic bone metastases and giant cell tumors (GCT). Hungry bone syndrome (HBS) is a severe and prolonged, postoperative hypocalcemia following parathyroidectomy. BT are a risk factor for HBS. We report the case of a young lady with BT masquerading as a GCT, from a tertiary centre in India.

Case study
A 25 year lady presented with pathological fractures of humerus, tibia and inability to weight bear. MRI in primary care, showed multiple hyperintense (T2 imaging) expansile lytic lesions over humerus,pelvis and femur with compression fracture of vertebræ. FNAC was suggestive of giant cell tumour. PET-CT confirmed hypermetabolic multifocal expansile bone lesions with fractures and osteoporotic vertebræ with no evidence of primary malignancy, raising a differential diagnosis of brown tumour. Biochemistry revealed elevated calcium (S.Ca 11.9 mg/dl, normal range (NR) 8.8–10.6), Alkaline phosphatase(304 IU/L,(NR 53–141)). Parathyroid hormone(PTH) was elevated: PTH 486 pg/ml (NR 10.0 – 65 pg/ml) with severe Vitamin D deficiency: 6.5 ng/ml(NR 30–100 ng/ml), low phosphorous 1.7 mg/dl(NR 2.5–4.5 mg/dl). A diagnosis of primary HPT with brown tumours was made. PET/CT, contrast enhanced CT and targeted ultrasound failed to localize a parathyroid adenoma. Sestamibi scan showed faint uptake at the right superior parathyroid. Preoperatively a loading dose of 300,000 units of Intramuscular and 200 units of oral cholecalciferol was given. Consent for targeted parathyroidectomy and possible full neck exploration was taken. Right superior parathyroid gland of 1.6 × 1.2 cm was excised, which was thin and flat (probably the reason for missing on CT/Ultrasound). Significant decrease in intraoperative PTH level (628.1–35.5 pg/ml) was observed. Intra-operative frozen section confirmed parathyroid adenoma. Post procedure she developed HBS (mean calcium 7.9 mg/dl) remaining asymptomatic. She required escalating dose of oral calcium upto 15 g of elemental calcium and 4 mg calcitriol with intermittent intravenous calcium and magnesium supplements. Proton pump inhibitors (PPI) were with-held. Post discharge calcium remained stable around 9 mg/dl with above dose of calcium and calcitriol. Pathological fractures are being managed conservatively.

Conclusion
BT is an important differential diagnosis for lytic expansile bone lesions with giant cell morphology on histology. BT often resolves with HPT treatment. Early diagnosis avoids complex surgical intervention.BT increases risk of post-operative HBS. Pre-operative loading of Vitamin D may have reduced duration and severity of HBS. However more evidence is needed to support this approach.

Correction of Hypomagnesemia and withholding PPI aids optimal absorption of oral calcium.

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EP191
Primary hyperparathyroidism in the setting of previous roux-en-Y gastric bypass: a case report
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Introduction
Primary hyperparathyroidism (PHPT) after roux-en-Y gastric bypass (RYGB) is poorly described. The diagnosis can be difficult as secondary hyperparathyroidism (SHPT) commonly occurs in patients after RYGB due to calcium hypoaosorption and vitamin D deficiency.

Observation
We present the case of a 50-year-old female with a history of normocalcemic hyperparathyroidism and nephrolithiasis. In 2005 the patient had undergone RYGB. During the first visit, an iso-hypoechoic nodule below the right inferior pole of the thyroid gland with a maximum size of 47 mm and internal vascularization was detected. Her biochemistry revealed a PTH of 930 pmol/l (NR 1–6.5 pmol/l). She was initially treated with 100 000 IU of Vitamin D3 intramuscularly once a month, but calcifediol, a hydroxylated form of vitamin D, was later prescribed due to the patient’s discomfort with the intramuscular injection. Further investigations demonstrated decreased bone density at the hip and distal radius and a single image suggestive for parathyroid adenoma detected by SestaMIBI scintigraphy. The patient underwent parathyroidectomy, and she was discharged with calcium carbonate and calcitriol therapy, but a few days later, she accessed our A&E for hypocalcemia. The hungry bone syndrome was excluded due to her normal phosphorus and magnesium. Histology confirmed a parathyroid adenoma with a maximum diameter of 5 cm. The patient was treated with a single 10% calcium gluconate vial, and subsequently, we preferred to start oral calcium. Osteoporosis was managed with alendronate. The patient was discharged with normal phosphorus and magnesium, but she was referred for treatment of vitamin D deficiency. She was later prescribed Calcitriol and 100 000 IU of Vitamin D once a week. Follow-up after 3 months showed normalization of PTH (65 pg/ml) with normalization of biochemical parameters and clinical improvement.

Discussion
Primary hyperparathyroidism (PHPT) post-RYGB is a rare complication. It is important to be aware of this rare presentation in order to make an early diagnosis and avoid complications. The main treatment for PHPT is surgical intervention. In selected cases, medical therapy may be sufficient. In our patient, the combined approach of surgery and medical therapy led to a successful outcome.
**Conclusion**

PHPT after RYGB is a rare condition, and concomitant SHPT can make diagnosis and follow-up difficult and predispose patients to more severe postoperative hypercalcemia.

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**EP192**

**Fahr Syndrome secondary to pseudohypoparathyroidism.**

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**Background**

Fahr’s Syndrome, also known as striatopallidodentate calcinosis is a rare form of neurological disorder characterized by abnormal calcified deposits in basal ganglia, cerebellar and cerebral cortex. Its prevalence goes from 2 to 12.5%. Etiology of this disorder is very wide and involves endocrinopathy, mitochondrial myopathies, dermatological abnormalities, infectious disease or may be idiopathic. We present a case of a patient with diffuse brain calcifications due to pseudohypoparathyroidism probably type 1b.

**Case description**

We present a case of a 37 years old man who presented in the Emergency Unit with epileptic generalized tonic-clonic seizure. He was known to suffer from epilepsy since 4 months of age but head CT was performed for the first time during this hospitalisation and diffuse bilateral brain calcifications were noticed. The patient has short stature with round face and brachydactyly of 4th metacarp. He also showed intellectual disability. Biochemical analysis showed hypercalcemia (6.1 mg/dl) with low-normal Vit D levels (29.8 ng/ml) and high PTH levels (152.1 ng/l). Hepatic and renal function were normal. Other electrolytes were also normal. Anterior hypophysis hormones were in their normal range. Because of hypocalcemia with high PTH levels and normal Vit D, magnesium levels and renal function, diagnosis of pseudohypoparathyroidism was made. Lack of other hormone resistances, and clinical appearance suggests pseudohypoparathyroidism type 1b. The patient was treated with IV calcium and Vit D3 firstly and then with calcitriol 0.25/daily. On follow up levels of serum ionized calcium and 24 calcium were improved.

**Conclusions**

Fahr’s Disease is a rare, neurological complication of chronic pseudohypoparathyroidism. In most cases the diagnosis is clinical-radiological with diffuse brain calcifications. It is suggested that PTH plays a protective role against calcifications in the brain. The mechanism is not fully explained but it is emphasized the importance of PTH receptor 2, found in brain cells and myocardium. After confirming pseudohypoparathyroidism, the patients should start treatment with cholecalciferol or ergocalciferol (firstly to fill the deposits) and calcium supplements. Because PTH is required for the renal conversion of calcidiol to calcitriol (active metabolite) calcitriol is often the treatment of choice.

**Key words**
calcium, PTH, hypoparathyroidism, pseudohypoparathyroidism, brain calcifications.

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**EP193**

**Late hypocalcaemia complicating the management of papillary thyroid carcinoma**

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**Introduction**

COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by an influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste.

**Severity**

It is highly variable, ranging from asymptomatic to severe or prolonged forms.

**We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.**

**Observation**

This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium. She received the first dose of astrazeneca in July 2021, after 4 h she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/l. As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 h and there was no recurrence.

**Discussion**

COVID-19 vaccines are as well tolerated in neuromuscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations. Campesium can be seen with COVID-19 vaccines, and is generally benign and transient. The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.

**Conclusion**

The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be monitored to avoid complications, particularly neuromuscular ones.

**References**


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**EP194**

**Vitamin D deficiency in the type 2 diabetic population of Northern Gran Canaria Island: Still highly prevalent but supplementation is on the rise.**

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**Introduction**

Vitamin D deficiency is associated with higher risk of severe COVID-19, and type 2 diabetic patients are a vulnerable group. We described an alarming rate of vitamin D deficiency (around 80.0%) with plasma calcifiedol <30 ng/ml in unsupplemented type 2 diabetes patients during the 2020 spring lockdown and the following winter in Northern Gran Canaria. There is an increasing awareness of this problem, both in family physicians and the general population, and the use of vitamin D supplements is rising.

**Objectives**

To assess the prevalence of vitamin D deficiency in type 2 diabetic patients from Northern Gran Canaria during the late autumn-early winter period (November 2021 to January 2022), and its relationship with vitamin D supplementation.

**Methods**

Plasma calcifiedol levels were sampled in an unsupplemented type 2 diabetic population, and recorded anonymously along with age, gender and vitamin D supplementation status. All included patients gave their informed consent.

**Results**

Data were obtained from 217 consecutive patients; only 2 (<1%) were excluded due to lack of consent.129 were female (59.4%), mean age was 58.6 ± 13.9 years. 138 (60.8%) were taking vitamin D supplements. Mean plasma calcifiedol was 35.7 ± 14.9 ng/ml; but it was lower than recommended (< 30 ng/ml) in 85 (39.2%) of the patients, deficient (< 20 ng/ml) in 35 (16.1%) and severely deficient (<12 ng/ml) in 8 (3.7%). In vitamin D supplemented patients, mean calcifiedol was 43.2 ± 11.6 ng/ml, with 20 patients (14.5%) <30 ng/ml, 6 (4.3%) <20 ng/ml, none < 12 ng/ml and 1 (0.7%) > 80 ng/ml. In unsupplemented patients, mean calcifiedol was 22.7 ± 9.3 ng/ml, with 65 (82.2%) < 30 ng/ml, 29 (36.7%) < 20 ng/ml and 8 (10.1%) <12 ng/ml. Plasma calcifiedol was significantly higher in supplemented patients (mean difference 20.5 ± 9.9 ng/ml, unpaired t-test, P < 0.0001) and the proportions of low, deficient and severely deficient patients were significantly lower (Fisher’s exact test, P < 0.0001, P < 0.0001 and P = 0.0002, respectively).

**Conclusions**

The prevalence of vitamin D deficiency during the late autumn-early winter months in our unsupplemented type 2 diabetic population remains extremely high. However, the use of supplements is increasing, about 60% of our patients at present (45% in our previous survey 1 year ago). In supplemented patients vitamin D status is satisfactory with 4% deficient, none severely deficient and < 1% above the recommended level.

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EP195
Management of denosumab discontinuation in a patient with osteonecrosis of the jaw and coexisting primary hyperparathyroidism
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Context
Patients with primary hyperparathyroidism (PHPT) may be treated with denosumab due to coexisting osteoporosis. Few studies have been conducted in this population.

Case presentation
An 84-year-old woman was seen in the outpatient clinic in March 2018 due to calcium levels at the upper limit of reference range (10.2 mg/dl) associated with elevated levels of PTH (112 pg/ml) and sufficient 25(OH)D (24 ng/ml) levels, findings consistent with mild PHPT. Her past medical history included: osteoporosis with vertebral fractures (T11 and T12 vertebral bodies) since 2009, hystero-annexectomy in 1973, quadrantectomy for breast carcinoma in 2009, bowel resection for adenocarcinoma in 2008, prior ischemic stroke, prior gastric ulcer treated with gastrectomy and current jejunum ulcer. The patient had been on Alendronate 70 mg weekly since 2008 and taking 1100 IU of vitamin D3, and furosemide 25 mg/day. Patient’s biochemistries were rechecked after three months: PTH was 61 pg/ml (12-88 pg/ml), serum Ca 11.3 mg/dl, serum phosphate 2.6 mg/dl, CTX 0.809 ng/ml. Due to age and comorbidities, the patient was not a good candidate for parathyroid surgery. Alendronate was stopped and denosumab 60 mg q6m was prescribed, the patient being evaluated every six months. In December 2020, a 2-cm area of active osteonecrosis appeared in the right mandibular region. Denosumab was promptly interrupted. To avoid potential rebound hypercalcemia the patient was immediately switched to cinacalcet at an initial dose of 30 mg per day, then increased at 60 mg per day after a few months, while checking serum calcium levels every 3 to 6 months, with safe control of serum calcium, PTH and overall symptoms.

Discussion
Denosumab is effective in improving BMD, lowering bone turnover and serum calcium in patients with PHPT, nonetheless, because of its mechanism of action, its discontinuation has been associated with rebound clinical fractures. Currently, limited data are available on the best management of patients discontinuing denosumab, although it is recommended to continue anti-osteoporotic treatment with oral or intravenous bisphosphonates. For our patient we could not consider these options due to coexisting active osteonecrosis. The patient had also two previous vertebral fractures. Hypercalcemia was managed with cinacalcet, and the patient has not sustained any fractures as of January 2022.

Conclusion
We suggest prompt cinacalcet use to manage potential rebound hypercalcemia following denosumab discontinuation in patients with PHPT, although these patients will remain at risk of rebound fractures.

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EP196
Impact of COVID-19 pandemic on waiting time from referral to definitive surgery in primary hyperparathyroidism: a large tertiary centre experience
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Background
The COVID-19 pandemic has resulted in widespread disruption to delivery of emergency and elective care in the last 2 years. Nevertheless, healthcare systems have quickly readapted to accelerate use of novel pathways for delivering clinical services. We reviewed the impact of COVID-19 pandemic on our time from community referral to definitive surgery in patients with Primary Hyperparathyroidism (PHPT).

Methods
We retrospectively reviewed the waiting times from General Practice (GP) referral to parathyroid surgery through our pathway which includes initial Endocrine review before referral for surgical review. Data was collected before COVID19 pandemic (2019) and compared with data during the pandemic (2020–2021). Results are reported as mean for continuous variables. The Mann Whitney U test was used for comparing continuous variables between groups. A P value of < 0.05 was considered statistically significant.

Results
28 patients were included in the pandemic cohort and 37 patients were in the pre-pandemic cohort. Time from GP referral to Endocrinology review was 60 days in the pandemic cohort (vs. 91 days in the pre-pandemic cohort, P = 0.03). Time from first Endocrinology review to referral for surgery was 26 days in the pandemic cohort, compared to 341 days in the pre-pandemic cohort (P < 0.01). There was no statistical difference in waiting times from surgical referral to surgical clinic review and hence to surgery between the pandemic and pre-pandemic cohort (54 days vs. 73 days and 181 days vs. 156 days, respectively). Overall, time from GP referral to definitive surgery was lower in the pandemic cohort at 314 days compared to 651 days in the pre-pandemic cohort (P < 0.01), with the most impact on this reduced waiting time being from GP referral to surgical referral by Endocrinology (84 days vs. 422 days, P < 0.01). There was no difference in our surgical pathway from time of referral for surgery to date of surgery in both cohorts (239 days vs. 229 days, P = 0.85).

Conclusion
Our waiting times from GP referral to definitive surgery in patients with PHPT are surprisingly lower during the COVID-19 pandemic when compared to pre-pandemic times. These improved waiting times can be attributed to innovative pathways and judicious use of resources by both the Endocrinology and Surgical teams in our tertiary centre.

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EP197
Correlation between vitamin D levels and severity of COVID 19 disease. Argentine Experience
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Objective
Vitamin D (VD) plays a role in immune response. Recent data shows that low levels of VD could worsen COVID-19 outcomes. This study aimed to establish an association between VD levels among COVID-19 patients with clinical outcomes and inflammatory markers.

Methods
Prospective multicentric cohort study. Consecutively recruit patients. Patients were grouped according admission status and level of VD [sufficient > 30 ng/ml (VDS), insufficient 20–30 ng/ml (VDI), deficient < 20 ng/ml (VDI)]. The variables evaluated were age, gender, oxygen mask requirement (O2), mechanical ventilation (MV), pre-existing comorbidities, inflammatory markers, severity of COVID-19 measured by News Score.

Results
365 patients were recruited (age 53 ± 16), 59% male, 88% from total were hospitalized, whose VD levels were significantly lower than ambulatories (19 ± 11 vs. 24.3 ± 14 ng/ml P < 0.006). The amount between groups was VDS (15%), VDI (27%), VDI (58%). VD levels correlated negatively with hospitalization days and evolution time (P < 0.0045). Severity of COVID-19 adjusted by comorbidities was linked to a lower VD status (P < 0.0001). Also an association with pronation requirement among patients with lower VD levels (P = 0.002) was observed. O2z risk was elevated among VDI (OR 2.9 95%CI 1.3–7) and VDI (OR 4.9 95%CI 1.4–6). Multiplying the odds in 2.6 and 3.7 in presence of 1 or more comorbidities with a higher need of ICU in VDD groups (OR 4.8 95%CI 1.2–20). multiplying the odds in 2.6 and 3.7 in presence of 1 or more comorbidities was linked to a lower VD status (P < 0.001). Also an association with pronation requirement among patients with lower VD levels (P = 0.002) was observed. O2z risk was elevated among VDI (OR 2.9 95%CI 1.3–7) and VDI (OR 4.9 95%CI 1.4–6). Multiplying the odds in 2.6 and 3.7 in presence of 1 or more comorbidities with a higher need of ICU in VDD groups (OR 4.8 95%CI 1.2–20). A negative relation between VD levels, basal ferritin and LDH was described (P = 0.018 and P = 0.045).

Conclusion
Among COVID-19 hospitalized VD level was significantly lower than ambulatory patients. There is an association between low VD with a worse course of disease needing more days of hospitalization, thus lengthening the time of sickness. VDI and VDD group had severe forms of COVID-19. VDD presented a higher risk for ICU attention. Further studies are needed to emphasize the importance of adequate levels of VD to improve COVID-19 outcomes.

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EP199
From chronic hypomagnesemia with secondary hypoparathyroidism to basal ganglia calcification
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As it is known, hypomagnesemia leads to decreased synthesis of Parathyroid hormone (PTH) and can cause PTH resistance. Chronic hypoparathyroidism itself may lead to basal ganglia calcification. We report a 58 years old male, who has suffered from convulsions for over 10 years, with a history of alcohol abuse (more than 25 units of alcohol/week). During this period there have been frequent aware convulsions, resembling to tetany, typical for hypocalcemia. Hypocalcemia and hypomagnesemia had been detected several times. Symptoms usually resolved by administration of Calcium and Magnesium. Patient used to stop taking supplements and continued alcohol abuse as soon as symptoms ameliorated. At the age of 58 patient had 3 tonic-clonic seizures with loss of consciousness, different from previous convulsions. The laboratory investigations showed severe hypocalcemia, hypomagnesemia, very low level of PTH and hyperphosphatemia (ionized Ca_0.60 mmol/l (1.15–1.29), Mg_0.56 mmol/l (0.66–1.07), PTH_2.5 pg/ml (15–65), Phos_1.54 mmol/l (0.81–1.45), 25(OH)D_24.0 ng/ml. Electromyelogram showed epileptiform activity (less common to hypocalcemia) and brain CT showed basal ganglia calcification, which may be manifestation of longstanding hypoparathyroidism. According to those findings, patient was diagnosed with structural generalized epilepsy. We believe it is a complication of longstanding hypomagnesemia with secondary hypoparathyroidism. Anticonvulsant (CBZ 200 mg TID) was added to prescription. Main cause of hypomagnesemia seems to be alcohol abuse, but other factors may also exist. Iv correction of hypocalcemia and hypomagnesemia was followed by oral Magnesium orotate (Mg_32.8 mg) two times a day, Calcium Carbonate (Ca_500 mg) three times a day, and Calcitriol 0.5 mcg/daily. Calcitriol was discontinued in several days after Calcium correction. On follow up visit (6–7 weeks later) elevation of PTH level was found, PTH 10.49 ng/l (12–50), Ca_1.12 mmol/l (1.12–1.32), Mg_1.66 mg/dl (1.6–2.6). No more seizures were noted. Non managed chronic hypomagnesemia with secondary longstanding hypoparathyroidism might lead to basal ganglia calcification, followed by development of epilepsy. In our case, it is not till clear, if hypomagnesemia is the only cause of hypoparathyroidism or not, because PTH level still stays below of reference range. However, it is clear, that administration of magnesium increased PTH secretion and decreased severity of hypoparathyroidism. We keep on observing.

Conclusion
Serum Magnesium level (as well as Calcium level) should be measured in all patients with seizures. Early diagnosis and management of hypomagnesemia with secondary hypoparathyroidism may prevent long-term irreversible neurologic complications.

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EP200
Management of hypocalcemia after thyroidectomy
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Introduction
Hypocalcemia is a well-known complication of total thyroidectomy. Usually, it’s a reversible and a transitory complication. However, it requires a regular check-up.

Objective
The aim of this study is to determine the epidemiological and the therapeutic characteristics of hypocalcemia after total thyroidectomy.

Methods
This is a retrospective study about 106 cases of total thyroidectomy that operated between the year of 2010 and 2019 in the ENT department in Kairouan.

Results
The average age was 44.11 [22–76 years] with a sex ratio of 0.1. The determination of serum calcium is done systematically at day 2 or 3 after surgery; earlier on if the hypocalcemia was symptomatic. The incidence usually occurs 3 days after surgery. Postoperative hypocalcemia was found in 36 patients (33.9%). Symptoms were found in 20 patients (55.5%): 18 of them presented with paresthesia of the extremities (90%). And the other 2 patients presented with tetany (10%). All patients presented with hypocalcemia were given calcium gluconate and vitamin D orally. The IV supplementation was only given in 22.2% of the symptomatic patients. The treatment took about 2 months on average. And only 6 patients developed definitive hypocalcemia. The multinodular goiter was the most found pathology in the cases of postoperative hypocalcemia (72%). In second place comes the Grave’s disease (16%). And in third place, cancer. In our study, 6 patients had total thyroidectomy with lymph node dissection. 4 of them, developed postoperative hypocalcemia.

Conclusion
Hypocalcemia is a frequent complication of total thyroidectomy, needing both, clinical and biological surveillance. Temporary oral supplementation usually does the trick.

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**EP201**

**Chronic asymptomatic hypocalcemia following thyroid surgery**

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**Introduction**

Postoperative hypoparathyroidism is a frequent complication of total thyroidectomy that must be detected and treated. The resulting hypocalcemia is quite severe and usually occurs within the first few days or weeks after surgery. Herein, we describe a case of chronic asymptomatic hypocalcemia related to postoperative hypoparathyroidism diagnosed years after total thyroidectomy.

**Observation**

We report the case of a 61-year-old woman who had a total thyroidectomy in 1997 for papillary carcinoma and was lost to follow up after surgery. She was referred to the endocrinology department (24 years later) to explore asymptomatic hypocalcemia (1.47 mmol/l) discovered incidentally in a biological check-up. She had no family or personal history of autoimmune disease. Physical examination showed no abnormalities but the electrocardiogram suggested prolongation of the QT interval. The patient was treated with i.v. infusion of calcium gluconate. Laboratory tests revealed, a controlling serum calcium: 1.65 mmol/l (55 mg/l), phosphate: 2.56 mmol/l (80 mg/l), PTH levels: 12 pg/ml. Further exploration showed long-term complications of hypoparathyroidism: a Fahr’s syndrome on the CT scan of the brain, dental anomalies, bilateral sub capsular cataract but no renal calculifications. The diagnosis of chronic hypocalcemia secondary to postoperative hypoparathyroidism was retained. She was put on calcium gluconate and alfalcacidol.

**Conclusion**

This case present a rare presentation of chronic asymptomatic hypocalcemia diagnosed 24 years after thyroid surgery and probably due to postoperative hypoparathyroidism.

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**EP202**

**Artificial intelligence technology for the early diagnosis of osteoporosis in cushing syndrome**

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In Cushing syndrome (CS), glucocorticoid-induced osteoporosis is suggested to be the main reason for drug-induced osteoporosis. This health condition creates weaknesses in bones which are then easily fractured.Studies estimate that osteoporosis is under diagnosed in the UK by around 50%, and according to the International Osteoporosis Foundation 2021, osteoporosis is a major healthcare burden in Europe with 4.3 million fragility fractures and healthcare costs more than 56 billion euros annually. Primary prevention rates are very low, and most patients only receive a Dual-Energy X-ray Absorptiometry (DEXA), scan following a first or second fracture. Osteoporosis is one of the most common comorbidities in CS patients. A recent Doctor of Philosophy (PhD) survey of CS members of a support group found 30 (42%) of the female members and 1 male member (6.6%), had been diagnosed with this condition. Only 12 of them initially had a DEXA scan to confirm their osteoporosis, and 23.8% reported that they had found an improvement in their condition after being prescribed medical therapy. However, the length of waiting time for a DEXA scan was between 8 months to 2 years. Over 70% of the women and 40% of the men in the survey reported bone pain, proximal muscle weakness, and mobility disabilities, and this had impacted on their social, personal, and working lives. The findings from recent clinical trials have shown that by using advanced physics modelling and Artificial Intelligence (AI), methods, accurate measure of bone mineral density from standard digital x-ray (DXR), images, example wrist and hip, can be achieved. This means for the first time, patients who undergo skeletal imaging can be opportunistically assessed for osteoporosis. Interestingly, in this PhD study, 55.3% n=24, of the other members including males, were referred for skeletal x-ray examinations mainly due to fractures which occurred following their CS diagnosis. AI technology could revolutionize the way in which the early onset of osteoporosis is identified and subsequently lead to earlier treatment and improved quality of life. Additional benefits being a reduction in the socioeconomic cost of long-term treatment for unnecessary radiation doses to patients. The recommendation from the PhD study being, that more research using AI technology is required and could become an integral part of the diagnostic workup for endocrine patients, thus avoiding the wait for a DEXA scan, as DXR equipment is more readily available.

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**EP203**

**A comparison of bone densitometry and mineral disorders in hemodialysis patients due to diabetes and non diabetics patients**

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**Introduction**

The chronic kidney disease (CKD) is associated to various bone and mineral disorders. Many studies showed that diabetes influence the bone and mineral metabolism.

**Methods**

This is a cross sectional study conducted in nephrology department of Taher Sfar university hospital in mahdia, Tunisia. The study involved 61 patients with chronic hemodialysis. They were invited to participate and were included after signing informed consent until the calculated sample size was reached. Patients were asked to undergo a hip and lumbar (L2-L4) densitometry by DXA to measure bone mineral density (BMD).

**Results**

The studied group of 61 patients was 26 females (42.6%) and 35 males (57.4%), there mean age was 53.9 [17-83] years, with mean dialysis duration 6.1 years. The mean onset age of hemodialysis therapy was 44.7 +/- 15.4 years. It was diabetic nephropathy in 25 cases (41%) vascular nephropathy in 15 cases and tubulointerstitial nephropathy in 21 cases (34.4). 23 patients (37.7%) had osteoporosis using the WHO criteria (T-score < -2.5), 26 patients (42.6%) had osteopenia and 12 patients had normal BMD. The mean bone mineral density of lumbar in diabetic patients and non-diabetics patients -1.72 vs -1.43 (P<0.005).

The mean bone mineral density of the hip in diabetics patients and non-diabetics patients -1.83 vs -1.21 (P<0.005).

**Conclusion**

Our study showed that chronic kidney disease has an important impact on bone and mineral metabolism. Second our study showed that diabetes can worsen patient bone mineral density.

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**EP204**

**Artificial intelligence technology for the early diagnosis of osteoporosis in cushing syndrome**

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In Cushing syndrome (CS), glucocorticoid-induced osteoporosis is suggested to be the main reason for drug-induced osteoporosis. This health condition creates weaknesses in bones which are then easily fractured. Studies estimate that osteoporosis is under diagnosed in the UK by around 50%, and according to the International Osteoporosis Foundation 2021, osteoporosis is a major healthcare burden in Europe with 4.3 million fragility fractures and healthcare costs more than 56 billion euros annually. Primary prevention rates are very low, and most patients only receive a Dual-Energy X-ray Absorptiometry (DEXA), scan following a first or second fracture. Osteoporosis is one of the most common comorbidities in CS patients. A recent Doctor of Philosophy (PhD) survey of CS members of a support group found 30 (42%) of the female members and 1 male member (6.6%), had been diagnosed with this condition. Only 12 of them initially had a DEXA scan to confirm their osteoporosis, and 23.8% reported that they had found an improvement in their condition after being prescribed medical therapy. However, the length of waiting time for a DEXA scan was between 8 months to 2 years. Over 70% of the women and 40% of the men in the survey reported bone pain, proximal muscle weakness, and mobility disabilities, and this had impacted on their social, personal, and working lives. The findings from recent clinical trials have shown that by using advanced physics modelling and Artificial Intelligence (AI), methods, accurate measure of bone mineral density from standard digital x-ray (DXR), images, example wrist and hip, can be achieved. This means for the first time, patients who undergo skeletal imaging can be opportunistically assessed for osteoporosis. Interestingly, in this PhD study, 55.3% n=24, of the other members including males, were referred for skeletal x-ray examinations mainly due to fractures which occurred following their CS diagnosis. AI technology could revolutionize the way in which the early onset of osteoporosis is identified and subsequently lead to earlier treatment and improved quality of life. Additional benefits being a reduction in the socioeconomic cost of long-term treatment for unnecessary radiation doses to patients. The recommendation from the PhD study being, that more research using AI technology is required and could become an integral part of the diagnostic workup for endocrine patients, thus avoiding the wait for a DEXA scan, as DXR equipment is more readily available.

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**EP205**

**Regional Migratory Osteoporosis- An under-diagnosed entity**

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**Introduction**

Regional Migratory Osteoporosis (RMO) is a rare condition, characterised by a self-limiting migratory arthralgia, which generally tends to involve the lower limbs. The arthralgia is usually, not associated with any history of trauma. Radiologically, Magnetic Resonance Imaging (MRI) is the investigation of choice. Bone Marrow Oedema (BMO) with subchondral sparing are the usual findings in patients with RMO. This condition is usually under diagnosed due to the complexity and lack of classical features.

**Case details**

We report the case of a 59-year-old gentleman, who presented to his General Practitioner (GP) with traumatic Right second toe pain, accompanied by significant deterioration in Quality-of-life (QOL). On X-Ray, there was no evidence of acute fractures. The symptoms at the time, were managed with analgesia and strapping. Subsequently, a year later, he incurred symptoms of pain and stiffness in the Right third and fourth toes, which was not preceded by a history of trauma. On this occasion, there was involvement of the Right hip as well. In total, at this point his QOL was severely impacted over the course of the last 18 months. He was then referred to the Tertiary sports and exercise specialist, for expert input. An MRI scan detected bone and soft tissue oedema centred on the second and third metatarsal heads involving the surrounding muscles.

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subcutaneous tissues and proximal and perhaps the middle phalanges. Mild plantar bone marrow oedema seen of the fourth metatarsal head. The appearances were highly suggestive of RMO, which instigated a referral to Metabolic bone services. A battery of investigations showed normal renal functions, Adjusted Calcium levels, Thyroid status and Vitamin D levels. Extended screening for Coeliac disease, Testosterone deficiency, Multiple Myeloma and Hyperparathyroidism were normal.

Management

A discussion in the Metabolic Bone Multi-Disciplinary setting advised repeat MRI and treatment with Bisphosphonates. The repeat MRI confirmed appearances in keeping with Transient BMO syndrome. Treatment with Intravenous Zoledronate alleviated his symptoms significantly and shortened recovery time, with Improvement in QOL.

Discussion

Till this date, the aetiology of RMO remains unclear. The key to diagnosis lies in a thorough clinical history supplemented by radiological findings. The radiology of RMO resembles Transient Osteoporosis of the Hip (TOH) and thus, the history of migratory arthralgia is key in distinguishing between both entities. Treatment options generally involve repletion of Vitamin D and Calcium levels, where appropriate. Bisphosphonates have been shown to improve symptoms and shorten recovery time.

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EP206
Osteoporosis in patients with Addison’s disease: Incidence and predictive factors


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Introduction

Because of a long-term glucocorticoid replacement over many years, patients with Addison disease may have an increased occurrence of osteoporosis. Furthermore, the prevalence of osteoporosis in patients with Addison disease may also be increased because of premature menopause associated autoimmune endocrinopathies and hypovitaminosis D. The objective of this study is to assess the incidence and risk factors for osteoporosis among patients with Addison disease.

Patients and methods

A cross-sectional study including 50 patients with Addison disease who had been receiving glucocorticoid replacement therapy for at least 5 years. Bone mineral density of the lumbar spine and both femoral necks were measured on osteodensitometry. The incidence of osteoporosis and its potential predictive factors were analyzed.

Results

Our study included 40 females and 10 males with a mean age of 49.5 ± 13.9 years (18-78 years). Average age at diagnosis was 35.5 ± 14.6 years (0-70 years). All patients were on hydrocortisone replacement, taking mean daily dose of 27.4 ± 6.7 mg (15-42.1 mg) corresponding to 0.388 ± 0.128 mg/kg. Mean cumulative hydrocortisone dose was 374.636 ± 283.821 mg (60 – 1184, 94 mg). No patient received antiresorptive therapy (oestrogen substitution therapy, bisphosphonates).

Low bone mineral density was observed in 24 (48%) patients, 12 (24%) of whom had osteoporosis. No osteoporotic fracture was observed. Patients who developed osteoporosis were significantly older than those with normal bone mineral density were (P = 0.018). Menopause was a significant predictor of incident osteoporosis (P = 0.006). Furthermore, osteoporosis was significantly more prevalent among females (P = 0.046). No statistically significant association was found between osteoporosis and disease duration neither the body mass index. Daily and cumulative hydrocortisone dose were higher in patients with osteoporosis than those with normal osteodensitometry (26.5 ± 8.3 mg/day vs 25.6 ± 6.3 mg/day; 462.2 ± 373.2 mg vs 344.6 ± 245.5 mg) but without statistical significance.

Conclusion

Identification of predictive factors of osteoporosis in patients with Addison disease is useful in the management of long-term glucocorticoid therapy’s bone impact. Then, further studies are needed to better analyze these factors and control bone mineral density during the course of Addison disease.

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EP207
rPTh(1-84) treatment-induced increased bone turnover in a young woman with post-surgical hypoparathyroidism

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Introduction

rPTh(1-84) replacement is the treatment of choice in adults with hypoparathyroidism not adequately controlled on standard therapy. Although increased bone turnover markers have consistently been reported in trials of safety and efficacy, marked elevations coupled with significant symptoms have been rare. We describe a case of increased treatment-induced bone turnover, necessitating significant therapeutic adjustments and monitoring.

Case report

A 26-year-old female suffered with severe hypoparathyroidism for 10 years, following total thyroidectomy and incidental parathyryectomy (three glands) for papillary thyroid cancer (PT1NO). Laboratory values on calcium carbonate 4g daily, alfacalcidol 3 mg daily, magnesium aspartate 60 mg bid and thymoxine 137 mg/d were as follows: TSH 0.33 IU/ml (0.27-4.7), thyroglobulin <0.1 ng/ml (<1), anti-TG negative, corrected calcium 0.5 mg/dl (8.4-10.1), phosphate 6.6 mg/dl (2.7-4.5), Mg 1.61 mg/dl (1.6-2.6), Cr 0.7 mg/dl, ALP 55 IU/l (23-104), PTH 5.1 pg/ml (15-65), 25(OH)D 34.9 ng/ml (20-50), 1,25(OH)2D3 29 pg/ml (18-80). Kidney ultrasound revealed nephrocalcinosis bilaterally and 24-h urine calcium was 539.7 mg/24h (<250 mg/24h). Following referral, rPTh(1-84) 50 mg daily was started and titrated to 100 mg daily within 6 months. The patient discontinued alfacalcidol and remained on 500 mg calcium carbonate and 1000U cholecalciferol daily, with excellent response. Within a week on 100 mg/d the patient reported severe bone pain in the knee joints and back, paralleled with successive increase in serum ALP at 160 IU/l, 231 IU/l and 611 IU/l (range 23 – 104 IU/l) and bone markers: CTx 1.50ng/ml (0.04-0.6ng/ml), PINP 623 ng/ml (15-60 ng/ml) and osteocalcin 157 mg/l (5.4-59.1ng/ml). Liver function tests and liver ultrasound were normal. rPTh(1-84) was reduced to 50 mg daily with gradual improvement in bone pain, but with immediate relapse of hyperparathyroid symptoms and worsened biochemical control. ALP levels normalized within 10 weeks to the upper normal range [113 IU/l (46-116 IU/l)]. Subsequently the dose was up titrated to 75 mg/d together with calcium carbonate 500 mg bid, magnesium 60 mg bid and alfacalcidol 1 mg/d. She has remained stable clinically and biochemically for the past 6 months. ALP values increased again but are maintained within 10% ULN.

Conclusions

Elevation of bone turnover markers are anticipated by rPTh(1-84) mechanism of action. However, they remain within normal range in the long term. The etiology for marked symptomatic increase in bone turnover in a minority of patients affecting treatment tolerability is unknown.

References


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EP208
Patient with mediastinal mass and hypercalcaemia

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Introduction

Hypercalcaemia is mostly caused by primary hyperparathyroidism and malignancy. Parathyromatosis is a rare condition characterized by multiple nodules of hyperfunctioning parathyroid tissue scattered throughout the neck and superior mediastinum, which can present a diagnostic and therapeutic challenge.

Case report

A 56-year-old woman visited the ER due to chest pain, left-sided neck edema, and hemoptema. The day before, she experienced left-sided neck pain and dysphagia. Her other complaints were recent weight loss and fatigue. Due to chest pain and high D-dimer level, CT pulmonary angiography was ordered, which showed a large heterogeneous soft tissue formation extending from the left side of the neck over the upper thoracic aperture and over the posterior mediastinum to just above the over the upper thoracic aperture and over the posterior mediastinum to just above.
the esophageal hiatus. The patient was admitted to Respiratory Medicine, where hypercalcemia (serum calcium 3.18 mmol/l; ref. 2.1-2.6 mmol/l) was found. At first, it was thought to be paraneoplastic, and an ultrasound-guided fine-needle aspiration biopsy of the mediastinal formation was performed, which was not diagnostic. FDG PET/CT two weeks after admission revealed a significant shrinkage of the mediastinal formation that showed low metabolic activity. Nothing abnormal was detected elsewhere. Finally, the patient was diagnosed with parathyroid hormone-dependent hypercalcemia (PTH 225 ng/l; ref. 10-65 ng/l), and transferred to Endocrine surgery for further diagnostic workup revealing a rare case of parathyromatosis at the lower part of the left thyroid lobe and around the esophagus extending caudally to Th3 level. Surgery revealed extensive parathyromatosis at the lower part of the left thyroid lobe and in the neck adipose tissue. Histopathology confirmed extensive parathyromatosis.

A surgical cure was not possible, and the patient continued treatment of persistent primary hyperparathyroidism with a calcimimetic. Cholecalciferol supplementation and zoledronate were given for osteoporosis.

Conclusion
We present a patient with mediastinal mass and hypercalcemia, which was first thought to be paraneoplastic. Further diagnostic workup revealed a rare case of spontaneous rupture and hemorrhage of a parathyroid adenoma with subsequent metabolically active process around the esophagus extending caudally to Th3 level was also present. Surgery revealed extensive parathyromatosis at the lower part of the left thyroid lobe and in the neck adipose tissue. Histopathology confirmed extensive parathyromatosis. A surgical cure was not possible, and the patient continued treatment of persistent primary hyperparathyroidism with a calcimimetic. Cholecalciferol supplementation and zoledronate were given for osteoporosis.

Complications of a rare condition, untreated due to difficult living conditions
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Introduction
Pseudohypoparathyroidism is a rare disorder characterized by end-organ resistance to parathyroid hormone, caused by molecular defects of the PTH receptor. Resulting chronic hypocalcemia and hyperphosphatemia require lifelong treatment with active vitamin D metabolites and monitoring, representing a challenge especially in difficult living conditions.

Case report
A 19-year-old woman presented to our clinic with carpopedal spasms and tachyary. Living in Switzerland since 5 years as a refugee from Eritrea, she reported having been treated with “pills” because of an undefined condition diagnosed in her early infancy. Her treatment was inevitably stopped when fleeing her native country during her pregnancy. Unfortunately, her current treatment with “pills” was stopped, and she was left untreated. The condition has high mortality and requires immediate treatment.

Case presentation
A 70-year-old woman presented in September 2021 with severe abdominal pain and confusion. She was diagnosed with acute pancreatitis precipitated by hypercalcemia. Her past medical history of hypertension, gastroesophageal reflux disease. Her regular medications are Atorvastatin and Ramipril. Her husband stated that she has been taken in several days to the dermatology clinic and was given Deflataine tablets “like sweets” for at least 2 years as an antiseptic (Deflataine or Remise tablets contain calcium carbonate and magnesium carbonate). On admission, she was found to have had very high serum adjusted calcium at 4 mmol/l (2.20 – 2.60), acute kidney injury with EGFR of 15 (her base line EGFR prior to admission was 45) and significantly high lipase and amylase. Her electrolyte investigations showed hypocalcemia of 1.59 mmol/l, serum albumin-corrected calcium 1.35 mmol/l [reference range 2.15-2.35], with an elevated parathyroid hormone (PTH) of 389 pg/ml [reference range 15-65], accompanied by hyperphosphatemia of 1.94 mmol/l [reference range 0.87-1.45] and vitamin D deficiency (25-OH vitamin D3 17 nmol/l [< 50]). Renal function, magnesium- and TSH-levels were normal. Hypercalcuria was absent. Brain MRI revealed severe calcification of basal ganglia. Molecular genetic analysis showed reduced methylation at the GNAS gene locus, which, in combination with the unremarkable clinical phenotype, pointed to pseudohypoparathyroidism type 1 B. Treatment with calcium carbonate, cholecalciferol and calcitriol was started and symptoms resolved with correction of serum calcium.

Comment and conclusion
Pseudohypoparathyroidism type 1 B is defined by predominantly renal resistance to parathyroid hormone, resulting in hypocalcemia and hyperphosphatemia with elevation of PTH caused by molecular defects (sporadic or inherited) at the GNAS locus of PTH receptor, a G-protein-coupled receptor (Gsa). As various endocrine receptors depend on stimulatory G-protein-coupled transduction, other hormonal resistance (TSH, gonadotropins, GH/IGF) can result, typically found in different subtypes in the heterogeneous group of pseudohypoparathyroidism disorders. The hormone resistance syndromes, in combination with specific somatic features (round facies, heterotrophic subcutaneous ossifications, brachydactyly) and development abnormalities, were first described by F. Albright in 1942, therefore known as Albright hereditary osteodystrophy. Although a rare disease (estimated prevalence: 0.79/100 000), pseudohypoparathyroidism must be suspected in asymptomatic hypercalcemia with elevated PTH. Our case report highlights the importance of correct diagnosis, medical treatment and patient information to avoid potentially fatal consequences. Unfortunately, this was delayed for several years in our patient due to difficult living conditions as a refugee and asylum seeker.

Acute confusional state as presenting feature in severe para-neoplastic hypercalcaemia
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Background
Hypercalcaemia is a common clinical problem. Severe hypercalcaemia or hypercalcaemia crisis is an endocrine emergency and can be life threatening if left untreated. The condition has high mortality and requires immediate therapeutic interventions and diagnostics. A rapid rise to the calcium levels can result in the impaired function of organ systems including central nervous system. Hypercalcaemia is mainly (more than 90%) caused by primary hyperparathyroidism or malignant conditions.

Clinical case
A 63-year-old man with background history of alcohol abuse presented to our institution with acute confusional state. Collateral history revealed that he was wandering in the streets. He was found pleasantly confused and disoriented by local police who brought him to the hospital. His physical examination revealed a Glasgow coma scale (GCS) score of 13/15 with no obvious localizing signs or symptoms.
neurological deficit. Initial investigations showed alcohol levels of less than 10 mg/dl, negative toxicity screen, unremarkable CT brain with normal blood glucose and serum amylase levels. He had decreased urinary output of 15-20 ml/hr with normal renal function but raised calcium levels of 3.72 mmol/l (2.20-2.60) and low phosphate levels of 0.77 mmol/l (0.85-1.5). He was treated as hypercalcemic crisis with intravenous fluids and given intravenous bisphosphonate (zolendronic acid 4 mg) in critical care unit. His calcium levels started decreasing with the treatment and his conscious level significantly improved. The diagnostics included low PTH levels with value of 6.7 pg/ml (15-65) and CT of thorax, abdomen and pelvis which revealed a left renal lesion of 15 x 12 cm² infiltrating into anterior and posterior perinephric soft tissue. He was referred to urology department for further investigations. Histopathology of renal biopsy specimen showed renal cell carcinoma and graded as advanced renal cancer (Stage IIIa). Unfortunately, due to his baseline status and compliance issues he was not deemed a candidate for surgery or systemic therapy and advised consideration for palliative approach.

Conclusion

The case illustrates the need to carefully review the differentials of hypercalcemia and consider immediate treatment interventions in situations of severe hypercalcemia or hypercalcemic crisis. Renal cell carcinoma should be considered as possible causative in hypercalcemia of unknown underlying pathology.

Key words: hypercalcemia, hyperparathyroidism, cancer

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EP212

A rare case of Pseudohypoparathyroidism
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Background

Pseudohypoparathyroidism includes a genotypically diverse group of syndromes of primary resistance to hormones whose actions are mediated by cyclic adenosine 3': 5'-monophosphate, in most cases caused by mutations and/or epigenetic changes at the complex GNAS locus on chromosome 20q13.3. Renal resistance to PTH leads to impaired formation of 1,25(OH)2D3, the fully active form of vitamin D, and reduces expression of sodium-dependent phosphate transporters in the renal tubules, leading to hypocalcemia and hyperphosphatemia, with elevated serum PTH levels. Patients with PTHT clinically manifest with tetany seizures, soft tissue calcifications and many congenital malformations. Early diagnosis and vitamin D3 or calcium treatment seem to be the most important for patient's condition.

Case

We describe a case of possible sporadic pseudohypoparathyroidism type II confirmed hashimoto thyroiditis, iron deficiency anemia, chronic erosive gastritis. 28 year old Caucasian female visited our clinic with complaints of frequent hospitalizations due to seizures and tetany since December 11, 2021. Patient was hospitalized at least 4 times and required Ca infusions. Patient complained of mild, intermittent and self-limited paresthesias, persistent asthenia, tachycardia, arthralgia since early years. She had been diagnosed at the age of 6 with hypocalcemia and possible pseudohypoparathyroidism, but diagnosis was not verified by genetic test. Initial lab investigation showed elevated PTH: 334.3 (15-65) pg/ml, hypocalcemia (iCa-0.73 (1.15-1.29) mmol/l), hyperphosphatemia (P-2.03 (N0.81-1.45) mmol/l), hypocalciuria (<0.2 mmol/l (N2.5-7.5), decreased bone mineral density on Dena Scan, T score L2=-2.4. Combined calcium and calcitriol supplementation was commenced, with symptomatic and laboratory improvement. Couple days after initiating Ca supplements and calcitriol, we achieved laboratory and clinical improvement (Ca-1.93 (2.15-2.5) mmol/l, P-1.85 (0.81-1.45) mmol/l (18.01.2022), Mg-0.65 mmol/l (0.6-1.07)). Moleculare identification is ordered and will be presented.

Conclusion

With initiated treatment, we hope for complete resolution of patient’s complaints and attaining symptomatic remission. A careful follow-up is needed to avoid complications and recurrence. Once correction of hypocalcemia and hyperphosphatemia is achieved, with no reported complications and recurrence, a good prognosis is anticipated, comparable to the general population.

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BMD. A significant higher incidence of reduced BMD was observed among menopausal women \( (P=0.049) \). Moreover, a higher mean PTH level was found in patients with decreased BMD but without statistically significant difference \( (56.2 \pm 21.8 \text{ pg/ml vs 48.1} \pm 25.4 \text{ pg/ml}, P=0.1) \). A lower mean vitamin D level was also found among those patients \( (19 \pm 10.2 \text{ ng/ml vs 25.2} \pm 16 \text{ ng/ml}) \). Cumulative hydrocortisone dose was higher among patients with reduced BMD compared to those with normal BMD, without statistical significance \( (408.9 \pm 324 \text{ mg vs 338.9} \pm 236 \text{ mg}, P=0.7) \). No significant correlation was identified between decreased BMD and duration of glucocorticoid substitution.

Conclusion
Bone loss is frequent in patients with Addison disease taking long-term glucocorticoid therapy and related to many factors affecting bone remodeling such as hydrocortisone dose and vitamin D deficiency. It seems imperative to ensure long-term follow-up of changes in BMD in patients with Addison disease.

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**EP251**

**Pregnancy and lactation-associated osteoporosis**

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Introduction
Pregnancy and lactation-associated osteoporosis (PLO) is a rare condition in which women have fragile fractures associated with significant reduction of BMD during pregnancy or postpartum period.

Case report
A 37-year-old female patient was admitted at our Clinic for further investigation of aetiology of osteoporosis in July 2019. Soon after delivery in February 2019 patient had felt left hip and foot pain as well as sharp intensive pain (intensity 9/10) in thoracic spine with propagation anteriorly into intercostal spaces. Pain was increased during body position changes, and was alleviated with ibuprofen intake. She also complained on morning stiffness. MRI of thoracic spine was performed in June and it showed irregularly decreased height of thoracic vertebrae 7 and 8, which seemed as compressive fractures. Osteodensitmetry showed osteoporosis with total T-score of spine -2.8 (L3 -3.1), Z-score -2.6(L3 -3.0) and osteopenia of the hip with T-score of neck of the femur -1.1. Z-score -1.1. Trabecular bone score indicated preserved microarchitecture of bones. On admission she complained of malaise, cold hands and feet, tingling in legs and dry mouth with occasional problem swallowing solids and liquids. First menstrual period after the delivery was in July and it is also when she stopped breastfeeding. In the previous years she had a spontaneous miscarriage and 3 tries of embryo transfer. Only in the first attempt she became pregnant. She wanted to give birth to another child. The median values of the T-score in the FN on the right before and after 12 months of using denosumab were, respectively: “-”2,5/“-”2.1/“-”1.85 \( (P=0.0001) \). On a first check-up 6 months later, X-ray of thoracic spine was performed and it showed new pathological fractures of thoracic vertebrae 9 and 11 so she received 2nd dose of zoledronic acid. Third dose was applied in December 2021. Next osteodensit_retry was scheduled for March 2022.

Conclusion
PLO is a rare condition and it should be considered as differential diagnosis in patients with back pain during or after pregnancy.

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**EP252**

**Results of denosumab used in postmenopausal women**

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The aim of the study was to assess the effectiveness of postmenopausal osteoporosis (PMOP) therapy with denosumab. Patients and methods 32 postmenopausal women with established PMOP for a period of 24 months or more received denosumab 60 mg subcutaneously once every 6 months combined with calcium and vitamin D. A quantitative assessment of bone mineral density (BMD) was carried out before treatment, after 12 and 24 months of observation, using dual-energy X-ray absorptiometry of the lumbar spine (L1 – IV) and femoral neck (FN) on the right and left. Changes in the severity of pain were assessed using a visual analog scale (VAS), the severity of the pain syndrome was assessed before treatment, after 12 and 24 months of observation. Statistical processing was carried out using the SPSS 23.0 software package.

Results and Discussion
The average age of women included into the study was 61.76 (59.35; 68.47) years. The average age at the onset of menopause was 47.52 (43.15; 49.83) years. The average duration of menopause at the time of the study was 12.64 (10.10; 21.62) years. The median values of the T-score in L1-IV before, after 12 and 24 months of treatment were, respectively: \(-2.5/=-2.1/=-1.85 \) \( (P<0.0001) \). The median values of the T-score in the FN on the right before and after 12 months of treatment were \(-1.9/=-1.1 \) \( (P=0.07) \); The median values of the T-score in the FN on the left before and after 12 months of treatment were \(-1.9/=-1.1 \) \( (P=0.04) \). The median values of the T-score in the FN on the right and left before and after 24 months of treatment were \(-1.9/=-1.1 \) \( (P=0.01) \). The median values of the T-score in the FN on the left before and after 24 months of treatment were \(-1.9/=-1.4 \) \( (P=0.01) \). The median values of pain severity according to VAS before, after 12 and 24 months of treatment were 5.5/4/2 points, respectively \( (P<0.0001) \). After 24 months of using denosumab, the mineralization indices of all the studied localizations significantly improved in comparison with the initial data.
Conclusions
Therapy with denosumab 60 mg subcutaneously 2 times a year with an interval of 6 months for 24 months in combination with calcium and vitamin D made it possible to significantly increase the BMD of the lumbar spine and significantly reduce the severity of pain syndrome according to VAS.

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EP219
Is obesity detrimental to postmenopausal bone health?

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Introduction
Despite available evidence for a relationship between bone health and obesity, the results of clinical trials remain conflicting. Thus, we conducted a cross-sectional study to analyze possible associations between waist circumference (WC), body mass index (BMI) and body weight (BW) with bone health in postmenopausal women.

Materials and Methods
The study included 84 women from Northeastern Bulgaria. Their mean age was 60.54 ± 7.07 years, and their mean duration of menopause was 11.45 ± 6.62 years. Bone health was assessed by dual-energy X-ray absorptiometry (DEXA), analysis of bone metabolic markers and fracture risk calculation.

Results
According to BMI 31% of the subjects were with normal weight, 50% were overweight and 20% were obese. In 82% of the women WC was over 80 cm. Significant positive correlations of bone mineral density (BMD) with WC (L1-L4 r = 0.264; P = 0.015, Femoral Neck r = 0.338; P = 0.002, Total Neck r = 0.393; P < 0.001), BMI (L1-L4 r = 0.295; P = 0.006, Femoral Neck r = 0.223; P = 0.042, Total Neck r = 0.330; P = 0.002) and BW (L1-L4 r = 0.446; P = 0.001, Femoral Neck r = 0.409; P = 0.001, Total Neck r = 0.457; P = 0.001) were found. However, after BW adjustment the correlations of BMD with WC and BMI became insignificant. Moreover, a negative association was found between Femoral Neck BMD and BMI after BW adjustment (r = -0.260; P = 0.018). On the other hand, the positive relationship between BMD and BW remained significant after WC and BMI adjustment. In addition, WC was inversely related to osteocalcin (r = -0.217; P = 0.046) and Beta Cross.Laps (r = -0.226; P = 0.039). Nevertheless, a positive relationship was found between WC and pyritrils D/creatinuria ratio (r = 0.277; P = 0.011), but it was associated with higher eGFR in obesity. Furthermore, higher BW was noted as a significant negative predictor of the 10-year risk of major osteoporotic fracture (MOF) (β = -0.730, P = 0.001) and hip fracture (HF) (β = -0.370, P = 0.001), but positive associations were found between BMI and the both fracture risks (for MOF β = 0.532, P = 0.009; for HF β = 0.441, P = 0.026).

Conclusion
We assumed that obesity might be detrimental to postmenopausal bone health, as it was associated with lower BMD, lower bone turnover and higher fracture risks.

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EP220
Endocrine disorders and osteoporosis: case series

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Introduction
Homeostasis of calcium and phosphor influence bone metabolism. They depend on several hormones, including parathyroid hormone, thyroid and sexual hormones. Low bone mass seems a common issue in endocrine disorders. The aim of this study is to identify the different endocrine disorders in patients with low bone mass.

Methods
Retrospective study collecting the medical files of patients followed in the endocrinology department of Charles Nicolle Hospital between the years 2018 and 2021. The exclusion criteria are: patients followed for a systemic disease or rheumatic disease and patients who received corticosteroid therapy.

Results
We have studied 50 consecutive patients (14 males, 36 females, sex ratio 0.38, aged 8-88 years). Postmenopausal women represented 56% of the study population. We measured bone mineral density (BMD) at the hip: 79% of patients had osteoporosis (36% males, 64% females) and 30% had osteopenia (12% males, 88% females). The average of T score was -2.78 (min -6; max 0.8) for the spine and -2.09 (min -4.7;max 0.7) for the femur neck with a significant correlation between them. 44% of patients were at a risk of fracture and 2% had a pathological fracture. According to the type of endocrinopathy: 62% of patients had hyperparathyroidism (63.5% osteoporosis; 36.7% osteopenia), 12% had hypogonadotropic hypogonadism (85.7% osteoporosis; 14.3% osteopenia), 10% had hyperthyroidism, 8% had primary ovarian insufficiency (25% osteoporosis; 75% osteopenia) and 2% had hyperadrenocorticism (50% osteoporosis; 50% osteopenia).

Conclusion
Additional studies are needed to further understand the endocrine secondary osteoporosis in order to establish evidence based guidelines about its diagnosis, evaluation, treatment and follow up.

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Table 1 Secondary efficacy outcomes

<table>
<thead>
<tr>
<th>Timeframe, months*</th>
<th>Outcome</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>CIB in volume of new HO lesionsa</td>
<td>IPN60130 vs placebo</td>
</tr>
<tr>
<td></td>
<td>CIB in number of HO lesionsb</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flare-up rate; number of flare-up days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number of body regions with new HO</td>
<td></td>
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<tr>
<td></td>
<td>CIB in pain intensity</td>
<td></td>
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<tr>
<td></td>
<td>Proportion of patients with new HO</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>CIB in HO volumeb</td>
<td>IPN60130 vs placebo and untreated natural history study (NCT02322255) participants</td>
</tr>
</tbody>
</table>

*aFrom Baseline up to the month given; bAssessed by low-dose whole-body computed tomography. CIB: change from Baseline; HO: heterotopic ossification.
EP222

**Brown tumour of the mandible as the first manifestation of primary hyperparathyroidism: a case report**

**Introduction**

Brown tumour is a rare, benign, tumour-like lesion of bones. The presence of brown tumour is a rare complication of uncontrolled primary, secondary or tertiary hyperparathyroidism. Brown tumours can be solitary or multifocal and are most commonly located in ribs, clavicles, pelvic girdle, extremities and facial bones (maxilla, mandible, and hard palate). A diagnosis of brown tumour in hyperparathyroidism is established by evaluation of serum calcium, phosphorus and parathyroid hormone levels. Very often a histologic diagnosis of a giant cell tumour is made in case of brown tumour. Treatment of these lesions is often directed to the management of the underlying hyperparathyroidism, which frequently results in regression and resolution of the lesion without surgical intervention. However, surgical treatment may be required in refractory cases or in large symptomatic lesions.

**Case presentation**

A 67-year-old male was referred to an oral surgeon for a right mandible mass and bleeding that was present for approximately one year. The patient’s past medical history was significant for recurrent nephrolithiasis. An incisional biopsy of the mass was performed and histologic examination suggested giant cell granuloma. Despite the histologic diagnosis, the experienced oral surgeon suspected brown tumour in hyperparathyroidism. The patient was referred to an endocrinologist and additional evaluation was performed. A laboratory examination showed hypercalcemia: total calcium level of 2.94 mmol/l (normal range: 2.14 – 2.53), ionized calcium level of 1.61 mmol/l (normal range: 1.18 – 1.32), hypophosphatemia: 0.66 mmol/l (normal range 0.79 – 1.42) and a high PTH level: 44.02 pmol/l (normal range: 1.59 – 7.24). The patient’s renal function was normal and the bone density test revealed osteoporosis. Neck ultrasound revealed an enlarged parathyroid gland and Tc-99 m MIBI SPECT/CT imaging of the neck and mediastinum showed pathological radiopharmacology uptake posterior of the left parathyroid gland and Tc-99 m MIBI SPECT/CT imaging of the neck and mediastinum showed pathological radiopharmacology uptake posterior of the left parathyroid gland and Tc-99 m MIBI SPECT/CT imaging of the neck and mediastinum showed pathological radiopharmacology uptake posterior of the left parathyroid gland and Tc-99 m MIBI SPECT/CT imaging of the neck and mediastinum showed pathological radiopharmacology uptake posterior of the left parathyroid gland.

**Conclusion**

A pathological fracture of the femur and multiple pelvic osteolytic lesions mimicking bone metastases as the first presentation of Primary Hyperparathyroidism

**Discussion**

Pathological fractures are uncommon in young patients and raise concern about malignancy. Brown tumour (osteitis fibrosa cystica) is a rare benign resorptive bone lesion reported in approximately 3% of patients with primary hyperparathyroidism (PHPT). These have become uncommon in contemporary practice and have the potential to be misdiagnosed because of radiological similarities to other bone diseases especially malignancy. We present a case where the first presentation of PHPT was a fracture of the left femur with multiple pelvic lesions masquerading as a metastatic malignancy.

**Summary**

Results from FALKON, estimated to complete in August 2025, will allow evaluation of the efficacy and safety of IPN60130 in patients with FOP.

**References**


**Funding**

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**EP225**

**Intrathyroidal parathyroid adenoma: a rare localization**

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Primary hyperparathyroidism is a frequent endocrine disorder but intrathyroidal parathyroid adenoma is extremely rare. Combining cervical ultrasound and MIBI scintigraphy allows localizing most parathyroid adenomas. Because intrathyroidal parathyroid adenomas mimic thyroid nodules the diagnosis can be challenging, requiring eventually the realization of a fine-needle cyto-puncture. We report here a case of an intrathyroidal parathyroid adenoma diagnosed via a combination of cervical ultrasound, cyto-puncture and MIBI scintigraphy. A 47-year-old female was addressed by her GP for diarrhea and asthenia associated with a 3.3 mmol/l hypercalcemia. Biologic assessment confirmed hypercalcemia associated with hypophosphatemia and elevated PTH, confirming primary hyperparathyroidism. The patient did not present ECG modifications. Abdominal ultrasound did not find renal lithiasis and osteopenia was found on DXA. Hypercalcemia was managed with iv hydration, bisphosphonate iv perfusion and Cinacalcet oral treatment. Cervical ultrasound did not find any parathyroid adenoma but showed a 24x18x15 mm, regular, smooth border, hypoechoic EUTIRADS 4 inferior nodule in the right lobe. Scintigraphy concluded to a MIBI focal uptake behind the lower part of the right thyroid lobe. A cyto-puncture of the thyroid nodule was performed and concluded to the presence of parathyroid tissue. The patient underwent right lobectomy. Pathological analysis confirmed an intrathyroidal parathyroid adenoma. Intrathyroidal parathyroid adenoma remains a rare entity. Different case reports and studies confirm the most common ultrasound features being a solid hypoechoic nodule, smooth and regular shaped, like the adenoma presented by our patient. One feature that is extremely characteristic for the intrathyroidal parathyroid adenoma is the presence of a hypoechoic EUTIRADS 4 inferior nodule in the right lobe. 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Discussion

NVD induced brown tumours are extremely rare in the developed world due to fortification of food. Hence only a handful of cases are reported in high risk individuals with poor dietary intake, malabsorption disorders and poor exposure to sunlight due to dressing habit. This gentleman was house-bound and completely lacked vitamin D containing foods in his diet for several years leading to this unusual presentation. Radiologically, OFC can be challenging to distinguish from primary bone tumor. Bone biopsy remains the gold standard for diagnosis. The mainstay of treatment is medical with correction of vitamin D and calcium supplementation during the acute phase to prevent hungry bone syndrome. Thorough education and long-term maintenance with Vitamin D supplements should be pursued in high risk individuals.

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**EP226**

**Ostitis fibrosa cystica as index presentation of severe vitamin D deficiency**

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Introduction

Ostitis fibrosa cystica (OFC) or brown tumour is a non-neoplastic fibro-cystic expansile lytic bone lesion caused due to excess parathormone (PTH). Brown tumour is classically known to occur in severe primary or secondary hyperparathyroidism due to end-stage renal failure with very high PTH level. OFC presenting as a mass due to nutritional vitamin D deficiency (NVD) is exceedingly rare.

Case presentation

47-year-old Caucasian gentleman presented with symptoms of generalised bone pain, particularly in the back and right knee progressing over two years with declining mobility but denied tingling, numbness or spasm. He is a strict vegetarian by choice with a significant past history of Vitamin B12 deficiency declining mobility but denied tingling, numbness or spasm. He is a strict vegetarian by choice with a significant past history of Vitamin B12 deficiency. He had diffuse tenderness in the pelvis and lumbar spines and height loss and a warm tender 6 cm swelling arising from the lateral aspect of tibial lesion was performed which showed extensive bone remodelling with areas of cellular and focally haemorrhagic stroma rich in osteoclast giant cells similar to brown tumour. He was treated with high dose intramuscular Ergocalciferol and went on to develop hungry bone syndrome, requiring parenteral calcium infusion.

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**EP227**

**Non-functioning parathyroid cystic tumour: a diagnostic and therapeutic challenge**

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Introduction

Parathyroid cysts (PCs) are uncommon lesions. They represent less than 0.5% of parathyroid lesions. Cysts are divided into two groups, functional and non-functional, in relation to their hormonal characteristics. Non-functioning ones make up 80 – 90% of PCs. We discussed three cases of non-functioning parathyroid cysts that we surgically excised.

Methods

We report 3 cases of non-functioning PCs treated in our department.

Results

Our series included 1 man and 2 women. The median age was 35 years [22 years – 45 years]. Patients presented a neck lump in the lower anterior neck. Dysphagia was noted in 2 cases. Clinical examination showed a soft, non-tender and well-limited anterior neck mass that move on swallowing. The mass had a median approximate size of 3 cm. Ultrasonography of the neck revealed a cystic lesion behind the left lobe of the thyroid gland in 1 patient and a right cystic thyroid nodule in 2 cases. Fine-needle aspiration (FNA) with detection of parathyroid hormone (PTH) in the cyst fluid was performed in one patient and the intracystic PTH level was high ([355 ng/l]). Recurrence was noted 1 month after the cyst aspiration. Serum calcium and PTH levels were normal in all patients. All patients underwent surgical treatment: surgical excision of the cystic mass in one case and right lobectomy in 2 cases. Histologic exam confirmed the diagnosis in all cases. PC was intrathyroidal in 2 cases. After median follow-up of 25 months [12 months – 41 months], no recurrence was noted.

Conclusion

Parathyroid cysts are extremely rare lesions. Our cases were nonfunctional parathyroid cystic lesions. FNA with detection of PTH in the cyst fluid (regardless of the level) is an important tool and confirmed the diagnosis in one patient in our study. Three therapeutic options are indicated: cyst aspiration, sclerotherapy and surgery.

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Introduction

Pseudohypoparathyroidism (PHP) is a rare disorder characterized by parathyroid (PTH) resistance, caused primarily by genetic defects involving the alpha-subunit of the stimulatory G protein. Biochemical and molecular analysis classify pseudohypoparathyroidism into types I-a, I-b, I-c and 2. We report a case of PHP I-b in an adolescent presenting with a neurological disorder.

Case Report

A 11-year-old female patient, with no relevant personal or family history, referred to a Neurology appointment for paroxysmal episodes of dystonia of the feet. She had hypocalcemia (corrected serum calcium 6.4 (8.6-10) mg/dl), hyperphosphatemia (serum phosphate 8.6 (2.5-4.5) mg/dl), elevated parathormone (PTH) 438 (15-65) pg/ml; low urinary calcium (<9 mg/24H), normal D vitamin (1.25-dioH-calciferol and 25-OH-calciferol), magnesium and kidney function. Thyroid function showed TSH 7.21, uT4 (0.4-4.6), free T4 11.1 pmol/l (12.22) and negative thyroid antibodies (TPO, TG). The laboratory results were suggestive of PTH resistance and partial TSH resistance. Supplementation with calcitriol, calcium carbonate and levothyroxine was initiated. No typical features of Albright hereditary osteodystrophy (AHO) were observed. A cerebral computed tomography scan revealed bilateral symmetrical calcifications of the cranial base nuclei involving the lenticular nucleus, globus pallidus, posteroexternal aspect of the thalamus and the cerebellar nuclei, suggestive of Fahr syndrome. Renal ultrasound revealed nephrolithiasis; thyroid ultrasound showed a maternally inherited 3-kb deletion, with loss of exon A/B, cause of autosomal dominant PHP I-b. Currently, the patient shows little compliance to therapy, despite the risks, and remains with asymptomatic hypercalcemia.

Conclusion

PHP I-b is most often a sporadic disorder, but sex-linked autosomal dominant inheritance has been reported. Patients with PHP I-b show, occasionally, thyroid stimulating hormone (TSH) resistance and typically lack of Albright hereditary osteodystrophy features.

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EP29

Multifactorial causes of secondary osteoporosis: a case report

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Introduction

Osteoporosis is a metabolic bone disease, characterized by reduction and changes in the bone mass quantity and quality, leading to an increased risk of fractures. It can be divided in primary (postmenopausal or senile), secondary and idiopathic. In the presence of osteoporotic fractures, particularly in men before the age of 65, it is essential to investigate the presence of secondary causes in order to establish an etiological therapy.

Case Report

A 62-year-old man was referred to an outpatient consultation for fractured osteoporosis after suffering spontaneous rib fractures during a coughing episode. He had history of arterial hypertension, diabetes mellitus, smoking, depressive disorder and an adrenal nodule under surveillance for 9 years. He was chronically medicated with metformin, enalapril, lecanapidine, nebivolol, hydrochlorothiazide, atorvastatin and fluoxetine. Physical examination revealed a mildly Cushingoid phenotype and deformation of the left tibia without local inflammatory signs. The analytical evaluation revealed bone alkaline phosphatase 97.6 (n <22.9 µg/l), serum cortisol 22.8 µg/dl and after 1 mg of dexamethasone 4.5 µg/dl, urinary cortisol 388 µg/24h (n <213.7), ACTH 8.7 (N: 7 – 63 pg/ml), hemoglobin A1c 8.1%, calcium 9.3 mg/dl, phosphorus 3.7 mg/dl, Vitamin D 10 ng/ml and PTHi 117 (N: 12-65 pg/ml). The thalamus and the cerebellar nuclei, especially dentate nucleus, suggestive of Fahr syndrome. Renal ultrasound revealed nephrolithiasis; thyroid ultrasound showed a maternally inherited 3-kb deletion, with loss of exon A/B, cause of autosomal dominant PHP I-b. Currently, the patient shows little compliance to therapy, despite the risks, and remains with asymptomatic hypercalcemia.

Discussion and Conclusions

In the reported case, the patient had several risk factors for low bone mass and fragility fractures, namely diabetes mellitus, functional hypercortisolism, secondary hyperparathyroidism, Paget’s bone disease and smoking. A multifactorial therapeutic approach was essential in order to reduce its high fracture risk.

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EP31

Association between serum magnesium levels and physical performance tests in patients with primary osteoporosis

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Introduction

Osteoporosis is the most frequent metabolic bone disease worldwide affecting primarily the senior population. The associated bone loss in combination with a decline in physical performance lead to increased incidence of falls and fragility fractures. Thus, improving physical performance is key to preventing osteoporotic fractures.
Methods
A total of 140 participants were enrolled in a cross-sectional study. Secondary causes of osteoporosis were excluded. All participants underwent dual x-ray absorptiometry analysis and later spine radiography (which resulted in 105 subjects being diagnosed with primary osteoporosis and 35 subjects with osteopenia or normal bone density). Each subject underwent several physical performance tests. Blood samples were obtained to perform biochemical and hormonal assessment.

Results
Statistically significant correlations were found between serum magnesium levels and 4-m Gait Speed values in patients suffering from osteoporosis with or without fragility fracture \((P=0.004, r=0.272)\). Linear regression showed a negative statistically significant correlation between serum magnesium levels and Timed Up and Go Test \((P=0.034, r=-0.207)\) in the osteoporosis subgroup. None of these correlations applied to subjects with osteopenia or normal bone density. All subjects except one had serum magnesium levels within the reference range.

Conclusion
Serum magnesium levels correlate with physical performance tests in patients suffering from primary osteoporosis. In the setting of hypomagnesemia being known to be associated with poor physical performance, the results of this study suggest more research is needed to establish whether magnesium supplementation should be an adjunct to osteoporosis therapies.

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patients for clinical symptoms so as to detect hypocalcaemia and treat it effectively and accordingly.

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EP235
Association between primary hyperparathyroidism with severe bone disease and osteomalacia: A case report.
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Introduction
Primary hyperparathyroidism is associated with multiple complications: severe bone disease is one of them. Osteomalacia is by definition a metabolic bone disease characterized by a softening of the bones. We herein report a rare case of an association between primary hyperparathyroidism with osteitis fibrosa cystica and osteomalacia caused by a severe vitamin D deficiency.

Observation
A 37-year-old woman was referred for investigation of weakness and loss of autonomy. She complained of generalized muscular and bone pain, height and weight loss for 1 year. On physical examination, she had waddling gait and hourglass chest deformity. X-ray examination showed looser zones at the pelvis, osteopenia and an aspect of osteitis fibrosa cystica. Computed tomography showed a brown tumor at the right ilium. The patient was diagnosed with primary hyperparathyroidism based on increased serum calcium 2.7 mmol/l (normal range: 2.20-2.60), increased parathormone concentration 2504 pg/ml (normal range: 15-72) and a low serum phosphate 0.67 mmol/l (normal range:0.80-1.45). The urinary calcium was 0.08 mmol/kg/24h. Renal ultrasonography showed a bilateral nephrolithiasis and BMD showed osteopenia with a high fracture risk: lumbar T-score -5.3 and Hip T-score -4. The diagnosis of osteomalacia was based on clinical and radiological presentation, low 25-OH vitamin D 3.28 ng/ml and elevated phosphatase alkaline 4590 UI/l (normal range 240). Cervical ultrasonography showed a 25x17 mm hypoechoic mass below the left lobe of the thyroid. Parathyroid scintigraphy confirmed increased uptake in the topography of left inferior parathyroid gland. The patient received vitamin D and calcium supplementation and therefore underwent a left lower parathyroidectomy. Postoperative pathology confirmed the diagnosis of parathyroid adenoma. The intraoperative serum PTH concentration was 106 pg/ml. She had hypocalcaemia on the third day after surgery: the serum calcium concentration was 1.9 mmol/l. She recovered well after calcium supplementation and was discharged 1 week after surgery.

Conclusion
This case report illustrates a rare case of a severe bone disease caused by an association of a chronic primary hyperparathyroidism and osteomalacia. Prevention, diagnosis and treatment of vitamin D deficiency and the early diagnosis of primary hyperparathyroidism are very important.

Key words
Primary hyperparathyroidism-bone disease-osteomalacia-vitamin D deficiency-case report

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EP236
Sporadic multiple-gland disease in primary hyperparathyroidism
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Introduction
In 80–90% of cases, the cause of sporadic primary hyperparathyroidism is adenoma of one parathyroid gland. Multiple-gland disease (MGD) is defined in patients with more than one pathological parathyroid gland. The frequency of occurrence of MGD is from 7% to 33%. Our aim is to report a case of primary hyperparathyroidism with MGD and to describe its diagnostic and therapeutic features.

Case Report
A 55-year-old man presented with 1-year history of bone pain and asthenia. He had history of diabetes and hypertension. He had not been suffering from pathological fractures, nephro lithiasis or gastropathy. No familial history of multiple endocrine neoplasia syndrome was noted. Physical exam showed a 2-cm left anterior neck mass. The laboratory workup revealed: serum calcium level was 3.05 mmol/l, serum phosphate level was 0.99 mmol/l and serum PTH level was 127 ng/l. Ultrasonography of the neck revealed a 26-mm parathyroid nodule behind the left lobe of the thyroid gland and another one behind the right lobe, measuring 15 mm. A 99 m technetium (99 m Tc) sestamibi scan has been performed: it showed an inferior right parathyroid adenoma with doubt on another left adenoma. The patient underwent inferior and superior right parathyroidectomy and left inferior parathyroidectomy. The intra-operative examination suggested parathyroid adenomas. The postoperative course was uneventful. The level of serum PTH (43 ng/l) and serum calcium (2.45 mmol/l) were normalized after the surgery. Histological exam confirmed the diagnosis of MGD: adenoma of the right superior parathyroid gland, pseudo adenomatus hyperplasia of the right inferior parathyroid gland and hyperplasia of the left inferior parathyroid gland. No recurrence was noted after 1 year of follow-up.

Conclusion
Identifying preoperatively patients at risk for MGD remains challenging. Intraoperative decisions are important for achieving acceptable cure rates and long-term follow-up is mandatory in such patients. Patients with MGD have an increased risk of complications at surgery and for persistence and recurrence after surgery.

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EP237
Particularities of primary hyperparathyroidism in multiple endocrine neoplasia type 1: Tunisian data
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Introduction
Multiple endocrine neoplasia type 1 (MEN1) is an inherited syndrome characterized mainly by the association of: Primary hyperparathyroidism (PHP), gastro-entero-pancreatic tumors (GEP) and pituitary tumors. The aim of our work is to specify the particularities of PHP in MEN1 among Tunisian population.

Patients & Methods
We performed a retrospective study on 16 patients with MEN1 during a 28-year period.

Results
The mean age at diagnosis of our patients was 36 years with a female predominance (Sex-Ratio = 1.3). PHP was the most frequent initial manifestation in MEN1 (5 cases) and it was present in all cases (7 cases). Four patients were asymptomatic at the time of diagnosis. PHP was complicated by urinary lithiasis in 3 cases and osteoporosis in 3 cases, which was severe in 2 cases. Surgical treatment was considered in six cases. This consisted of parathyroid adenoma removal in 4 cases and subtotal parathyroidectomy in two cases. The anatomopathological study concluded to multiple adenomas in 3 cases. A therapeutic failure with persistent hypercalcaemia was observed in 2 cases. The genetic study was done in 4 patients. It showed the presence of a novel mutation, not previously described in the literature, of the MEN1 gene at exon 4 in three cases.

Conclusion
Our work illustrates the particularities of PHP in MEN1 and subsequently confirms the results of the literature.

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EP238
Primary hyperparathyroidism and rheumatoid arthritis
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Rheumatoid arthritis is a systemic autoimmune inflammatory disease characterized by severe pain, if left untreated. Primary hyperparathyroidism is a systemic disorder characterized by disordered calcium metabolism leading to increased serum calcium and PTH levels. Primary hyperparathyroidism may be due to the presence of a parathyroid adenoma or parathyroid hyperplasia. The aim was to present a cohort of patients with rheumatoid arthritis who presented with primary hyperparathyroidism. A cohort of patients with rheumatoid arthritis is presented. Three patients with active rheumatoid arthritis are described. Patients were female, aged 58, 65 and 67 years old. They had seropositive rheumatoid arthritis, anti-CCP positive, rheumatoid factor positive and had severe pain on treatment with methotrexate and corticosteroids. During laboratory evaluation increased calcium levels were observed along with increased PTH levels. In further evaluation an ultrasoundogram revealed the presence of a parathyroid adenoma adjacent to the thyroid in two of the patients, while in the other scintigraphy with 99mTc-SESTAMIBI was performed which revealed an adenoma beneath the left lobe of the thyroid gland. Surgical removal of the parathyroid adenoma was planned. For the management of rheumatoid arthritis biologic therapy was introduced. Primary hyperparathyroidism in the context of rheumatoid arthritis is rare. If diagnosed it may require surgical removal of the parathyroid adenoma as increased calcium levels may aggravate pain in the setting of systemic inflammation. The diagnosis of primary hyperparathyroidism in the setting of rheumatoid arthritis may be due to routine screening for calcium levels on biochemical evaluation in modern times.

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EP239
How we managed malignant hypercalcemia in a hyperparathyroid in heart failure in the emergency room
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Introduction
We report a case of malignant hypercalcemia complicated by acute pancreatitis, in a patient whose cardiac insufficiency obliged us to use an unconventional therapeutic means: calcimimetics.

Case Report
Mrs. Halima, 74 years old, had a history of arterial hypertension complicated by ischemic heart disease at the stage of heart failure. She consulted the emergency room for typical pancreatic pain, the biological workup found a lipasemia at 30 times normal and acute renal failure, the abdominal CT scan was in favor of an acute pancreatitis stage E of Balthazar. The etiological investigation found malignant hypercalcemia (140 mg/dl) secondary to primary hyperparathyroidism (PTH: 679 pg/ml). the patient was put on fasting, with analgesic treatment. For the presence of kidney failure faced with the reduced therapeutic choices, our attitude was to prescribe cinacalcet at a progressive dose: 30 mg per day then 60 mg per day, the calcimia went in two days from 140 mg/l to 120 mg/l then to 100 mg/l.

Discussion
Cinacalcet is an oral calcimimetic that mimics the effects of calcium on the calcium receptors of the parathyroid cell. It lowers blood calcium and reduces PTH concentration. [1] Initially used in hyper parathyroid hypercalcemia associated with end-stage renal disease is actually FDA approved to treat secondary HPT in patients with parathyroid carcinoma (2011) [2], and hypercalcemia in patients with primary HPT who are unable to undergo Parathyroidectomy, but its use in malignant hypercalcemia in emergency situations has not been recommended, in some cases, and when the classical treatment of hypercalcemia is not possible, as in our patient’s case, calcimimetics, and in particular cinacalcet, can be the most effective therapeutic option to save the patient.

Conclusion
We suggest that the use of this therapeutic class may be useful in urgent situations in patients with cardiac or kidney failure when hyper hydration is not possible.[1] Wada M., and Nagano N.: Control of parathyroid cell growth by calcimimetics.

EP240
Post covid 19 vaccine cramps in a patient followed for hypoparathyroidism: who is to blame?
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Introduction
COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by a influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste. Its severity is highly variable, ranging from asymptomatic to severe or prolonged forms. We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.

Observation
This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium. She received the first dose of astrazeneca in July 2021, after 4 hours she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/L. As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 hours and there was no recurrence.

Discussion
COVID-19 vaccines are as well tolerated in neuro muscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations. Campesium can be seen with COVID-19 vaccines, and is generally benign and transient. The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.

Conclusion
The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be avoided to manipulate complications, particularly neuromuscular ones.

References

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EP241
Pseudo hypoparathyroidism discovered in adulthood
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Introduction
Pseudohypoparathyroidism (PHP) is a part of a very rare heterogeneous group of endocrine disorders. It is caused by alterations in the PTH receptor, which is encoded by the GNAS1 gene inducing target tissue resistance to PTH. Pseudohypoparathyroidism typically gets discovered during early childhood, rare are the cases discovered in adulthood.

Observation
Herein the case of a 35-year-old man, descendant of a non-consanguineous marriage, with a medical history of bilateral cataract surgery at the age of 33 years-old, who consulted the emergency department for an epileptic seizure then he was transferred after discovering a severe hypocalcemia with Fahr’s syndrome at the CT-Scan. The patient didn’t present neither cramps or paresthesia. Chvostek
and Trousseau signs were negative. He had a short stature (Height 153 cm vs Target height 180 cm), dental hypoplasia and soft tissue calcifications on the dorsal part of the hands confirmed by the X-Ray imaging. The patient was in sinus tachycardia at 115 bpm with a non-prolonged corrected QT interval (353 ms). The biochemistry showed a low corrected calcium level at 1.94 mmol/l, an elevated level of phosphorus (1.89 mmol/l), a high level ofPTH (170 pg/ml) and a normal renal function (creatinine 69 umol/ml), in favor of the diagnosis of PHP. The patient was treated with the association of calcium (6g/day) and alphacalcidol (2ug/day), and the corrected calcium level when he was discharged was at 2.14 mmol/l.

Conclusion
In PHP the target tissue is resistant to PTH, resulting in hypocalcemia and hyperphosphatemia. Five different types of PHP, each with specific features, have been described. The best-known type of PHP is type Ia, where biochemical disruptions are combined with a phenotype called Albright’s hereditary hyperphosphatemia. Five different types of PHP, each with specific features, have been described. The best-known type of PHP is type Ia, where biochemical disruptions are combined with a phenotype called Albright’s hereditary osteodystrophy (AHO), including short stature, round face, brachymetacarpia, and subcutaneous ossifications. But the diagnosis of certainty in our case remains genetic.

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EP242
Primary vs tertiary hyperparathyroidism in a patient with medullary necroacinarisosis and chronic renal failure
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Background
Nephrocalcinosis is characterized by the deposition of calcium products in kidney parenchyma and tubules. It may cause acute or chronic kidney injury or be incidentally detected radiographically in a patient with normal kidney function. Most patients with nephrocalcinosis do not progress to end-stage kidney disease, but with certain underlying conditions, may be associated with progressive kidney dysfunction.

Methods
The patient was diagnosed with primary hyperparathyroidism on the basis of blood analysis, biochemical analysis, scintigraphy, calcium levels and parathyroid hormone (PTH).

Case presentation
A 70 year old female patient came to the Emergency Unit with fatigue, diffuse abdominal pain, vomiting, diarrhea and decrease in the amount of urination.

Laboratory analysis revealed hyperkalenaemia, hyponatremia, high azotemia (286 mg/dl) and creatinemia (7.2 mg/dl), high uricemia and phosphatemia. PTH = 832 g/l (high), 25-hydroxyVit D = 6.3 mg/dl (low), total Ca =9 mg/dl(normal). Cell blood count showed normocromic normocytic anaemia. Diuresis was 1 liter/24 - hours (low) and diagnosis of acute renal failure was made. Hemodialysis was started and after first session the patient was hospitalized to nephrology department. The patient was well known for a 20 years of recurrent renal calculosis and has had three interventions of renal calculus and has had three interventions of renal calculosis and has had three interventions of renal calculosis.

Conclusion
The patient underwent hemodialysis. She was planned for three and half gland parathyroidectomy.

Medullary necrocal.binosis is a well known manifestation of primary hyperparathyroidism. When this happens, hyperplasia of parathyroid gland also occurs and if primary hyperparathyroidism wasn’t diagnosed, tertiary hyperparathyroidism can develop and differential diagnosis become very difficult. In our case, medullary necrocalcinosis is a strong evidence of primary hyperparathyroidism and correlates with scintigraphy, but raising values of PTH during years also suggests secondary hyperparathyroidism due to chronic renal failure. In this scenario tertiary hyperparathyroidism can also happen. Treatment of choice is three and a half parathyroidectomy which is a definitive solution for adenoma (primary vs tertiary), and calcium lowering therapy even in the background of parathyroid hyperplasia.

Keywords
Medullary necrocalcinosis, primary hyperthyroidism, parathyroid adenoma, calcium, PTH, kidney, parathyroid glands, calculi, chronic renal failure.

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EP243
Paralytic sciatica revealing hyperparathyroidism: a case report
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Introduction
Primary hyperparathyroidism (HPT1) is a frequent endocrinopathy. Diagnosed incidentally or in front of a urinary or bone symptomatology, we report a case of primary hyperparathyroidism in the mode of revelation makes the originality “a paralyzing scatica”.

Observation
The patient was 44 years old and was undergoing neurosurgery for chronic low back pain that was resistant to etiological treatment. In view of the persistent and hyperalgic nature of the disease, a detailed radiological work-up was carried out: CT scan of the spine with multiple somatic lesions in the lumbosacral region and in the iliac wings. The diagnosis of multiple myeloma was ruled out and on the phosphocalcic workup: primary hyperparathyroidism was diagnosed (with parathyroid hormone (PTH) elevated to 1033 pg/ml, hypercalcemia at 116 mg/l compared to albuminemia at 36 g/l, high calcitriol at 392 mg/ml, low phosphorous level at 12 g/l with total protein at 76 g/l); A cervico-thoraco-abdomino-pelvic CT scan showed a left parathyroid nodule measuring 3.6 cm with thyroid nodules classified as TIRADS 2, 3, and 4, the patient benefited from a total thyroidectomy with excision of the parathyroid nodule, on anamnystopathological examination: aspect of a parathyroid adenoma subsequently substituted in calcium and vitamin D.

Discussion
Primary hyperparathyroidism results from an increased secretion of parathyroid hormone (PTH), associated with hypercalcemia, most often related to a parathyroid adenoma, hyperplasia of the parathyroid glands and parathyroid carcinoma are very exceptional. The classic presentation associating bireocystic osteitis, chondrocalcinosis, nephrocalcinosis, renal colic, and the digestive and neuropsychic clinical signs of hypercalcemia is less and less frequently encountered in Western countries, but remains frequent in some countries. The diagnosis of severity and the etiological diagnosis allow the indications and the modalities of surgical treatment to be determined; any symptomatic form (bone, kidney or hypercalcemia-related signs) constitutes an indication for surgery. Minimally invasive parathyroidectomy is the first-line treatment for most patients.

Conclusion
The presence of diffuse cervical and lower extremity polyarthralgia may not be due to osteoarthritis alone. This deserves a thorough investigation such as a blood calcium and PTH measurement.

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EP244
Symptoms alleviation of primary hyperparathyroidism intensified by COVID-19 pandemic effects using a balanced diet: a case report
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Introduction
Hyperparathyroidism happens when one or more of parathyroid glands secrete excessive parathyroid hormone, causing calcium levels in blood to rise. A diagnosis may be missed or delayed because there are no symptoms or they are vague, like depression, tiredness, losing your appetite in addition to hypercalcaemia symptoms e.g. vomiting, bone and joint pain, dehydration, hyretension, etc. Surgery to remove the parathyroid gland is usually the only way of treating primary hyperparathyroidism. Patients who are unable to have surgery, cinacalcet tablet may help control the condition while being sure to have a healthy and balanced diet.

Method
A 57 years old female patient with 115 kg weight and 160 cm height and a history of osteoarthritis, osteoporosis, joint pain and inability of movement in addition to depression was referred to our endocrinology clinic. Since COVID-19 pandemic, she had to leave her job as a teacher and staying at home. This situation dramatically deteriorated her mental health and intensified weight gain procedure. Considering her history and laboratory examination results, especially high plasma level of calcium, hyperparathyroidism was diagnosed. Nevertheless, no
medicine was prescribed for her. Analyzing her routine nutrition, we found that her daily liquid intake was very low, 2 glasses, accompanied by irregular meals with almost no snack. Instead, an intense diet of 1500 kcal per day with high carbs, magnesium and B-complex and low calcium and high liquid consumption was designed in order to change her nutrition style for 6 months. The diet was planned to balance her meals with 3 main meals and 3 snacks in the meantime. She was recommended to consume more citrus and lemons and no spinach to prevent renal calculi formation. Her health condition was monitored every week by our dietitian staff.

Results
After one month of this intense diet, the patient lost 5 kg of her weight. She reported a kind of lightheadedness feeling, amelioration of joint’s pain while she could walk 10 minutes at home each day. By 6 months follow up, she reported a remarkable improvement of her QOL and losing 12 kg of the weight, no more joint pains and no renal problem.

Conclusion
EP245
A recurrent hypercalcemia after subtotal parathyroidectomy revealing a Munchhausen syndrome
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Introduction
Primary hyperparathyroidism is the most common manifestation of multiple endocrine neoplasia (MEN) type 1, with a frequent involvement of all the parathyroids. In cases where the four glands weren’t resected, a close monitoring should be performed for an early diagnosis of recurrence. Elevated calcium levels with elevated parathormone (PTH) levels in this context makes the physician suspect an adenoma or a hyperplasia of the remaining parathyroid. We herein describe the case of a suspected recurrent hyperparathyroidism which revealed a Munchhausen syndrome.

Observation
We report the case of a 34-year-old man carrying a heterozygous missense mutation of the third exon of the MEN1 gene. He didn’t have gastric nor intestinal tumors. He had two millimeters pituitary nodule with normal prolactin and IGF1 levels. For the adrenal tumors, there was a non-functional micronodular hyperplasia. There was no thymic nor bronchopulmonary tumor. The patient presented four years ago a hypercalcemia at 3 mmol/l with functional micronodular hyperplasia. There was no thymic nor bronchopulmon-ary tumor. The patient presented four years ago a hypercalcemia at 3 mmol/l with elevated PTH levels at 400 pg/ml, and he was operated on with resection of three parathyroid gland containing each an adenoma; the fourth parathyroid gland wasn’t found during surgery. During four years, calcium and PTH levels were normal, with the last normal control respectively at 2,5 mmol/l and 84,5 pg/ml. During four years, calcium and PTH levels were normal, with the last normal control respectively at 2,5 mmol/l and 84,5 pg/ml (2018).

Results
After one month of this intense diet, the patient lost 5 kg of her weight. She reported a kind of lightheadedness feeling, amelioration of joint’s pain while she could walk 10 minutes at home each day. By 6 months follow up, she reported a remarkable improvement of her QOL and losing 12 kg of the weight, no more joint pains and no renal problem.

Conclusion
EP246
Association between interleukin-6 and renal function in patients with diabetes mellitus
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Background and Aims
To assess the relationship between level of interleukin-6 (IL-6) and the renal function in patients with diabetes mellitus (DM).

Method
A total of 416 patients with DM, aged 34 to 75 years, were examined. Control group included 60 healthy patients the same age. All patients underwent standard clinical and laboratory examination, with an assessment of the levels of natriuretic peptides (BNP, proBNP) and level of IL-6. Renal function was assessed based on the levels of serum creatinine, cystatin C, eGFR, which was calculated according to the CKD-EPI formula, and albuminuria, which was assessed as albumin/crea-tinine ratio. Statistical data analysis was performed using smSTATA 14.2 for Mac (2018).

Results
The levels of IL-6 in patients with DM were higher than in control group (3.14 [1.7; 7.9] vs. 1.5 [1.5; 1.7] mg/ml). The level of IL-6 increased with GFR decreasing from 1.7 [1.5; 1.9] mg/ml in CKD 1 to 11.4 [8.9; 32.1] mg/ml in CKD 5 and significantly different between all groups. At the same time, IL-6 values in patients with CKD 1 were also significantly higher compared to the control group (1.7 [1.5; 1.9] mg/ml vs. 1.5 [1.5; 1.7], at p < 0.001). IL-6 significantly correlated with cystatin C (r = -0.71, p < 0.001). A strong negative correlation was also observed between IL-6 and eGFR (r = -0.73, p < 0.001). Multiple linear regression analysis revealed a significant association of creatinine and IL-6 (ß = 0.29, p < 0.001). To find the optimal cut-off threshold for reducing eGFR, a classification analysis using ROC curves was used. At the level of IL-6=2.6 mg/ml, the sensitivity and specificity were 76.7% and 73.9%.

Conclusion
IL-6 might be an independent predictor of decreased renal function in patients with diabetes. Further study of the role of pro-inflammatory cytokines in the development of renal impairments will make it possible to finally decode the mechanisms of their pathogenesis, which will further allow us to understand their complex effect on the body and obtain information for the development of new effective and safe specific medicines.

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EP247
COVID-19 triggered inborn errors of metabolism in adults: a case report of mitochondrial fatty acid oxidation disorder
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Introduction
Autosomal recessively inherited disorders in the metabolism of mitochondrial fatty acid β-oxidation constitute a group of rare diseases with different clinical manifestations and prognosis depending on the type of enzyme deficiency. Hypoketotic hypoglycemia is common to all these types of disorders and is associated with increased consumption of glucose and impaired synthesis of ketone bodies from fatty acids during the fasting periods, infection, or prolonged physical exertion. The analysis of acylcarnitines using tandem mass spectrometry is the gold standard diagnosis of FAO disorders; however, it can be supplemented by the determination of acylglycines, organic acids and other metabolites to clarify the type of enzyme deficiency. The study aims to discuss a clinical case of genetic FAO disorder, first diagnosed after coronavirus disease (COVID-19) as a trigger for the development of clinical signs of the disease. Case report
A previously healthy 18-year-old male patient was admitted to the intensive care unit in a hypoglycemic coma with a blood glucose level of 1.8 mmol/l. Upon examination, COVID-19 with moderate bilateral pneumonia was diagnosed. Biochemical investigations showed the significantly elevated levels of creatine phosphokinase, liver enzymes, creatinine and urea. After clinical stabilization and
Resolution of SARS-CoV-2 infection the renal biomarkers, liver enzymes and creatine phosphokinase were normalized, and the patient was transferred to the endocrinology department for further examination. After exclusion of insulin-producing tumors, adrenal insufficiency and other common causes of hypoglycemia, a fasting test was performed. Decreasing the glucose level to 3.4 mmol/l, insulin to 5.5 IU/l and C-peptide to 0.7 ng/ml, accompanied by severe headache, nausea and recurrent vomiting in the patient, led to the decision to stop fasting after 28 hours. In cases of suspected congenital metabolic disorders, the profiles of acylcarnitine in plasma and organic acid in urine during a period of fasting were measured. Elevated levels of plasma acylcarnitines and increased excretion of ethylmalonic, glutaric and isovaleric acids indicated multiple deficiency of acylcoenzyme A dehydrogenase.

Conclusions
Along with the risk of a severe course of COVID-19 in individuals with metabolic dysfunction, COVID-19 can be a trigger for the initial detection of rare inherited metabolic disorders. This study describes for the first time a clinical case of a newly diagnosed multiple deficiency of acylcoenzyme A dehydrogenase in an adult during the development of SARS-CoV-2 infection.

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Correlation between pulse wave velocity and cardiovascular risk in type 2 diabetes
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Introduction
Diabetes increases the risk of high blood pressure, atherosclerosis, coronary heart disease and stroke. Therefore, People with diabetes have an increased cardiovascular risk. Arterial stiffness is a marker of cardiovascular risk and has been shown to have an independent prognostic effect on cardiovascular disease. The aim of this study was to examine the relationship between cardiovascular risk and arterial stiffness in type 2 diabetes.

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®/XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Our population were divided into two groups: high cardiovascular risk 27.3% and very high cardiovascular risk and arterial stiffness in type 2 diabetes.

Discussion and Conclusion
Arterial stiffness is often increased in type 2 diabetes. It is currently considered an essential link in the development of atherosclerosis and represents a new marker of cardiovascular risk. Carotid-femoral pulse wave velocity is the “gold-standard” method for assessing arterial stiffness in both populations; diabetics and the general population.

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Diabetes Mellitus and COVID-19: Is there a bidirectional relationship?
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Introduction
Diabetes mellitus is a well-known risk factor for worse clinical outcomes in patients with Coronavirus Disease 2019 (COVID-19). However, the relationship between these two entities seems to be bidirectional. The aim of this study was to identify the relationship between diabetes and COVID-19.

Methods
We conducted a prospective study including all patients admitted at the COVID-19 departments of The University Hospital Taher Sfar (Tunisia), between November 2020 and December 2021. We used “The RAPID CORE CASE REPORT FORM” developed by the World Health Organization.

Results
A total of 422 patients were included with a mean age of 59.8 ± 14.7 years (53.2% were females). The type 2 diabetes mellitus (T2DM) was present in 32.5% of cases. During hospitalization, 62.5% patients with T2DM presented a poor glycemic control with a mean rate of blood glucose level of 12.7 ± 9 mmol/l and a mean rate of hemoglobin A1c of 8.4 ± 2.5%. Hyperglycemic complications among patients with T2DM included diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome in 48.5% and 12.1% of cases respectively. A quarter of non-diabetic patients affected by COVID-19 was diagnosed with new-onset diabetes. Our survey showed a significantly higher death rate among patients with T2DM (P = 0.015).

Discussion and Conclusion
The ongoing pandemic of COVID-19 has significantly affected blood glucose control in patients with T2DM. The results of this effects can be classified into direct effects by the viral infection and indirect effects especially by the use of treatments for the COVID-19 infection like corticosteroids, which affect glucose homeostasis and can also induce diabetes. Furthermore, diabetes is a risk factor for worse outcomes and even death in patients with COVID-19.

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EP251  
Canagliflozin and liraglutide effect on myocardial damage in diabetic rats with experimental myocardial infarction  
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Background  
Cardiovascular events are the major cause of mortality among patients with type 2 diabetes mellitus (DM2). Menopause in women additionally increases cardiovascular risk. Despite myocardial infarction (MI) treatment approach in diabetic patients is not specific, some glucose-lowering drugs could have cardioprotective properties. In general, most glucagon-like peptide-1 receptor agonists (GLP-1Ra) and sodium-glucose co-transporter-2 inhibitors (SGLT-2i) have cardiovascular advantages. Particularly, liraglutide (LIRA), semaglutide, empagliflozin, canagliflozin (CANA), dapagliflozin decrease MI incidence. However, SGLT-2i and GLP-1Ra influence on MI manifestations, damage volume and severity in patients with DM2 remains the subject for further investigation. Moreover the cardiotropic properties of these drugs in menopause diabetic subjects undergoing MI is even less studied.

Aim  
To evaluate the effect of CANA in comparison with LIRA on myocardial damage area in menopause type 2 diabetic rats in experimental MI.

Materials and methods  
Female Wistar rats were subjected to bilateral ovariectomy on order to induce menopause. DM2 was modelled by high-fat diet and streptozotocin 60 mg/kg i.p. injection. Rats in control group were fed with standard chow. The following groups were formed: “DM+M” (ovariectomized rats with DM2 treated with CANA 25 mg/kg for 8 weeks, n = 5), “DM+M+LIRA” (ovariectomized rats with DM2 treated with LIRA 0.06 mg/kg for 8 weeks, n = 5), “DM+M+LIRA” (ovariectomized rats with DM2 treated with LIRA 0.06 mg/kg for 8 weeks, n = 4), “CRL” (females without any procedures, n = 5). After 16 weeks of treatment transient global myocardial 30-min ischemia of isolated heart was modelled in all rats. Myocardium necrosis area was evaluated after 90 min of reperfusion.

Results  
Necrosis area was significantly larger in “DM+M” group (42.00 (34.00; 70.00) % of total heart area) in comparison to “CRL” group (33.00 (22.60; 40.00) %, P = 0.003). Both LIRA and CANA administration led to decrease of myocardial damage area (31.67 (15.50; 46.00) % and 31.75 (24.00; 59.00) %, respectively) in comparison with “DM+M+LIRA” (42.00 (34.00; 70.00) %) group (significantly for LIRA groups, P = 0.07). Importantly, there was no significant difference in myocardial damage area between “DM+M+LIRA” and “DM+M+LIRA” groups, P = 0.2. Glucose control was similarly satisfactory in both treatment groups.

Conclusions  
Both LIRA and CANA similarly decrease heart necrosis area in menopause diabetic rats with myocardial infarction.

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EP252  
Comparative analysis of characteristics of pregnant women with pathologocal oral glucose tolerance test vs negative oral glucose tolerance test in a trimester of 2019  
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Introduction  
Gestational diabetes mellitus (GDM) is the metabolic disorder most frequently associated with pregnancy, presenting important maternal and fetal implications. Strict glycemic control through lifestyle measures and/or pharmacotherapy is essential to achieve adequate obstetric-perinatal results. The objective of this study is to compare baseline characteristics and perinatal results in patients diagnosed with GDM after performing oral glucose tolerance test (OGTT) vs patients with negative OGTT, in a trimester of 2019.

Materials and method  
Retrospective observational study comparing baseline clinical-laboratory characteristics and obstetric-perinatal results of 258 women referred to our center during the September-October-November trimester of 2019 due to a positive O’Sullivan test to perform the confirmatory test with 100 g OGTT.

Results  
Exposed in Table 1. Of the 258 OGTT performed, 217 were negative and 41 were positive (16% positive). Among the most relevant findings, the BMI before pregnancy of the 41 women diagnosed with GDM was 29.08 ± 5.82 kg/m² compared to 27.64 ± 7.03 kg/m² in the 217 with negative OGTT (P = 0.046). Weight gain during pregnancy was significantly lower in the group with GDM (P = 0.001): 6.79 ± 5.3 kg vs 10.33 ± 5.26 kg. Of the 41 women diagnosed with GDM, 11 received treatment with insulin. 1 with metformin and 29 with dietary measures. No differences were found in obstetric or perinatal outcomes in both groups.

Conclusion  
Through diagnosis and treatment of GDM, perinatal and obstetric results achieved were similar to those of women without GDM. Although women diagnosed with GDM started with higher BMI values, they presented significantly less weight gain during pregnancy than those with negative OGTT, after undergoing a specific treatment.

Table  

<table>
<thead>
<tr>
<th>Pathological OGTT (n=41)</th>
<th>Negative OGTT (n=217)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous BMI (kg/m²)</td>
<td>29.08±5.82</td>
<td>27.64±7.03</td>
</tr>
<tr>
<td>History of GDM (n=111)</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>History of DM (n=224)</td>
<td>14</td>
<td>46</td>
</tr>
<tr>
<td>Weight gain (kg)</td>
<td>6.79±5.3</td>
<td>10.33±5.26</td>
</tr>
<tr>
<td>Treatment with insulin</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Treatment with metformin</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Birth gestational age (weeks)  
Prematurity (n=228)  
Newborn weight (3258±449)  
Newborn height (50.2±1.95)  
Births (n=224); eutocic; instrumental, cesarean  
Fetal percentile (53.52±27.92)  
Neonatal hypoglycemia; neonatal jaundice; distress  
Neonatal admission; neonatal ICU admission; deaths  
Dystocia (1 (n=35))  

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EP253  
PSMA6 and KEAP1 genes methylation in patients with type 1 diabetes and diabetic retinopathy  
Deimante Kardonaite1, Rasa Verkauskienė1, Lina Radzevičienė1, Laura Daugintyte-Petrusiene1, Vilma Jurate Balciuniene1, Jelizaveta Sokolovskaya2 & Natalia Paramonova3  
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EP254
Effects of semaglutide on glycemic control and weight loss in a patient with Prader-Willi Syndrome: a case report
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Background
Prader-Willi syndrome (PWS) is the most frequent genetic cause of obesity and is often complicated by glucose metabolism alterations. Conventional therapies prescribed in type 2 diabetes mellitus (T2DM), like oral hypoglycemic agents and insulin, frequently failed to achieve adequate glycemic control in patients with PWS. Beneficial effects of the glucagon like peptide-1 receptor agonists (GLP1RAs) exenatide and liraglutide have been reported for the management of T2DM in PWS, but no data are currently available on the use of semaglutide, belonging to the same class of drugs, in this particular population.

Case presentation
We report for the first time the use of semaglutide 1 mg per week in an adult patient with genetically confirmed PWS complicated by poor controlled diabetes and severe obesity. At baseline his HbA1c was 11.1%, body weight 99.5 kg, BMI 37.5 kg/m2. He was on a multi-injection insulin therapy, with a total daily insulin dose of 180 IU, in addition to metformin 3000 mg/day. After 6 months of semaglutide treatment, his weight had fallen to 93.9 kg (-5.6 kg, BMI 39.1 kg/m2) and HbA1c had dropped to 7.0% (-4.1%).

Results
As assessed by bioimpedentiometry, there was also a notable decrease in fat mass (-4.9 kg), without significant changes in lean mass, and a progressive reduction in insulin requirements up to 140 IU (-40 IU/day). The patient well tolerated the therapy and no adverse events were reported.

Conclusions
Interestingly, our patient had previously tried liraglutide therapy in conjunction to metformin and insulin therapy reporting no substantial efficacy.

EP255
Central nervous system condition in children with diabetes mellitus type 1
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Diabetes mellitus is a metabolic disease that is accompanied by brain injury manifested as cognitive, emotional and vascular impairment.

Purpose
To study prevalence and degree of disorders of central nervous system in children with diabetes mellitus type 1 (T1DM).

Methods and materials
Examination of nervous system in 100 children - age 7-18 yrs [9.0-17.8] with T1DM was provided. The control group consisted of healthy children (n=30). The condition of central nervous system was determined on the basis of cognitive and emotional function tests; studying of cerebral circulation was performed using extravascular Doppler study according to standard techniques. The degree of compensation of diabetes was estimated according to criteria ESPAD Consensus Guidelines (2018).

Results
Optimal level (HbA1c <7.0%) of compensation was revealed in 62% of children (group I) and nonoptimal in 38% of children (group II). Decrease of cognitive functions, disturbance of emotional sphere and deterioration of cerebral circulation was established in 12 children (19%) in group I and 16 patients (42%) in group II (P=0.02). The performed correlation analysis revealed association of cognitive, emotional dysfunction and cerebral circulation disorders with the HbA1c level (r=-0.41; -0.5 and -0.47 accordingly, P<0.001).

Conclusions
Diabetic children with nonoptimal HbA1c level frequently cognitive, emotional and cerebral circulation disorders (42%). Prevalence of cognitive, emotional and cerebral circulation increased parallel to HbA1c level.

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EP256
Association of sarcopenia with peripheral nerve functions in type 2 diabetes mellitus patients in East India: A prospective cross sectional study
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Diabetic peripheral neuropathy (DPN) is considered to be the risk factor for the development of sarcopenia. Various previous studies showed the correlation between DPN and muscle disorders, but the study regarding the association between sarcopenia and nerve conduction parameters in diabetic peripheral neuropathy is limited.

Aim
This study was planned to detect the association between sarcopenia with peripheral nerve functions in type 2 diabetes mellitus (T2DM) patients.
Subclinical left ventricular dysfunction in patients with obesity and chronic obstructive pulmonary disease
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The purpose of the work was to compare the changes in the global longitudinal strain of the left ventricle in obese patients with and without COPD.

Material and methods of research
Group I consisted of obese patients without COPD (n=50; 21 males, mean age - 48.8 ± 9.1 years). Group II – 40 patients with obesity and COPD, comparable in age, gender. Group III – 37 patients with COPD without obesity, comparable in age, gender and risk group of COPD. Group A was in 7 group B – in 16, group C – in 5, group D – in 9 patients (GOLD, 2021).

Exclusion criteria
Secondary forms of obesity, persons with a BMI <18 kg/m2, BMI waist circumference, hip circumference, their ratio, visceral obesity index (VAI) and percentage of adipose tissue content according to Deurenberg, cardiometabolic risk on the CMDs scale, fat-free mass index (FFMI) and appendicular skeletal muscle mass index (ASMI) were evaluated. All patients in remission underwent standard echocardiography (EchoCG) with estimated global LV strain in the longitudinal direction (Global Longitudinal strain-GLS) using the “AFI” option.

Results
Primary: In the non-obese group with COPD, the mean GLS was −1.76 ± 0.74%. In group I, the mean GLS was −1.8 ± 0.74%. In Group II, the mean GLS was −1.3 ± 0.74% (p = 0.003). There was a significant difference in the GLS between the non-obese group with COPD and the non-obese group (p = 0.003). In the non-obese group, the percentage of adipose tissue content was significantly higher than in the group without COPD (p = 0.003).

Conclusion
The deterioration of global LV longitudinal strain is determined in 66% of patients in the presence of metabolically unhealthy obesity (vs 26% without obesity, p < 0.001). The negative dynamics of GLS is associated with the severity of COPD, visceral obesity and low muscle mass.

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EP259
The intestinal microbiome and the adipomyokine profile of different phenotypes of obesity
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Currently, it has been established that obesity is a heterogeneous disease. There are metabolically healthy (MHO) and metabolically unhealthy obesity (MNHO) depending on the presence of cardiometabolic disorders. Potential factors that differentiate obesity into phenotypes include the gut microbiome and endocrine activity of adipose and muscle tissue. The purpose of the study was to compare intestinal microbiome and adipomyokine profile in patients with different obesity phenotypes and in healthy people. A cohort cross-sectional study was performed. The study involved 265 participants (men=44 (16.6%), women=221 (83.4%), average age - 47.1±4.8 years). Formed clinical groups: group 1 (n=129) - healthy people with normal body weight, group 2 - obese patients (n=136). In order to isolate different obesity phenotypes, patients of group 2 were divided into 2 subgroups based on the NCEP-ATP III criteria: subgroup 2a (n=40) - MHO, subgroup 2b (n=55) - MNHO. Quantitative and qualitative assessment of the state of the gut microbiome was performed by metagenomic analysis. Measurement of adipokines and myokines was performed by multiplex ELISA on a Magpix analyzer. Statistical analysis was conducted in the R version of the RStudio program. As a result, in patients with MHO the presence of Lentaishpaeae was less often observed and the number of Bacteroidetes was lower, but the amount of Firmicutes was higher compared to MNHO subgroup (P<0.05). In obese group, the number of Bacteroidetes, Proteobacteria was increased and the amount of Actinobacteria, Firmicutes, TM7, Fusobacteria was decreased, and the phyotypes of Tenericutes, Planctomycetes and Lentaishpaeae were more often verified compared with similar indicators in healthy people (P<0.05). When comparing the studied adipokines and myokines in patients with different obesity phenotypes, significant differences were found for adiponectin and leptin (P<0.05). In patients with MHO, the level of adiponectin and leptin was significantly higher compared with the MNHO. In patients with MHO and MNHO, the level of adiponectin was significantly lower, and leptin and asparin - higher compared with the control group (P<0.05). No significant differences in the content of myokines in different obesity phenotypes were found in our study. The obtained results indicate changes in the composition of the intestinal microbiome and adipokine profile in different obesity phenotypes. Further research is required, both to confirm the obtained results and to identify correlations between metabolic parameters with individual phyotypes of the gut microbiome and the profile of adipomyokines.

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EP260
Maternal weight gain during pregnancy and neonatal birth weight among women with gestational diabetes mellitus
Olfa Lajili, Aroua Temessek, Rim Rachdi, Yosra Htira & Feika Ben Mami

Introduction
Body mass index (BMI) and gestational weight gain are increasing globally. However, the association between gestational weight gain consistent with the Institute of Medicine (IOM) guidelines and neonatal birth weight among women with gestational diabetes (GDM) remain unclear.

Objective
The aim of our study was to assess gestational weight gain among tunisian women with GDM and its effect on neonatal birth weight.

Methods
A prospective and longitudinal study including 220 women with GDM followed at the gestational diabetes research unit of department C at the National Institute of Nutrition of Tunis, The Research Unit of GDM (Department C), Tunis, Tunisia.

Results
The mean gestational BMI was 28.8±5.2 kg/m². The mean term of discovery of GDM was (24 gestational week + 2 day)±(7 gestational week + 2 day). The average weight gain in late pregnancy was 12.2±4.6 kg. More than half of the patients (56.1%) had inadequate weight gain and 44.5% had excessive weight gain in late pregnancy. The mean birth weight was 3368.2±551.2 g [1022g -5000 g]. The main neonatal outcomes were macrosomia (13.5%) and transient respiratory distress (11.4%). Patients with macrosom newborns tended to have higher pre-gestational BMI but with no significant difference between the two groups (29.3±4.8 kg vs 28.5±5.2 kg; P=0.4). Furthermore, there was no correlation between the weight gain in late pregnancy and the birth weight (P=0.679). Similarly, we did not observe an association between the incidence of macrosomia and the weight gain in late pregnancy (P=0.559).

Conclusion
The half of women (65.1%) had inadequate weight gain in late pregnancy. These data point out the interest to follow the recommendations of weight gain during pregnancy in patients with GDM to prevent pregnancy outcomes including macrosomia.

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EP261
Correlation between pulse wave velocity and microangiopathy in type 2 diabetes
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Introduction
Microangiopathy is defined as damage to small blood vessels, and more particularly arterioles and arteriolar capillaries that supply organs. It can occur under different conditions and it represents a complication of diabetes. The aim of this study was to examine the relationship between microangiopathic complications and arterial stiffness in type 2 diabetes.

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®/XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPWV).

Results
The mean age of the study population was 57.53±9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Microangiopathic complications were found in 58.2% of the patients. In this group, cPWV was at 14.41±2.84 m/s VS 12.56±2.42 m/s in patients without microangiopathic complications (P<0.001). Moreover, the presence of arterial stiffness multiples by 4 the risk of microangiopathic complications (Odds Ratio = 4). The ROC curve that we established to find a threshold value of the cPWV from which this correlation appears, had an area under the curve equal to 0.694. The discriminate threshold value having the best sensitivity/specificity pair was 13.45 m/s.

Conclusion
Arterial stiffness is often increased in type 2 diabetes. Its presence contributes to the development of microangiopathic complications. Which leads us to believe that the early prevention of arterial stiffness may delay microangiopathy.

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EP262
Evolution of combined impaired fasting glucose and impaired glucose tolerance in 58 β-thalassemia major (ß-TM) patients during a mean 7.7 year follow-up
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1 Quisisana Hospital, Ferrara, Italy; 2 College of Medicine, Sultan Qaboos University, Muscat, Oman; 3 Hamad Medical Center, Pediatrics, Doha, Qatar; 4 Department of Diabetes and Endocrinology, Whittington Hospital, London, United Kingdom; 5 Hamad Medical Center, Hematology, Doha, Qatar; 6 National Kapodistrian University of Athens, First Department of Paediatrics, Athens, Greece

Background
In patients with β-thalassemia major (ß-TM) glucose dysregulation (GD) develops insidiously, aggravating prognosis and quality of life.

Objectives
The objectives of this study were to retrospectively review the extent to which β-TM patients, having combined impaired fasting glucose (IFG) and impaired

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The combination IFG/IGT in β-TM patients with severe iron overload constitutes a high-risk state for developing diabetes.

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### EP263

**Hormonal-metabolic and functional predictors of unfavorable cardiovascular prognosis in young patients with type 1 diabetes mellitus.**

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**Background**

Patients with type 1 diabetes have a significantly higher risk of coronary events, as well as diseases of the cardiovascular system. Purpose of the study – to show the relationship between metabolic, structural, and functional parameters of the cardiovascular system in young patients with DM1.

**Methods**

The study included 60 patients without CVD: 40 patients with DM1 and 20 patients without DM1, the groups were comparable in age, sex, AMT, heart rate, blood pressure. All patients underwent a laboratory examination, which also included an assessment of the levels of adiponectin, resistin, electrocardiography, biometrical and ergospirometry.

**Results**

In the group of patients with DM1, an increased content of adipose tissue (P=0.003) was revealed in the absence of a statistical difference with the group without DM in terms of BMI and correlations between the level of maximum power of exercise performance (METs) with the content of muscle tissue P=0.004 and with adipose tissue P=0.049. In the control group, correlations were revealed - METs to % of muscle tissue P=0.004. The decrease in the functional parameters of the cardiorespiratory system in young patients with DM is noteworthy: the time to reach the anaerobic threshold (AP) (P=0.008) and the maximum oxygen consumption (VO2 max) (P=0.034) compared with the group of patients without DM1. Correlations were revealed in the group of patients with DM1: METs to VO2 max P=0.001 and to AP P=0.004. In the control group: METs to VO2 max P=0.001, AP P=0.008 and VO2 max to AP P=0.003. It should also be noted an increase in the level of resistin in the group of DM1 patients compared with the group without DM1 (P=0.044). When conducting a correlation analysis in the group of patients with DM1, a correlation was found between VO2 max and the level of adiponectin P=0.021.

**Conclusions**

Young patients with DM1 have lower functional indicators of the cardiorespiratory system, compared with patients without DM, while maintaining a high tolerance to physical activity. Also, in young patients with DM1 who do not have cardiovascular diseases, there is a significant increase in the level of resistin, which has pro-inflammatory activity and, according to many studies, is associated with an increase in cardiovascular risk.

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### EP264

**Association of adherence to the Mediterranean diet and body composition in type 1 diabetes mellitus**

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**Introduction**

Body composition is gaining more interest in some pathologies such as Type 1 Diabetes Mellitus (DM1). Adherence to the Mediterranean diet has been shown to be effective in improving the prognosis of cardiovascular disease, which is the main cause of mortality in these patients. To assess whether adherence to the Mediterranean diet in DM1 is associated with improvement in disease control parameters, body composition, anthropometry, dynamometry, and other cardiovascular risk factors.

**Patients and methods**

Cross-sectional study in 32 patients with DM1. Demographic parameters, variables related to the disease, anthropometrics, dynamometry and body composition were collected using vectorial electrical impedance analysis. In addition, adherence to the Mediterranean Diet was evaluated using the validated 14-point test of the PREIDMED trial. Statistical analysis was performed using the SPSS program (SPSS, inc, v 25.0).
Results
32 DM1 patients under follow-up in the Endocrinology consultation of the HUSC of Granada were selected. Mean age was 41.5 ± 15.2 years, 20 women (62.5%) and 12 men (37.5%). Mean BMI was 26.0 ± 5.1 kg/m², mean HbA1c was 7.4 ± 1.1%, mean phase angle was 5.9 ± 0.7°. Patients were divided according to their adherence to the Med Diet into high adherence (≥ 9 points) or low adherence (< 9 points) according to the results of the PREDIMED trial. 19 patients (59%) obtained 9 or more points. There were significant differences between the groups in terms of total insulin dose (37.1 ± 14.1 vs 49.9 ± 15.5, P = 0.024), insulin/kg (0.53 ± 0.2 vs 0.67 ± 0.15, P = 0.034) and insulin sensitivity factor (50.6 ± 20.2 vs 37 ± 15.56, P = 0.05), standardized phase angle (1.2 ± 1.5 vs 0.02 ± 0.84, P = 0.019) and C-reactive protein (1 ± 0.5 vs 2.4 ± 1.3, P = 0.047). A tendency to the difference between the groups in terms of HbA1c and lipid profile was found, without finding statistical significance. A statistically significant difference was found between the groups, with those who were less adherent presenting higher levels of the TG/HDL ratio.

Conclusions
In our sample, type 1 DM patients who presented greater adherence to the Med Diet showed lower insulin needs and greater sensitivity to it with improvement in the inflammatory pattern and better preservation of cell membranes measured indirectly by the angle of phase. Based on these preliminary results, we should reinforce diabetes education programs to increase adherence to the Mediterranean diet in our DM1 patients.

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EP266
Glycemic variability in pregnant women with gestational diabetes mellitus
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Introduction
Glycemic variability (GV) is a more accurate parameter for assessing the risk of developing diabetic complications than traditional parameters for assessing compensation. In most cases, diet therapy is used to treat DM, while the glycemia in a pregnant woman should correspond to the glycemic level in healthy pregnant women. The aim of our work is to compare two-week glycemic profiles and GV in pregnant women with GDM on diet therapy and in healthy pregnant women using the FreeStyle Libre flash monitor system.

Materials and methods
Analysis of the glycemic profile of 62 pregnant women aged 33.2 ± 6.1 years. The average gestational age of the women included in the study was 12.6 ± 6.4 weeks of gestation. The pregnant women were divided into 2 groups: 30 pregnant women with GDM and 12 healthy pregnant women. According to the self-monitoring diary using a glucometer, all pregnant women with GDM had target glycemic values. Each group underwent a two-week glucose profile monitoring using the FreeStyle Libre continuous monitoring system. To assess GV, the following parameters were used, reflecting various characteristics of the glycemic curve: SD characterizes the degree of scatter in glycemic values; MAG - reflects the rate of change in glycemic levels; CONGA - duration of glycemic increase; HBGI – hyperglycemia risk index; LGBI – hypoglycemia risk index; ADDR is the average value of risks. Results
Taking into account the peculiarities of control in GDM, the threshold values of the normal range were changed in accordance with the target values for pregnant women with GDM. Indicators of glycemia and glycemic variability were significantly higher in the group of pregnant women with GDM compared with pregnant women without carbohydrate metabolism disorders, but within the target range. The average level of glycemia in the groups was 4.72 ± 0.37 mmol/l vs 4.24 ± 0.34 mmol/l, respectively (P < 0.0001). Comparative analysis of GV parameters in groups: SD - 0.8 vs 0.7213 (P < 0.05); LS - 1.4 vs 0.8 (P < 0.05); LGBI 5.56 vs 4.6 (P < 0.05); HBGI - 0.43 vs 0.42 (P = 0.06); J-index - 9.08 vs 7.64 (P < 0.001); MOOD - 0.96 vs 0.79 (P = 0.07); MAG - 2.3 vs 1.8 (P < 0.05); ADDR - 1.02 vs 0.2410 (P < 0.05); MAG - 3.8 vs 2.6 (P < 0.001), CONGA index 3.9 vs 3.7 (P = 0.09), respectively.

Conclusions
Flash glycemic monitoring can be used to obtain more detailed information about the glycemic profile, especially when it is difficult to assess the degree of GDM compensation.

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EP267
GLUCUBE: Usability validation of a non-invasive device for blood glucose measurement
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1Virgen Macarena University Hospital, Endocrinology and Nutrition Department, Seville, Spain; 2University of Seville, Department of Signal Theory and Communications, Biomedical Engineering Group, Seville, Spain

Introduction
The Biomedical Engineering Group of the University of Seville, the Endocrinology and Nutrition Unit of the Virgen Macarena Hospital (ENU-VMH) and the company Igluco Tech are developing the GLUCUBE device, a new non-invasive sensor for blood glucose measurement.

Objective
First validation of usability and accessibility of the device by patients in a controlled clinical environment.

Material and Methods
General user-centered methodology. Design of questionnaires and semi-structured interviews to collect opinions, requirements and improvements

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suggested by users. Selection of subjects for validation based on the heterogeneity of the sample, age, gender, socioeconomic characteristics and digital culture. From a preliminary prototype, iterative development carried out in parallel to the validation incorporating the identified improvements to the user-sensor interfaces.

Results
Study characteristics: 96 people with type I diabetes, 142 type II, 1 LADA, 19 without diabetes; 123 women; 84±19 kg weight (mean ± standard deviation); 5±11 years; 166±13 cm height, 35±10 years; 169±14 cm height, 27±7 BMI. Group of people over 50 years old: 72 people with type I diabetes, 12 type II, 6 without diabetes; 43 women, 47 men; 86±18 kg weight; 65±5 years; 165±12 cm height, 31±6 BMI. The usability and accessibility tests showed that 81% of the volunteers under the age of 50 expressed interest in having the results preferably displayed on the screen of a mobile phone, while 19% indicated the device screen as a preference. On the other hand, in the age group of people over 50 years old, only 13% of the volunteers preferred the screen of a mobile phone compared to 87% who preferred a visual interface on the device. 100% of the users positively valued the non-invasive nature of the proposed prototype and the ease of use. Regarding general aspects of the prototype, 97% of the patients indicated that the device did not need improvements and 2% suggested that voice prompts be included. 20% of users indicated a long battery life as a desirable feature for the device.

Conclusions

The introduction of user usability and accessibility validation in the design, from its early stages, guarantees the ease of use and adherence of the patient to the use of the final device.

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EP268
Psychological impact of obesity in adult women
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1Hedi Cheker University Hospital, Endocrinology, Sfax, Tunisia; 2Hedi Cheker University Hospital, Community Medicine, Tunisia

Introduction
Obesity is a global epidemic with a growing prevalence in recent decades. In Tunisia, obesity is a major problem as it is increasing in adults as well as in children and adolescents. It therefore appears important to deepen the knowledge on this pathology and especially on the psychological profile, since studies concerning the mental health of obese subjects remain rare.

Purpose

Study the psychological impact of obesity in adult women

Patients and Methods

Descriptive observational study using the quantitative approach, including 115 obese female adults who consulted the clinic of Sfax. A validated questionnaire was proposed to these patients concerning 6 dimensions: depression and anxiety (HAD scale), social phobia (LSAS score), self-esteem (RSE score), body image (BSQ-8c short version) and eating disorders (BITE scale).

Results

The average age of our population was 47.14 years. Seventy-eight percent of our patients were married. The median body weight was 93.15±17.6 kg and 54.7% of our population had stage 1 obesity. Stage 2 and 3 were present in 20.7% and 24.7% respectively. Abdominal obesity was present in 94.7% of cases. Fifty-one patients were on a diet that was prescribed mainly by family and friends (41%) and only 8% sealed medical care. Depression was present in 17.4% of our population and anxiety in 76.5%. All our patients had low self-esteem and social phobia, of which 90.4% had very low self-esteem and 40.9% had intense social phobia. Preoccupation with body image was described in 90% of our female patients and 32% had severe body image concerns. Sixty percent of our population suffered from eating disorders, of which 12.2% had bulimia.

Conclusion
Obesity is a growing concern, not only in terms of physical and social health, but also in terms of psychological health, throughout the world.

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EP269
Should we systematically detect hypothyroidism in obese subjects?
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Hedi Cheker University Hospital, Endocrinology, Tunisia

Introduction
Hypothyroidism has always been considered one of the most common endocrine etiologies of obesity. That said, would screening for hypothyroidism be justified in the face of obesity? The purpose of our study was to study the thyroid profile of obese people.

Patients and methods

We conducted a retrospective study which patients with obesity hospitalized in the diabetology endocrinology department, CHU Hedi Cheker of Sfax, between 01/10/2022 and 31/12/2022. for all patients who had consulted for obesity in which a thyroid assessment was requested as part of an endocrinological survey.

Results
The total number of patients was 70 obese, (12 men and 58 women), aged on average 44.57 years (±15 years). The average BMI of our patients was 38.38±6.09 kgm². In our study population, 30% of patients were moderately obese; 34.3% were severely obese and 35.7% were morbidly obese. No subject was known to have a history of dysthyroidism. Among patients, 6.7% (n=5) had subclinical hypothyroidism with TSH higher than 4 µIU/l and a normal FT4. In the latter, a thyroid check-up was done after one month returning normal. The rest of the patients (n=65) had no abnormalities in their thyroid function. The analytical study did not find a correlation between TSH blood level and the BMI of patients (P=0.134).

Conclusion
Our study shows that hypothyroidism remains a secondary cause to look for in the face of obesity with signs of appeal in favor of diagnosis instead of a systematic screening that proves to be unjustified.

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EP270
Un unexpected cause of mild hypoglycaemia in an adult
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A 36-year-old Caucasian male was referred in November 2021 to our clinic, for investigations regarding his recent genetic diagnosis of congenital hyperinsulinism, revealed by genetic testing, performed after the birth of couple’s second child presenting with recurrent hypoglycaemia. The female newborn diagnosed with fetal macrosomia (birth at 38 weeks, 4.3 kg), required follow-up and further examinations. A massive parallel sequencing on panel of 4867 genes using Roche platform, performed on the entire family, revealed the presence in the heterozygous state of the variant c.4432G>A, p.Gly1478Arg in the ABCC8 gene in the newborn, her father and the couple’s first child, born in 2018 (3.6 kg at 36 weeks), which inherited the variant, but had no suspicious event of hypoglycaemia. In our patient, the condition is transmitted in the autosomal dominant mode. Each child of a carrier individual has a 50% risk of inheriting the anomaly. However, the expressivity is variable and the penetrance incomplete, therefore the severity of the phenotype cannot be predicted. Venous blood sample showed non-fasting sugar level at 62 mg/dl (3.4 mmol/l) with inappropriate normal value of C-Peptide (0.954 nmol/l) and insulin (92.9 pmol/l). 7-day continuous glucose monitoring (CGM) with Dexcom G5® Mobile CGM System, highlighted several hypoglycaemic events, confirmed by fingerstick measurement, going as low as 45 mg/dl (2.5 mmol/l) linked mostly to meals, occasional alcohol consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition consumption or after a 5-hour fasting period.
hypoglycemic events. The understanding of the genetic basis of familial hyperinsulinism should borne in mind that certain patients with hypoglycemia might present genetic features with late-onset (or late diagnosis), such as congenital hyperinsulinism. Mild hypoglycemia in an adult can be easily missed, but the underlying cause can be rare with important further implications for the patient and his offspring.

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EP271
Impact of emotional eating in the weight of woman
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Introduction
Obesity is nowadays one of the most important challenges in public health and, therefore, the investigation of their causes is most relevant. Among the various behavioral roots of obesity, the emotional over ingestion determined by emotional factors, i.e. emotional eating (EE), is one of them.

Objectives
To study how emotions contribute to obesity in woman.

Methods
We gathered a convenience sample 220 woman in the hospital and community settings, of which, 43 had normal weight, 37 overweight, 19 grade 1 obesity, 35 grade 2 obesity and 86 grade 3 obesity. The mean age was 39.3 ± 10.4 years and BMI was 35.3 ± 9.8 kg/m2. We applied the Emotional Appetite Questionnaire (EMAQ) that evaluates the EE determined by positive and negative emotions and by positive and negative situations. Statistical analysis was performed with the One-way ANOVA with Bonferroni correction test and Pearson’s correlation test for variable association. P values ≤ 0.05 were considered as statistically significant.

Results
We found a positive correlation among age and BMI (P < 0.001) and the mean of negative situations (P < 0.001). We observed a negative correlation among BMI and education (P < 0.005), the mean positive emotions (P < 0.001) and positive situations (P < 0.005). We noticed a significant age difference among normal weight vs grade 2 obesity and grade 3 obesity (P < 0.001) participants. Normal weight and grade 3 obesity groups had different education levels (P < 0.02). In terms of EE we observed significant differences between normal weight and grade 3 obesity (P < 0.005) and between overweight and grade 3 obesity (P < 0.03). Normal weight and grade 3 obesity participants had significant differences in the positive situations (P < 0.03).

Conclusions
In this sample older and lower education participants showed a higher BMI. Woman with higher BMI appear to have more EE determined by negative emotional situations. Ingestion originated by positive emotions and situations results in lower BMI. Attending to all groups of weight classes concerning the EE, only the positive emotions distinguish the normal weight of the grade 3 obesity and the overweight. The positive situations distinguish the normal weight and the grade 3 obesity. According with some the literature, this study, corroborates the results in lower BMI. Attending to all groups of weight classes concerning the EE, woman with higher BMI appear to have more EE determined by negative situations.

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EP273
Serum xanthinoxidase activity (sxo)-glucose homeostasis association in patients with type 2 diabetes mellitus (t2dm)
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Introduction
Hyperuricemia is increasingly being considered a potential pathogenic factor for T2DM, metabolic syndrome, and several adverse consequences of vascular disease. It has been suggested that xanthine oxidase may underlie the urine acid-T2DM association. The study aimed to determine the associations between clinical parameters, glucose homeostasis, and SXO activity in patients with T2DM.

Methods
125 patients with T2DM, age (58.9 ± 9.4) years. Determined WC, HC, ratio WC/HC, BMI, FG, PGB, fasting insulin, serum urine acid (SUA), HOMA_IR, QUICKI, Caro, HOMA_S%, HOMA_S%, and SXO activity. Results
We found a significant age difference among normal weight vs grade 2 obesity and grade 3 obesity (P < 0.001) participants. Normal weight and grade 3 obesity groups had different education levels (P < 0.02). In terms of EE we observed significant differences between normal weight and grade 3 obesity (P < 0.005) and between overweight and grade 3 obesity (P < 0.03). Normal weight and grade 3 obesity participants had significant differences in the positive situations (P < 0.03).

Conclusions
In this sample older and lower education participants showed a higher BMI. Woman with higher BMI appear to have more EE determined by negative emotional situations. Ingestion originated by positive emotions and situations results in lower BMI. Attending to all groups of weight classes concerning the EE, only the positive emotions distinguish the normal weight of the grade 3 obesity and the overweight. The positive situations distinguish the normal weight and the grade 3 obesity. According with some the literature, this study, corroborates the importance of the positive EE as a differential factor in the woman’s weight. Therefore, the investigation of their causes is most relevant. Among the various behavioral roots of obesity, the emotional over ingestion determined by emotional factors, i.e. emotional eating (EE), is one of them.

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Endocrine Abstracts (2022) Vol 81
EP274
Liraglutide improves binge-eating and increases ghrelin levels in obese diabetic patients
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Background and aims
Liraglutide belongs to glucagon-like peptide-1 receptor agonists (GLP-1 RA) and is widely used for diabetes type 2 (DT2) management as well as for obesity treatment. GLP-1 RA reduce body weight and suppress eating behavior by delaying gastric emptying and affecting arcuate nucleus in hypothalamus. Binge eating disorder (BED) is the most common eating disorder (ED) in individuals with obesity and DT2. BED is characterized by consuming large amounts of food with an associated sense of loss of control. A well-known appetite-stimulating hormone is ghrelin, secreted within the gastric mucosa. Some studies report about decreased ghrelin levels in obese, diabetic patients as well as in individuals with BED. Our aim was to evaluate the effect of liraglutide on BED and ghrelin level after 3 months of administration in obese diabetic 2 patients.

Materials and methods
75 individuals (mean age – 60.1 ± 6.4 years; BMI - 33.4 ± 3.6 kg/m²; history of diabetes <5 years) with DT2 were recruited into the study. After completing Binge eating scale (BES) 18 patients were screened positive for BED. 8 binge-eaters (1st study group) started therapy with metformin and liraglutide 1.8 mg daily. Other 10 participants (2nd study group) used metformin and SGLT-2 inhibitors as glucose-lowering therapy. Ghrelin level was assessed at the 1st and 12th week of the study.

Results
the 1st study group which used dual therapy with liraglutide demonstrated greater weight loss compared to the 2nd group (4.3 ± 1.3 kg vs. 1.7 ± 0.8 kg, p <0.05). BES-scoring improved in the 1st study group and 5 participants (37.5%) were categorized into non-binge-eaters. Baseline ghrelin level in the liraglutide group (18.8 ± 10.3 ng/ml) increased (24.9 ± 10.8 ng/ml) significantly (P <0.05) but not in the 2nd group.

Conclusion
liraglutide is effective and safe for the use in obese diabetic 2 individuals with BED. It reduces body weight and stabilizes eating behavior which makes them potential candidates for the application in diabetic 2 patients with BED. Changes in ghrelin level reflect the recovery of energy homeostasis due to weight loss.

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EP275
A potential complication of diabetes: ischemic colitis
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Background
Ischemic colitis (IC) is a disorder characterized by a decrease in blood flow of the large intestine. Many factors can contribute to decreased blood flow in the arteries supplying the large intestine, such as nonocclusive causes like hypertension and atherosclerosis and occlusive causes like embolism from myocardial infarction. With Ischemic colitis’s high mortality rate and its association with many cardiovascular diseases, it’s important to understand the comorbidities that might lead to these events. Diabetes is known to cause atherosclerosis and other cardiovascular events. Thus, Diabetes might play a role in the development of ischemic colitis. This study aims to find and assess comorbidities like diabetes associated with admission for ischemic colitis.

Methods
We conducted a cross-sectional study of adults with IC listed as the primary ED diagnosis from 2005 to 2014 using the Nationwide Readmission Database (NRD).

The characteristics of the IC-related ED visits were analyzed.

Results
The estimated number of ED visits with a primary diagnosis of IC from 2005-2014 was 541,267 people. Our results showed that the mean age of the cohort was 62 +/- 14 years, suggesting that most patients affected with ischemic colitis are elderly. 101,758 out of 541,267 ischemic colitis patients were found to have uncomplicated diabetes, amounting to 18.8% of the ischemic colitis population.

Conclusions
A notable comorbidity associated with ischemic colitis was uncomplicated Diabetes. Diabetes is marked by hyperglycemia, which can result in atherosclerosis. Atherosclerosis may lead to hypoperfusion of organs and ultimately ischemic colitis. Constipation is not only the most common gastrointestinal symptom of diabetes, but most common precipitating factor of ischemic colitis in the elderly. Most of the patients affected with ischemic colitis are elderly, based on the results. Thus, uncomplicated diabetes may be regarded as a comorbidity associated with ischemic colitis, constitution being the resulting precipitating factor.

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World Health Organization for children aged 6 to 19 years. Body composition was assessed in all participants using an Inbody 770 analyser (Inbody Co. Ltd, Korea). Statistical processing of the results was performed using SPSS Statistics 25.0.

Results
Fat parameters in girls and boys from the obese and overweight groups were comparable to the SDS BMI values. The 11% of normal weight girls (n = 146) had increased body fat mass, 32.2% had increased body fat percentage, and 7.5% had visceral obesity (VO). As for boys, 43.9% had decreased muscle mass. Boys with normal body weight (n = 147) had increased fat mass in 17.7% cases, 34.7% of those examined had increased percentage of fat mass and 2.1% had visceral obesity. Among all boys surveyed, 17.5% had decreased muscle mass. Weight deficient children, irrespective of gender, had no excess fat mass but all had deficit muscle mass.

Conclusions
The results obtained in the survey are probably related to lifestyle aspects of modern children, such as low physical activity and an unbalanced diet. The revealed changes in body composition in children with normal SDS BMI indicate the need for more active diagnostic tactics and the use of additional tools to diagnose these deviations and their correction. The use of bioimpedance measurement will allow early detection of signs of visceral obesity in children, irrespective of BMI.

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EP278
Evolution of glucose-insulin homeostasis in children with β-thalassemia major (β-TM): A twenty-year retrospective ICET- A observational analysis from early childhood to young adulthood
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We studied retrospectively the changes of glucose-insulin homeostasis from early childhood to young adulthood in β-thalassemia major (β-TM) patients with impaired fasting glucose (IFG) vs those with normal OGTT.

Methods
All data entered in the database of β-TM patients’ records from September 1983 to September 2021 were included in the study.

Results
The occurrence of dysglycemia (GD) (IFG, IGT and IFG + IGT) after 20 years of follow up was markedly higher in the group with IFG at the beginning of the study compared to the group with normal OGTT. There was no case of diabetes mellitus. In patients who had normal OGTT at baseline, a small proportion developed GD (2/9 at 15 years and only 1/8 at 20 years). On the other hand, 3 out of 9 patients with baseline IFG, had persistent IFG at 5 years. One had persistent isolated IFG and 3 developed IGT 10 years later. 5/9 had IFG after 15 years, and finally 6/8 had GD after 20 years. (table/indices of insulin secretion and sensitivity (MI, HOMA-IR, ddi) were statistically different (P < 0.001) between the two groups. HOMA-IR was higher in patients who had IFG vs (69 patients had HOMA-IR > 2.24) the group with normal OGTT (2/6 patients had HOMA-IR > 2.24). This suggested a degree of insulin resistance in the etiology of GD. In both groups of patients, no correlation was observed between serum ferritin (SF), ALT and indexes of insulin sensitivity or insulin resistance.

Conclusion
Our data advocates that baseline IFG predicts future development of GD because almost half of patients with IFG at the outset had abnormal glucose handling 15 years later. Understanding the sequence of abnormalities in the progression from normal glucose homeostasis to GD and identifying the risk factors for the glycol-metabolic defects in thalassemia patients might help in the formulation of interventions.

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EP279
Malnutrition risk using morphofunctional evaluation in hematopoietic stem cell transplantation
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Background
Malnutrition affects 50-50% of patients with hematological malignancies; it is due to the disease itself, the treatment-related catabolic process and chemotherapy side effects (nausea, vomiting, diarrhea and mucositis). Patients with poor nutritional status have increased morbidity (treatment complications, infections, mucositis) and mortality.

Aim
To evaluate the nutritional status of all patients that underwent hematopoietic stem cell transplantation (HSCT) in our center during April-November 2021

Methods
A novel morphofunctional nutritional evaluation (including electrical bioimpedance, handgrip dynamometry, biochemistry, abdominal adipose ultrasound and rectus femoris muscle ultrasound) was performed baseline and 24±9 days after HSCT.

Results
Forty-eight patients were included; mean age 50.2±14.6; 62.5% males. Lymphomas was the most common cause of HSCT (35%), and most patients underwent an autologous transplant (56.3%). At baseline severe and moderate malnutrition (using the GLIM criteria) were observed in 21% and 37.5% of patients respectively, despite only 21% presented with BMI <20 kg/m2. Patients lost weight during the study period (5.6±3.1%; p<0.05), especially fat free mass (16.7±2.3 vs 18.4±6.5; p<0.05), serum albumin levels, superficial and deep abdominal adipose tissue, as well as the occurrence of rectus femoris significantly decreased in most patients during follow-up (p<0.05).

Conclusions
Malnutrition is observed in more than 50% of patients before the HSCT despite normal or increased BMI. Significant weight loss during the first days after HSCT worsens the nutritional status of these patients. The novel morphofunctional nutritional evaluation provides early and additional information that could have prognostic value. Routine nutritional evaluation should be performed in all patients before HSCT.

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EP280
C-peptide response to standardized test meal in patients with newly diagnosed type 2 diabetes mellitus
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Background
Optimal testing of beta-cell dysfunction is still elusive. Oral based solid-food tests could superiorly approximate real-life stimulation by incorporating incretin activation. Increased body fat was recently associated with better preserved beta-cell secretory response, due to gluco-lipotoxicity induced adaptation.

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EP282

Nurses knowledge in diabetes self-management education in Sfax, Tunisia

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Introduction

Diabetes mellitus is a major public health problem affecting all ages worldwide. In Tunisia, 18% of the population has diabetes mellitus. In fact, it is one of the first ten causes of death in our country. Therefore, self-management education for diabetic patients plays an important role in reducing diabetes complications and mortality rate. The education is conducted not only by doctors, but also by nurses.

Purpose

The aim of this study is to determine the nurses’ knowledge in diabetes self-management education (DSME) methods.

Methods

We are presenting a descriptive study including 32 nurses, 17 nurses from the endocrinology department of Hedi Chaker hospital, Sfax, Tunisia, and 15 nurses from the healthcare dispensary Mohamed Ali Sfax, Tunisia.

Results

The majority of nurses: 62.50% were young, aged between 25 and 40 years old, 78% of them were female and 78.5% were married. We discovered that only 63% of the nurses were involved in nurse-led DSME and did actually have specific training in DSME. The nurses believed that the purpose of DSME is essentially to prevent complications (36%), to lead as normal a life as possible (30%), and to obtain a balanced blood sugar (18%) and to improve the patient’s life (16%). Only 6.25% of the nurses had real good knowledge in DSME vs 18.75% having average and poor knowledge respectively. The majority of the female nurses (56.25%) had average knowledge in DSME vs 18.75% in the male group, and only 6.25% of the female nurses knew how to properly educate the diabetes patients vs 20% in the male nurses. Total absence of DSME knowledge was mostly described in the youngest group of nurses (25-40 years old) with an average of 18.75% vs 0% in older nurses (> 40 years old). We noted that nurses having more than 10 years work experience were more efficient in educating the patients than those with less work experience. Finally, we asked the nurses to provide solutions on how to get more information about DSME; 50% of them proposed attending seminars, 44% proposed organizing ongoing training sessions and 6% didn’t comment.

Conclusion

In recent years, great emphasis has been placed on the role of non-pharmacological self-management in the care of patients with diabetes. Studies have reported that nurses, compared to other healthcare professionals, are more likely to promote preventive healthcare seeking behaviors.

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EP283

Pharmacogenomics and efficacy outcome of therapy with glucagon-like peptide-1 receptor agonists in type 2 diabetes

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Introduction

Individual variability in drug efficacy and safety due to genetic diversity is a major challenge for clinicians. Pharmacogenomics deals with inherited differences in the efficacy and safety responses to drugs. The incidence of type 2 diabetes (T2D) is increasing worldwide and the disease is reaching pandemic proportions. T2D is treated by oral and/or injectable drugs. The interindividual variability of T2D drug actions may be caused, at least in part, by genetic factors. This review outlines the contribution of pharmacogenomics to the efficacy outcome of glucagon-like peptide-1 receptor agonists (GLP1RAs) therapy in T2D.

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Methods
A systematic search of literature was conducted using the search terms pharmacogenomics, type 2 diabetes, glucagon-like peptide-1 receptor agonists, and efficacy.

Results
Pharmacogenomics has identified the relevance of approximately 56 genes in the response to 7 pharmacological classes of antidiabetic drugs. More than 460 million people worldwide have T2D. According to the American Diabetes Association and the European Association for the Study of Diabetes, GLP1RAs are recommended as a second-line treatment in the management of T2D when there is no evidence for combination therapy. The identified genes influencing the efficacy outcome of GLP1RAs treatment included single nucleotide polymorphisms (SNPs) of GLP1R (increased or decreased efficacy with rs6923761, rs3765467, rs10305420, and rs761386 SNPs), TCF7L2 (increased efficacy with rs7903146 SNP), CNR1 (increased efficacy with rs1049333 SNPs), 5OR3C (increased efficacy with rs1416406 SNPs), and WFS1 (decreased efficacy with rs10010131 SNP).

Conclusion
Pharmacogenomics is an important tool in medicine. Education of clinicians is essential for the implementation of genetic testing into clinical practice. The use of genotype-guided dosing can help obtaining better efficacy and safety outcomes with drugs. Potential genomic markers for targeted GLP1RAs therapy have been identified. However, the number of studies is relatively limited and more comprehensive research including larger populations is needed to determine the therapeutic implication of incorporating precision medicine with the utilization of GLP1RAs in T2D.

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EP284
Factors affecting glycemic outcomes using closed-loop systems in real-world
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Aims
To evaluate real-world efficacy of closed-loop systems (CLS) (Minimed™ 780G, DBLGI -Diabeelloop- and Control-IQ™ Tandem) as well as to assess those predictive factors related with the achievement of near-normal glycemic control.

Methods
A prospective, longitudinal, and observational study was performed. It included T1D adults who initiated CLS between April 2021 and December 2021 in our hospital and provided data for ≥3 months (ninety of 130 CLS users were included). We evaluated the initial and three-months data regarding glycemic outcomes and their baseline characteristics.

Results
Ninety T1D were included (54 female, 45.1 ± 11.3 years, 76.2 ± 16.0 kg weigh, 27.4 ± 4.9 kg/m² BMI, baseline HbA1c 7.5 ± 0.9%). 41% were previously under multiple daily injections (MDI), 91% used continuous glucose monitoring (CGM) and 56% used an insulin bolus advisor. Different commercial CLS were used: 54 DBLGI, 18 Control-IQ™ and 18 Minimed™780G. After three months, HbA1c significantly decreased to 6.9% ± 0.7% (+0.6% ± 0.1%, p<0.001). 58% achieved HbA1c ≤7%, 25% HbA1c 7-7.5% and 17% HbA1c >7.5%. Mean glucose management indicator (GMI) was 7.0% ± 0.4% (45% GMI <7%, 13% GMI =7% and 100% GMI ≤7%). Mean time in-range (TIR) was 73% ± 10% (67% TIR >70%) and mean time below range 54-69 mg/dl (TBR) was 1.4% ± 1.0%. Optimal glycemic control was observed among people with higher education level (GMI 6.8% ± 0.3% vs 7.1% ± 0.4%, p<0.04) and among people under 45 years old (HbA1c 6.7% ± 0.1% vs 7.1% ± 0.1%, p<0.04). We observed a positive trend towards better glycemic control in women (TIR >70% 71% vs 61%) and in those people who exercise regularly (HbA1c ≤7% 75% vs 54%; TBR <4% 0% vs 8%). overweight didn’t affect glycemic control. Regarding prior treatment, a higher percentage of patients with insulin pump obtained optimal glycemic control compared with MDI (HbA1c ≤6.5% 34% vs. 22%). Similarly, the previous use of insulin bolus advisor related to a higher proportion of optimal HbA1c (HbA1c ≤6.5% vs 21%). We observed a better glycemic control with the Minimed™780G system (GMI =6.7% vs. 7.0% DBLGI and 7.0% Control-IQ™, TIR >70% 81% vs 65% DBLGI and 59% Control-IQ™ (n.s.), better TAR and TBR, but no differences in HbA1c.

Conclusions
In almost all cases the use of a CLS improved glycemic control substantially. Factors that lead to an optimal glycemic control are higher education level, younger age and the CSL system used. Other factors that could influence glycemic outcomes are female sex, previous use of insulin pump and/or insulin bolus advisor and regular exercise. Partially funded by ISCIII (PI18/01118).

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EP285
Predicting the effectiveness of metformin in patients with type 2 diabetes mellitus from molecular genetic positions
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Purpose
To assess the possibility of predicting the effectiveness of pharmacotherapy with metformin in patients with type 2 diabetes mellitus (DM2) depending on the single nucleotide polymorphism of the nitric oxide synthase gene.

Materials and methods
186 patients were examined, referred for planned hospitalization, the duration of DM2 was 6-8 years, the target level of glycated hemoglobin was 7.5%, the actual level was 8.3%. All patients were prescribed metformin. Single nucleotide polymorphism of the gene (SNP) eNOS3 C786T (rs 2070474) was determined by real-time PCR, the level of Klotho protein was determined by ELISA, and the level of glycated hemoglobin was determined by BioRad. According to the results of the genetic study, the patients were divided into three groups: with the CC, TC and TT genotypes (SNP) eNOS3 C786T (rs 2070474).

Results
Patients with genotype CC achieved and maintained glycated hemoglobin levels below the target in 86% of cases when metformin was used at a dose of 1700 mg per day. In the same group, the Klotho protein level was significantly higher than in the other groups (P<0.05).

Conclusions
The use of metformin as monotherapy at a dose of 1700 mg/day may sometimes be sufficient in the presence of the CC genotype. The patients with TC and TT genotypes need to the combined hypoglycemic pharmacotherapy at the start.

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EP286
Age-related changes in proinsulin processing in non-diabetic individuals
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Introduction
To understand the pathological changes associated with glucose homeostasis in old age, it is necessary to know the natural changes in the processing of proinsulin into mature insulin. Surprisingly, while there is abundant information about insulin function in diabetics, the situation in healthy adults and old humans was rarely examined.

The study aimed
to determine how the proinsulin secretion in individuals with normal glucose tolerance changes during the process of natural aging.

Methods
A total of 761 individuals (539 women, 222 men) with normal glucose tolerance were divided into groups according to age: 1) 18-30 years 355 persons, 2) 30-45 years 234 persons, 3) 45-60 years 103 persons, 4) 60-75 years 58 people, 5) 75-90 years 11 people.

Basal blood glucose, proinsulin, insulin, C-peptide levels, HOMA-R, BMI and proinsulin/insulin, proinsulin/C-peptide,
proinsulin/glycemia ratios were monitored. Parameters were compared between age groups, separately for women and men. Statgraphics software (Kruskal-Wallis, Dunn’s test, P<0.05).

Results

Blood glucose levels increased with age. The age categories up to 30 and up to 45 years had the lowest levels and differed from the older groups. The older categories no longer differed. HOMA-R increased with age and matched the development of BMI in the categories. HOMA-R was highest in women in the 60-75 category and men in the 45-60 category. Basal insulin and C-peptide levels depended on gender. For women, the highest levels were in the category of 60-75 years, for men already in the category of 45-60 years. Proinsulin levels were highest in the youngest women under the age of 30, then decreased with age and the differences were no longer significant. In men, proinsulin levels did not differ with age. The proinsulin/insulin ratio was highest in both sexes under 30 years of age. The proinsulin/glycemia ratio was also highest at age 30, but only in women. The insulin/C-peptide ratio did not change with age.

Conclusion

A cross-sectional analysis of basal proinsulin secretion in normoglycemic individuals showed that its levels were surprisingly highest in the 18-30 age group, especially in young women. The proinsulin/insulin ratio was also highest in the youngest, both sexes. All people, including normoglycemic, develop insulin resistance with age. We showed a slight age-dependent increase in insulin and C-peptide secretion, the peak of which was different in men and women. However, in normoglycemic subjects, proinsulin secretion did not increase with age. 

Table 6

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Children with β-TM and NGT (n: 9)</th>
<th>Children with β-TM and isolated IFG (n: 9)</th>
<th>Controls (n:9)</th>
<th>P-value A vs. B</th>
<th>P-value A vs. C</th>
<th>P-value B vs. C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological age (yrs)</td>
<td>5.41 ± 0.72</td>
<td>5.59 ± 1.73</td>
<td>5.14 ± 0.4</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (Males/Females)</td>
<td>4/5</td>
<td>6/3</td>
<td>5/4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.5 ± 2.9</td>
<td>18.1 ± 2.7</td>
<td>18.1 ± 3.1</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Serum ferritin (ng/ml)</td>
<td>1,867 ± 654.9</td>
<td>1,848 ± 307.0</td>
<td>-</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>ALT (UI)</td>
<td>117.3 ± 92.9</td>
<td>74.11 ± 46.67</td>
<td>-</td>
<td>NS</td>
<td>NS</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>84.7 ± 7.3</td>
<td>198.4 ± 5.0</td>
<td>76.3 ± 7.4</td>
<td>&lt; 0.001</td>
<td>NS</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Plasma glucose 2-h after OGTT (mg/dl)</td>
<td>105.6 ± 13.6</td>
<td>107.1 ± 18.6</td>
<td>86.0 ± 12.0</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>8.88 ± 1.96</td>
<td>10.5 ± 2.7</td>
<td>3.7 ± 2.7</td>
<td>NS</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MATSUEDA INDEX (MI O-120)</td>
<td>6.70 ± 2.24</td>
<td>6.38 ± 2.28</td>
<td>17.11 ± 6.7</td>
<td>NS</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.92 ± 0.53</td>
<td>2.85 ± 0.77</td>
<td>0.72 ± 0.52</td>
<td>&lt; 0.05</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Insulinogenic Index (IGI)</td>
<td>0.53 ± 0.29</td>
<td>0.74 ± 0.68</td>
<td>0.75 ± 0.16</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Oral disposition index (ODI)</td>
<td>3.45 ± 2.11</td>
<td>4.01 ± 3.82</td>
<td>12.92 ± 5.11</td>
<td>NS</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

DOI: 10.1530/endoabs.81.EP286

DOE: 10.1530/endoabs.81.EP287
We assessed glyemia and insulin markers in 18 young children with beta thalassemia major (BTM). Insulin markers measured included: the Homeostatic Model Assessment index of insulin resistance (HOMA-IR), Matsuda index (MI), the insulinogenic index (IGI), and the oral disposition index (oDMI). 9/16 had normal fasting glucose (FG) and 9 had impaired fasting glucose (IFG).

Results
HOMA-IR, a marker of IR was significantly higher in children with BTM compared to normal controls. Fasting insulin was significantly higher in children with BTM patients vs normal children. Despite higher fasting insulin compared to controls thalassaemic children (group A) had higher fasting glucose levels. Both findings support an insulin resistance state early in these patients. oDMI was significantly lower in children with BTM (with and without IFG) compared to normal controls.

Conclusion
These findings supported the presence of significant insulin resistance in children with BTM on repeated blood transfusion and iron chelation

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**EP290**

Glycemic changes in relation to hepatic iron status in patients with non-transfusion dependent (NTD-SCD) and transfusion dependent sickle cell disease (TD-SCD).

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Introduction
We evaluated glyemia and the iron status in patients with NT-SCD and 6 patients with TD-SCD by measuring serum ferritin level (SF), liver iron content (LIC), alanine transferase (ALT) and fasting blood glucose (FBG) over 5 years of follow up.

Results
At the initial assessment, 16 adults with (age: ± 14 years), and six of TD-SCD (n = 6, age =± 10 years) were studied. SF of NT-SCD had SF > 500μg/L, and 5/6 had high LIC (> 36 μmol Fe/kg dry weight). FBG had elevated ALT concentrations. High ALT had high in 2/6, 1/6 had IFG. Five years later, 3/6 of NTSCD had DM and 2 had IFG. Those who developed DM had had LIC at 13, 75, and 22 mmol/kg 5 years before the development of DM. The 2/6 who developed IFG had had LIC at 27 and 39 mmol/kg DW. In TD-SCD, 2/6 developed DM and 1/6 had IFG. Those who developed DM had had LIC at 127 and 20 mmol/kg and normal FBG 5 years before the development of DM. The one with IFG had previously had LIC at 22 mmol/kg and normal FBG 5 years back. Echocardiography revealed abnormalities of the left ventricle, dilated left atrium and dyskinesis in 5/22.FBG was correlated significantly with the age of patients (r = 0.68, P < 0.01) but did not correlate with ferritin, LIC or BMI. LIC was correlated significantly with SF (r = 0.89, P < 0.001).

**Table**

<table>
<thead>
<tr>
<th></th>
<th>(A) Age yr</th>
<th>HB g/dl</th>
<th>SF ng/ml</th>
<th>FPG mmol/l</th>
<th>LIC mmol/kg d.w.</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTD-SCD</td>
<td>33.0 ± 14*</td>
<td>10.1 ± 1.9</td>
<td>772 ± 1300</td>
<td>4.7 ± 0.7</td>
<td>1.9 ± 1.7</td>
</tr>
<tr>
<td>TD-SCD</td>
<td>24.8 ± 10</td>
<td>8.5 ± 0.8</td>
<td>3310 ± 2078*</td>
<td>4.6 ± 0.7</td>
<td>11.1 ± 13.3*</td>
</tr>
<tr>
<td>(B)</td>
<td>NTD-SCD</td>
<td>38.3 ± 14*</td>
<td>9.5 ± 1.2</td>
<td>550 ± 467</td>
<td>6.4 ± 2.0</td>
</tr>
<tr>
<td>TD-SCD</td>
<td>30.6 ± 10</td>
<td>8.9 ± 0.9</td>
<td>2767 ± 2925*</td>
<td>5.9 ± 1.1</td>
<td>16.1 ± 8.9*</td>
</tr>
</tbody>
</table>

*p < 0.05 NTD-SCD vs. TD-SCD

Conclusions
A significant number of our patients with ND-SCD and TD-SCD develop dysglycemia (IFG, and DM) that is correlated with age but not correlated with BMI. Glycemic data and iron status in patients with NT-SCD vs TD SC at the beginning of the study (A) and after 5 years of follow-up (B) (mean ± SD).

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**EP291**

Description of patients with diabetic foot of neuropathic and vascular cause cared for in a multidisciplinary Diabetic Foot Unit

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Objective
6% of people with diabetes present with diabetic foot as a complication, which means greater morbidity and mortality compared to those who do not. Its diagnosis and management by multidisciplinary teams including surgeons can improve these patients’ care. The objective was to analyze the main characteristics of patients and health results obtained, as well as to evaluate the impact of PAD (peripheral artery disease) existence in patients cared for in our multidisciplinary Diabetic Foot Unit.

DOI: 10.1530/endoabs.81.EP289
Research Design and Methods
Observational prospective study. 273 patients from two different populations (with and without PAD - classified according to the presence of distal pulses) attended in a 14-month period in the multidisciplinary Diabetic Foot Unit were included. Data on patient’s characteristics and outcomes were analyzed in order to compare them. For inference study, a comparison of medians with the non-parametric test for independent samples for the quantitative variables and an X2 test for the comparison of proportions in qualitative variables were performed.

Results
n = 273

| Table |
|------------------|------------------|
| With pulse       | Without pulse    |
| N                | 135              | 138              |
| Male             | 108(80%)         | 95(69%)          |
| Age*             | 60(54-67)        | 64(75-81)        |
| HbA1c(%)         | 7,6(6,7-9,5)     | 6.9(5,6-8,0)     |
| Type 2 Diabetes  | 118(87%)         | 128(93%)         |
| Previous ulcers* | 71(52%)          | 37(27%)          |
| Hypertension*    | 88(65%)          | 114(82%)         |
| Dyslipidemia*    | 78(60%)          | 107(77%)         |
| Smoking history  | 83(61%)          | 63(46%)          |
| Nephropathy      | 47(35%)          | 48(35%)          |
| Retinopathy*     | 45(30%)          | 28(32%)          |
| Coronary disease*| 11(8%)           | 40(29%)          |
| Cerebrovascular disease* | 9(7%)       | 25(18%)          |
| Number of consultations* | 3(1-6) 38(28%) | 1(1-2) 49(35,5%) |
| Amputation Major amputation* | 31(23%) | 2(1,4%) 43(31%) 17(12,3%) |
| Antibiotherapy* Intra-venous antibiotic Revascularization* | 87(64,4%) 38(28%) | 71(51,4%) 44(32%) 28(20%) |

*p < 0.05

Conclusions
Patients with PAD are older, and presented with a greater macrovascular burden and a history of previous ulcers. However, patients with neuropathic foot presented with more microvascular complications, with similar metabolic control in both groups.

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EP293

HbA1c response after initiation of flash glucose monitoring in adults with diabetes

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Hospital General La Mancha Centro, Alcázar de San Juan, Spain

Introduction and Objective
Flash glucose monitoring is a form of interstitial glucose monitoring and it is indicated in patients with diabetes mellitus. The objective of the study was to assess the effect of introducing flash glucose monitoring in adults with diabetes with respect to change in hemoglobin Alc (HbA1c).

Material and Methods
Prospective observational study of adults with diabetes in our center, in whom a prescription for a flash glucose monitoring sensor was collected, started between June and November 2020. Primary outcome was change in HbA1c 12 months after initiation of flash glucose monitoring. Changes in fasting blood glucose 12 months after the start of monitoring were also studied.

Results
77 subjects (55.8% men) were analysed with an average age of 47.3±13 years old with diagnosis of diabetes (71,4% DM1, 26% LADA, 2,6% DM2). The average of month with diagnosis of diabetes of our subjects were 169.8±10.3 months. Only 26% of subjects were well trained in the correct calculation of carbohydrate portions. We observed how the average HbA1c baseline 7.87±1.2%, and 12 after initiation of flash glucose monitoring was 7.33±1.2%, this results was statistically significant finding (P<0.001). Likewise, statistically significant changes in fasting blood glucose were found, baseline 108.9±7.4 mg/dl and 12 months after initiation of flash glucose monitoring 140.3±48.9 mg/dl. No changes were observed in either weight or insulin dose.

Conclusions
Flash monitoring is associated with significant reduction in HbA1c and fasting blood glucose in people with diabetes. Multiple causes can justify said improvement, and more studies are necessary to demonstrate the reason for these changes.

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EP294

The melatonin receptor gene polymorphism rs10830963 is not associated with significant differences in sleep patterns and biorhythms.

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1Institute of Endocrinology, Department of Molecular Genetics, Prague, Czech Republic; 2Faculty of Science, Charles University, Molecular Biology and Biochemistry, Prague, Czech Republic; 3Institute of Physiology, The Czech Academy of Sciences, Biological Rhythms, Prague, Czech Republic

The average of month with diagnosis of diabetes of our subjects were 169.8±10.3 months. Only 26% of subjects were well trained in the correct calculation of carbohydrate portions. We observed how the average HbA1c baseline 7.87±1.2%, and 12 after initiation of flash glucose monitoring was 7.33±1.2%, this results was statistically significant finding (P<0.001). Likewise, statistically significant changes in fasting blood glucose were found, baseline 108.9±7.4 mg/dl and 12 months after initiation of flash glucose monitoring 140.3±48.9 mg/dl. No changes were observed in either weight or insulin dose.

Conclusions
Flash monitoring is associated with significant reduction in HbA1c and fasting blood glucose in people with diabetes. Multiple causes can justify said improvement, and more studies are necessary to demonstrate the reason for these changes.

DOI: 10.1530/endoabs.81.EP294
Introduction
Melatonin is a crucial hormone for controlling sleep rhythms and disruption of its normal secretory rhythmity is considered to be one of the causes of type 2 diabetes mellitus. The MTNR1B gene encodes the melatonin receptor. Polymorphism rs10830963 in this gene shows an association with fasting blood glucose and impaired glucose tolerance. Current studies suggest that carriers of the minor allele G have a slightly shifted cycle of melatonin secretion toward a later rise in the evening and a slower decline in the morning, which may interact with social factors on early morning activity and thus adversely affect glucose regulation. The aim of this study was to determine whether the polymorphism is projected into sleep patterns, biorhythms and chronotype evaluated through a questionnaire.

Methods
A total of 268 volunteers completed the MCTQ (Munich chronotype questionnaire) to determine sleep habits and chronotype. The average age did not differ significantly between the compared genotype groups. The ratio of women/men in the groups was also similar. Genotyping was performed on a TaqMan instrument (LC480, Roche), data were evaluated by NCSX/Pass 2020.

Results
Minor variant G was present in a heterozygous constellation in 124 participants (46%) and in a homozygous constellation in 26 (10%) with an allele frequency of 59.2%. The remaining 118 individuals (44%) were homozygous in the common variant C. The average length of sleep on weekdays and days off did not differ between the groups, nor did the mid-sleep phase on weekdays and days off. The chronotype calculated from the mid-sleep phase values corrected for sleep debt accumulated during working days was also comparable. The time of subjective maximum daily activity was similar in all three genotype groups, with a median at 11 a.m. The social jat lag resulting from the discrepancy between the natural biorhythm and work/social duties averaged 0.85 ± 0.698 h regardless of genotype. Interestingly, while in the groups with CG and CC genotype there were about 9% of people with very low caffeine consumption, in the group of homozygous GG carriers, individuals with low caffeine requirement were completely absent.

Conclusion
In the sample of the Czech population, we did not observe significant differences in sleep patterns and chronotype between the groups formed depending on the rs10830963 SNP genotype of the MTNR1B gene. Grant support: N2U20-01-00308 and MZ CZ RVO UE0023761

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EP296
Impact of glucoregulation and duration of diabetes on the incidence of diabetes chronic complications in Republic of Srpska/Bosnia and Herzegovina
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Background/Aim
Importance of glucoregulation quality in diabetes complication prevention was proven in numerous clinical studies. Aim of this study is to determine impact of glucoregulation and duration of diabetes on the incidence of chronic complications of diabetes in Republic of Srpska (RS).

Method
Study model included subjects with T1D and T2D who participated in the two-year project in the RS. It was a cross-sectional study with 1088 participants. Specially designed questionnaire included data obtained by objective trial, clinical examination, data on antihyperglycemic treatment, and patient’s record data regarding diabetes and diabetes complications. The quality of glucoregulation was assessed based on glycosylated hemoglobin (HbA1c) values.

Results
Finally, study included 1037 subjects, 4.6% with T1D and 95.4% with T2D, 576 women (55.5%) and 461 (44.5%) men. Poor glycemic control (HbA1c ≥ 6.5%) was found in 61.1% of subjects (χ2 = 4.874, df = 1, P = 0.027) and percentage of this patients increased with longer diabetes duration. Among patients with diabetes, more than 10 years’ duration, poor glucoregulation (HbA1c ≥ 6.5%) was recorded in 84.6% with T1D and 76.1% with T2D; with less than 5 years’ duration was recorded in 58.30% of patients with T1D and 48.0% with T2D. The most common complication was neurosensory foot (55.8%), statistically significantly more frequently observed in patients with HbA1c ≥ 6.5% (χ2 = 5.229, df = 1); microalbuminuria (49.2%) was reported most frequently in diabetes of 5-10 years’ duration. Polyneuropathy (42.5%) and microalbuminuria were more common in T2D (χ2 = 10.217, df = 1, P = 0.001), while retinopathy (25%) was more common in T1D. Microvascular complications were statistically significantly more common in patients with unsatisfactory glucoregulation as well as longer duration of diabetes, especially in patients with T2D and disease duration over 10 years. Cardiovascular disease was recorded in 82.0% of T2D patients with HbA1c ≥ 6.5% and in 82.1% of those with HbA1c ≤ 6.5%, with no statistically significant difference with regard to glucoregulation quality.

Conclusion
It can be concluded that 3/5 of diabetes patients in RS (61.1%) have poor glucoregulation. Microvascular complications, have higher incidence in patients with poor glucoregulation. Longer T2D duration significantly increases incidence of microvascular complications, especially disease duration of 10 years or more. Cardiovascular complications are present in high percentage regardless of quality of glycemic control. These results are similar to results from developing countries and indicate the need for implementation of additional, interventional measures for improving glucoregulation and reducing chronic complications in patients with diabetes in RS.

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EP297
Cochleo-vestibular disorders in diabetic patients
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Introduction
Cochleovestibular disorders in patients with diabetes is not well known as compared to other complications. The aim of this study was to evaluate the epidemiological, clinical and paraclinical characteristics of cochleovestibular dysfunction in diabetes.

Materials and Methods
This is a retrospective study of 100 diabetic patients. The patients had a clinical otological and vestibular examination as well as a tonal audiometry and a video nystagmography.

Results
The mean age of our patients was 50.97 years with extremes ranging from 17 to 82 years. A female predominance was noted with a sex ratio of 0.66. The mean

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duration of diabetes was 10 years with extremes ranging from 5 to 27 years. The diabetes was type 1 in 22 cases and type 2 in 78 cases. Degenerative complications were noted in 20% of cases. These included diabetic retinopathy alone in 7% of cases, diabetic neuropathy in 6% of cases and both complications in 7% of cases. Deafness was noted in 32 cases (32%). It was a sensorineural hearing loss in all cases, more important in the medium to high frequencies. The hearing impairment was more severe in type 1 diabetes. Vestibular involvement (peripheral and/or central) was present in 24 cases (31.5%). An analytical study analyzing epidemiological characteristics, metabolic control, and the presence of degenerative complications did not find statistically predictive factors for cochleovestibular involvement.

Conclusion
In our study, we did not find any predictive factor for vestibular impairment in diabetics. However, this is only preliminary data, because our study did not include non-diabetic controls.

DOI: 10.1530/endoabs.81.EP297

EP298
Precipitating factors of diabetic ketoacidosis
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Introduction
Diabetic ketoacidosis (DKA) is one of the most serious acute complications of diabetes mellitus (DM). In some studies, infections have been shown to be a precipitating factor in half of the subjects. On the other hand, several recent studies emphasise that poor treatment adherence is also a common cause of DKA.

Objective
To identify the most common precipitating factors for DKA in the Republic of Croatia.

Patients and Methods
This retrospective, multicentre study included DM type 1 or DM type 2 patients diagnosed with DKA between January 1, 2014, and December 31, 2018, and treated in 5 different hospital treatment centres: Dubrovnik, Našice, Split, Zagreb, and Osijek. Only the first episode of DKA was included in the analysis. Patients suffering from steroid DM and DM due to endocrine disorders such as acromegaly and Cushing’s syndrome were excluded.

Results
The study included 160 patients (55% men), 68% of whom had DM type 1. The median age of the respondents was 42 years (18-89). The most common cause of DKA was infection (57%), followed by poorly controlled DM (37%) and first presentation of DM (10%). In 6% of the patients DKA was due to other causes such as insulin pump failure, stroke or myocardial infarction. In the group of patients with infections, urinary tract infections (30%), gastrointestinal infections (30%), and respiratory tract infections (19%) were the most common, while 21% of patients had other sources of infection. In 39% of these patients, previously poorly controlled diabetes was present along with the infection, and in 12% of them, DKA caused by the infection was the first manifestation of the disease. In patients with DM type 2, infections were more frequently the cause of DKA than in patients with DM type 1 (P<0.05). In patients with DM type 1, poorly regulated glycaemia is obviously more often the cause of DKA (31.2%) than in patients with DM type 2 (17.7%).

Conclusion
The most common precipitating factors for the development of DKA are infections and poor diabetes management, likely due to lack of patient cooperation with insulin treatment and inadequate education about the use of insulin therapy in acute illness.

DOI: 10.1530/endoabs.81.EP298

Is the 2009 CKD-EPI more accurate with or without the race coefficient for black adults from outside the United States?
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Introduction
Diabetes is the leading worldwide cause of chronic kidney disease, which is diagnosed by measuring albuminuria and estimating glomerular filtration rate (GFR) with creatinine-based formulas, such as the 2009 CKD-EPI developed in the United States of America (USA). Nonetheless, the race coefficient (RC), present in the 2009 CKD-EPI, may overestimate GFR in other countries.

Aim
The goal of this systematic review and meta-analysis was to assess the accuracy, measured by P30 (percentage of estimated results within 30% of measured GFR), of the 2009 CKD-EPI in estimating GFR with and without the RC in black adults outside the USA.

Methods
A bibliographical search of PubMed and Embase was performed and last updated on December 5th, 2021. Eligible studies included 2009 CKD-EPI P30 accuracy values with or without the RC for black adults outside the USA. Studies which used inadequate measuring methods of GFR were excluded. Our study is registered in PROSPERO (CRD42021236613) and reported according to the PRISMA-DTA guideline. The data was extracted by independent pairs of reviewers and was pooled using a random-effects model.

Results
Our systematic review included 11 studies, with a total of 1834 black adults from Africa, South America and Europe. Eliminating the RC in the 2009 CKD-EPI formula significantly increased P30 accuracy results in these populations (from 61.9% [95% CI, 53% to 70%] to 72.9% [95% CI, 66.7% to 78.3%]; P<0.03).

Conclusion
Outside the USA, the 2009 CKD-EPI should not be used with the RC, even though it is not sufficiently accurate (P30 below 75%). Thus, we endorse KDIGO guidelines to use exogenous filtration markers in black patients outside the USA when a more accurate estimation of GFR may impact clinical conduct.

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EP300
A patient with aniridia and Type 1 diabetes mellitus
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Introduction
Aniridia is a rare congenital condition which is characterized by a complete or partial absence of the iris and fovea and malformations of the lens and anterior chamber. It is usually related to mutations in PAX6, a member of a multigene family of transcription factors, which is important for the development of the nervous system, the eyes and also the endocrine pancreas and it is found to be associated with mild glucose intolerance. Complete loss of insulin secretion is rarely described and here we present such a case.

Presentation
A seventeen years old male, with congenital bilateral aniridia, and no other past medical history, referred to our department due to polydipsia, polyuria, fatigue and weight loss (10 kilograms the last five months) gradually worsening. On clinical examination his BMI was 27.73 kg/m2, blood pressure 120/70 mmHg, pulses 82/min and he was dehydrated. From his laboratory exams his blood glucose was 391 mg/dl, glycosylated hemoglobin (HbA1c) 9.5%, C-peptide 0.6 ng/ml, Glutamic acid decarboxylase antibodies (Anti-GAD) and Pancreatic Islets antibodies (Anti-ICA) were both positive. On these findings the diagnosis of type 1 diabetes mellitus (T1DM) was made and the patient was started on insulin (basal – bolus regime). His father was fifty two years old and had also congenital aniridia and diabetes mellitus (T1DM) was made and the patient was started on insulin (basal – bolus regime). His father was fifty two years old and had also congenital aniridia and type 2 diabetes mellitus treated with oral hypoglycemic agents. A genetic test for the PAX6 gene was sent and results are expected.

Conclusion
Aniridia is a rare inherited condition and is mostly related to glucose intolerance and mild diabetes, but complete loss of insulin secretion and T1DM can also be found. Patients with aniridia need a close follow up, so that any disorder of glucose metabolism be detected on time.

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**EP301**

Endogenous hyperinsulinism and diabetes remission: A report of 2 cases

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Introduction

Diabetes is a chronic, progressive disease characterized by elevated levels of blood glucose. In type 1 diabetes, some patients experience a “honeymoon period” shortly after diagnosis, wherein insulin needs decrease significantly and a few studies have demonstrated that drug-free glycemic control can be achieved in type 2 diabetes. We describe 2 unusual cases of endogenous hyperinsulinism and diabetes remission.

Case presentation 1

A 43 year-old female who was referred to our hospital for evaluation of recurrent episodes of hypoglycemia. She was diagnosed with type 1 diabetes at the age of 17 after an episode of Diabetic Ketoacidosis. She was treated with insulin for 6 years. During the last year, she experienced recurrent episodes of hypoglycemia that have persisted regardless of the progressive withdrawal of insulin therapy with no episodes of hyperglycemia. In the first 48 hours of glycemic control in hospital care, a symptomatic hypoglycemia was documented and a blood sample showed that her plasma glucose was 62 mg/dl, insulin level was 3.3 mU/ml and C-peptide was 1.04 ng/ml. These levels confirmed endogenous hyperinsulinism.

Case presentation 2

A 24 year-old female who was admitted to the hospital for hypoglycemia. She had diabetes mellitus at the age of 33 and treated with insulin for the last 10 years. During the last year, she continued to have frequent hypoglycemic episodes, despite repeated dose reductions and finally she stopped the insulin therapy. Two months later, her fasting plasma glucose was 2.4 mmol/l. On admission, a blood sample showed that her plasma insulin level was 24.1 µU/ml, C-peptide was 0.43 ng/ml and cortisol was 49 nmol/l, while glucose level was 33 mg/dl. These levels were consistent with endogenous hyperinsulinism.

Conclusion

These cases highlight the possibility of diabetes remission induced by endogenous hyperinsulinism. Diabetes remission after years of insulin therapy is uncommon and it should be investigated thoroughly.

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**EP302**

Effects of glucagon-like peptide 1 analogue on eating behavior in patients with obesity

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Introduction

One of the objectives of weight loss in obesity is to prevent metabolic disorders. An important component in the maintenance of the achieved results is a change of eating behavior.

Goal

To study the effect of liraglutide 3.0 mg on the dynamics of metabolic parameters and eating behavior in patients with obesity.

Materials and methods

The study enrolled 42 obese patients in whom anthropometric parameters, metabolic parameters, and eating behavior were assessed with Dutch Eating Behavior Questionnaire (DEBQ). Patients were divided into 2 groups, one of which received liraglutide 3.0 mg with lifestyle modification for 3 months. The other group was recommended to receive only lifestyle modification. The participants were re-examined after 3 months.

Results of the study

In the liraglutide group in addition to a significant decrease in body weight, BMI and waist circumference, there was a statistical trend toward lower glucose, insulin and HOMA-IR levels. When comparing the dynamics of parameters between the groups, Δ body weight, BMI and glucose in the liraglutide group were significantly superior. In reassessment of eating behavior after 3 months of treatment, no statistically significant differences were found with the initial severity of restrictive, emotional, and/or external types in both groups and, despite a more pronounced decrease in body weight in the liraglutide group, between them.

Conclusions

Three months of isolated lifestyle modification and/or its combination with liraglutide 3.0 mg is not sufficient to make a lasting change in eating behavior. However, considering that obesity is a chronic and relapsing disease, the need for eating behavior correction remains relevant to prevent disease recurrence. This substantiates the need for more long-term intervention in obesity, including drug therapy.

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**EP303**

Prevalence of sarcopenia with different DXA indices in a population with high-risk obesity

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Background

Sarcopenic obesity (SO) is an entity characterized by excess fat mass (FM) and low muscle mass (LMM) and function. Excess FM itself can lead to loss of muscle mass (LMM) and function. Excess FM itself can lead to loss of muscle mass (LMM) and function.
mass and function at any age. The combination of obesity and sarcopenia is a proven risk factor for frailty, comorbidities and mortality. New diagnostic criteria have been developed for this entity.

Aims
To assess the prevalence and severity of SO with different indices by DXA, in a group of individuals with high-risk obesity (HRO).

Methods
Prospective observational study of individuals with HRO (BMI > 35 kg/m²) under follow-up by the obesity unit of the Complejo Asistencial Universitario de León. We collected demographic and anthropometric variables, body composition by dual energy X-ray absorptiometry (DXA, A Lunar Ida; GE Healthcare, USA), hand grip strength (HGS) (Dynex®DynApgrx) and physical performance with the timed up and go test (TUG). For the diagnosis of LMM with DXA, the equations appendicular skeletal muscle mass (ASM: lean mass arms and legs–bone mass arms and legs), appendicular skeletal muscle mass index (ASM/ASMheight²), total skeletal muscle mass index (TSMI; TSM/height²), TSMI/ASM:1.33), lower extremity skeletal muscle mass index (LESMI/LESM/height²), LEM: lean mass–bone mass index, appendicular lean mass index (ALMI/ALMheight²), ALM: lean mass arms + lean mass legs), skeletal muscle mass index (SMI;ASM/weight)<100) and appendicular lean mass/width (ALMC/ALM/weight×100) were used.

Results
124 subjects were included, 71.8% women, mean age 42.6 (SD 9.0) years, mean BMI 46 (SD 5.2) kg/m². The cut-off points and percentage of patients diagnosed with low strength, muscle mass and low physical performance are shown in the table below.

The prevalence of low muscle mass with DXA varies according to the parameter and setting used. The adjustment of DXA-derived parameters for muscle mass should be made according to the investigated cohort in terms of ethnicity, BMI, sex and age range. In this population, if we take into account the two criteria, muscle mass (with SMI) and muscle function (HGS), 13% of women and 17% of men will have sarcopenia, 4.5% and 11.4% severe sarcopenia respectively.

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**EP304**

Empagliflozin and arterial stiffness in type 2 diabetic patients: a real clinical practice case-control study

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Background
Sodium-glucose cotransporter-2 (SGLT2) inhibitors demonstrated beneficial effects on cardiovascular and renal events in patients with type 2 diabetes mellitus. The mechanisms underlying these effects are not fully elucidated. Aim of this study was to investigate whether empagliflozin is able to affect arterial stiffness/pulse wave velocity in type 2 diabetic patients.

Methods
Pulse wave velocity and other parameters of arterial stiffness were assessed before and after a 3-month treatment with empagliflozin in 16 consecutive T2DM outpatient; data were compared with 16 T2DM outpatients not treated with SGLT2 inhibitors.

Results
The sex of the patients and the duration of diabetes mellitus did not differ between groups. However age was significantly higher in the empagliflozin group at baseline compared to controls (64.1±8.68 vs 74.45±8.13, P < 0.05). Empagliflozin treatment significantly decreased HbA1c after 12 weeks of treatment (7.9±1.78 vs 7.04±1.09%, P < 0.008). After 12 weeks’ treatment, empagliflozin significantly improved PWV compared to controls not treated with SGLT2 (ΔPWV -0.68±1.1 vs 0.89±1.6, P < 0.004, P = 0.0065 with age and HbA1c as covariates). Moreover body weight significantly decreased in the empagliflozin group (-8.75 ± 16.16 vs 81.71 ± 16.5 kg, p = 0.001) compared to controls (in whom remained unchanged) as long as BMI (30.48 ± 5.4 versus 28.75 ± 5.66 kg/m², P < 0.002) compared to controls (in whom remained unchanged). Estimated glomerular filtration rate (eGFR) remained unchanged in the two groups during the study whereas urine Albumin to Creatinine ratio significantly improved with empagliflozin (17.8 ± 46.8 vs 12.2 ± 35.7 mg/mmol, P = 0.049).

Conclusions
In this real clinical practice study the potential effect of empagliflozin treatment on arterial function in T2DM patients was extensively investigated. Arterial stiffness was significantly decreased in the group treated with the empagliflozin and the difference was significant compared to the control group. Significantly improvement in urine Albumin to Creatinine ratio suggest an improvement of endothelial function in these patients that could be involved in reducing arterial stiffness.

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**EP305**

Association of single nucleotide polymorphisms (SNPs) of the intestinal fatty acid-binding protein (FABP2) gene with peripheral atherosclerosis in patients with type 2 diabetes mellitus.

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Relevance
There is a search for candidate genes that contribute to the progression of atherosclerosis in patients with diabetes mellitus. It has been suggested that the FABP2 Ala54Thr polymorphism may be associated with the risk of atherosclerosis.

Objective
To evaluate the relationship between polymorphism of the intestinal fatty acid-binding protein (FABP2) gene Ala54Thr with peripheral atherosclerosis in patients with type 2 diabetes mellitus.

Materials and methods
We examined 40 patients with type 2 diabetes, who were in the endocrinology department of the Regional Clinical Hospital. N. A. Semashko in September-November 2021. The duration of diabetes mellitus is from 2 to 18 years, glycated hemoglobin is 8.1 ± 0.93%. The patients’ age ranged from 43 to 76 years old. All patients had grade 1-2 obesity, dyslipidemia, 36 patients were diagnosed with arterial hypertension. Patients had micro and macrovascular complications of diabetes mellitus of varying severity. Glycemic indicators (HbA1c, glycemic fluctuations using FreeStyle monitoring), lipid profile, body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP) were determined, ultrasound examination of the vessels of the lower extremities and the brain was performed. Molecular-genetic study was carried out on the basis of the Regional Clinical Hospital named after N. A. Semashko. We saw FABP2 (rs1799883) Ala54Thr. DNA samples isolated from whole blood leukocytes using the DNA-Express-Blood-Plus reagent kit were used for analysis, followed by analysis of the isolated DNA by polymerase chain reaction (PCR) on a CFX-96 amplifier (Bio-Rad, USA). Used reagent kits (LifeTech, Moscow) in accordance with the instructions.

Results
A positive association of Ala54Thr with body mass index, blood pressure level was revealed. In 50% of cases, patients were diagnosed with GG SNP (Ala/Ala), in 28% of cases – GA SNP (Ala/Thr), in 22% - AA SNP (Thr/Thr). Indicators of glycemic control, levels of triglycerides and low density lipoproteins were significantly higher in patients with the AA (Thr/Thr) group. In the same group, a lower ankle-brachial index was noted (P = 0.04).

Conclusions
AA SNP genotype (Thr/Thr) is associated with an increased incidence of peripheral atherosclerosis in patients with type 2 diabetes.

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**EP306**

Retrospective analysis of association between coronary artery disease and Glycemic Control in South Indian T2DM population

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Background
Type 2 diabetes mellitus (T2DM) is independently associated with an increased risk for cardiovascular disease caused mainly by early development of vascular changes leading to atherosclerosis. Coronary artery disease (CAD) is one of the common complications. However, the exact correlation between glycemic control and the risk of developing CAD remains unclear. This study sought to assess the correlation of glycemic control and risk of developing CAD in South Indian population.

Methods
This retrospective analysis was conducted amongst 1888 patients with type 2 diabetes who visited a diabetes and cardiology care center in Tamil Nadu, India between January 2017 and December 2021. This study assessed glycemic and cardiometabolic parameters including HbA1c, blood pressure, lipid levels, electrocardiogram, and ECHO reports. The statistical analysis was conducted using SPSS software and Chi-square test was used.

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Diabetes mellitus and depression are two major public health problems which can coexist and influence each other. Identification of the predictive and associated factors with depression among diabetics can facilitate the task of clinicians.

**Objective**

Evaluate the socio-demographic and clinical factors associated with depression among patients having diabetes mellitus (DM).

**Materials and Methods**

A cross sectional study was conducted among 260 diabetic patients followed in the Endocrinology Department at “Taher Sfar University Hospital” in Mahdia, Tunisia. Patients with a psychiatric history were excluded at the outset. Depression was diagnosed according to DSM-V criteria and the severity determined via the Hamilton score scale.

**Results**

Our patients were aged between 20 and 91 years old. 62.7% of the participants in the study were women. The mean duration of the diabetic disease was of 9 years (from 1 to 50 years). Type 2 diabetes was found among 92.3% of patients. According to DSM-V diagnosis criteria, we found that 15% of our patients suffered from Major Depressive disorder (MDD). Among this group having MDD, 71.8% were female, 31% belonged to the age group 35-45 years and 53.8% were married. Matrimonial status wasn’t significantly linked to MDD but correlated with the severity of depression ($P = 0.048$). We also found that the majority of patients with MDD (84.6%), had at least one chronic disease in addition to diabetes and that a good proportion of them (69%) was treated with insulin. Both MDD and severity of depression were significantly linked to chronic complications of DM ($P \leq 0.001$ for both). Distal neuropathy was present among 39% of patients and this complication had a significant relationship with depression ($P = 0.025$).

**Conclusion**

Our study showed that diabetic patients suffering from MDD are mostly women but since proportion of women was most important in our study, these results should be evaluated. The relationship between depressive symptoms and insulin therapy can be explained by the arduousness of the injections and the increased risk of hypoglycemia causing depressive symptoms in one hand, and in the other by the failure to reach glycemic targets via other medications among depressive patients having poor treatment compliance. The risk of depression seems to be increased in diabetic patients suffering from chronic diabetic complications and screening for depression would be necessary in this case. Other studies should be conducted to determine if early screening of depression could delay insulin therapy or help prevent diabetes complications.

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**EP307**

**Predictive factors for distal and symmetric polyneuropathy in diabetic patients**

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**Introduction**

Diabetic neuropathy is the most common cause of neuropathy worldwide and is known to affect approximately half of all diabetic patients. It significantly impairs the quality of life of patients.

**Aim of the study**

To establish the predictive factors of distal symmetric polyneuropathy (DSPN) in diabetic patients.

**Methods**

This is a descriptive cross-sectional study including 116 patients. The diagnosis of PNDS was established according to the MNSI (Michigan Neuropathy Screening Instrument) and DN4 (Neuropathic Pain Diagnostic Questionnaire) scores. We divided the patients into two groups; group one (G1) patients with DSPN ($N = 67$) and group two (G2) without DSPN ($N = 49$). Then, using SPSS software, we were able to perform a multivariate study on independent predictive factors of DSPN as well as a univariate study of factors associated with this complication.

**Results**

Among the sociodemographic factors, only age was predictive of DPN with $P = 0.005$ (mean age: G1 64.85 +/- 12.56 years versus 58.27 +/- 11.88 years for G2). The analysis of the history showed that: nephropathy ($P = 0.002$), retinopathy ($P < 0.001$), myocardial infarction ($P = 0.037$), stroke ($P = 0.020$), hypertension ($P < 0.001$) and dyslipidemia ($P = 0.006$) were associated with DSPN. Symmetrical and peripheral polyneuropathy was found in 64 subjects with a diabetes duration of more than five years ($P = 0.015$), in 57 with unbalanced diabetes ($P = 0.024$) and in 34 with a history of hospitalization ($P < 0.001$). Regarding treatments, biguanides ($P = 0.001$), sulfonylamides ($P = 0.001$) and insulin ($P < 0.001$) were associated with symmetrical and peripheral polyneuropathy. Comparison between the two groups according to biological data showed a significant difference in creatininemia ($P = 0.011$), blood glucose ($P = 0.030$) and a significant increase in HbA1c in the neuropathy group with $P = 0.001$. On multivariate analysis, the independent predictors of DSPN were retinopathy and hypertension.

**Conclusions**

Age, nephropathy, retinopathy, history of myocardial infarction and stroke, and the presence of other cardiovascular risk factors such as dyslipidemia and hypertension, as well as the length of time the patient has had diabetes, are the main predictive factors for distal and symmetrical polyneuropathy in patients living with diabetes.

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**EP309**

**Prevalence and risk factors of diabetic painful distal symmetrical polyneuropathy**

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**Introduction**

Distal and symmetrical peripheral polyneuropathy is the most frequent type of diabetic neuropathy. Its painful form (PDN) is the most common cause of non-traumatic neuropathic pain and can place a heavy burden on patients’ lives. Despite the major impact that it can have on the quality of life, PDN is generally underdiagnosed because of a large interindividual variability of symptoms and in the absence of well-established diagnostic criteria.

**Aim**

To determine the prevalence of PDN and to identify the different risk factors of its occurrence within Tunisian diabetic patients.

**Methods**

This was a cross-sectional study conducted in the endocrinology-diabetology department of Hedi Chaker hospital Sfax Tunisia, in which we collected adults with diabetes. The DN4 Questionnaire was used to diagnose PDN.

**Results**

A total of 185 patients were recruited. The mean age of patients was 54.9 years with a slight female predominance (54.1% Vs 45.9%). Patients with type 2 diabetes represented 82.7% against 17.3% with type 1 diabetes. The mean duration of diabetes’ evolution was 12.31 years. The average of HbA1c level was 10.27%. Among diabetes’ complications, PDN was the most frequent in our study (48.1%). The mean DN4 score was 3.57. Significant predictors of PDN included advanced age ($P = 0.004$), high waist circumference ($P = 0.01$), long history of diabetes ($P = 0.000017$), insulin therapy in patients with type 2 diabetes ($P = 0.001$), high platelet count ($P = 0.025$), high cholesterol ($P = 0.048$) and the absence of well-established diagnostic criteria.

**Conclusion**

Diabetic painful distal symmetrical polyneuropathy is a major public health problem in Tunisia which affects 1 out of 8 diabetic patients.PDN must be well managed and early screening and treatment should be introduced in diabetic patients to prevent its occurrence and reduce its burden on patients’ quality of life.
diabetic neuropathy is very high among our population. This emphasizes the need
for greater prevalence and worsened quality of life in this population.

Conclusion

We found a higher prevalence of LUT symptoms in patients with diabetic neuropathy, which is consistent with prior studies. Diabetic neuropathy is associated with elevated pressure on the bladder and exacerbates LUT symptoms. The study highlighted the need for closer monitoring and intervention in patients with diabetic neuropathy to improve their quality of life.

Key words
diabetic neuropathy, LUT symptoms, prevalence, quality of life.

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EP309
Obesity and abdominal adiposity are associated with lower urinary tract symptoms in Tunisian patients with type 2 diabetes: a cross-sectional study
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Background and Aims

Lower urinary tract (LUT) dysfunctions are highly prevalent, especially in women. Diabetes is a well-established risk factor for developing LUT symptoms. Several studies suggest that a high body mass index (BMI) may worsen the urinary discomfort in patients with type 2 diabetes (T2DM). The current survey aims to investigate the relationship between obesity and LUT dysfunctions in patients with T2DM.

Patients and Method

We conducted a descriptive and analytical cross-sectional study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administered the Urinary Symptom Profile (USP) questionnaire to all patients to assess LUT symptoms.

Results

The mean age was 59.3 ± 10.6 years, with a female predominance (55.5%). Dyslipidemia (57%) and hypertension (49.7%) were the most common comorbidities. The duration of the evolution of diabetes was 11.0 ± 7.9 years. Oral antidiabetic agents (OAD) and insulin therapy were prescribed in 40% and 13.6%, respectively. Most of the patients were receiving a mixed insulin-OAD treatment (44.2%). A glyceric imbalance was noted in 79.7%. As high as 79.5% of patients with T2DM reported symptoms related to LUT dysfunctions. We compared the body composition in two subgroups:
- G1: patients with LUT dysfunction (n = 159),
- G2: patients without LUT dysfunction (n = 41).

The mean weight in G1 was significantly more elevated than in G2 (77.5 ± 13.8 versus 70.3 ± 11.1 kg; P = 0.003). Similarly, G1 displayed a substantially higher BMI (G1: 29.2 ± 5.8 versus 26.4 ± 4.2 kg/m²; P = 0.03). The prevalence of obesity (BMI >30) was significantly higher in G1 (34.0%) compared to G2 (14.6%) (P = 0.016). Abdominal adiposity with significantly associated with LUT symptoms, since the average waist circumference was higher in G1 in comparison with G2 (103.5 ± 95.7 cm; P = 0.01).

Conclusion

Diabetes and the female gender are largely linked to the onset of LUT dysfunctions in the general population. Our work highlights an additional risk of urinary dysfunction due to weight gain, high BMI, and visceral adiposity in patients with T2DM. Increasing weight is associated with urinary incontinence and other LUT symptoms, most likely because of elevated pressure on the bladder and straining the muscles that support the urethra. These mechanisms, along with hyperglycemia-related omoistic polyuria and diabetic neuropathy are responsible for a greater prevalence and worsened quality of life in this population.

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EP311
Difference of serum glucose, sodium and potassium levels in diabetic ketoacidosis
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Background and aims

Diabetic ketoacidosis is acute complication of diabetes mellitus. Hyperglycemia is one of the diagnostic features of diabetic ketoacidosis. Electrolyte disturbances are common as well. Aim of this study is to examine whether there is a difference in serum glucose, sodium and potassium concentrations with respect to age, gender and severity of diabetic ketoacidosis.

Materials and Methods

Medical records from 1 January 2017 to 31 December 2019 were reviewed and patients with the diagnosis of diabetic ketoacidosis were selected. Results

The study included 52 patients. Most patients belonged to the younger age group (18-24 years, 37.3%), there were more women (54.9%) and moderate diabetic ketoacidosis dominated (66.7%). The average glucose concentration was 27.10 mmol/l (median). Glucose concentration was significantly higher in the age group of 25 to 44 years and > 65 years compared to the group of 18 to 24 years (P = 0.02). No difference in glucose concentration was found with respect to gender. The average sodium concentration was 130.00 mmol/l (median). Sodium concentration was significantly higher in the age group 18 to 24 years and > 65 years compared to groups 25 and 44 to 65 years (P = 0.002). The average potassium concentration was 4.80 mmol/l (median). Women had significantly higher sodium concentrations (P = 0.002). Potassium concentration was significantly higher in the age group 25 to 44 years compared to other groups (P = 0.01). Men had significantly higher potassium concentrations (P = 0.01). The mean pH concentration was 7.19 (median). There was no association of pH levels with regards to age and gender. No significant relationship was found between glucose, sodium and potassium concentrations with regard to severity of diabetic ketoacidosis.

Conclusion

Diabetic ketoacidosis was most common in the age group 18 to 24 years and in women and was most often of moderate severity. The highest average concentrations of glucose and sodium were found in those older than 65 years, whereas potassium was high in the group 25 to 44 years. Women had significantly higher sodium concentration, while men had significantly higher potassium concentration. The severity of diabetic ketoacidosis was not related to glucose, sodium and potassium concentration.

Key words
diabetic ketoacidosis, glucose, sodium, potassium, diabetes mellitus

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EP312
Clinical characteristics and glycemic control in Tunisian patients with type 2 diabetes suffering from lower urinary tract dysfunctions: a comparative population-based survey
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Background and Aims

Several studies have pointed a significant relationship between diabetic complications, glycemic imbalance, and the onset of lower urinary tract dysfunction (LUTD) in this population. The current survey aims to assess the clinical and biochemical characteristics related to glycemic control in patients with type 2 diabetes presenting with symptoms of LUTD.

Patients and Method

We conducted a comparative cross-sectional study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administered the Urinary Symptom Profile (USP) questionnaire to all patients to assess LUT symptoms. We compared the clinical and biological factors related to diabetes in two subgroups:
- G1: patients with LUTD (n = 159),
- G2: patients without LUTD (n = 41).

The mean age was 59.7 ± 11.8 years old; P = 0.36. A slight female predominance was noted in

Results

No difference in gender and severity of diabetic ketoacidosis.

Key words
diabetic ketoacidosis, glucose, sodium, potassium, diabetes mellitus

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Conclusion
Glycemic imbalance, diabetic microangiopathy, and diabetic neuropathy were found to be significant baseline characteristics associated with the onset of LUTD in the diabetic population. Glycemic control and therapeutic patient education are the most efficient preventive measures to reduce the incidence of LUTD in patients with T2DM. A multidisciplinary approach including a team of diabetologists, urologists, and physiatrists may ensure well-coordinated management of patients presenting with LUTD.

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EP313
Comparison of admissions for diabetic ketoacidosis in patients older and younger than 25 years of age at San Cecilio Clinical University Hospital in Granada
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Introduction and objectives
Diabetic ketoacidosis (DKA) is a severe acute complication of Diabetes Mellitus (DM) and as such, on a large number of occasions will require hospital admission. As we know, it happens when there is an absolute or relative insulin deficit, although it is true that the characteristics described in the literature of these episodes are very different. Our aim was to compare the characteristics of DKA occurring in patients under 25 years of age with those of patients over 25 years of age in our setting.

Material and Methods
Retrospective observational study comparing patients older than 25 years with DM admitted for DKA at San Cecilio Clinical University Hospital in Granada, Spain with those aged 16-24 years from January 1, 2019 to December 31, 2021. Variables related to the disease (type of DM, time of evolution, associated complications...) and to the episode of DKA (precipitating factor, hospital admission time, ICU stay...) were analyzed. Analyses were carried out with SPSS 15.0.

Results
We included 39 patients older than 25 years and 22 younger than 25 years (49% women in both groups). The time of evolution of DKA was significantly shorter in patients younger than 25 years (10.86 vs 19.69 years, *P* < 0.05). As comorbidities, 40.5% of those older than 25 years had alterations in the psychiatric sphere (vs 14.3% of the other group, *P* < 0.05). Regarding previous treatment, those older than 25 years had significantly lower total slow insulin doses (22.48 vs 30.71 IU, *P* < 0.05). There were no significant differences in terms of need for ICU stay (59% in both groups). The most important precipitating factors in both groups were: treatment omission, diabetic transgressions and concomitant infections. Metabolic control in terms of HbA1c was worse in the group under 25 years of age (11.74 vs 10.54%, *P* < 0.05). No significant differences were observed in analytical parameters (blood glucose, pH, HCO3 and lactate acid) at admission.

Conclusions
In our work, it was observed that admissions for DKA in our center were more frequent in patients older than 25 years, as well as that these present worse metabolic control in terms of HbA1c and higher insulin needs. On the other hand, there is a tendency for the majority of DKA episodes in patients over 25 years of age to be associated with infections, while the main risk factor in younger patients is the omission of treatment.

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EP314
Gestational diabetes mellitus : Association between maternal insulin resistance with pregnancy outcomes and maternal characteristics
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Introduction
Gestational diabetes mellitus (GDM) is the most common metabolic disturbance during pregnancy. The prevalence of GDM is rising and correlates with the increase in maternal obesity over recent decades. The aim of our study was to assess the association between maternal insulin resistance with pregnancy outcomes and maternal characteristics among tunisians women with GDM.

Methods
A prospective longitudinal study carried out during the year 2020 at the research unit of GDM of Department C at the National Institute of Nutrition of Tunis. The study was conducted among 135 women diagnosed with GDM with 75 g oral glucose tolerance test (OGTT 75) between 24–28 weeks. Insulin resistance was evaluated using the homeostasis model assessment of insulin resistance (HOMA-IR). Patients are followed during pregnancy and until post partum. Statistical analyses were performed using SPSS 20.

Results
The mean age was 32.3 ± 5.3 years. The mean pre-gestational BMI was 28.31 ± 4.9 kg/m². Two thirds of the patients (72.4%) were overweight and 29.9% were obese. The means of fasting blood glucose and the number of abnormal glycaemia values at time of OGTT 75 were respectively 0.96 ± 0.11 mg/dl and 1.45 ± 0.63. The means of fasting blood glucose, HbA1c and total cholesterol were 4.85 ± 0.63 mmol/l, 5.32 ± 0.43% and 1.25 mmol/l. One third of patients (36.3%) were diagnosed before 24 gestational weeks. The mean HOMA-IR was 3.18 ± 1.7 and 55.3% of women had insulin resistance. Macrosomia and pregnancy induced-hypertension were noted in 15.8% and 3.8% of cases. The univariable analysis showed an association between the HOMA-IR and the pre-gestational BMI, fasting blood glucose and the number of abnormal glycaemia values at the time of OGTT 75, levels of HbA1c, fasting glucose value, C-peptide and total cholesterol and also with an earlier diagnosis of GDM before 24 gestational weeks (respectively *P* < 0.01, *P* = 0.044, *P* < 0.01, *P* < 0.01, *P* < 0.01, *P* = 0.049 and *P* = 0.019), however, there was no association between the HOMA-IR and pregnancy outcomes.

Conclusions
Our study showed that The HOMA-IR was associated with advanced maternal age, higher pre-gestational BMI, higher fasting blood glucose, HbA1c, and C-peptide levels. Women followed for GDM with higher HOMA-IR remain a high risk population and more researches are necessary to improve outcomes in this group.

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EP315
Analysis of glycemic control in type 1 diabetes patients using flash glucose monitoring
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Introduction
Flash glucose monitoring expansion to an increasing number of patients with type 1 diabetes, coupled with its increased accuracy and ease of use, has increased available data on glycemic control in this population and allows detection of improvement areas in diabetes education and treatment.

Objective
To analyze main parameters standardized by ATTD consensus (2019) in our population of patients with type 1 diabetes using flash glucose monitoring.

Material and methods
Cross-sectional study carried out on May 7, 2021. Glucose profile of patients with medical follow-up in Endocrinology service in Virgen de la Victoria Hospital in Malaga were analyzed on Libreview platform. Those patients without download available in previous two weeks were excluded.

Results
1,562 patients were analyzed. 51.2% were male. Average number of readings was 10.98 ± 8.13 daily readings with 84.11 ± 20.74% active time. Mean glucose was 165.34 ± 39.04 mg/dl with a standard deviation (SD) 61.81 ± 18.80 mg/dl and a coefficient of variation 37.31 ± 7.52%. time in range (TIR) was 58.96 ± 18.86%, time above range (TAR) was 35.66 ± 19.92%, and time below range (TBR) was 7.52%.
5.38 ± 6.25%. 28.83% patients achieved an TIR greater than 70%, 63.5% a TBR less than 5% and 33.74% a TAR less than 25%. Average interquartile range was 88.09 ± 31.14. Mean hypoglycemia number is 0.65 ± 0.54 daily events, with a mean duration of 90.53 ± 54.51 minutes.

Conclusions
Glycemic control in our cohort of patients, although similar to populations with same characteristics, is still far from parameters recommended in ATTD consensus. We must exploit flash glucose monitoring to detect possible areas for improvement both individual and populationally.

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EP316
Did the COVID-19 pandemic affect the management of gestational diabetes?
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Introduction
Researchers argue that increased morbidity is noted in pregnant women during the current COVID-19 pandemic. Reports indicate that the pandemic has led to disruptions in care of persons with diabetes. Glycated hemoglobin A1c (A1c) is not sufficient in screening for gestational diabetes mellitus (GDM) but may be of use in monitoring glycemia in GDM. To the best of our knowledge no studies had been done on late pregnancy glycaemia (via A1c), as a surrogate of the access/quality of care for women with GDM, have been put forth.

Aim
To assess whether care for women with GDM during the COVID-19 era (via measurement of A1c in late pregnancy) was compromised, compared to the pre-COVID-19 period.

Subjects & Methods
We accessed the medical records of 90 pregnant women (49 before and 41 during the COVID-19 era; mean age ± SD: 34.01 ± 5.50 years) with GDM, in whom A1c was measured after the 34th week of pregnancy. We noted the following parameters: age, body weight change (diffBW) during pregnancy, presence of thyroid disease (TSH), and diabetes mellitus type (DM T1 or T2). Statistical evaluation was done with two way analysis of variance (ANOVA), analysis of covariance (ANCOVA) and with the chi square test.

Results
Fifteen of 49 and 15/49 women in the pre-COVID-19 era had thyroid disease and were on INS, respectively, whereas 10/41 and 20/41 in the COVID-19 era had thyroid disease and were on INS, respectively (P < 0.1, Chi square). Mean ± SD A1c was 5.26% ± 0.42% before and 5.37% ± 0.58% during the COVID-19 era (P < 0.1, ANCOVA), with no significant effect or differences in age, diffBW or presence of thyroid disease (P > 0.1 ANCOVA). The only factor that had an effect on A1c was the mode of treatment (NT or INS) both in the pre-COVID-19 era; mean age 54.51 minutes. Patients on M experienced greater weight loss (-3.4 ± 2.3 versus -2.3 ± 1.2 kg, P < 0.05) and reduction in BMI (-1.9 ± 1.1 versus -1.0 ± 0.9 kg/m², P < 0.05). A 6-month M therapy significantly changed the levels of glucose, insulin, lipids, uric acid, HOMA-R and resulted in significantly reduced AS (P < 0.01). BP decreased more in M-treated patients than in the D group (SBP -6.7 ± 5.1 versus -2.2 ± 4.2 mmHg; DBP -6.4 ± 3.1 versus -1.9 ± 4.2 mmHg, P < 0.05 for both). By linear regression analysis changes in BP on M was associated with HOMA-R and AS changes (0.362, P < 0.05, 0.423, P < 0.05 respectively).

Conclusions
The diet alone wasn’t enough for a reduction in weight and BP in obese hypertensive patients. Weight-loss program with metformin is more effective and shows additional antihypertensive effect in those individuals. The reduction in BP on metformin is mediated by improvement insulin/glucose homeostasis, it is accompanied by lowering of aldosterone, uric acid and lipid-lowering effects, what results in cardiovascular risk reduction.

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EP318
Role of incretins, gut microbiota and permeability in the remission of type 2 diabetes mellitus after bariatric surgery
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Introduction
Bariatric surgery is an effective therapy for patients with type 2 diabetes mellitus (T2D). Many mechanisms have been proposed for its metabolic benefits, such as caloric restriction, weight loss, increased secretion of gut hormones like glucagon-like peptide 1 (GLP-1) and 2 (GLP-2), bile acid diversion, decrease of pancreatic and hepatic fat deposits and changes in gut microbiome. Aims
Evaluate changes after surgery in gut microbiome profile, incretin secretion, intestinal permeability, systemic inflammation and succinate levels. Assess the associations between former variables and determine predictors of metabolic outcomes.

Material and Methods
Prospective single-center, non-blinded randomized controlled trial study, including patients with grades II and III obesity and T2D undergoing metabolicRYGB (mRYGB). At baseline and at one year after surgery we performed antrrophicometric, body composition, biochemical analysis including fasting IL-6 and C-reactive protein, a standard meal test (SMT) and lipid test (LT) with plasma insulin, C-peptide, plasma GLP-1, GLP-2, succinate, and the study of gut microbiota was performed.

Results
13 patients were evaluated, 9 females and 4 males, mean age 52.6 ± 6.5 years, mean BMI 39.3 ± 1.4 kg/m², initial HbA1c of 7.6 ± 1.5% with 69.2% under insulin treatment. Twelve months after surgery a reduction of 33% of total weight loss at the expense of fat mass was observed. Diabetes remission was achieved in 69% of patients. Fasting plasma succinate and zonulin significantly decreased after surgery. After SMT and LT a significant increase in AUC for GLP-1 and GLP-2 and C-peptide was observed after surgery whereas AUC for glucose significantly decreased. Patients achieving T2D remission had higher initial C-peptide but similar proportion of insulin treatment and incretin response. In the
response of the body. Physicians should advise the patients about the complications of diabetes mellitus during fasting especially hypoglycemia, the aim of this study is to determine the relation between type 2 diabetes mellitus and hypoglycemia and to evaluate whether this correlation is significant or not.

Patients and Methods
This is a cross-sectional prospective study, which included 304 Muslim patients with type 2 diabetes mellitus who decided to fast Ramadan during 2019 in two cities, 122 patients were from Duhok city and 183 patients from Erbil city, Kurdistan region of Iraq.

Results
Majority of patients fasted the Ramadan and the mean days of fasting were 26.96. Most patients had no attacks of hypoglycemia (85%), 4.6% have a single attack, and 8% had 4 attacks. There was no significant correlation between the hypoglycemic attacks and the variables studied in this article, such as the duration of diabetes, oral hypoglycemic agents, days of fasting, and fasting before Ramadan.

Conclusion
Physicians must warn patients about the possible risk of hypoglycemia during fasting and it’s the patient’s own decision to continue fasting or not, however the high risk group should be advised against fasting. Lastly, the other role of physician is to adjust the dose of anti-diabetic drugs during fasting in order to minimize the risk of hypoglycemia.

References

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**EP319**

What is the impact of being overweight on the progressive genius of Crohn’s disease?
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2Medicine, University of Dohuk, Duhok, Iraq

**Conclusion**

0.55).

P

remission was similar in the two groups (group 1: 12.5% vs group 2: 8.3%,
P

0.76), the number of severe relapses (Z

P

0.02). After a mean follow-up of 36.82 months [6–52 months], there was no significant difference between the 2 groups concerning the occurrence of complications of CD (P

8.1). The comparison of these groups shows no significant difference in terms of age, sex ratio, tobacco consumption, the duration of development of disease, disease phenotype, presence of anoperineal lesions, presence of upper digestive tract, the severity of the initial flare or the degree of initial intestinal damage assessed by the Lemann score. However, a significant association was demonstrated between overweight and a colonic localization of the disease at the time of diagnosis, compared to other localizations (P

0.02). After a mean follow-up of 36.82 months [6–52 months], there was no significant difference between the 2 groups concerning the occurrence of complications of CD (P

0.76), the number of severe relapses (P

0.21), course of intestinal damage (P

0.59), use of systemic corticosteroid therapy (P

0.75), immunosuppressants (P

0.58), biotherapy (P

0.34) or surgical treatment (P

0.37). Extra-digestive manifestations were more frequent in overweight patients compared to patients with a normal BMI but without statistically significant difference (group 1: 37.5% vs group 2: 27.1%, P

0.41). The possibility of achieving deep remission was similar in the two groups (group 1: 12.5% vs group 2: 8.3%, P

0.55).

**Conclusion**

According to these results, being overweight in CD does not significantly alter the long-term course of the disease. Studies on larger scales are therefore necessary.

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**EP321**

The effect of insulin resistance syndrome in obese children on the development of hypertension
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**Objective**

To investigate the state of blood pressure in children with obesity and insulin resistance.

**Materials and Methods**
127 obese children, age from 6 to 15 years, average age 11.5 years. Anthropometry, calculation of body mass index (BMI), waist/hip volume ratio, measurement of blood pressure (SBP, DBP), study of the level of immunoreactive insulin, glucose were carried out. Insulin resistance was determined with hyperinsulinemia above 22.0 microns/ml, a high NOM index. Results.

obesity in the observed children was of varying degrees, the average BMI was 26.9±2.2, while the predominantly abdominal type of distribution of the subcutaneous fat layer was revealed. Impaired glucose tolerance and fasting glycemia were detected in 14 (11.0%) obese children. The 2 diabetes mellitus in 1 child (0.8%) with hyperinsulinemia was detected in 45 (35.4%) children, while the average insulin level was 56.5±6.8 um/ml. An increase in the HOMA index was detected in 64 (50.4%) patients, the average indicator was 12.0±1.9, which made it possible to verify their insulin resistance syndrome. An increase in blood pressure was detected in 46.5 ± 4.4% of obese children, in 55.2 ± 8.1 children with obesity and insulin resistance. The frequency of elevated SBP values in obese children was registered in 39.1%, DBP - in 24.6%. In children with obesity and the presence of insulin resistance, high rates of SBP were recorded in 53.4%, DBP - 39.7%. Also, among children with insulin resistance, there were high values of SBP and pulse pressure, which indicates the indirect influence of insulin resistance syndrome in the formation of increased peripheral vascular resistance and the development of arterial hypertension.

**Conclusion**

arterial hypertension is a fairly common concomitant pathology in obese children. When burdened with insulin resistance syndrome in obese children, the frequency of arterial hypertension increases and is recorded in every second sick child, which indicates a direct and / or indirect effect of insulin resistance on an increase in blood pressure.

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**EP320**

Incidence of hypoglycemia among patients with type 2 diabetes who fasted during Ramadan
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**Background and Objectives**

Fasting causes a major change in the dietary habits including the frequency, the timing, and the patterns which will result in a major change in the metabolic

**Conclusion**

8.1 children.
**EP322**

**Lipid abnormalities in hospitalized patients with diabetes**

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**Introduction**

Lipid abnormalities are frequent in type 2 diabetes. They increase the risk of cardiovascular events, morbidity and mortality in these patients. The aim of this study was to determine the lipid profile in patients with diabetes during hospitalization.

**Method**

We conducted a prospective study in the department of diabetology in the National Institute of Nutrition in Tunis from October 2021 to January 2022. This work was carried out on the medical records of hospitalized patients. Hypercholesterolemia was defined when the total cholesterol >5.2 mmol/l, Hypertriglyceridemia when a triglyceride level >1.7 mmol/l, and Low HDL cholesterol level by an HDL cholesterol level <1 mmol/l and <1.3 mmol/l in men and women respectively.

**Results**

We included 97 patients with diabetes with a sex ratio (M/F) of 0.6 and a mean age of 51.2 ± 17.5 years. The majority were type 2 diabetes (72%). The mean age of diabetes was 12.2 ± 8.8 years [0.34]. Pre-obesity, class I, class II and class III obesity were found in 28%, 30%, 3% and 3% of patients, respectively. The lipid profile showed hypercholesterolemia in 19% and hypertriglyceridemia in 29% of cases. Hypertriglyceridemia was correlated significantly with diabetes imbalance (P = 0.005) and with poor compliance with dietary rules (P = 0.002). Then, no significant correlation with obesity was found (P = NS). In addition, Low HDL cholesterol concerned 55% of the patients. LDL cholesterol was ≥ 0.7 g/l in 86% of cases and it was correlated with the presence of coronary artery disease (P = 0.03). Statins were prescribed for 54% of diabetics: 49% of patients were on atorvastatin while 3% of diabetics were on simvastatin. Only one patient was on rosuvastatin.

**Conclusion**

Achieving glycemic control in patients with diabetes is compulsory to improve lipid profile. Lipid-lowering drugs, especially statins are often necessary to reduce in the risk of developing diabetes and dyslipidemia, cardiovascular diseases, sleep apnoea, osteoarticular, gynecological and mood disorders.

DOI: 10.1530/endoabs.81.EP322

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**EP324**

**Features of the course and outcome of pregnancy in gestational diabetes mellitus in real clinical practice**

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**Background and aims**

Published data on the prevalence of GDM and its complications in real clinical practice in Russia are insufficient. To assess the prevalence of GDM among pregnant women in one of the districts of Moscow, the structure of risk factors, the course and outcomes of pregnancy in women with GDM.

**Materials and Methods**

A retrospective analysis of data from the primary documentation of 510 pregnant women who were diagnosed with GDM during 2019.

**Results**

GDM was diagnosed in 510 pregnant women out of 5000 observed (10.2%). The mean age of women was 31.9 ± 4.8 (95% CI 31.5-32.3). The diagnosis was made in the 1st trimester of pregnancy - 224 pregnant women (43.9%), in the 2nd trimester - 31.8% (162), in 18.6% (95) in the 3rd trimester. Mean values of venous plasma glucose - 5.43 (5.25-5.7) mmol/l, FBGlc - 5.19 ± 0.4 (95% CI 5.15-5.24).

Treatment with diet therapy - 84.5%, the rest - insulin therapy (in all cases, aspart and detemir were used). The structure of risk factors: burdened hereditary history - 206 (40.4%), GDM in previous pregnancies - 54 (10.6%), macrosomia in history - in 6.3% of cases; antenatal fetal death in history - 3 (0.59%). Obesity was found in 120 (23.5%) women: BMI 30.4-39.9 kg/m² was recorded - 14.3%, BMI 35-39.9 kg/m² - in 5.1%, BMI 40 kg/m² or more - 4.1%. Pregnancy complications were observed in 123 women (24.1%) in 64 (12.5%) cases - fetoplacental insufficiency; preeclampsia - 54 (10.6%); 1 of the pregnant women - eclampsia; the threat of abortion and the threat of premature birth - 1.56% and 1.96%. In 12 pregnant women (2.35%) - polyhydramnios, in 18 cases (3.62%) - oligohydramnios. Adverse pregnancy outcomes were registered in 153 women with GDM. GDM prevalence was 509.0. This was due to the presence of diabetes mellitus and related conditions. One of the pregnant women - eclampsia; the threat of abortion and the threat of premature birth - 1.56% and 1.96%. In 12 pregnant women (2.35%) - polyhydramnios, in 18 cases (3.62%) - oligohydramnios. Adverse pregnancy outcomes were recorded in 153 women with GDM out of 213 analyzed (71.8%): caesarean section in 22.5% of cases; premature rupture of amniotic fluid - in 58 (27.2%); macrosomia - 16.43%; ruptures of the pelvic organs - 41.31%; clavicle fracture - 2 cases; cephalohematoma - 3 cases; diastasis syndrome - in 6 newborns (2.82%); congenital malformations - in 2 newborns. CNS depression syndrome (7.98%), fetal cerebral ischemia - in 8.92%.

**Conclusions**

Totally unfavorable pregnancy outcomes were significantly more common in the group with earlier manifestation of GDM (60.7%) compared with the 2nd group (37.7%) (p <0.001). A detailed comparison of pregnancy complications in these groups showed no statistically significant difference.

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**EP325**

**Mitochondrial Diabetes: a case report**

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**Introduction**

Mitochondrial diabetes represents about 1% of diabetes but still very often misunderstood. The most frequent mutation is 3234A > G of the mtDNA, which is responsible for the maternally inherited diabetes and deafness syndrome (MIDD). We report an observation of a patient with strong suspicion of mitochondrial diabetes.

**Case presentation**

43-year-old female patient, with diabetes for 5 years on an Insulin Therapy. Anamnesis: Diabetes discovered at the Age of 38 years by an acid ketosis decompensation.- Strong heredity of diabetes: grandmother, two uncle, two aunts, tree cousins, all on the mother’s side. - Hypoacusis in an uncle and two sisters on the mother’s side. - Blindness in grandmother and diabetic retinopathy in mother - Diabetic nephropathy in aunt on the mother’s side.

**Clinical examination**

is without particularity with BMI at 37.86 kg/m². Diabetes typing immunological test is negative

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Discussion
Various abnormalities (mutations or deletions) in mtDNA are thus responsible for multi-organ syndromes that include diabetes among other abnormalities. Maternally Inherited Diabetes and Deafness (MIDD) is the most common form of mitochondrial diabetes. The 3243A > G mutation affects the tertiary structure of tRNA. The consequence is a cellular energetic deficit that mainly manifests in very active metabolically organs such as the endocrine pancreas. Mitochondrial diabetes should be suspected in view of the young age of onset of diabetes, maternal transmission, and association with other extra-pancreatic disorders (neurosensorial deafness, reticular macular dystrophy, neurological and muscular disorders, cardiomyopathy). The purpose of searching for the mutation is to confirm the clinical diagnostic, to deduce the risk of maternal transmission and to propose a genetic diagnostic to the relatives.

Conclusion
Knowing mitochondrial diabetes is essential for early diagnosis, systematic screening for multi-organ damage, specific and multidisciplinary management, and to offer genetic counseling.

Bibliography
1. Ming Li Yee, Rosemary Wong1. Mitochondrial disease: an uncommon but
3. P.-J. Guillausseau, Diabetes mitochondriaux. 10-366-D-25 EMC.

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EP327

Growth Assessment and Metabolic Syndrome (MetS) Criteria in children with steroid-sensitive Nephrotic syndrome (SSNS) and frequent relapses treated with long-term prednisone therapy (LTPT): Comparison between children who developed obesity versus those who did not develop obesity

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Introduction
Long term prednisone therapy (LTPT) can be associated with overweight, obesity, and short stature. Both LTPT and obesity are considered risk factors for the occurrence of the different components of the metabolic syndrome (MetS).

Aim
We studied steroid-associated metabolic and clinical adverse events in children with NS and frequent relapses treated with LTPT (obese vs non-obese).

Methods
Data of 30 children with SSNS was analysed retrospectively. 16/30 were obese after LTPT and 14 were not obese. The cumulative dose of steroids over 5 years was calculated for each child. Growth and different components of the metabolic syndrome (MetS) including impaired fasting glucose (IFG), high LDL and cholesterol, lower HD and high blood pressure were studied over this period and compared with the data for 66 age-matched obese non-nephrotic children.

Results
Analysis of data showed that children with NS who developed obesity during therapy were significantly taller than the normal weight group. The obese group had higher cholesterol, TG and LDL level compared to the non-obese group. Both groups had high prevalence of hypertension (40% in the obese group vs 35.7% in

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<td>1.97*</td>
<td>32.53</td>
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<td>37.57</td>
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<td>7.69</td>
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<td>3.54</td>
<td>0.72</td>
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*P < 0.05 group 1 vs group 2. Group 1 Children with NS who became obese on LT prednisone therapy. Group 2: Children with NS who did not become obese on LT prednisone therapy.
the non-obese group)
Conclusion
In children with SSNS on LTPT the development of obesity was associated with higher components of the MetS compared to the non-obese group advocating a higher risk to develop the cardiovascular and metabolic consequences.
DOI: 10.1530/endoabs.81.EP327

EP328
Treatment adherence in patients with type 2 diabetes and its associated factors
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Introduction
Treatment adherence is fundamental in diabetes control. The aim of our study is to evaluate treatment adherence in patients with type 2 diabetes and to determine its associated factors.

Methods
Cross-sectional study enrolling 80 type 2 diabetes patients followed up in the outpatient department of the national institute of nutrition. The Morisky questionnaire was used to evaluate treatment adherence. Age, gender, body mass index (BMI), diabetes duration and treatment, glycosylated hemoglobin (HbA1c), serum lipid profile, microvascular and macrovascular complications were assessed.

Results
The mean age was 60 ± 8 years. Of the study population, 60% were females, and 65% were insulin-treated. The mean diabetes duration was 14.9 ± 7.7 years, mean glycated hemoglobin was 10.4% ± 1.6 and mean BMI was 30.1 ± 6.2 Kg/m². High adherence was reported in 37% of cases, medium adherence in 28% of cases and low adherence in 35% of cases. Patients with good adherence had higher BMI (31.74 ± 6.7 Kg/m² vs 27.99 ± 5.55 Kg/m²; P = 0.03) and better serum lipid profile including a lower triglycerides levels (1.94 ± 1.11 mmol/l vs 1.3 ± 0.52 mmol/l; P = 0.003). Lower HbA1c levels (10.89% ± 1.4 vs 10.42% ± 1.5; P = 0.25), lower total cholesterol levels (4.08 mmol/l ±1.06 vs 4.47 mmol/l ± 1.60; P = 0.17) and higher HDL cholesterol levels (1.14 ± 0.32 vs 1.02 ± 0.2; P = 0.13) were associated to a better adherence but not significant. The presence of peripheral neuropathy, gastroparesis and genital autonomic neuropathy were significantly associated with low adherence (P = 0.015, P = 0.007 and P = 0.02 respectively). Patients with good adherence had lower prevalence of macrovascular complications including acute coronary syndrome (15.4% vs 35%; P = 0.01), stroke (4.8% vs 7.7%; P = 0.6) and peripheral arterial disease (38.5% vs 52.4%; P = 0.2).

Conclusions
Our study highlights the beneficial impact of good adherence on lipid, and glycemic control. More awareness campaigns and counseling services should be provided by health professionals to improve treatment adherence and diabetes management.
DOI: 10.1530/endoabs.81.EP328

EP329
Metropletin treatment in woman with familial partial lipodystrophy and severe hypertriglycerideremia
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Introduction
Metropletin, a recombinant analogue of leptin, is the only drug available for the treatment of generalized or partial lipodystrophy. Familial partial lipodystrophy (FPL) is a rare genetic disorder characterized by selective loss of subcutaneous adipose tissue, ectopic fat deposition, decreased leptin levels, and varying metabolic disorders, which in some patients can be quite severe and life-threatening. We present here such a woman with FPL who is treated with metrepletin.

Presentation
A 53-year-old woman diagnosed with FPL (LMNA gene variant) 8 years ago, had the typical phenotypic features of the syndrome, type 2 diabetes mellitus (T2DM) (HbA1c = 8.7%) and severe hypertriglycerideremia (triglycerides = 1113.6 mg/dl) despite maximum treatment and good adherence to it. She also had extensive visceral fat, fatty liver with a marked increase in liver size, ectopic fat disposition with increased fat in the mediastinum and significant increase in pericardial fat, fibrosis of the heart septum and myocardopathy. The patient commenced treatment with metrepletin 5.8mg per day subcutaneously. Three months after the initiation, she showed improvement in body weight and metabolic parameters (HbA1c = 6.1% and triglycerides = 33.9 mg/dl). A year on metrepletin treatment, improvement of fatty liver infiltration and a significant reduction of its size (from 25cm to 20 cm) was observed as well as a significant reduction of the fat in the mediastinum and pericardium. Body composition measured by dual energy X-ray absorption (DXA), showed a fat redistribution with an increase in the upper and lower extremities and a decrease in the trunk. At two years on the same dose of metrepletin, she was metabolically stable (HbA1c = 5.7% and triglycerides = 320 mg/dl), with a further reduction of liver size, at 18 cm.

Conclusions
FPL is a rare disease with varying phenotype and a broad spectrum of metabolic disorders which at times can be quite severe and life-threatening. The use of metrepletin in these patients can significantly improve such metabolic aberrations and their potentially fatal consequences.
DOI: 10.1530/endoabs.81.EP329

EP330
Study of the effects of long-term therapy DPP4i on the morphofunctional state of pancreatic endocrinocytes in the older age group in the clinic and experiment in conditions of type 2 diabetes.
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Almazov National Medical Research Centre, Saint Petersburg, Russian Federation

Introduction
DPP4i improves the function of β-cells and α-cells. However, there have been short-term follow-up and young subjects in many experimental and clinical studies. The imbalance of pancreatic endocrinocytes increases in adulthood and changes become less reversible. We decided that it would be useful to study the morphofunctional features of pancreatic endocrinocytes while taking DPP4i in the older age group in the clinic and experimentally.

Materials and methods
Male Wistar rats with streptozotocin-nicotinamide-induced type 2 diabetes (DM type 2) (n = 20, age over 12 months) received group therapy for 24 weeks. 1. Control - healthy control group. 2. DM type 2 - DM type 2 without therapy. 3. DPP4i - Vildaglaptin 1.5 mg per kg. Pancreatic preparations were made after the end of therapy. Immunohistochemical study was carried out with antibodies to glucagon, insulin. Patients (n = 36, over 50 years of age) were divided into groups depending on the therapy. 1. DPP4i for more than a year in combination with Metformin. 2. Metformin + sulfonylurea preparation(SU).

Insulin, glucagon, C-peptide levels were examined before and after a standard breakfast. The HOMA IR and HOMA β indices were calculated.

Results
Experiment. A statistically significant difference in the volume of β-cells (significantly less in the group DM type 2 (P < 0.05)), in the volume of α-cells (significantly more in the group DM type 2 (P < 0.05)) was revealed when comparing DM type 2 group with a healthy control group. A statistically significant difference (P < 0.05) was obtained when comparing the DM type 2 group without therapy and the DPP4i group. The number of β-cells was significantly higher with iDPP4 therapy, and the number of α-cells was significantly lower. There was no statistically significant difference in the number of β- and α-cells (P > 0.05) when comparing the DPP4i group with the control group. Clinical part of the study. We obtained a significant difference in fasting glucagon and insulin levels between the Metformin + DPP4i and Metformin + SU groups (P < 0.05). More significant hyperglucagonemia and hyperinsulinemia were observed in the group receiving Metformin + SU.

Discussion.Long-term use of drugs DPP4i contributed to the normalization of the number of β- and α-cells in the experiment. And also DPP4i reduced the secretory imbalance of insulin and glucagon in a clinical study. Our results show that DPP4i contributes to the normalization of the functional state of pancreatic endocrinocytes, including in older age groups.
DOI: 10.1530/endoabs.81.EP330

Endocrine Abstracts (2022) Vol 81
Diabetes mellitus (DM) is a most significant medical-social worldwide problem. Absence of reliable screening program for identification of persons with the higher risk of DM dictates a necessity of sensitive tests of early DM diagnosis. Following genealogical analysis, two experimental groups were formed: patients with type 1 DM with the familial burden (probands) and those at risk (siblings) were included into the 1st and 2nd groups, respectively. Apparently healthy subjects without carbohydrate metabolism disorders served as the controls. The screening program consisted of determination of immunological and genetic biomarkers, to name presence of specific autoantibodies to β-cells of Langergance islets (ICA) and to decarboxylase glutamic acid (GAD), A49/G polymorphisms of CTLA4 gene and INS gene rs689 in patients with the familial DM burden and persons at high DM risk. The familial DM burden was found in 71.7% of patients with type 1 DM. In the probands, significant increase of mean concentrations of ICA and GAD autoantibodies, as compared to the controls (P < 0.001) was found. Among the patients having siblings with DM as the first line relatives, concentrations of the GAD autoantibodies were found almost two times higher than in those with DM but without familial DM burden. Analysis of results of genotyping for CTLA4 gene A49/G polymorphisms and those of INS gene rs689 in patients with genetically determined DM burden demonstrated association of G allele and heterozygous AG genotype of CTLA4 gene and T allele and heterozygous AT genotype of INS gene with the risk of DM onset. The findings are the evidence for importance of biomarkers under study for identification of genetically determined DM forms and prognosis for its progression at early preclinical stage.

EP331
Development of complex of biomarkers for screening program for early diagnosis of familial diabetes mellitus
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1Institute of Biophysics and Biochemistry under Mirzo Ulugbek National University of Uzbekistan, Metabolomics, Tashkent, Uzbekistan; 2Specialized Scientific-Practical Medical Center of Hematology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; 3Ya.Kh. Turakulov Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; 4Tashkent Pediatric Medical Institute, Uzbekistan Ministry of Education, Tashkent, Uzbekistan

EP332
The impact of the interventions based on mobile apps in physical activity among people with Type 2 diabetes mellitus
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University of West Attica, Department of Nursing, Athens, Greece

EP333
Contraception in diabetic women: A review of 100 cases
Fadwa Atfi & Imane El Abbassi
CHU Ibn Rochd, Maternity Department, Casablanca, Morocco

EP334
A Rare Case: Non Ketotic Hyperglycemic Chorea
Filiz Mercan Sardag1, Mehmet Akif Otegeçili1, Ensar Aydemir1, Coskun Ates1, Etham Hocaoğlu1, Soner Cander1, Özen Öz Gü1, Canan Eroğlu1 & Erdinc Erturk2
1Bursa Uludag University, Endocrinology and Metabolism, Bursa, Turkey; 2Bursa Uludag University, Internal Medicine, Bursa, Turkey

Discussion
The problem of contraception must be systematically addressed in a diabetic woman of childbearing age, during each consultation. Oestrogen-progesterone treatments should not be excluded from the contraceptive regimen in women with diabetes, type 1 or type 2, and under 35 years of age. Potential adverse impacts on blood glucose, lipid profile and microangiopathy are apparently modest. The effects on macroangiopathy need to be integrated with other cardiovascular risk factors. The evaluation of knowledge concerning contraception will have to be the subject of several more in-depth studies in order to properly define the issue and to propose practical solutions to generalise the information with the aim of reducing the risk of unforeseen consequences on pregnancy in these women who most often have complicated diabetes.

Conclusion
The prescribing practitioner should be the subject of several studies in order to propose practical solutions to improve knowledge and contraceptive practices with the aim of reducing the unforeseen risks of pregnancy in these women.

Materials and Methods
This is a prospective survey having concerned 100 diabetic women surveyed in the Maternity ward of the CHU Ibn Rochd of Casablanca, during a five-month period, between April and September 2021.

Results
The average age of the women was 35.2 years. Obesity was noted in 26%, hypertension in 51%, dyslipidaemia in 35% and in 35% and 5% of the women were smokers. Type 1 diabetes accounted for 35% and type 2 for 65%. Diabetes was unbalanced in 91% and complicated in 68%. Hormonal contraception was used in 42%, the intrauterine device in 28%, local methods in 20%, tubal ligation was performed in 9%. The maternal-fetal risks linked to unbalanced diabetes were known in 66%, the need for obstetrical and diabetic pregnancy monitoring in 63%, and the obligation to start insulin in pregnant diabetic women in 47%. Women who used hormonal contraception despite having a contraindication to the pill represented 39%.

Aim
The purpose of this study was to identify the impact of the interventions based on mobile apps in physical activity among people with T2DM which included in randomized controlled trials (RCTs).

Methods
The international bibliography was examined to present the impact of the intervention based on mobile app in physical activity among people with T2DM comparing with usual diabetes care. This study is a narrative review and for this purpose the electronic database of PubMed was searched using keywords such as “Type 2 diabetes”, “mobile applications”, “physical activity” in English and Greek language for studies for the past 5 years. The inclusion criteria were all RCTs associated with a comparison of mobile app-based interventions and with usual diabetes care in adults with T2DM. The exclusion criteria were those not being RCTs or those which were study protocols and pilot studies.

Results
A total number of 26 RCTs were reviewed in this study. By using the search terms and by applying the eligibility criteria 6 RCTs were chosen and screened for developing this study and the non-relevant cases of 20 articles were excluded according to exclusion criteria. In the 6 RCTs that were included in the narrative review, 1,005 people participated with T2DM. Finally, these studies had separated the participants to intervention group based on mobile app and control group with usual diabetes care. The intervention group who received the mobile app with physical activity advice had increased their physical exercise and had decreased their hemoglobin Alc (HbA1c) compared to the control group with the usual diabetes care. Moreover, changes were observed between these two groups to their biomarkers and anthropometry measures such as weight, waist circumference and body mass index (BMI) in favour of the intervention group.

EP334
A Rare Case: Non Ketotic Hyperglycemic Chorea
Filiz Mercan Sardag1, Mehmet Akif Otegeçili1, Ensar Aydemir1, Coskun Ates1, Etham Hocaoğlu1, Soner Cander1, Özen Öz Gü1, Canan Eroğlu1 & Erdinc Erturk2
1Bursa Uludag University, Endocrinology and Metabolism, Bursa, Turkey; 2Bursa Uludag University, Internal Medicine, Bursa, Turkey

Introduction
Hemichorea-hemiballismus, secondary to hyperglycemia, is a rare but easily treatable condition that is usually associated with poorly controlled type II diabetes mellitus. Diagnosis is based on clinical assessment and imaging. Etiology includes primarily cerebrovascular diseases, metabolic, degenerative,
Flash glucose monitoring and glycemic control in type 1 diabetes: Real world data

Antonio Ballesteros Martín-Portugués, Marta Iturregui, Lourdes García-García-Douceel, Concepción Cruzado-Begines, Silvia Ponce-Delgado & Maria Gloria Baena-Nieto
Jerez Hospital, Endocrinology Unit, Jerez, Spain

The use of Flash Glucose Monitoring system (FGM) for the management of type 1 diabetes mellitus (T1D) is rapidly increasing. FGM enables people with diabetes to regularly track their glucose levels without needing to perform capillary finger-stick measurements (SMBG). Clinical studies have shown improvement of glycemic control and hypoglycemia reduction, as well as better comfort and quality of life in people with type 1 diabetes (T1D) using this technology. Objectives: to assess the degree of achievement of glycemic targets in T1D patients using the flash sensor properly (>70% of the time) in our center.

Methods

We analyzed registry data collected at a tertiary diabetes centre in Spain. People with T1D routinely using FGM to manage their diabetes were included in the analysis. Downloaded LibreView data of patients were collected: data regarding glucose management indicator (GMI), time within range 70-180 mg/dl (TIR), coefficient of variation (CV) and hypoglycemic events.

Results

A total of 712 patients were included in the study. 80 patients did not download any sensor data. The downloaded data were prior to 6 months in 20 patients and sensor use was <70% of the time in 116 patients. We analyzed data from patients who used the sensor appropriately (>70% of the time). Data from 488 patients (68.53%) were analyzed. The percentage of patients with a GMI < 7% was 48%, those with CV <36% were 49.8% and those with TIR>70% were 31.6%. All targets were met only in 22.5% of patients. In addition, 87.9% of patients had a high risk of hypoglycemia and 27.5% had experienced at least 1 daily hypoglycemic event.

Conclusions

There is a high percentage of T1D patients using FGM who do not use it properly. Only 15% of T1D patients with adequate use of the sensor have good glycemic control. Metabolic control in T1D patients should be improved and strategies for proper use of FGM must be implemented.

DOI: 10.1530/endoabs.81.EP336
Patients with type 2 diabetes mellitus (DM) are one of the most vulnerable categories of patients in terms of adverse outcomes of COVID-19 infection. 

Aim
To assess the features of laboratory and instrumental data in patients with COVID-19 and type 2 DM (unvaccinated) depending on the value of glycated hemoglobin (HbA1c) at the time of the onset of oxygen deficiency.

Materials and methods
The study involved 78 patients with type 2 DM and COVID-19. All the participants were divided into 2 groups. Group 1 (n = 47) included patients with HbA1c<7.0%, group 2 (n = 31) - >7.0%. The patients underwent computed tomography scan of the lungs (CT), assessment of blood oxygen saturation level (SpO2), HbA1c, C-reactive protein (CRP), ferritin, D-dimer, complete blood count on the 6–9th day of the disease.

Results
Analyzing the obtained results it was revealed that in patients of group 1 the duration of type 2 DM was 7.0 [6.0; 7.5] years vs 8.9 [7.0; 10.0] years in group 2 (P = 0.031). The HbA1c was significantly higher in group 2 – 8.5 [8.0; 8.9]% vs 7.0 [6.7; 7.0]%, (P = 0.001). So, in group 1 at the time of hospitalization SpO2 was 91.0 [90.0; 93.0]%, vs 87.0 [86.0; 89.0]% (P = 0.005). All the patients had bilateral interstitial pneumonia, the median value of the percentage of lung tissue damage in group 1 was 45.0 [40.0; 55.5]% vs 65.0 [60.0; 70.0]% in group 2 (P = 0.002) (Fig. 1). 

Introduction
COVID-19 pandemic: Impact on follow up care of insulin-requiring diabetic patients
Asma Kardi, Radhouen Gharbi, Ben Salem Maram, Manel Jemel, Hajar Kandara, Maria Clibout & Ines Kammoun
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EP340
COVID-19 pandemic: Impact on follow up care of insulin-requiring diabetic patients
Asma Kardi, Radhouen Gharbi, Ben Salem Maram, Manel Jemel, Hajar Kandara, Maria Clibout & Ines Kammoun
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Introduction
COVID-19 is a novel pandemic affecting globally. It has led to an unprecedented global health crisis assessing health system’s preparedness to deal with health disasters. The aim of our study was to evaluate the impact of COVID-19 on the follow up care of diabetic patients.

Methods
We conducted a retrospective study in 100 insulin-requiring diabetic patients. Data regarding treatment availability, weight, glycemic control and follow up care during two years before (T1: 2018-2019) and during the pandemic of COVID-19 (T2 : 2020-2021) were collected.

Results
The study population included 60 women and 40 men. The mean age was 58.6 ± 1.3 years. Among our 100 patients, 30% have type 1 diabetes mellitus and 70% have type 2 diabetes mellitus. Fifty-seven patients were using insulin alone and 43 patients were treated by insulin with metformin. Hypertension and dyslipidemia prevalence was respectively 55% and 56%. Insulin had always been available. However, metformin, anti-hypertensive drugs and anti-dyslipidemic drugs disponibility in public health facilities decreased, with respectively 57%, 36% and 75% of cases before pandemic versus 79%, 59% and 85% in T2 (P = 0.022, P = 0.004 and P = 0.332 respectively). Eight patients missed at least one medical consultation in T1 versus 46 patients in T2 (P < 10-3). Fundoscopy and screening for microalbuminuria were performed respectively in 83% and 89% of patients in T1 and in 41% and 87% in T2 (P < 10-3, P = 0.839 respectively). Glycosylated hemoglobin increased in 75% of patients. Its mean raised from 8.9% to 9.3% (P < 10-3). The percentage of patients with well-controlled diabetes decreased from 29% in T1 to 19% in T2 (P = 0.013). A weight gain was documented in 57% of patients. The mean of weight increased from 76.9 Kg to 78.3 Kg (P < 10-3). Out of 100 patients, cardiovascular events were documented in one patient in T1 and in five patients in T2 (P = 0.219).

Conclusion
A significant impairment in the follow up care of diabetic patients and their glycemic control has been revealed through our study. This can be partially explained by the impact of lockdown on treatment facilities availability, healthy lifestyle habits and by the stressful condition related to this pandemic. However, effective preparedness are needed in future so that complications can be minimized.

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**EP341**

Diabetes distress and its clinical determinants in Type 2 diabetes patients

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Introduction

Diabetes distress (DD) refers to the emotional burdens and worries, often hidden, that are part of the spectrum of the patient experience when managing a chronic and demanding disease like diabetes. The objective of this work was to determine the prevalence of DD and its clinical determinants in type 2 diabetic patients.

Patients and methods

Cross-sectional study conducted on 92 type 2 diabetic patients who consulted on an outpatient basis between April and June 2021. DD was assessed using the Diabetes Distress Scale (DDS).

Results

The average duration of diabetes was 10.35 years. 69.6% of patients presented with moderate to severe distress related to diabetes. The dimension of lifestyle distress had the highest score among the DDS subscales. There was a correlation between age, level of education, social coverage, rate of follow-up, HbA1c level and DD. HbA1c levels and rate of follow-up were the main predictors of DD.

Discussion and conclusion

The results of this work underscore the importance of identifying DD in type 2 diabetics. High levels of DD have been significantly associated with poor glycemic control, poor diabetes self-management, and poor quality of life. More work is needed to better explore and manage psychological comorbidity in type 2 diabetics.

DOI: 10.1530/endoabs.81.EP341

**EP342**

A diabetic foot case with bilateral charcot arthropathy

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Uludag University Medical School, Bursa, Turkey

Background

Diabetic foot infections are an important cause of morbidity and mortality associated with poor glycemic control, polyneuropathy and micro/macrovascular diseases. The clinical, laboratory, radiological, pharmacological and/or surgical evaluation is required. We report a case of diabetic foot infection with bilaterally charcot joint.

Case

A 52-year-old female patient with type 2 diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD) and peripheral artery disease (PAD) applied to our endocrine clinic with ulcerated lesion on the sole of the right foot. Eight years previously she had undergone a left first metatarsophalangeal (MTP) joint arthroplasty due to underlying diabetic foot. On examination, she had a bilaterally neuropathic arthropathy (Charcot joint). Her plasma glucose level was 272 mg/dl, HbA1c of 7.8, erythrocyte sedimentation rate (ESR) of 46 mm/h and C-reactive protein (CRP) of 42.1 (normal range, 0-5) mg/l with normal renal and liver function tests in the first laboratory evaluation. Two-sided X-Ray and magnetic resonance imaging (MRI) of the ankle and foot revealed destructive joint disease without osteomyelitis (Figure 1). The diagnosis of diabetic foot infection was made, and treatment with intravenous piperacillin/tazobactam and teicoplanin for two weeks, then the patient improved. After clinical and biochemical improvements, the patient was discharged with oral antibiotics.

Discussion

Uncontrolled diabetes mellitus is the most common cause of non-traumatic amputations. Chronic, progressive and destructive arthropathy may develop in diabetic patients associated with sensory, autonomic and motor neuropathy. Treatment of charcot neuroarthropathy is based on multidisciplinary team management. Inappropriate and late approach of diabetic foot infection often results to amputation of any limb.

DOI: 10.1530/endoabs.81.EP342

**EP343**

Foot risk assessment in diabetic patients

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²Military Hospital of Instruction of Tunis, Hygiene Service, Tunis, Tunisia;
³National Institute of Nutrition Of Tunis, Department B, Tunis, Tunisia;
⁴National Institute of Nutrition Of Tunis, Outpatient Department and Functional Explorations, Tunis, Tunisia;
²Military Hospital of Instruction of Tunis, Endocrinology Department, Tunis, Tunisia

Background

The management of diabetic foot starts with prevention, mainly based on the early detection of peripheral neuropathy and peripheral arterial disease, called podiatric risk assessment. This risk must be evaluated in all type 2 diabetics since the discovery. The aim of this study was the assessment of diabetic foot ulcer risk according to International Working Group on the Diabetic Foot (IWGDF) and the identification of risk factors for developing foot lesions.

Methods

We conducted a descriptive, cross-sectional study that concerned 60 diabetic patients hospitalized in the Department C of the National Institute of Nutrition between July and September 2021.

Results

Mean age of patients was 59.1±12.23 years with sex ratio 0.66. Half patients were hypertensive, 64.4% had a personal history of dyslipidemia and 34% were smokers. All patients had Type 2 diabetes with evolution duration 9.53±6.26 years. The majority of patients (91.7%) had uncontrolled diabetes and 66.7% had microangiopathy (retinopathy and nephropathy). Thirteen patients (21%) had a foot at risk. On clinical examination, neuropathy was found in 21% of cases, while lower limb arteriopathy in 14.3%. Patients were classified into four risk groups according to IWGDF criteria as follows: grade 0: 78.3%; grade 1: 13.3%; grade 2: 6.7% and grade 1: 1.7%. There was statistically significant relationship between LDL cholesterol (P = 0.035), microangiopathy (P = 0.003) and foot risk grade. Patient's sex, BMI, diabetes duration, smoking, and HBA1c did not have significant association with risk of diabetic foot ulcer.

Conclusion

Diabetic foot remains a major health problem and a frequent cause of limb amputation. Podiatric risk assessment represents a key tool to avoid many dreaded complications.

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**EP344**

Relationship between kidney function and the level of amylinemia in patients with diabetes mellitus

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Background

Chronic kidney disease (CKD) is one of the leading causes of disability and mortality in patients with different types of diabetes mellitus (DM). However, relationships between kidney function and serum amylin levels are still controversial, especially in patients with heterogeneous types of diabetes. The objective of the study was to determine the features of the glomerular filtration rate (GFR) in patients with DM depending on the level of amylinemia.

Methods

89 patients with DM and CKD were examined, as well as 15 representatives of the control group. The patients were divided into three groups by the types of DM (25 patients with classical type 1 diabetes mellitus (T1DM), 36 patients with latent autoimmune diabetes in adults (LADA), 28 patients with type 2 diabetes (T2DM)) and by the GFR stages (G1-21, G2-49, G3a-48, G3b-17, G4-10). GFR was determined by the CKD-EPI formula. Serum amylin levels were measured using the ELISA method.

Results

The level of amylinemia in patients with GFR stages G1 and G2 probably did not differ in comparison with the control and among themselves. In the group of patients with GFR stage G3a, the level of serum amylin was 7.7 times higher than the control, 3.7 times higher than the G1 group, but did not differ from the one in group G2. In patients with GFR of stage G3b, the above indicator was 14.7 times higher relative to the control, 7.2 times higher relative to the group of individuals with GFR of stage G1, 3.5 times higher than the G2 stage and 1.9 times higher.
Acute pancreatitis revealing major hypertriglyceridemia at 94 g/l!

Kaouther Rifai, Loubna Guissi, Salma Ahallat, Hind Iraqi & Medina Rivero1, Isabel Mateo Gavira2 & Esteban Sanchez Toscano2
Abir1, Nadia Ben Amor 1, Rihab Yamoun2, Faten Mahjoub2, 3
DOI: 10.1530/endoabs.81.EP346

Introduction

Hypertriglyceridemia (HTG) is a rare but well-known cause of acute pancreatitis, which can be fatal with an overall mortality rate of 36-50% in the most severe forms.

Case presentation

A 29-year-old patient was admitted to the emergency department with abdominal pain, bilious vomiting and alteration of general condition. Physical examination showed hemodynamic shock with diffuse abdominal tenderness. The Laboratory results showed a serum lipase of 546 U/l (higher than 6 times the upper limit of normal), a severe hypertriglyceridemia at 94 g/l and hypercholesterolemia at 11 g/l. Abdominal ultrasound did not show lithiasis, abdominal CT scan revealed Balthazar grade E pancreatitis and magnetic resonance cholangiopancreatography (MRCP) did not show microthelithiasis of the gallbladder and biliary ducts. Pancreatic autoantibodies were negative. The diagnosis of acute pancreatitis due to major hypertriglyceridemia was made. The patient was managed with fasting, intravenous hydration, heparin and ibutrate therapy. The evolution was marked by a clinico-biological improvement.

Discussion

The association between acute pancreatitis and HTG is widely recognized. It presents 12-38% of all acute pancreatitis. The symptomatology of this acute pancreatitis is unremarkable. The management of major hypertriglyceridemia is based on symptomatic treatment combining effective analgesia, parenteral nutrition, adequate hydration and lipid-free nutrition. Other therapies have been reported, such as heparin infusion and insulin. Plasma exchange may be useful, although its clinical efficacy has not been proven.

Conclusion

Hypertriglyceridemia is a rare cause of acute pancreatitis. It requires specific treatment to overcome the acute phase and prevent recurrence.

Acute pancreatitis revealing major hypertriglyceridemia at 94 g/l!

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The association between acute pancreatitis and HTG is widely recognized. It presents 12-38% of all acute pancreatitis. The symptomatology of this acute pancreatitis is unremarkable. The management of major hypertriglyceridemia is based on symptomatic treatment combining effective analgesia, parenteral nutrition, adequate hydration and lipid-free nutrition. Other therapies have been reported, such as heparin infusion and insulin. Plasma exchange may be useful, although its clinical efficacy has not been proven.

Conclusion

Hypertriglyceridemia is a rare cause of acute pancreatitis. It requires specific treatment to overcome the acute phase and prevent recurrence.

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A new case of hypoglycemia of unrelated etiology.

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Male, 29 years old. Go to consultations in our center for a second opinion for obesity recurrence after bariatric surgery, as an alternative management to obesity. The efficacy of liraglutide for weight loss in a patient with relapse in obesity after bariatric surgery – case report

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Introduction

Obesity is a chronic disease which has become a global epidemic. Approximately 7% of deaths per year is associated with obesity, especially because of its complications such as cardiovascular diseases, type 2 diabetes or cancer. Lifestyle interventions are the first line of management but additional pharmacotherapy or bariatric surgery should be considered in more severe cases.

Case report

A 40-year-old woman was referred to Endocrinology Outpatient Clinic because of severe obesity. She underwent laparoscopic sleeve gastrectomy few years ago which led to weight loss. However, a return to unhealthy eating habits as well as an insufficient physical activity, have caused obesity recurrence. The patient has been treated with metformin 1 g because of insulin resistance, perindopril 5 mg due to hypertension and venlafaxine 150 mg because of depression. Despite of metformin implementation, diet and activity interventions, the reduction of weight has not been achieved. At the first endocrinology consultation, the patient had a body weight of 124 kg and a body mass index of 43.97 kg/m². Blood pressure was 137/85 mmHg under treatment. The laboratory tests revealed normal liver and renal function. The pituitary function (corticotropic, thyroid, gonadal, and somatotroph axes) was also confirmed as normal. US abdomen examination showed signs of hepatic steatosis and lack of gall bladder which has been removed due to cholestolithiasis. Fastening laboratory test results showed: total cholesterol of 183.0 mg/dl, LDL-cholesterol of 110.2 mg/dl, triglycerides of 109.0 mg/dl, HDL-cholesterol of 51 mg/dl. Oral glucose tolerance test at time 0-60-120 min, after a 2-week break in the use of metformin, revealed glucose levels: 100-278.99 mg/dl and insulin levels 10.8-75.19-18.4 µU/ml, with mild insulin resistance at fasting (HOMA-IR 2.67). Thus, considering severe obesity, unresponsive to diet and lifestyle interventions, complicated by hypertension, impaired fasting glucose, hepatic steatosis and depression, a GLP1-receptor agonist therapy with liraglutide has been proposed, from a starting dose at 0.6 mg up to a final dose at 3.0 mg per day. No side effects have been registered during therapy so far. At the last follow-up visit, four months after introducing liraglutide, the patients' weight was 108 kg (BMI 38.29 kg/m²), with a total weight loss of 16 kg (~12.9%).

Conclusions

Liraglutide effectively reduces body weight and may be a safe option of treatment in patients with severe obesity. It should be also considered in subjects with obesity recurrence after bariatric surgery, as an alternative management to reoperation.

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Assessment of the Podiatric Risk on Diabetics: Cross-Sectional Study in According to 200 Patients

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Endocrine Abstracts (2022) Vol 81
Introduction
The diabetic foot is a frequent, serious and costly complication of diabetes. The prevention of diabetic foot involves a systematic podiatric evaluation of diabetic patients to identify the foot at risk. The aim of our study was to determine the podiatric risk in a Tunisian diabetic population according to the classification of the International Working Group on the Diabetic Foot (IWGDF) and the factors associated with podiatric risk.

Methods
It was a prospective cross-sectional, descriptive and analytical study conducted over a three-month period including patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes, hospitalized in nutrition department A between 1 August and 31 October 2021. Subjects under 18 years of age or hospitalized for conditions other than diabetes were excluded from the study.

Results
The study enrolled 200 patients and the sex-ratio was 0.72. The average age of the cohort was 53 years. 74.2% of the patients were running type 2 diabetes. Of them, 75% had dyslipidemia and 82% were overweight or obese. High Blood Pressure was found in 51% of cases. The capillary blood glucose and glycated hemoglobin were respectively around 12.26 mmol/l and 10.8%. Prior ulceration and/or amputation were noted in 9% of cases. The gradation of the foot risk according to the International Working Group on the Diabetic Foot (IWGDF) was established as follows: grade 0 (76.3%), grade 1 (12.6%), grade 2 (6.3%), grade 3 (4.8%). Risk factors most associated with foot injury occurrence included diabetic peripheral neuropathy (P = 0.000), the absence of pulse perception (P = 0.000), chronic peripheral artery occlusive disease (PAOD) (P = 0.000), diabetic retinopathy (P = 0.002) and diabetic nephropathy (P = 0.017).

Conclusion
The prevention of diabetic foot in emerging countries is accessible by a systematic clinical examination of all diabetic feet and the awareness of adapted footwear. Long-term studies are needed to evaluate whether the intervention of podiatrists starting at an early phase would lead to a reduction in major foot problems.

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EP349
Cutaneous manifestations of diabetes mellitus
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Introduction
Diabetes mellitus (DM) is the most common endocrine disorder. The skin manifestations of diabetes can vary depending on the duration of the disease and the control of blood glucose levels. Almost all patients with DM eventually develop skin changes due to the long-term effects of hyperglycemia on microcirculation and skin collagen. This study was conducted to find the hospital based prevalence of mucocutaneous manifestations in patients with diabetes mellitus, their clinical pattern and relationship with glycemic control and duration of the disease

Methods
It was a longitudinal observational study including 200 patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes, admitted in nutrition department A for any reason between 1 August and 31 December 2021. Subjects under 18 years of age or hospitalized for conditions other than diabetes were excluded from the study.

Results
Among 200 patients with DM, 88(44%) were males and 112(56%) were females. The mean age of the patients was 51.85 ± 18.35 years and mean total duration of diabetes was 11.87 ± 9.9 years. Of them, 135 (67.5%) had one or more dermatoses. The common skin disorders for which patients sought treatment were: xerosis (55.5%), plantar hyperkeratosis (41.3%), onychomycosis (39.2%), and inter-toe intertrigos (18.2%). Risk factors most closely associated with mucocutaneous manifestations included High Blood Pressure (P = 0.000), diabetic peripheral neuropathy (P = 0.018) and obesity or overweight (P = 0.000). But there is no statistically significant relationship with nephropathy (P = 0.14) or retinopathy (P = 0.58).

Conclusion
Skin problems are quite common among diabetic population. Diabetes-related skin lesions can serve as a gateway for microorganisms and possible secondary infections. The early detection of mucocutaneous manifestations in DM is important to be able to avoid and manage the complications and prevent disability.

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EP350
Dapagliflozin can Induce and Maintain Type 2 Diabetes Remission
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Introduction
Type 2 diabetes mellitus, has gained a lot of attention in recent years as one of the most important chronic progressive diseases in the world, which slowly carries towards longevity and which involves many chronic complications, which are dangerous to health and the economy. Sodium-glucose cotransporter-2 (SGLT2) inhibitors represent a category of newly discovered drugs that work by preventing glucose reabsorption in the proximal renal tubules. (SGLT2) Inhibitors may induce type 2 diabetes remission. Design: Randomized, -controlled trial, 6-month trial.

Materials and Methods
100 type 2 diabetes patients were randomized into 2 groups.

Results
The results show a statistically significant decrease of A1C levels after 3 and 6 months treatment with dapagliflozin and significant change in A1C levels after 3 months treatment of glimepiride but a no significant change in the next 3 months. The results also show a statistically significant decrease in BMI in the dapagliflozin group after 6 months of treatment.

Conclusion
As type 2 diabetes is one of the most disabling diseases, it is necessary to find a drug that can lead to remission. Dapagliflozin can lead to type 2 diabetes remission.KeywordsDapagliflozin, Inhibitors, Type 2 Diabetes

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EP351
Double Trouble. Metformin and empagliflozin induced lactic acidosis - A case report
Bhavna Sharma, Michele Mantega, Mahesh Deore, Ian Seetho, Shivasanthar Seechurn, Elaine Hui, Mushitaq Rahman & Asjid Qureshi
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63 years old with sarcoidosis since 2018 and type 2 diabetes was referred by GP for hypercalcaemia related to likely dehydration and sarcoidosis. She was started on a weaning dose of prednisolone and empagliflozin. She had already been on metformin for several years. She was discharged after calcium improved from 2.97 mmol/l to 2.83 mmol/l. She was advised to follow up in Ambulatory care in 1 week for repeat calcium levels. On follow up, noted to have calcium levels of 2.67 mmol/l. Lactate noted to be 6.9 with a pH of 7.3 (calculated anion gap 13.1 mmol/l). Patient noted to be completely asymptomatic with normal systemic exam. Given fluids in ambulatory care, however, lactate noted to be rising at 7.7 with negative ketones and normal sugars. Empagliflozin was stopped and insulin was initiated with normalization of lactate with minimal fluid therapy. A literature review noted a similar case by Tomigana et al with lactic acidosis after initiation of empagliflozin along with metformin. Cellular dehydration with inhibition of enzymes may contribute to high lactate in the patients treated with metformin and an SGLT2 inhibitor. Lactate should be checked in unwell patients on metformin and an SGLT2 inhibitor. The effect of this complication on mortality/morbidity is unclear and further research is needed.

Reference

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EP352
Long-term impact of digitally administered Breathe Well-being Diabetes Reversal Program (BDRP) in individuals with type 2 diabetes mellitus
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Introduction
Breathe Well-being Diabetes Reversal Program (BDRP) delivers personalized lifestyle management (LSM) curriculum including education, lifestyle, and health-related content, based on patient’s health profile and preferences. The program assists the physicians in making clinical decisions by providing comprehensive lifestyle data, which facilitates patient adherence and aids in achieving positive health outcomes.

Objective
To estimate the long-term impact of digitally administered BDRP on lifestyle measures in individuals with T2DM in India

Methodology
BDRP provides a 4-month digitally administered LSM intervention with additional stress reduction module – a “Happiness and Lifestyle Coach” combined with meditation. Individuals with T2DM were divided in 3 cohorts (1:1:1) treated with (a) BDRP with doctor-prescribed medication (n = 60), (b) BDRP with doctor-prescribed medication and personalized stress reduction module (n = 61), (c) Only doctor-prescribed medication (control group; n = 60). After 4-months of intervention, cohorts 1 and 2 with high (H > 70%) and medium (M: 50-70%) adherence and cohort 3 were followed up to 19 months. Informed consent was obtained.

Results
Of 60 and 61 individuals in cohorts 1 and 2, 46.7% (28) and 54.1% (33) showed H and M adherence. In H and M cohort 1, BMI (kg/m²) reduced from 32.6 and 31.2 at baseline to 29.5 and 28.7 at 19 months (P < 0.001; P = 0.000, respectively). In H and M cohort 2, BMI reduced from 32.9 and 31.9 at baseline to 29.7 and 28.7 at 19 months (P = 0.001; P = 0.000, respectively). Body weight (kg) in H and M cohort 1 reduced from 90.2 and 85.4 at baseline to 81.6 and 78.4 at 19 months (P = 0.003; P = 0.000). For H and M cohort 2, body weight reduced from 88.1 and 88.0 at baseline to 79.8 and 79.2 at 19 months (P = 0.001; P = 0.000). In control group, BMI and body weight reduced from 32.0 and 88.1 to 31.8 and 87.5 (P = 0.029; P = 0.025). At 19 months, HbA1c levels < 6.5% were observed in 78.6% and 81.8% individuals in H and M cohorts 1 and 2. Penn State Worry Questionnaire (PSWQ) score average changed from 57.5 and 55.5 to 42.1 and 42.1 for cohort 1 (H and M), and 54.9 and 59.8 to 33.9 and 41.0 for cohort 2 (H and M) at 19 months, respectively.

Conclusion
Clinically meaningful reductions in BMI, body weight, HbA1c, and stress levels were observed in both cohorts. Cohort 2 showed greater improvement in stress levels than cohort 1. Study findings supported the promising role of digitally administered BDRP on lifestyle measures of individuals with T2DM.

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EP353
Sodium-glucose cotransporter-2 (SGLT-2) inhibitor-induced diabetic ketoacidosis and Fournier’s gangrene
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Introduction
The Food and Drug Administration (FDA) had issued warnings on the increased risk of diabetic ketoacidosis and Fournier’s gangrene with patients using Sodium glucose cotransporter-2 (SGLT-2) inhibitors. Herein, we report a case of simultaneous Fournier’s gangrene and diabetic ketoacidosis after initiation of treatment with Empagliflozin.

Case Presentation
We report a case of a 54-year-old woman with type 2 diabetes on empagliflozin presented feeling unwell. Blood glucose level raised at 32.7 and ketones of 2.2 mmol on admission. Blood gas showed acidosis of pH 7.242 (7.35 - 7.45), bicarbonate of 21.2 mEq/l (22 - 26) and base excess of - 6.5 mmol/l (-2 to 6). She was started on diabetes ketoacidosis treatment. Empagliflozin was suspended. Blood results showed raised C-reactive protein of 353 mg/l. She reported new pain in the perineum, inflammation of left labia with a patch of necrosis in left groin crease. She was commenced on broad spectrum intravenous antibiotics. CT scan showed marked diffuse subcutaneous fatty infiltration and oedema on the left side of the perineum and left buttock with suspected fluid collection of the left labia measuring 29x14mm, multiple enlarged left inguinal lymph nodes. She underwent surgical drainage and debridement. Histology showed ulceration and necrotizing abscess with fat necrosis which confirmed the diagnosis of Fournier’s gangrene. Humulin M3 twice daily was initiated. She then recovered well.

Conclusion
To our knowledge, only 4 cases reported in the literature worldwide presented with simultaneous Fournier’s gangrene and diabetic ketoacidosis after initiation of treatment with (SGLT2) inhibitors. Health care professionals should be aware of this extremely rare but life-threatening adverse events. They should assess patients for Fournier’s gangrene if suspected.

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EP354
Impact of depression in type 2 diabetes with Covid 19: 38 cases
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Introduction
Diabetes, like any chronic disease, generates in addition to the somatic consequences, serious psychological repercussions, depression and diabetes emerging respectively in the 4th and 9th rank of the most important causes of disturbances in number of years of life corrected for the disability factor. (DALYS).

Patients and methods
Descriptive retrospective study of 38 post-Covid diabetics collected from the endocrinology – diabetes department of CHU Hedi Chaker, Sfax, Tunisia.

Screening for depression using the Beck Scale (BDI).

Results
The average age of our patients was 45.5 years with a sex ratio (M/F) of 1.5. All of our patients had type 2 diabetes. The mean duration of diabetes was 9.5 years. The majority of patients (77%) were on an HbA1c > 7%. According to the Beck scale, 63.6% of our patients had experienced a feeling of sadness after Covid, of which almost 25% were unable to cope. Feelings of discouragement, failure and guilt were found, respectively, in 64%, 64% and 45% of cases. A state of fatigue was noted in half of our patients and 42.4% were unable to work. Overall, all of our patients experience post-Covid depression to varying degrees: it was severe in 30.3%, moderate in 54.5% and mild in the rest of our diabetic patients. None of our patients admitted to having a suicide plan and 45% felt that death would set them free. Only 25% of nurses are interested in the psychological side of post-Covid diabetic, 40% of whom encourage them to consult a psychiatric hospital.

Conclusion
All people with diabetes should be screened for symptoms of depression or anxiety. Screening for and managing the psychological consequences of diabetes is essential. Screening for and managing the psychological consequences of diabetes in adolescents is essential for improving the quality of life of these patients and better controlling their disease.

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EP355
Distinct inflammatory signatures of upper- and lower-body adipose tissue in postmenopausal women with normal weight and obesity
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Background
Abdominal obesity is associated with insulin resistance and increased cardiometabolic disease risk, whereas lower-body fat accumulation seems
protective against metabolic derangements. Differences in upper-body and lower-body adipose tissue (AT) function seem to underlie these opposing associations. Here, we investigated the inflammatory signature of upper- and lower-body AT in women with normal weight and obesity, as well as in human primary abdominal (ABD) and femoral (FEM) adipocytes.

Methods

Twenty-one healthy postmenopausal women (aged 50-65 years) with normal weight (BMI 18-25 kg/m²) and obesity (BMI 30-40 kg/m²) were recruited. The in vitro secretion of adipokines from ABD and FEM subcutaneous AT was determined after an overnight fast using the arterio-venous balance technique. Furthermore, adipokine expression and adipocyte size in ABD and FEM AT were examined. Finally, the expression and secretion of adipokines were investigated in vitro using differentiated human primary ABD and FEM subcutaneous adipocytes derived from the same individuals.

Results

Plasma leptin (P < 0.001) and PAI-1 (P = 0.036) concentrations, as well as abdominal and femoral adipocyte size were higher in women with obesity compared to normal weight. No significant differences in fat cell size and blood flow were found between ABD and FEM AT. There was significant net release of leptin and MCP-1 across ABD and FEM AT (all P = 0.001), and fractional release of MCP-1 was higher in ABD than FEM AT (P = 0.023). Gene expression of leptin (P = 0.010), PAI-1 (P = 0.080) and TNF-α (P = 0.090) were lower in ABD than FEM AT and increased in obesity. In vitro, IL-6, PAI-1 and leptin gene expression was higher, while adiponectin and DPP-4 gene expression were lower in adipocytes derived from the ABD compared to FEM region. Finally, ABD adipocytes derived from women with obesity secreted less MCP-1 compared to femoral adipocytes (P = 0.013).

Conclusions

The present study demonstrates for the first time that there are differences in the expression and secretion of pro-inflammatory adipokines between ABD and FEM AT and human primary adipocytes in postmenopausal women, independent of adipocyte size.

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EP356

A unique family with early-onset, severe obesity and hypopituitarism harboring different POMC pathogenic mutations.

Lauriane Le Collier1,2,3, Brigitte Delemer1, Christine Poitou-Bernert4,5, Tozzi1, Sabrina Basciani2, Rebecca Rossetti2, Angela Balena2, Vol 81

Plasma POMC activity according to in vitro analyses. Patient A is currently being treated effectively with an MC4R agonist, decreasing BMI from 41.5 kg/m² to 25 kg/m² after three years.

Conclusions

We described the segregation of three different pathogenic POMC mutations within the same family with a CPHD phenotype and severe, early-onset obesity. One of them was challenging to identify because of the limitations of targeted NGS.

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EP357

An evidence-based framework to evaluate melanocortin-4 receptor (MC4R) pathway relevance for obesity-associated genes

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Introduction

The MC4R pathway is the principal regulator of mammalian energy balance through its modulation of energy intake and energy expenditure. Variants in genes associated with the MC4R pathway can result in rare genetic diseases of obesity. Clinical data in patients with certain genetic defects in the MC4R pathway indicate that setmelanotide, an MC4R agonist, may effectively reduce weight and hunger in scientifically rationalized obese subpopulations in which MC4R-pathway deficiency is a contributing factor to obesity. Here we introduce an evidence-based framework designed to evaluate various genes' relevance to the MC4R pathway to identify those genetic patient populations most likely to benefit from long-term setmelanotide therapy.

Methods

This framework utilizes a set of clinical (human genetics) and non-clinical experimental evidence to evaluate MC4R pathway relevance and is based on the core principles of the NIH ClinGen Gene-disease Clinical Validation approach which is the industry standard for assessing gene-disease relationships. Human genetic evidence helps define the contribution of the gene to human obesity, while experimental evidence assesses involvement of the gene in the function of MC4R pathway. The cumulative weight of this evidence is used to classify MC4R pathway genes into 4 strength-based tiers: very strong, strong, moderate, weak. The nature, quantity, and quality of evidence required for each tier builds upon that of the previous tier, with higher ranked genes being more likely to define patient populations potentially responsive to long-term setmelanotide treatment.

Results

Based on a comprehensive literature review, 118 MC4R pathway genes were identified and rank ordered: 8 “very strong”, 29 “strong”, 22 “moderate”, 59 “weak”. Importantly, clinically meaningful weight and hunger score reductions following treatment with setmelanotide have been previously demonstrated in patients with obesity due to variants in 6 genes, all initially classified as “very strong” or “strong”, lending credence to this framework for the selection of patient populations most likely to benefit from long-term setmelanotide therapy.

Conclusions

This framework provides robust means of selecting MC4R pathway relevant genes and supports clinical investigation of setmelanotide responsiveness in an additional 31 “very strong/strong” genes including LEP, SIM1, MAFA2, and KSR2. A clinical trial is currently underway for patients with these gene variants.

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EP358

Reduction in Oxytocin levels predict body weight loss in patients with obesity after a very low carbohydrate ketogenic diet (VLCKD).

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Objective

We describe two first cousins presenting with neonatal corticotrophic deficiency and severe, early-onset obesity. This study aims to identify the molecular etiology of these disorders in both cases and highlights the limits of genetic investigations.

Methods

We collected the clinical-biological data of the family and, more particularly, of the two first cousins (A and B). We performed several constitutive Next-generation Sequencing (NGS) protocols focused on genes causing monogenic forms of pituitary deficits or obesity. The pathogenicity of variants was assessed via the guidelines of the American College of Medical Genetics and Genomics.

Results

Patients A and B had very early-onset obesity (≥ + 3DS at 1year) with neonatal corticotrophic deficiency and Combined Pituitary Hormonal deficiency (CPhD). The initial sequencing of three genes causing pituitary deficiency (TPT1, PROP1, LHX3) was negative. Then, by another targeted sequencing protocol, we found that Patient A carried a pathogenic compound heterozygous variant in POMC (NM_001035256.3: p.Tyr139* and p.Cys228*). However, Patient B only carried the POMC p.Tyr139* variant at heterozygous state, inherited from her mother (aunt of Patient A). Whole-exome sequencing in Patient B allowed us to identify a second pathogenic heterozygous variant in the proximal promoter of POMC (c.-11C>A) that was inherited from her father. This non-coding variant was previously reported pathogenic in the literature, with a deleterious effect on POMC activity according to in vitro analyses. Patient A is currently being treated effectively with an MC4R agonist, decreasing BMI from 41.5 kg/m² to 25 kg/m² after three years.

Conclusions

We described the segregation of three different pathogenic POMC mutations within the same family with a CPHD phenotype and severe, early-onset obesity. One of them was challenging to identify because of the limitations of targeted NGS.

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metabolic syndrome has been associated with reduced fasting serum oxytocin in larger scale mixed gender studies.

Aim

Data regarding the oxytocin system in rodent obesity models and human subjects with obesity appear divided. This study aimed to investigate the concentrations of OXT in a population affected by obesity before and after a very low carbohydrate ketogenic diet (VLCKD) induced weight loss.

Materials and methods

Subjects with obesity were enrolled at the Center of High Specialization for the treatment of Obesity (CASCIO), Umberto I Polyclinic, Sapienza University of Rome. At baseline (t0) and after eight weeks of VLCKD (t1), all patients underwent clinical evaluation, biochemical routine assessment, DXA examination for body composition (Hologic Inc., Bedford, MA, USA, QDR 4500W) and venous blood sampling in EDTA plus 500 KIU/ml of aprotinin (Abcam ab146286) for plasma OXT determination (Abcam, Ab133050, ELISA kit).

Achievement of ketosis was monitored by measuring urinary β-OH-butyrate.

Results

40 patients (26 females and 14 males) suffering from obesity were enrolled, (age = 55.5 ± 7 years and BMI = 35.7 ± 4.3 kg/m²). OXT level at baseline (t0) was 1166 ± 403 pg/ml, with no differences between males and females. At t0 OXT positively correlated with BMI and hip circumference. After VLCKD, a significant weight reduction was seen (mean BMI = 32.7 ± kg/m², mean weight loss = -8.8 kg) and OXT (t1) significantly decreased (728.2 ± 201.7 pg/ml, P < 0.001). Baseline OXT positively correlated with (r = 0.316, P = 0.046). A strong inverse adjusted correlation between weight loss and baseline OXT was also reported (r = -0.458, P < 0.005). A regression analysis showed that the reduction in OXT between t1 and t0, the grade of ketosis during VLCKD and baseline%fat mass were all predictors of weight loss (R²0.422, P = 0.025).

Conclusion

Our study demonstrated that higher OXT levels associates with BMI and with ketosis induction. A lower OXT reduction during a VLCKD seems to be unfavorable for achieving weight loss. Differences in assay method used for measuring OXT, as well as expression patterns of oxytocin receptors, could explain the partial discrepancy of our results with the literature. Peripheral actions of oxytocin deserve further investigations.

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EP359

Response of the human gastric epithelium to sleeve gastrectomy surgery

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The gastric mucosa is a dynamic and regenerative tissue that functions in extreme conditions of low pH, mechanical insults and bacterial exposure. The mucosa is composed of pit and neck cells which secrete protective mucus, parietal and chief cells that secrete acid and digestive enzymes, enteroendocrine cells that affect motility, secretion and satiety, rare tuft cells, and at two-stem-cell compartments. We studied the response of the gastric mucosa to sleeve gastrectomy surgery: a bariatric surgery, and identifies a new set of signals involved in the gastric mucosa adapts to the new anatomy. We observed an increase in the gastric mucosa adapts to the new anatomy. We observed an increase in the transcriptional program and express hormones and neurotransmitters that were positively correlated with BMI and hip circumference. After VLCKD, a significant weight reduction was seen (mean BMI = 32.7 ± kg/m², mean weight loss = -8.8 kg) and OXT (t1) significantly decreased (728.2 ± 201.7 pg/ml, P < 0.001). Baseline OXT positively correlated with (r = 0.316, P = 0.046). A strong inverse adjusted correlation between weight loss and baseline OXT was also reported (r = -0.458, P < 0.005). A regression analysis showed that the reduction in OXT between t1 and t0, the grade of ketosis during VLCKD and baseline%fat mass were all predictors of weight loss (R²0.422, P = 0.025).

Conclusion

Our study demonstrated that higher OXT levels associates with BMI and with ketosis induction. A lower OXT reduction during a VLCKD seems to be unfavorable for achieving weight loss. Differences in assay method used for measuring OXT, as well as expression patterns of oxytocin receptors, could explain the partial discrepancy of our results with the literature. Peripheral actions of oxytocin deserve further investigations.

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EP360

Long-term safety of diazoxide choline extended-release (DCCR) tablets in patients with prader-willi syndrome

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Background

Prader-Willi syndrome (PWS), a rare genetic neurobehavioral-metabolic condition, is characterized by hyperphagia, accumulation of excess fat, hypotonia, and behavioral/psychological complications. There are no currently approved medications to treat hyperphagia in patients with PWS; DCCR is under development as a treatment for PWS.

Objectives and Methods

The objective was to evaluate long-term safety of DCCR in individuals with PWS. 125 participants with genetically-confirmed PWS ≥ 4 years old with hyperphagia were treated with oral daily DCCR in multi-center studies conducted at 29 sites in the US and the UK: a 13-week, Phase 3, double-blind, placebo-controlled study (DESTINY PWS) and its long-term, open-label extension study (to 52 weeks and beyond). The target DCCR dose was 4.2 - 5.8 mg/kg. 103 patients received DCCR for 52 weeks and 54 patients received DCCR for at least 78 weeks.

Results

Overall, DCCR was well tolerated with the majority of adverse events (AEs), (77.6%) having grade 1 or 2 severity. Treatment-emergent adverse events (TEAEs) occurred in 98.4% of participants. Drug related TEAEs occurred in 80.0% of participants. Twenty participants experienced serious adverse events (SAEs), for which only two participants were considered drug-related (one patient with peripheral/pulmonary edema and another with fluid retention). There were no SAEs leading to death. The most common TEAEs were hypertrichosis (61.6%), peripheral edema (34.4%), and hyperglycemia (22.4%). TEAEs infrequently resulted in discontinuation of study drug (7.2% of participants). These results are consistent with the observed safety profile of DCCR from prior studies. Consistent with the expected safety profile of diazoxide, fasting glucose rose through Week 26 (mean change from baseline 5.2 SD mmol/l) = 0.35 ± 0.81) and returned nearly to baseline by 15 months of treatment (0.11 ± 0.06). HbA1c followed a similar pattern, increasing at 26 weeks and returning nearly to baseline by 15 months. In participants experiencing hyperglycemia, the AE resolved with continued treatment in about half of cases. About 90% of peripheral edema cases resolved while treatment continued, requiring infrequent dose adjustment (7%) or the need for diuretic treatment (3%). Most cases of hypertrichosis (> 80%) were mild and only in one instance led to discontinuation. About 35% of cases of hypertrichosis were resolved/resolving at Week 52.

Conclusions

DCCR was well tolerated beyond 52 weeks of administration. The most common treatment-emergent adverse events were expected based on prior studies of DCCR. These included hypertrichosis, peripheral edema and hyperglycemia, which were typically mild and resolved without treatment in most cases.

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EP361
Menstrual cycle characteristics in women with type 1 diabetes mellitus
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Background
Women with diabetes mellitus type 1 (DMt1) are known to have a higher prevalence of reproductive disorders, including delayed menarche, menstrual cycle abnormalities and polycystic ovary syndrome (PCOS)-like phenotype.

Objective
To evaluate the menstrual cycle characteristics of women with type 1 diabetes mellitus as well as to compare them with healthy women of reproductive age.

Methods and patients
The study included 37 women with DMt1 and 38 clinically healthy women serving as a control group. A detailed gynecological anamnesis was obtained: age at menarche, menstrual cycle interval (MC), menstruation length, dysmenorrhea, pregnancies, births, miscarriages. Oligomenorrhea was defined as having a menstrual cycle longer than 35 days throughout at least the past year. Primary dysmenorrhea was defined as painful menstruation unrelated to a secondary pelvic disease. The metabolic control was evaluated by the glycated haemoglobin (HbA1C). Anthropometric measurements, basal levels of testosterone (T), thyroid-stimulating hormone (TSH) and serum prolactin were studied in all participants. Body mass index (BMI) was calculated.

Results
There was no statistically significant difference in terms of age (P = 0.26) and BMI (P = 0.57) in the studied population. Euthyroid function and normoprolactinemia were reported in all participants. Women in the DMt1 group had statistically significantly higher T and HbA1C levels than healthy controls (P = 0.000). There was no significant difference in the age at menarche or menstruation length in women with DMt1 compared to the control group. The mean duration of MC in DMt1 group was 32.73 + 5.9, compared to the control group (30.29 ± 2.53), without reaching statistical significance (P = 0.07). 14 women (37.8%) with DMt1 reported oligomenorrhea. A statistically significant difference between the relative proportion of diabetic women with dysmenorrhea (51.4%) compared to healthy controls with oligomenorrhea (23.7%) (z-test; P < 0.05) was observed. Women with DMt1 had a higher number of pregnancies (P = 0.005), births (P = 0.03) and miscarriages (P = 0.03) compared to healthy controls. A significant correlation was found between T and dysmenorrhea (r = 0.508, P = 0.001) and with oligomenorrhea (r = 0.664, P = 0.000). There was also a positive significant relationship between dysmenorrhea and oligomenorrhea (r = 0.648, P = 0.000).

Conclusion
Despite satisfactory metabolic control, women with DMt1 have higher frequency of menstrual cycle irregularities. Early and precise examination of menstrual cycle characteristics of women with DMt1 is essential for developing a better approach towards the reproductive disorders observed in diabetic women.

Key words
type 1 diabetes mellitus, oligomenorrhea, dysmenorrhea, menstrual cycle, testosterone.

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EP362
Imidazole-osmium reduces elution of lipids from cryofixed rat hepatic tissue for ultrastructural analysis.
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Introduction
Transmission electron microscopy (TEM) is the main tool for studying the ultrastructural properties of metabolically diseased tissue. For impactful micrographs as well as for interpretation of TEM specimens, the integrity of cellular components is crucial. Elution of substances is a major problem in TEM preparation with no universal solution found so far. Investigating fatty liver disease in a rat model, an important factor is the depiction of undamaged lipid droplets. Imidazole, a highly polar heterocyclic compound, is hypothesized to enhance the binding ability of osmium tetroxide. This study aimed to investigate the effect of imidazole-osmium application before cryopreparation to prevent elution from lipid droplets.

Methods
Perfusion-fixed (4.5% phosphate buffer formaldehyde, pH 7) hepatic tissue from male Sprague-Dawley rats (n = 6; 8 weeks old) on high fat diet (60% of calories as fat; fed for 4 weeks) was processed for TEM. Prior to the procedure of high pressure freezing and freeze substitution, samples (n = 3) were pre-exposed to 1% OsO4 <cf:eq = 1-ganima41-ganima41-ganima41>4<cf:end> in 0.1M imidazole for 30 min. For comparison, a control group was not subject to such pre-exposure (n = 3). Specimens were embedded in Agar 100 resin, and the ultrastructure was analyzed in ultrathin sections (70 nm, Leica EM UC7; ZEISS Libra 120 TEM).

Results
Screening a multitude of ultrathin sections from steatotic rat livers from three separate animals revealed expletive electron dense material within the membrane of lipid droplets in imidazole-osmium pre-treated tissue. At variance to this, the conventional approach without imidazole pre-treatment displayed translucent areas with minimal granular content.

Conclusion
The chemical bond between osmium tetroxide and imidazole obviously reduced the elution of contrastable lipid molecules from lipid droplets prior to preparation and high pressure freezing with freeze substitution. This procedure promises a major advantage in the ultrastructural study of fat accumulation in hepatic tissue. Further investigations including NanoSIMS (Nanoscale secondary ion Mass Spectrometry) will be conducted to confirm this hypothesis.

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EP363
Homocysteine level in diabetic subjects with venous thrombosis
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Introduction
Homocysteine is an intermediate sulfur amino acid in the metabolic pathways of cysteine production from methionine, which is increasingly involved in various pathological processes (arterial thrombosis, depression, schizophrenia, dementia). We are interested in the course of our work to study the variation of homocysteine levels in diabetic subjects with venous thrombosis.

Materials and methods
This is an observational case-control study, comparing 47 healthy control subjects with 47 patients admitted to the internal medicine department for the management of deep vein thrombosis confirmed by radiological examination. These two groups were matched according to age, sex and body mass index. The homocysteine assay and fasting blood sugar were done by an enzymatic method. The assay of glycated hemoglobin was carried out by the reference method (high performance liquid chromatography).

Results
The mean age of patients and controls was 40.8 ± 10.5 years with ranges of 18 and 59 years. The two groups consisted of 27 men (57.5%) and 20 women (42.5%) with a sex ratio of 1.35. The diabetic subjects in our population were 14.8% in the patient group and 12.7% in the control group (without statistically significant difference). Hyperhomocysteinemia was significantly correlated with the presence of diabetes with P = 0.006 with a mean level of 26.28 ± 10 μmol/l in diabetic subjects against a mean level of 12.3 ± 5.9 μmol/l in non-diabetic subjects.

Conclusion
Homocysteine is a sulfur amino acid involved in many cardiovascular pathological processes which should be systematically screened for in all diabetics.

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EP364
Development of an electrochemical immunoassay based on competition assay for the detection of biomarkers in human urine samples
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Introduction

Diabetes mellitus (DM) is a disease characterized by increased glucose levels, mostly either due to insulin deficiency (type 1 DM) or a decreasing ability of insulin receptor binding (type 2 DM) or both. Biomarker measurements such as fasting glucose and haemoglobin A1C are vital to detect and monitor DM. In addition to these parameters and antibody testing, insulin determination has been used for classifying different types of DM. However, the disadvantage of insulin measurement is a rapid degradation in the blood through hepatic metabolism. Moreover, interferences may arise from exogenous insulin injection. In contrast, C-peptide is co-secreted along with insulin in equimolar quantity, consisting of 31 amino acids and a longer half-life of 30 minutes compared to 3-5 minutes with insulin. Therefore, it can be detected in urine samples, reflecting insulin metabolism by non-invasive samples, as this is also not subjected to exogenous insulin interference.

Objective

We aim to validate urinary C-peptide as a reliable and sensitive biomarker for determination of the beta cell function using a point-of-care approach.

Method

The proof-of-concept for electrochemical detection of C-peptide is based on competition format. We utilize a self-assembled monolayer for covalent attachment of the coating C-peptide onto the screen-printed electrodes. Various concentrations of C-peptide were measured using an antibody against C-peptide, labelled with an enzyme to generate the signal, and a laptop/mobile phone used as the output reader.

Result

We are able to show that our proof-of-concept works for C-peptide determination. The developed sensor obtained a limit of detection of 3.5 ng/ml in spiked urine samples. In addition, the assay showed a high specificity to C-peptide with no known cross-reactivity to other related structures such as insulin.

Conclusion

Further evaluation of the assay is ongoing in our laboratory to further improve the sensitivity of the assay. Overall, our proof-of-concept for the determination of urinary C-peptide is a reliable and it can be miniaturized for easy-to-use portable assay which can be used to support diagnosis and monitoring of DM to prevent the progression of the disease and further complications.

Conclusion

These results indicate substandard diabetic care for patients in Libya. It also outlines a high rate of diabetic ketoacidosis (DKA), a life-threatening condition for diabetic patients and requires intensive care that is lacking in Libya. Improvement in emergency care for diabetic patients in Libya is advocated to avoid future morbidity and mortality.

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EP366

Characterization of a cohort of patients with type 1 diabetes during their unstructured transition to adult care

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Background and aims

Transition of patients with type 1 diabetes (DM1) from pediatric to adult care is challenging and international guidelines recommend effective transition programs. The aim of this study is to describe our baseline situation, without a structured transition program, and to identify factors associated with worse glycemic outcome.

Materials and Methods

This is an observational, retrospective study of patients with DM1, aged 14 or more on 09/03/2020. We analyzed demographic variables and variables related with metabolic outcomes and complications. A descriptive statistical analysis was performed and comparisons were made pre- and post-transition (Students t, Wilcoxon test), using R Core Team 2020, 3.6.3. Factors associated with changes in HbA1c and admissions were assessed (Spearman R. Mann-Whitney’s test, chi-squared). A p-value < 0.05 was considered significant.

Results

We have currently included 67 patients (58.21% male), 64.2% of whom had adult-care follow-up. HbA1c was 7.7% +/- 1.1 before transition and 8.5% +/- 1.8 (P = 0.007) thereafter, despite an increase in their daily insulin dose (10.8 +/- 0.3 UI/kg vs 9.2 +/- 0.3 UI/kg, P = 0.008). During transition, 29.8% of patients had at least one admission to the hospital for acute complication, mainly diabetic ketoacidosis (DKA) or hyperglycemia. Patients who had a continuous glucose monitor (CGM) (24.6%) had a significant improvement in HbA1c during transition (-0.34% +/- 1.3) when compared to those without (+ 0.84% +/- 1.53%, P = 0.045) and had no admissions for DKA (vs 26.1% without CGM (p = 0.028)). Worse glycemic control was also associated with a lower height percentile (Spearman’s R 0.38, P = 0.003), higher levels of triglycerides (Spearman’s R 0.33, P = 0.031), LDL-cholesterol (Spearman’s R 0.62, P < 0.001) and total cholesterol (Spearman’s R 0.59, P < 0.001). Admissions due to acute complications were associated with loss of follow-up (P = 0.043, OR 4.29, IC 1.19 - 15.41) and a longer time between last pediatric visits and first adult appointment (151 +/- 246.18 vs 449.87 +/- 420.26 days, P = 0.037).

Conclusion

Despite the small size of this cohort, we observed a worsening of glycemic and metabolic outcomes during the unstructured transition. We also observed an increased risk for acute complications in patients with loss of follow-up. The association between the use of CGM and improved glycemic control and lower risk of hospital admission has to be interpreted with care, given the retrospective nature of the study, but it could be related with the “booster” education received with the device.

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EP367

Levels of IL-10 in CD4+ and CD8+ in patients with Type 2 diabetes mellitus and their correlation with mediterranean diet and anthropometric variables

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Introduction

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia due to absolute or relative insulin deficiency. Mediterranean diet (MD) is a healthy, traditional diet that is becoming increasingly popular. The aim of the present study was to assess the levels of IL-10 in CD4+ and CD8+ in patients with type 2 diabetes mellitus (T2DM) and their correlation with MD and anthropometric variables.
Regarding body composition, a significant inverse correlation was shown between fat mass and CD4 free mass and CD4 C. Regarding body composition, a significant inverse correlation was shown between fat mass and CD4 free mass and CD4 C. Regarding body composition, a significant inverse correlation was shown between fat mass and CD4 free mass and CD4 C. Regarding body composition, a significant inverse correlation was shown between fat mass and CD4 free mass and CD4 C. In T2DM patients, significant differences were also found regarding sex, specifically in O mg/ml and Ferritin: values than in healthy controls (1.304 C Z 0.052), as well as a significant direct correlation between fat mass and 

Exceptions

Conclusions

IL-10 expression was increased in CD4 + and CD8 + populations in T2DM, and significant correlations were found between Mediterranean diet and body composition.

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EP369

Development of THE allele-specific PCR method for studying insulin gene rs689 polymorphism

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Background

Insulin gene (INS) is known to be responsible for production of insulin by the pancreatic β-cells. It includes variable number of tandem repeats (VNTR) of oligonucleotide consequence (ACAGGGGGT/GC/TGCGG) in the promoter region (Bell et al., 1981,1982); being the gene involved in the susceptibility to various pathologies. The allele-specific PCR allows direct diagnosis of some genetically determined disorders is rather simple and precise. However, by today, there have been no data on the use of the allele-specific PCR for the INS gene rs689 polymorphism.

AIM

The work was initiated to develop a protocol for simple, quick and precise PCR method to determine INS gene rs689 polymorphism.

Materials and methods

To study INS gene rs689 polymorphism, we used a modified method of allele-specific PCR. Original design of primers was performed by means of bioinformation analysis of NCBL database, Genome Browser with Biodit app. The genotyping was performed using Applied Systems-7200 programmed thermocycler.

Results

To pick up the INS gene nucleotide sequence from the NCBL database is the first step of the procedure. Oligoprimers was synthesized at the Academician S.U. Yunusov Institute of Chemistry of Plant Substances, Uzbekistan Academy of Sciences. The INS gene polymorphic region (rs689) was amplified by means of allele-specific PCR. The primers synthesized as the result were the basis for development of novel test-system intended for determination of INS gene rs689 polymorphism by allele-specific PCR. The efficacy of the method was assessed in the studies in the frames of research grant for patients with diabetes mellitus.

Conclusion

The modified protocol based on the allele-specific PCR intended for study on the INS gene rs689 polymorphism was developed. The protocol can be used in study on various pathologies in diabetes mellitus, insulin resistance, polycystic ovarian syndrome, adrenocarcinoma esophagogastric junction, neurodegenerative disorders, etc.

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EP370

Compliance and quality of life in people with type 2 diabetes

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Introduction
Type 2 diabetes mellitus (DM2) is the most common disease in the spectrum of metabolic disorders, with its prevalence increasing significantly in recent years. It is estimated that by 2035, 592 million people will have type 2 diabetes. People with type DM2 have high rates of depression and a quality of life that is poorer than that of the general population. Another important factor in the quality of life of people with DM2 is the compliance of patients with the treatment which affects the outcome in the management of diabetes.

Purpose
The purpose of this study was to investigate the quality of life in people with DM2, the compliance with medication and other guidelines of health care professionals, and finally correlate these variables.

Material and Method
This cross-sectional study included two questionnaires, regarding the compliance and quality of life in a Greek population with DM2. The procedure was performed in two phases by distributing the questionnaires twice, three to five months apart. The convenience sample consisted of 73 adult patients with DM2.

Results
The results of the present study showed greater impact in the quality of life regarding sex life, freedom to eat and freedom to drink while less impact was observed on dependence from others. In terms of compliance with the medical instructions and medication, it was found to be statistically increased after a 15-minute nursing intervention. Regarding the glycosylated hemoglobin levels, the mean value was lower in the second measurement in a statistically significant degree after the intervention. Age, gender, lower level of education and low financial status did not seem to be associated with low quality of life scores in the present research study.

Conclusions
Health care professionals should consider not only the clinical parameters but also the lifestyle of each person with DM2 considering the physical, spiritual, cultural, social background and gender differences. Individualized care plans should be developed with a focus on patients, aiming on diet, exercise, and individual counseling to achieve optimal quality of life and compliance with the treatment.

Conclusions
Postpartum weight loss was observed in 74.4%, glycemic control was observed in 60% and significantly associated with exclusive breastfeeding (P < 0.000), as breastfeeding has benefits for infant health, but also for maternal health, lactation and quality of life in patients with DM2. Additionally, we found a positive impact on glycemic homeostasis and weight loss. This can be explained by the needs of milk production. The mammary gland needs glucose to make lactose. The objective of this study is to evaluate the impact of breastfeeding on glycemic control and weight loss.

Results
The results had indicated that the mean age of 35 years, predominantly type 2 diabetes (89%), a mean weight at conception was 80kg. Only 13% of the patients had planned their pregnancy, 57% of the patients were on insulin, 83% of the patients were breastfeeding. 36% of them were exclusively breastfeeding, the predominant duration of breastfeeding was more than 12 months (37%), postpartum weight loss was observed in 74.4%, glycemic control was observed in 60% and significantly associated with exclusive breastfeeding (P = 0.000), as

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well as with the duration of breastfeeding of more than 12 months ($P = 0.000$), the latter was correlated with postpartum weight loss ($P = 0.02$).

**Conclusion**

Our results underline the positive impact of breastfeeding on weight loss and glycemic control, hence the need to systematically insist on breastfeeding in women with diabetes.

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**EP374**

**Modulation of antimony mediated therapy for an optimal insulin secretion during visceral leishmaniasis**

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Objective

Visceral Leishmaniasis is a macrophage associated disorder for the treatment of which antimony based drug like Sodium Antimony Gluconate has been the first choice in the recent past. About 5% of the patients may develop insulin dependent diabetes mellitus. It appears to have a direct action on pancreatic beta cells, resulting in initial insulin release followed by impaired insulin secretion. Within this context we looked into alternate therapies of treatment along with SAG on triggering the CD2 epitope.

Methods

We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug resistant or susceptible strain of Leishmania donovani with 3 million parasites via-intra-cardiac route. Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments. Insulin levels were also determined on the same intervals.

Results

The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-$\gamma$ was not statistically different between combination vs monotherapy ($P = 0.208$) but CD2 treatment even alone significantly influenced IFN-$\gamma$ production than either SAG treatment ($P = 0.045$) or with CD2 adjunct SAG treatment ($P = 0.005$) in Ld-S strain as well as in Ld-R strain. The influence of CD2 adjunct treatment was also documented in anti-leishmanial functions in macrophages. Interestingly insulin levels were observed to be optimal on supplemting SAG along with CD2.

Conclusion

SAG along with CD2 could be used as a potential therapy to overcome incidences of Diabetes mellitus during Visceral Leishmaniasis.

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**EP375**

**Phenotypical variability in hepatocyte nuclear transcription factor 1 beta (HNF1b) gene mutation – A five case report**

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Introduction

MODY 5 is a rare form of autosomal dominant monogenic diabetes with a broad phenotypical spectrum that occurs with pancreatic and extra-pancreatic clinical manifestations, such as: malformation and dysfunction of the pancreas, nephrologeric anomalies, impaired renal function, hepatopathy and neurocognitive defects. It is caused by a mutation of the gene encoding hepatocyte nuclear transcription factor 1 beta (HNF1b).

**Case 1**

Male, 8 years-old with a history of developmental delay, facial dysmorphia, macrocephaly and pielic dilatation. At the age of three a genetic test revealed 17q12 microdeletion associated with HNF1b mutation. Blood analysis revealed a HbA1c 4.7% and C-peptide (C pep): 1.0mg/ml (RR: 1.1-4.4). To date, at the age of eight, he remains euglycemic, with a HbA1c 5.5% and a C pep 0.94 ng/ml, without any treatment.

**Case 2**

Male, 15 years-old, diagnosed with renal cysts and motor skills disorder. At age of 14 a genetic test revealed 17q12 deletion. To this date the patient remains euglycemic, with a HbA1c 5.2%, without any treatment.

**Case 3**

Female, died at 49 years of age with sepsis, with a history of developmental delay, diabetes diagnosed at 16 years of age, kidney chronic disease and hepatopathy of unknown etiology. Started hemodialysis at the age of 43, renal transplant at 46 years-old. Genetic test revealed a 17q12 deletion associated with HNF1b mutation. She was on insulin therapy.

**Case 4**

Male, 16 years-old, diagnosed with CKD G2A2 KDIGO, multiple bilateral renal cysts and pielic dilatation. At age of six, a diagnosis of diabetes was made (insulin deficiency symptoms and no acute complications) and started insulin. Abdominal CT scan revealed pancreatic agenesis. C pep <0.02 ng/ml. Genetic test revealed: HNF1b – c.301G>b. (p.S101*) Currently the patient is on functional insulin therapy. HbA1c: 7.2%.

**Case 5**

Male, 23 years-old with progressive renal dysfunction due to bilateral renal cysts, underwent kidney transplant at the age of 19. After a few weeks diabetes was diagnosed (HbA1c 8% and C pep: 3.89 ng/ml) and started on insulin. Genetic test revealed: HNF1b – variant c.443C>T (p.S148L). Last visit: HbA1c 8.3%, C pep 4.06 ng/ml. Cr: 2.5 mg/dl and GFR: 36 ml/min/1.73 m2.

Conclusion

HNF1b gene mutation phenotype is variable and there are no pathognomonc manifestations, nevertheless, it should be suspected in patients with unusual diabetes and multisysstem involvement unrelated to diabetes, especially, renal disease. Diabetes in these mutations can develop at any age. Neurodevelopmental disorders, diabetes, nephrologeric anomalies and hepatic abnormalities may raise suspicion of a 17q12 deletion syndrome.

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**EP376**

**The growth effects of long-term (five years) prednisone therapy in frequently relapsing nephrotic syndrome of childhood: impact on statural growth and weight gain**

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Nephrotic syndrome (NS) in children usually has an onset between 2-8 years of age and steroids form the mainstay of management. Therapy may affect growth in children with relapsing NS.

**Table 1 Longitudinal growth data of NS patients on LTPT**

<table>
<thead>
<tr>
<th>Age years</th>
<th>WT</th>
<th>WTSD</th>
<th>HT</th>
<th>HTSD</th>
<th>BMI</th>
<th>BMISD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3.99</td>
<td>17.66</td>
<td>0.19</td>
<td>102.17</td>
<td>-0.38</td>
<td>16.67</td>
</tr>
<tr>
<td>SD</td>
<td>2.19</td>
<td>6.40</td>
<td>0.77</td>
<td>16.35</td>
<td>1.09</td>
<td>1.34</td>
</tr>
<tr>
<td>Mean</td>
<td>6.72</td>
<td>26.97</td>
<td>0.70</td>
<td>118.98</td>
<td>-0.35</td>
<td>18.29</td>
</tr>
<tr>
<td>SD</td>
<td>2.50</td>
<td>11.77</td>
<td>1.37</td>
<td>15.16</td>
<td>1.02</td>
<td>4.22</td>
</tr>
<tr>
<td>Mean</td>
<td>8.93</td>
<td>34.88</td>
<td>0.42</td>
<td>126.91</td>
<td>-0.79</td>
<td>19.98</td>
</tr>
<tr>
<td>SD</td>
<td>3.85</td>
<td>21.30</td>
<td>1.28</td>
<td>21.44</td>
<td>1.10</td>
<td>5.68</td>
</tr>
</tbody>
</table>

**Table 2 Percent abnormalities after 3 and 5 years of LTPT**

<table>
<thead>
<tr>
<th></th>
<th>Beginning</th>
<th>After 3 yr.</th>
<th>After 5 yr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMISD &gt; 2</td>
<td>2/32</td>
<td>7/32</td>
<td>8/32</td>
</tr>
<tr>
<td>% Obesity (OB)</td>
<td>6.25%</td>
<td>21.88%</td>
<td>25.00%</td>
</tr>
<tr>
<td>BMISD &gt; 1&lt;2</td>
<td>6/32</td>
<td>7/32</td>
<td>10/32</td>
</tr>
<tr>
<td>(OW)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% OB</td>
<td>18.75%</td>
<td>21.88%</td>
<td>31.25%</td>
</tr>
<tr>
<td>Total OB and OW</td>
<td>8/32</td>
<td>14/32</td>
<td>18/32</td>
</tr>
<tr>
<td>%</td>
<td>25.00%</td>
<td>43.75%</td>
<td>56.25%</td>
</tr>
</tbody>
</table>

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Aim
This study was carried out to investigate linear growth and weight gain in children with NS and multiple relapses who receiving long-term prednisone therapy (LTPT) for 5 years.

Methods
Data of 30 children with SSNS was analysed retrospectively. They received prednisolone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. (height, HtSDS, weight, BMI and BMISDS) were recorded each clinic visit along the treatment period. Growth data were correlated with the cumulative dose of steroid.

Results
The mean cumulative prednisone = 125 +/- 28 mg/kg/yr given over an average duration of 5 years. The HtSDS was not affected after 3 years (from -0.38 to -0.35 respectively) but decreased to -0.79 after 5 years (-0.4 SD loss). The BMISDS increased from 0.65 to 0.97 and 1.1 after 3 and 5 years respectively. Obesity (OB) and overweight (OW) increased from 25% pre-treatment to 59.2% after 5 years of treatment. Hypertension was detected in 12.5% and 23% of patients after 3 and 5 years of treatment.

Conclusion
Long term prednisone therapy (for 5 years) with a mean cumulative dose of prednisone = 125 +/- 28 mg/kg/yr, was associated with a small decrease in the HtSDS but significant increase in the BMISDS, OW, obesity and hypertension.

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EP377
Degenerative complications after insulin therapy: are there benefits to prescribing analogue insulin compared to human insulin?
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Introduction
Over the past two decades, the development of genetic engineering techniques has led to the emergence of insulin analogue that have the advantage of improving diabetes quality of life compared to human insulin. The aim of our study was to compare the frequency of occurrence of degenerative complications in two groups of patients with type 2 diabetes (T2D) on human insulin (NPH) and analogue insulin, and thus determine whether or not there are benefits to prescribing analogue insulin.

Materials and methods
Prospective comparative study involving 88 T2D patients, carried within the National Institute of Nutrition in Tunis and hospitalized for insulin therapy. Patients were divided into two groups: (G1) including 44 patients on human insulin and (G2) including 44 patients on analogue insulin. The presence or absence of degenerative complications was noted in both groups 18 months after insulin.

Results
Median age was 55.6 years in G1 versus 52.8 years in G2 (P = NS). Median diabetes duration was 7.1 years in G1 compared to 8.92 years in G2 (P = NS). Peripheral neuropathy was the most common complication in both groups (59.1% in G1 versus 68.2% in G2; P = NS). Diabetic retinopathy was present in 36.6% in G1 versus 40.4% in G2 (P = NS). Diabetic nephropathy was more present in G1 than in G2 (28.9% versus 20%; P = NS). Impaired renal function was more present in G1 than in G2 (41% versus 39%; P = NS). Coronal heart failure was the most common macrovascular complication in both groups (29.6% in G1 and 25.3% in G2). There was no statistically significant difference (P = NS) between the two groups for each of the macrovascular complications.

Conclusion
The two groups were comparable for the frequency of occurrence of different micro and macro vascular complications. In addition, patients on insulin analogue were less likely to develop diabetic nephropathy, renal failure and coronary heart failure.

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EP378
Diabetes in the elderly: adherence and particularities of treatment
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Introduction
Elderly diabetics are often fragile patients at high cardiovascular risk. The medical, human and socio-economic impact of diabetes is heavy in the elderly. Symptoms in this particular population are often insidious and atypical, which can delay diagnosis and the establishment of effective treatment. Indeed, management is not always easy because it must take into account multiple parameters. The objective of our study was to study the observance and particularities of treatment in elderly diabetics.

Methods
We conducted a retrospective observational study at the National Institute of Nutrition and Food Technology in Tunis, over a period from January 2018 to September 2021. Data were collected from patients’ medical observation records. We prepared an information sheet which was used for the statistical analysis of the data.

Results
We collected 35 elderly diabetic patients. The age of the patients varied from 70 to 89 years with an average age of 76.2 ± 4.5 years. Our population was characterized by a female predominance (66%). The average duration of diabetes in our population was 5.89 ± 3.91 years with extremes ranging from 1 to 14 years. The average age of discovery was 70.29 ± 4.44 years with extremes ranging from 65 to 79 years. All of our patients were type 2 diabetics. Glycated hemoglobin varied between 6.5% and 13.9% with an average of 8.9 ± 1.9%. More than half of the population had an HbA1c greater than 8.5%. About half of the study population were on oral antidiabetics alone. Insulin therapy was prescribed in 54% of the population, of which only two patients were on insulin analogues. For patients on insulin therapy, the most prescribed therapeutic regimen in our population was the basal regimen (50%) with an average daily dose of basal insulin in the order of 0.47 ± 0.25 U/Kg/d. Therapeutic non-compliance was mentioned in 54% of patients. The main reasons for stopping treatment were the unavailability of drugs at local dispensaries (26%) and adverse effects (21%) dominated by digestive disorders due to metformin.

Conclusions
Diabetes in the elderly remains an area to be discovered. Few studies have been carried out to date. The field therefore remains open to many studies, especially in terms of therapy.

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EP379
Effect of ISGLT-2 on renal function and lipid spectrum in patients with type 2 diabetes mellitus
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Diabetes mellitus (DM) is a global medical and social problem of our time, which is faced by medical science and healthcare in almost all countries of the world. The situation in Uzbekistan follows the global trend. According to 2019 data, 230 610 patients with diabetes are registered in the country: 18 349 patients with type 1 diabetes and 212 261 - with type 2 diabetes. According to screening studies, the prevalence of type 2 diabetes in Uzbekistan over the past 14 years has increased 1.6 times and, according to the latest data (2015).

Aim
To study the functional state of the kidneys and lipid metabolism while using ISGLT-2 in patients with type 2 diabetes mellitus with diabetic nephropathy.

Materials and Methods
We studied 40 patients with T2DM with DN (CKD C2, A2). The average age was 52.7 ± 3.78 years; diabetes experience - 8 years; BMI-30 ± 0.17; Hb1C-9.2 ± 0.4%; fasting glycerina −10.2 mmol/l; eGFR-78 ml/min; TG-2.7 ± 0.44; total cholesterol-3.4 ± 0.72; MAE1 32 ± 0.125.

Results
6 months after the start of ingestion of ISGLT-2, the patients showed an improvement in renal function and lipid metabolism. According to laboratory data, there is a significant (P < 0.001) decrease in creatinine levels by 7.4 μmol/l (93.8 ± 0.05) and an increase in eGFR by 5.3 ml/min/1.73 m 2. Despite the fact that the doses of statins did not change, we observed a significant (P < 0.05) decrease in total cholesterol levels by 1.04 mmol/l and triglycerides by 1.17 mmol/l.

Conclusion
In our study, we observed a significant decrease in the level of atherogenic fractions of the lipid spectrum. Also, the dynamics of creatinine and eGFR levels confirms the safety of the drug and some nephroprotective effect, which manifests itself with a sufficiently short observation period.

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EP380
Patient experience and outcome of teleconsultation in management of T2DM during COVID-19 Pandemic in Semi urban and village population in Kerala
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Background
Coronavirus pandemic had pushed both doctors and patients to adapt to teleconsultation for routine consultations in management of type 2 diabetes (T2DM). Telemedicine is believed to be an effective resource in health access but its experience to the patient and its outcome of management are not well understood in semi urban and village population of India. Thus, this study aims to assess the experiences and outcomes of T2DM management by tele-consultation in these population.

Methods
This Cross-sectional observational study was conducted involving 250 patients with type 2 diabetes who availed teleconsultation services in two diabetes care centers in Tirur, Kerala between March 2021 to August 2021. Patient experience was obtained through an online survey questionnaire and the glycemic outcomes are gathered from base line and end of 3 months.

Results
About 135 (54%) of the patients were male, while 115 (46%) were female. Majority of the teleconsultation occurred in the 45–65-year age group. The mean duration of diabetes was 9.1 ± 4.2. Majority of T2DM patients were on ≥2 OADs (61.2%). Around 32.8% patients were using Insulins along with oral therapy. Patient experience survey response was received from 210 patients. 190 (90.47%) of patients were happy with the quality of conversations with their physician in terms of advice and instructions. Further 175 (83.33%) were satisfied with the duration of consultation. Around 195 (92.85%) would be happy to use teleconsultation again, while 200 (95.23%) would recommend teleconsultation to their friends and family. The reduction of HbA1c was 0.7% [TCV1-9.2 ± 13 vs TCV2-8.5 ± 2.2]. There was minimal change in BMI 0.73 kg/M2 [TCV1-29.87 ± 4.2 vs TCV2 29.14 ± 2.5] was observed. The self-reported hypoglycemia events were less 15 (6%) patients, no documented severe hypoglycemia.

Conclusions
The patient experience and outcomes result of the study indicate that telemedicine may confer better diabetes management during and beyond COVID-19 pandemic in sub-urban and village population in Kerala

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EP381
Mistakes revealed during continuous glucose monitoring in patients with poorly controlled Type 1 diabetes
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Introduction
There is no doubt that continuous monitoring systems can improve diabetes control. The aim of the study was to determine typical deviations of glucose and mistakes in insulin treatment, self-control, predisposing to the poor blood control. Materials and methods
30 patients with type 1 diabetes were included, mean age 21 ±7.8, mean age of diabetes manifestation 19.2 ± 13.9 years, mean duration of diabetes – 15.3 ± 7.5. Including criteria: type 1 diabetes, basal-bolus regimen of insulin injection, HbA1c above individual target level for more than 1 year. Excluding criteria: acute diseases, failure of chronic diseases. We conducted constant glucose monitoring (CGM) using blinded system (patients didn’t see results during monitoring). CGM lasted 7 days in all patients and 1988 readings were measured by the device. According to the protocol patients should have recorded in provided for them diary carbohydrates (CH) amount, doses of insulin and measure glucose levels with glucometer at least 4 times a day.

Results
We revealed statistically significant difference between HbA1c (8.9 ± 2.1%) measured in laboratory during CGM and calculated HbA1c (7.0 ± 1.2%) measured during monitoring (according to the results of standardized protocol) (P < 0.05). As far as patients were instructed to record CH, insulin doses and blood glucose levels measured at least 4 times a day it’s possible to assume that one or all parts of this daily routine are lost in patients with diabetes who didn’t achieve target HbA1c. Increased blood glucose levels during night (47.0 ± 29.0%) were associated with higher HbA1c during CGM (r = 0.5, P < 0.05). The higher dose of basal insulin (21.3 ± 9.1 IU) was associated with higher HbA1c measured in laboratory (r = 0.5, P < 0.05) and increased glucose during night (r = 0.5, P < 0.05).

Conclusion
1. Calculated HbA1c and laboratory HbA1c differ for approximately 2% in patients with poorly controlled diabetes. 2. Nocturnal hyperglycemia is associated with higher HbA1c level and higher doses of basal insulin.

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EP382
Medication Adherence in Patients with Type 2 Diabetes
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Introduction
Medication Adherence (MA) is the extent to which patients follow medical instructions. Poor MA is frequently encountered in the majority of chronic diseases, including diabetes. The aim of our study was to evaluate MA in patients with poorly controlled type 2 diabetes mellitus (T2DM).

Patients and methods
We conducted a cross-sectional study over a period of 2 months, including patients with poorly controlled T2DM, followed at the endocrinology department of university hospital Taher Sfar Mahdia. MA was assessed using the Morisky compliance questionnaire.

Results
A total of 59 patients were included with a mean age of 64.1 ± 9.6 years (56.8% were females). The mean duration of diabetes was 15.7 ± 7.6 years. Diabetes was complicated in 81.4% of cases. The average hemoglobin Alc was 10.63%. Polymedication was observed in 76.5% of patients with an average of 9.6 medications per day. Therapeutic education was performed in only 38.6% of patients. According to the Morisky score, 26.4% of patients had a good MA, 41.7% had medium MA and 31.9% had low MA. Forgetting is the first cause of this bad MA. Patients on insulin had a better MA compared to those on oral antidiabetic medications (P = 0.001).

Discussion and conclusion
MA is a challenge in the management of diabetes to achieve therapeutic goals and to prevent long-term degenerative complications. Hence the interest of therapeutic education, a process that must be continuous in the course of care in order to optimize this MA.

DOI: 10.1530/endoabs.81.EP382

EP383
Does the insulin pump improve glycaemic control in patients with type 1 diabetes?
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Introduction
Insulin pump therapy is recommended more and more in type 1 diabetic patients in order to achieve and maintain optimal glycaemic control. The objective of our study was to determine the effectiveness of insulin pump therapy in improving metabolic control in type 1 diabetic patients.

Patients-Methods
This is a retrospective, descriptive and analytical study including 20 patients with type 1 diabetes treated by insulin pump, between 2017 and 2021. All patients received a clinical evaluation, analysis of the glycaemic cycle and a dosage of HbA1c at the time of the start of insulin pump and during the evolution. Statistical analysis was performed by SPSS version-21.

Results
The mean age of the patients was 16.8 ± 8.1 years with a sex ratio (M/F) of 0.42. Thirty per-cent were children. The mean duration of diabetes was 5.8 ± 4.8 years. Seventy-five per-cent of patients practiced functional insulin therapy. The indications for insulin pump treatment were mainly hypoglycaemia and instable diabetes. During follow-up, we found a statistically significant decrease in insulin requirements, improvement in mean HbA1c and maintenance of control during
Liver autophagy, as assessed by accumulation of LC3-II and p62 proteins, is positively correlated with the severity of nonalcoholic steatohepatitis (NASH) in humans. Since growth hormone (GH) is negatively associated with liver steatosis and NASH development, and our laboratory has reported that steatosis and NASH develop in a mouse model of adult-onset, hepatocyte-specific GH- receptor knockdown (aHepGHRkd), we sought to determine if GH directly regulates the hepatocyte autophagy program, and whether this regulation is mediated via STAT5B activation. To this end, adult GHRfl/fl male mice were treated with adenovirus-associated viral vectors to generate GHR-intact control (AAV8-TBGp-null), aHepGHRkd (AAV8-TBGp-Cre) or aHepGHRkd mice with constitutive activation of STAT5B (AAV8-TBGp-Cre + AAV8-TBGp-Stat5bCA). Livers were analyzed 7 days post AAV injection, a time when steatosis is observed in aHepGHRkd mice. We first evaluated the level of p62 and LC3-II proteins in liver lysosomal fractions by western blot, from mice euthanized at 1800h (end of the normal sleep cycle, natural fasting), a time of enhanced autophagy. In this condition, we did not observe any differences in p62 or LC3-II protein levels between control, aHepGHRkd or aHepGHRkd + Stat5bCA. Since p62 and LC3-II are involved in the initiation of autophagy, but are rapidly cleared in the autolysosome, we repeated the study after treating the mice with leupeptin, that blocks Cathepsin B, H and L, and impairs amphotysin-lysosome fusion, leading to a build-up of p62 and LC3-II. In this scenario, we observed that aHepGHRkd resulted in an increase in accumulation of p62 and LC3-II, compared with GHR-intact controls, and Stat5bCA partially reversed this effect. Current literature suggests that autophagy increases in the steatotic liver to protect against NASH progression. Therefore it is possible that the increase in autophagy observed in aHepGHRkd mice is not directly due to loss of GHR signaling but secondary to the development of steatosis, since Stat5bCA also reduces steatosis in aHepGHRkd mice. Therefore, although additional studies are required to determine if GHR/STAT5B plays a direct role in regulating the autophagy process in the liver, our data suggest this remodeling process could be altered in the context of GH signaling alteration during NAFLD development.

Funding
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EP384
Regulation of glycemia in patients with type 2 diabetes with oral antidiabetics, insulin and combination therapy
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Sarmento-Cabral1,2,3,4,5,6, Elena Gutierrez-Casado5,6, Mercedes GC27
OncObesity and Metabolism, Córdoba, Spain; 2University of Córdoba, Department of Internal Medicine, Córdoba, Spain; 3Osijek Health Center Osijek, Osijek, Croatia

Aim of the study
The objectives of this study were to determine the regulation of glycemia (measured by fasting glucose levels and HbA1c) in patients with type 2 diabetes and to examine whether there is a difference in therapy (oral antidiabetics, insulin, combination) on HbA1c and median glucose levels. The study included patients with type 2 diabetes who were examined in the Health Center Osijek, Croatia.

Materials and Methods
The following data were collected in family medicine clinics: age, sex, body weight and height, as well as data from laboratory findings (fasting glucose levels, HbA1c, AST, ALT, urea, creatinine, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides). Results
HbA1c and median glucose levels were lowest in subjects on oral antidiabetic therapy (6.9% and 7.9 mmol/l), in subjects on insulin (7.4% and 8.2 mmol/l), while in subjects on combination therapy, the values were highest (9% and 9.8 mmol/l); the difference in HbA1c was also statistically significant (Kruskal-Wallis test, \( P = 0.02 \)). An association between HbA1c and glucose values with age, sex, and body mass index has not been established.

Conclusion
A statistically significant difference was observed between HbA1c values and the type of therapy, i.e., the difference was observed between subjects on oral antidiabetics and those on combination therapy, which indicates the importance of additional education of patients on self-control and achieving fasting and postprandial glycemic targets. No statistically significant difference was observed in the parameters of glycemic regulation (fasting glucose, HbA1c) with respect to age, sex and body mass index of the subjects.Key words: type 2 diabetes; glycemia; HbA1c; insulin; oral antidiabetics
DOI: 10.1530/endoabs.81.EP384

EP385
Adult-onset loss of the hepatocyte growth hormone receptor (GHR) is associated with increased autophagy in livers of male mice in the context of natural daytime fasting
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Liver autophagy, as assessed by accumulation of LC3-II and p62 proteins, is positively correlated with the severity of nonalcoholic steatohepatitis (NASH) in humans. Since growth hormone (GH) is negatively associated with liver steatosis and NASH development, and our laboratory has reported that steatosis and NASH develop in a mouse model of adult-onset, hepatocyte-specific GH-Receptor knockdown (aHepGHRkd), we sought to determine if GH directly regulates the hepatocyte autophagy program, and whether this regulation is mediated via STAT5B activation. To this end, adult GHRfl/fl male mice were treated with adenovirus-associated viral vectors to generate GHR-intact control (AAV8-TBGp-null), aHepGHRkd (AAV8-TBGp-Cre) or aHepGHRkd mice with constitutive activation of STAT5B (AAV8-TBGp-Cre + AAV8-TBGp-Stat5bCA). Livers were analyzed 7 days post AAV injection, a time when steatosis is observed in aHepGHRkd mice. We first evaluated the level of p62 and LC3-II proteins in liver lysosomal fractions by western blot, from mice euthanized at 1800h (end of the normal sleep cycle, natural fasting), a time of enhanced autophagy. In this condition, we did not observe any differences in p62 or LC3-II protein levels between control, aHepGHRkd or aHepGHRkd + Stat5bCA. Since p62 and LC3-II are involved in the initiation of autophagy, but are rapidly cleared in the autolysosome, we repeated the study after treating the mice with leupeptin, that blocks Cathepsin B, H and L, and impairs amphotysin-lysosome fusion, leading to a build-up of p62 and LC3-II. In this scenario, we observed that aHepGHRkd resulted in an increase in accumulation of p62 and LC3-II, compared with GHR-intact controls, and Stat5bCA partially reversed this effect. Current literature suggests that autophagy increases in the steatotic liver to protect against NASH progression. Therefore it is possible that the increase in autophagy observed in aHepGHRkd mice is not directly due to loss of GHR signaling but secondary to the development of steatosis, since Stat5bCA also reduces steatosis in aHepGHRkd mice. Therefore, although additional studies are required to determine if GHR/STAT5B plays a direct role in regulating the autophagy process in the liver, our data suggest this remodeling process could be altered in the context of GH signaling alteration during NAFLD development.

Funding
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EP386
Predictive factors of postoperative septic complications after flexible ureteroscopy for urinary stones
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Introduction
The recent advent of flexible ureteroscopy made endoscopic approach to kidney and proximal ureteral calculi evolve to a real effective procedure. However, this technique is not free of postoperative complications. The aim this study was to assess the predictive factors of septic postoperative complications following flexible ureteroscopy for upper urinary tract stones.

Methods
This is a descriptive retrospective study concerning 92 patients who underwent flexible ureteroscopy for renal and proximal ureteral stones in the urology department of the military hospital of instruction of Tunis between January 2015 and December 2021. Septic complication we defined as the occurrence of postoperative fever, urrosepsis, septic shock or death. We used multivariate logistic regression to assess predictive factors of septic postoperative complications.

Results
The mean age was 50 years (20 - 82). Regarding the medical history of our patients: Diabetes was found in 29 cases (32%), occupying the first place, followed by high blood pressure in 24 cases (26%) and chronic renal failure (20%). We identified postoperative complications following 26 interventions (28%) of which 13% were septic. Predictive factors of postoperative Sepsis after flexible ureteroscopy were: Diabetes (\( P = 0.032 \)), a history of urolithiasis (\( P = 0.023 \)), a history of extracorporeal shock wave lithotripsy (\( P = 0.009 \)). In our study, a quarter of diabetic patients had developed postoperative sepsis. This complication was found in only 7.9% of non-diabetic patients. Statistically, the difference was significant (\( P = 0.032 \)).

Conclusion
In light of our studies, diabetic patients have a significantly higher risk of occurrence of postoperative infectious complications. This population may require specific perioperative preparatory measures to reduce operative morbidity.

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Screening for distal and symmetric polyneuropathy in the diabetic patient: 116 cases
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Introduction
The prevalence of diabetes in the world population is increasing day by day so that its frequency reaches epidemic proportions. As a result, the complications of diabetes are becoming more and more frequent. Diabetic neuropathy, the most common complication which affect up to half of the patients.

Purpose of the study
To establish the prevalence of distal symmetrical polyneuropathy (DSPN) in diabetic patients and demonstrate the importance of screening for this complication.

Methods
This is a descriptive cross-sectional study conducted among 116 patients during their usual appointment at the consultation. Data collection was done over a period of 2 months from August 1 to September 30, 2021. All patients had a complete neurological examination. We used the Michigan Neuropathy Screening Instrument (MNSI) and the DN4 Neuropathic Pain Diagnostic Questionnaire to establish the prevalence of the disease in our population.

Results
We included 116 participants divided into 47 men and 69 women. The mean age was 62.07 (24 - 89 years). Type 2 diabetes was noted in 79% of the population. The average duration of diabetes was 12.35 years. The average blood sugar was 7.9 mmol/l, HbA1c ≤ 7% was noted in 27% of cases. The mean MNSI History score was 3.76 and 23% of patients had a score ≥ 7 indicating the presence of diabetic neuropathy in them. The mean MNSI physical score was 3.82 and 51% of patients with a score ≥ 2.5 had diabetic neuropathy. The mean DN4 score was 3.25. Our results showed that 42 patients (36%) had neuropathic pain with a score ≥ 4. Thus, PNDS was diagnosed in 57.8% of our patients. This prevalence was established on the basis of DN4 and or MNSI scores. The pediatric risk was grade 2 in 29% and grade 3 in 12%.

Conclusion
Distal and symmetrical polyneuropathy is very frequent in diabetic patients and causes a consequent morbidity. It is therefore imperative to detect it early enough for a better management.

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Diabetic muscle infarction: a case study
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Introduction
Diabetic muscle infarction (DMI) is a rare complication of long-standing, poorly controlled diabetes, and it’s more common in patients with micro-vascular complications. Herein, we present a case of DMI occurring in patient on hemodialysis, Case presentation
A 44-year-old man on maintenance hemodialysis presented with an acutely painful and swelling in his left calf. He had a 21-year history of poorly controlled diabetes, with micro-vascular complications (neuropathy and retinopathy). On physical examination: his skin was pale, his temperature was 37°C, his heart rate was 80 beats per minute and his blood pressure was 150/80 mmHg. His left calf was swollen and tender with no edema or inflammatory signs. Biochemical findings showed: C-reactive protein (CRP) 42 mg/l, CPK 179 U/l (39-308) and LDH 382 U/l (140-280). A Doppler ultrasound showed no sign of deep vein thrombosis, but demonstrated edema of the superficial tissues which prompted the practice of an MRI showing thickening of the lateral gastrocnemius muscle with edema. It is the seat of a lack of enhancement extending over 3 cm with the interposition of a few fibers of marked enhancement. The thickening and muscle edema was more important in the posterior compartment of the leg. It also showed edematous infiltration of fascia and subcutaneous cellulitis without significant enhancement and minimal fatty degeneration of the different muscle compartments of the leg. The patient was put on analgesics and activity restriction in the acute phase followed by gradual mobilization.

Conclusion
Diabetic muscle infarction is a rare and under-reported condition that should be suspected in any diabetic dialysis patient who develops a painful, swollen muscle.

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Gestational diabetes: a review of 64 cases
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Introduction
Gestational diabetes (GD) is the consequence of an exaggerated insulin resistance associated with a defect insulin secretion. It is a high-risk pregnancy due to its maternal and foetal complications, the pathogenesis of which involves maternal hyperglycaemia.

Materials and methods
This is a retrospective study of 64 parturients, carried out from January 1, 2019 to January 1, 2020 in the gynaecology obstetrics of the LaLa Meryem maternity hospital of CHU Ibn Rochd of Casablanca.

Results
The average age of our parturients was 31 years, and they were multiparous in 81.24% of cases. Obstetrical complications were dominated by HTAG (14.06%), urinary tract infections (12.50%); while macromasia (51%) and foetal death in utero (14.06%) are the two major foetal complications. The caesarcan section rate was 75%.

Discussion
These high rates of maternal-foetal complications lead us to insist on early diagnosis of gestational diabetes in order to ensure a normal course of the pregnancy and to reduce the risk of complications, without forgetting the interest of follow-up and monitoring of complications in the far postpartum period for both the mother and the child. The improvement of obstetrical and perinatal prognosis depends above all on multidisciplinary care involving the cooperation of different professionals, in particular diabetologists, gynaecologists, obstetricians, attending physicians dieticians, etc. The pharmacist also has a role of listening and advising, which can be useful to the patient. In addition, his involvement could be one of the solutions in the future in the screening of gestational diabetes. Through this study, we were able to identify the epidemiological and therapeutic characteristics, the risk factors involved, screening modalities and maternal-foetal morbidity, which allowed us to deduce the difficulties encountered during screening, diagnosis, and treatment

Conclusion
Gestational diabetes is a public health problem whose prevalence is increasing in our societies. Its short and long-term impact on children and mothers requires appropriate diagnosis and management.

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Uricemia in hypertensive type 2 diabetics: the forgotten metabolic parameter
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Introduction
Hyperuricemia is a common metabolic feature in patients with metabolic syndrome.

Aim
The aim of our work is to study the correlation between uric acid level and the metabolic profile in hypertensive type 2 diabetics.

Methods
This is a retrospective descriptive study of hypertensive type 2 diabetic patients followed in the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia between 2019 and 2021. Hyperuricemia was defined as uric acid level ≥ 360 μmol/L.

Results
100 patients were included. Mean age was 62.14 ± 12.7 years with a sex ratio (M/F) of 0.65. Diabetes has been diagnosed since 13.73 ± 9.6 years on average with a mean HbA1c of 11.06 ± 2.5%. Hyperuricemia was found in 23.75% of cases overall and in 29.41% of patients with diabetic nephropathy (DN). Uricemia was correlated primarily with renal function in type 2 diabetics. Our results also showed a significant association between uric acid levels and triglyceride and HDL levels, which could be attributed to a fructose-enriched diet.
Conclusion
Hyperuricemia has been found to correlate with major metabolic parameters in patients with diabetes notably those with DN. Its importance contrasts with the paucity of studies about its cardiovascular effects and the lack of clear guidelines regarding its management.

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EP391
Cardiovascular risk in diabetic patients with chronic kidney disease: One more turn of the screw
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Background
Poor glycemic control in patients with diabetes mellitus(DM) is a well-documented responsible factor for microvascular complications, especially eye and kidney damage. The onset of chronic kidney disease(CKD) marks a serious turning point in the clinical history of DM in terms of cardiovascular prognosis. Our study aims to assess the cardiovascular risk(CVR) in diabetic patients with CKD.

Method
We conducted a retrospective descriptive study on 88 type 2 diabetic patients with CKD, admitted during 2019-2020 to the Endocrinology-Diabetology Department of the Hedi Chaker University Hospital, Sfax, Tunisia.

Results
The mean age was 68.7±10.9 years with a male predominance(52.3%). Active smokers represented 12.5%. We noted a family history of CKD and early cardiovascular events in 12.5% and 5.7% of cases, respectively. The mean duration of the evolution of diabetes was 13±9 years. We highlighted a glycemie imbalance in 80.2% of patients with a mean fasting plasma glucose of 2.78±1.5g/l and an average HbAIC level of 9.68±2.5%. Dyslipidemia and hypertension were encountered in 94% and 86.4% of cases, respectively. Obesité affected 35.7% of the patients with a mean BMI of 28.53 ± 5.11 kg/m². Macroangiopathy was documented in 29.5%, mainly ischemic heart disease (19.1%) and stroke (9.1%). Diabetic retinopathy was diagnosed in 53.5%. The mean glomerular filtration rate(GFR) was 32.2±13.81 ml/min/1.73 m². Most patients were Stage 3 CKD (56.8%) whereas 30.5% were stage 4 and 12.5% stage 5. Hemodialysis was undergone for 7.9%. Albuminuria was positive in 52.2% with mean proteinuria of 1.46±2.4 g/g24 h. According to the European Society of Cardiology 2021 CVR assessment, all patients are among the very high CVR range.

Discussion
Diabetic nephropathy (DN) is the first leading cause of CKD in the world. Chronic hyperglycemia is responsible for the vascular damage and progression of CKD to terminal-stage and recourse to hemodialysis. In addition to traditional CVR factors, GFR impairment and albuminuria are independent markers of CVR and overall morbidity in diabetic patients. This risk is proportional to the severity of CKD and would be maximal in hemodialysis patients. We recommend screening annually for DN using a urine dipstick test and serum creatinine measurement. Achieving the best glycemic control (A1c <7%), treating high blood pressure (<130/80 mmHg or <125/75 mmHg if proteinuria >1.0 g/g24 h and increased serum creatinine), using neprroprotective renin-angiotensin-aldosterone system blockers, and treating dyslipidemia (LDL-cholesterol <0.55 g/l) are effective measures for preventing the development of microalbuminuria, delaying the progression to more advanced stages of CKD and reducing the overall cardiovascular mortality in diabetic patients.

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EP392
Diabetic foot: a tunisian experience
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Introduction and aim
Diabetic foot (DF) is associated with increased morbimortality and cost of diabetes management. The aim of this study is to describe the epidemiological, clinical and paraclinical characteristics and follow-up outcomes of patients with diabetic foot in a Tunisian center.

Methods
It is a monocentric retrospective study of 210 patients with diabetic foot followed at the endocrinology department of the Hedi Chaker Sfax University Hospital between 1997 and 2020.

Results
Patients were predominantly men (79.6%), aged 59.1±12.2±4 years on average. Over 85% of patients were type2 diabetics, 90.4% of whom had a chronically imbalanced condition. In our population, diabetes has been diagnosed since 13.2±8.2 years while DF was the revealing factor of diabetes in 7 patients (3.4%). Approximately one third of the patients lived in poor socioeconomic conditions and 24% were illiterate. Half of the patients were obese and 25.2% were smokers. The mean time to consultation was 45.83 days (median = 15 days). The most common reason for admission was major hyperglycemia associated with DF (75.1%) while ketaocidosis was found in 29 patients (14.1%). Half of patients had lower limb arterial disease (LLAD) upon admission while peripheral neuropathy was present in 81.6% of patients. The most frequent triggers of DF were ulcer trauma (26.7%) and foot-shoe conflict (12.1%). The involvement was bilateral in 51 patients. Clinical findings showed DF infection, ulceration and plantar perforation were present in 72, 62 and 59 cases respectively. Eighteen percent patients were at gangrene stage upon admission. Lab investigation showed a mean blood glucose level at 15 ± 6.81 mmol/l. The most frequently isolated germ was Staphylococcus aureus (29 cases). Antibiotic therapy was prescribed in 62.1% of cases for a mean duration of 19.9 ± 18.6 days. Amputation was the outcome for 44 patients and the mortality rate was 1.9%. In monovariate analysis, the predictive factors for amputation were the presence of LLAD (OR = 6; P = 0.02), osteitis (OR = 34; P < 0.001) and gangrene (OR = 18; P < 0.001).

Conclusion
Despite major advances in therapeutic options, DF remains a major public health issue. Therapeutic education and primary prevention are essential to reduce the frequency and severity of DF complications and urge early management.

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EP393
Diabetic nephropathy and hypertension
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Introduction
Diabetic nephropathy is a dreadful complication of diabetes and it is the leading cause of chronic kidney disease worldwide. Hypertension is a major cause of progression of this complication.

Objective
To determine the prevalence of diabetic nephropathy, to search a correlation between the presence and duration of arterial hypertension and the occurrence of diabetic nephropathy.

Patients and methods
This is a retrospective study carried out about 184 type 2 diabetic patients, followed at the department C of the National Institute of Nutrition in Tunis. Results
The mean age was 61 ± 10 years, with a sex ratio M/F of 0.56. The mean duration of diabetes was 14 ± 8 years, the mean glycated hemoglobin (HbAIC) was 10.6%. Nephropathy was present in 37% of cases. In the subpopulation of patients with nephropathy, it was noted that 67% of patients were at the stage of microalbuminuria, 44.2% were in renal failure, mean clearance of creatinine was 57 ml/min and 79% were hypertensive. The presence of nephropathy was correlated with the duration of evolution of hypertension (74% had a duration of evolution of more than 05 years) and 62% of patients were in blood pressure imbalance.

Conclusion
Blood pressure control is crucial in diabetic patients, it allows nephroprotection and an improvement of the cardiovascular prognosis.

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EP394
The association of hypertension and type 2 diabetes
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Introduction
The association of hypertension and type 2 diabetes is frequent. These two pathologies constitute each a cardiovascular risk factor with a cumulative effect which increases the cardiovascular morbi-mortality of hypertensive diabetics.

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Objective
To measure and compare the frequency of degenerative complications of diabetes in hypertensive and non-hypertensive diabetics.

Patients and method
The study was descriptive, retrospective and included 184 type 2 diabetic patients followed at the service C of the National Institute of Nutrition of Tunis.

Results
The mean age was 61 ± 10 years, with a sex ratio M/F of 0.56. The mean duration of diabetes was 14.2 ± 8 years, the mean glycated hemoglobin (HbA1c) was 10.6%. It was noted that 69.5% of patients had hypertension. The prevalence of macroangiopathy was globally higher in hypertensive diabetics than in non-hypertensive patients (retinopathy: 33.6% vs 8.9%; neuropathy: 26.6% vs 17.8%; nephropathy: 43% vs 3.6%). Similarly, the prevalence of macroangiopathies was higher in hypertensive diabetics (stroke: 3.9% versus 0.54%; coronary artery disease: 18.8% versus 1.6%; and cerebral artery disease: 6.3% versus 1.8%).

Conclusion
Hypertension is often associated with type 2 diabetes. It worsens the cardiovascular prognosis and accelerates the onset of degenerative complications. Adequate management of arterial hypertension is therefore necessary to reduce the cardiovascular risk of diabetic patients.

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EP395
The blood lead level is the meaningful indicator to metabolic syndrome in healthy populations
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Background
Lead is known as an environmental toxic pollutant and hormonal regulatory confounder associated with obesity. Recent China scientific report shows that blood lead level (BLL) is closely related with body mass index. Therefore, we investigated the association between the prevalence of metabolic syndrome and blood lead levels in healthy general population without hypertension, dyslipidemia, and diabetes.

Methods
We assessed the socio-demographic (height, weight, alcohol and smoking, income, education and living area, waist circumference), cardio-metabolic variables (blood pressures, fasting plasma glucose, glycated hemoglobin and HDL cholesterol, triglyceride, high sensitivity C-reactive protein), BLL, after fasting over eight hours from 1,381 healthy subjects without hypertension, dyslipidemia, and diabetes, among 8,238 subjects in 2017 KHANES (Korea Health Analysis and Nutrition Examination Survey) dataset. Chi-square tests for categorical variables, Pearson’s correlation analysis, student t-test for continuous variables were performed. P-value <0.05 was considered as significant at both sided using by SPSS packages for windows (version 18, USA).

Results
As a total of 1,381 subject (43.22 +/- 0.39 years, female 55.3%), mean BMI and WC were 23.52 +/- 0.099 kg/m², 79.98 +/- 0.285 cm. The BLL was correlated with BMI, WC, age, sex, income, education, living location, alcohol, smoking, occupation, systolic pressures, diastolic pressures, fasting plasma glucose, total cholesterol, HDL-cholesterol, (P < 0.05) The BLL was very significantly correlated with BMI, WC after controlled for age, income, education, marriage, smoking, alcohol, occupation, energy intake. (P < 0.05, P < 0.001) In addition, we found hypertension, hyperglycemia, hypercholesterolemia, and hypertriglyceridemia, high sensitivity-CRP, high glycated hemoglobin, and low HDL-cholesterolemia in higher group than lower group in BLL (P < 0.05) Furthermore, it was more evident for the significant difference between two groups in women than men. (P < 0.01)

Discussion and Conclusion
As the endocrine regulator related with metabolism, the blood lead level might be associated with body weight. However, the clear mechanism between them would not be determined. BLL was closely related with metabolic syndrome in healthy general population without diabetes, hypertension, and dyslipidemia. Further controlled longer clinical trial would be considered in the future.

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EP396
Impact of bariatric surgery on body composition and cognition: a pilot study
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Aim
Bariatric surgery (BS) modifies body composition. The aim of the study was to establish the first step toward the introduction of the ultrasound (US) and bioelectrical impedance analysis (BIA) in the evaluation of body composition before and after BS. In addition, as obesity was shown to be related to global cognitive decline, we aim to determine possible changes in cognitive test before and after BS.

Material and Methods
A prospective pilot study of patients with obesity who underwent BS in our hospital. Fat mass (FM) and lean mass (LM) were calculated by BIA, and skeletal muscle index (SMI) was used for estimating muscle mass. We measured thigh muscle thickness (TMT) and subcutaneous fat (SF) of quadriceps by US. In the same visit, Montreal Cognitive Assessment (MOCA) test was done. All subjects were assessed 1 month before surgery and 12 months after it.

Results
32 patients were included (75% female, mean age: 40.15 years, mean BMI: 43.79 kg/m²). BS reduced BMI 6.63 ± 1.25 kg/m² on average (P = 0.001). About body composition, significant reductions in FM (7.26 ± 0.99 kg, CI 95% 5.23 to 9.29, P = 0.001) and SF (0.24 ± 0.08 cm, CI 95% 0.07 to 0.41, P = 0.007) were found. Conversely, although a significant increase in LM (3.76 ± 0.72 kg, CI 95% 2.29 to 5.23, P = 0.001) was observed, TMT (0.05 ± 0.12 cm, CI 95% -0.3 to 0.19, P = 0.634) and SMI (0.33 ± 0.17 kg/m², CI 95% -0.01 to 0.68, P = 0.057) did not change. When BIA and US were compared, we found a significantly correlation between the FM and SF (pre-surgical: r = 0.42, P = 0.01; post-surgical: r = 0.52, P = 0.003) and between SMI and TMT (pre-surgical: r = 0.35, P = 0.04; post-surgical: r = 0.38, P = 0.03). Lastly, MOCA score significantly increased after BS (1.13 ± 0.52, CI 95% 0.06 to 2.19, P = 0.04).

Conclusions
Our results suggest that US evaluation of TMT and SF may be complementary to BIA-derived SMI assessment for estimating muscle mass. Likewise, we also detected a possible improvement in the cognitive function of patients after BS.

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EP397
Correlation of obesity with diminished neutralizing antibody count
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The obesity epidemic, which has persisted for more than 45 years, is now being faced concurrently with the coronavirus pandemic, with deadly effects. The complex changes caused by obesity, such as chronic inflammation, are known to be detrimental in patients with COVID-19. 33.2% of the Georgian population is obese (1). Therefore, we aimed to explore the synergistic effects between obesity and SARS-CoV-2. The objective of our study is to compare the presence of neutralizing antibodies among obese and non-obese individuals 22 weeks after COVID-19 vaccination. The findings should have important implications for fine-tuning revaccination protocols for people with obesity.

Materials and Methods
In-vitro chemiluminescence immunoassays were used to quantify the serum neutralizing antibodies to SARS-CoV-2 in 30 individuals in an outpatient setting. Only patients who had received the second COVID-19 vaccine dose at least 22 weeks earlier were included in the study. Patients were divided into two subgroups according to BMI, with 15 patients with BMI >30 kg/m² in the obese group and 15 patients with BMI <30 kg/m² in the control group. In both subgroups, 40% of patients had recovered from COVID-19. The exclusion criteria for the study were the presence of autoimmune diseases, current use of immunosuppressants, or a history of COVID-19 in the prior 8 weeks.

Table 1. Values are presented as mean. BMI: body mass index.

<table>
<thead>
<tr>
<th>Parameter</th>
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<td>6/9</td>
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<td>Age</td>
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<td>Duration since Second Dose (weeks)</td>
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<tr>
<td>No</td>
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<tr>
<td>nABs (µg/ml)</td>
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<td>1,8362</td>
</tr>
</tbody>
</table>

Limitations

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of this study include the small study population size and the lack of baseline data
confirming the presence of antibodies 3 weeks post-vaccination.

Results
The serum samples of immunized patients with obesity showed lower antibody
counts than those in the non-obese group. The mean amount of neutralizing
antibodies in the obese group was 1,8362 µg/ml, compared with 19,3846 in the
control group.

Conclusion
Our study showed a strong correlation between BMI and a sustained immune
response, because most immunized patients with obesity had diminished amounts
of neutralizing anti-SARS-CoV-2 antibodies after 22 week.

EP398
Berberis vulgaris: perspectives in the treatment of non alcoholic fatty liver disease

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Introduction
Berberis vulgaris is a plant, of the family Berberidaceae. Berberine is the main
active compound of the barberry. It is an isoquinoline alkaloid of intense yellow
color. Berberis vulgaris is used in several medical purposes, including liver
protection, anti-oxidant, antimicrobial agent. It also seems to reduce the level of
cholesterol in the blood and triglycerides. Our study aims to investigate the effect
of the dietary supplement 'Berberis Vulgaris' made from the extract of the dried
root bark, on the metabolic parameters in patients with hepatic steatosis (NAFLD).

Patients and Methods
This is a double-blind randomized clinical trial conducted on 60 patients with
NAFLD, divided into two equal groups: (G1) treated with berberine and (G2)
treated with placebo. All patients received 3 capsules each day before meals.

Weight, body mass index (BMI), Waist circumference (WC), liver transaminase
levels and lipid profile were recorded in both groups before and after treatment.

Results
Our population included 17 men (28.33%) and 43 women (71.67%). The average age
of patients included in G1 is 47.71 years for men and 58.48 years for women while in
G 2 it is 58.9 years and 76 years respectively. The majority of patients in both groups
have a family history of metabolic diseases. The majority of NAFLD patients had
metallic diseases such as diabetes in 40% of G2 patients and dyslipidemia in 40%
of G2 patients and hypertension in 58.9% of G2 patients and obesity in 40%
of G2 patients and hypertension in 40%

Impact of obesity severity on the metabolic profile of obese patients

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Introduction
Obesity is one of the major public health issues worldwide and is known to be
associated with an increased risk of severe metabolic and cardiovascular
complication. The aim of our study was to assess the impact of obesity severity
on the metabolic profile of obese patients.

Materials and methods
Cross-sectional descriptive study involving 68 obese patients carried within the
National Institute of Nutrition in Tunis. The patients were divided into two
groups: 34 patients with a BMI between 30 and 34.99 kg/m² (G1) and 34 patients
with a BMI ≥40 kg/m² (G2). Each patient underwent clinical examination,
fasting blood sampling for metabolic profile and an abdominal ultrasound for fatty
liver disease.

Results
Median age was 47.67 years in G1 versus 46.85 years in G2 (P = NS). A clear
female predominance was noted in both groups with an F/H sex ratio of 4.66 in
G1 and 16 in G2. The average BMI was 32.67 kg/m² in G1 compared to 44.55
kg/m² in G2. The average waist circumference was significantly higher in G2 than in
G1 (130 cm vs 112.94 cm, P < 0.01). The prevalence of diabetes was 35.29%
in G1 and 23.53% in G2 (P = NS). Mean fasting blood glucose levels were
comparable in both groups (7.79 mmol/l in G1 and 7.4 mmol/l in G2, P = NS).
The prevalence of dyslipidemia was higher in G2 (23.53%) than in G1 (17.65%),
P = NS. The mean total cholesterol level in mmol/l was comparable between the
two groups (3.48 in G1 vs 2.87 in G2, P = NS). The mean triglyceride levels in
mmol/l was significantly higher in G2 than in G1 (1.33 in G1 vs 2.17 in G2, P = 0.0024). The average HDL cholesterol level in mmol/l was higher in G1 than in
G2 (1.28 in G1 vs 1.20 in G2, P = NS). The mean uric acid level in micromol/L
was significantly higher in G2 than in G1 (350.61 in G2 versus 284.64 in G1, P = 0.03). Fatty liver disease prevalence was higher in G2 than in G1 (11.76% vs
5.88%) with no statistically significant difference (P = NS).

Conclusion
Our study showed that the severity of obesity is associated with a higher
prevalence of metabolic disorders justifying early management of obesity in order
to delay the onset of these abnormalities.

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Introduction
Obesity is one of the most important problems worldwide in recent times. Groupal lifestyle intervention programmes are efficacious in the management of obesity. While exercise and healthy dietary habits have consistently been shown to improve various metabolic markers, adherence to these behaviors is low and methods that increase adherence to health behaviors are needed.

Objective
The primary objective of this study is to evaluate the effectiveness of a groupal weight loss programme for weight loss in obesity and its efficacy in improving health parameters related to obesity.

Materials and Methods
All participants received a groupal lifestyle intervention focused on diet, physical activity, and behavior change strategies. The duration of program was 6 months. Clinical and biochemical parameters were evaluated before and after the intervention.

Results
A total of 112 patients were included. At baseline, the mean body-mass index (BMI) for all participants was 46.1 ± 14.2 kg/m², and the mean weight was 125.8 ± 22.1 kg. The mean age was 46.9 ± 14.3 years and 72.5% were women. 60.4% had hypertension and 23.1% were diabetic. Of the 112 patients, 82 patients completed the follow-up (78.5%). 21.4% of the patients did not attend the appointments and left the program. The percentage of participants who lost 5% or more of their initial weight was 47.6%. In 18.8% of them the weight loss was < 5% and 19.6% of patients did not lose weight. Of the 39 patients who achieved the weight loss goal, a significant decrease in BP, basal glycemia, Hba1c, uric acid, T- cholesterol, and triglycerides was observed. The patients who completed the follow-up and had the best results were the oldest and those with the most comorbidities.

Conclusions
The establishment of a groupal weight loss programmes achieves objective weight loss in most patients with a benefit in analytical parameters. Less adherence to our protocolized programme was shown in younger patients, which could be due to less interest and lack of awareness of the disease. Future studies with a longer follow-up period would be interesting.

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EP403
Covid-19 infection in an individual with Down Syndrome, obesity, and hypothyroidism: a case from the UAE
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Covid-19 infection severity has been associated with pre-existing conditions including obesity. Individuals with Down Syndrome (DS) are potentially at high risk. Reports on the outcomes of Covid-19 infection in individuals with DS are scant. Here we present such a case. MA is a 27-year old Emirati male with DS, obesity and hypothyroidism. He was brought to the ER with a history of hemoptysis (2 days), fever and cough (1 week). He tested positive for Covid-19. Initial investigations showed high CRP (44 mg/l), and mildly elevated ferritin (541 mcg/l) and D-dimer (0.93 mcg/ml). A chest CT scan showed classic Covid-19 pneumonia features with moderate severity score of 10/25. On Day 7 post-admission, his condition deteriorated; septic shock secondary to gram negative septicemia with multi-organ failure developed. He required ventilator support and was intubated in ICU. Oliguria/anuria acute kidney injury (creatinine 882 mmol/l) followed, requiring hemodialysis; thrombocytopenia and deranged liver function tests were reported. He was discharged full course COVID-19 regimen with multiple courses of broad-spectrum antibiotics and antifungal medication. After 10 days, MA was extubated but remained on oxygen supplementation, until finally weaned off oxygen completely. His renal function gradually recovered; his transaminits and thrombocytopenia resolved. His severe hypanremia (sodium 170 mmol/l) improved on hypotonic fluid. MA was discharged after 5 weeks with a 10-day ICU stay. Post-Covid, swollen legs, uncontrolled headache, hair loss, and weight loss (9 kg) were noted. Hypothyroidism was inadequately controlled (TSH 11.72 mIU/l) 3 months post-discharge requiring thyroxine dose increase (150 to 175 mcg OD). This report highlights management challenges of COVID-19 infection in individuals with DS who often have other co-morbid conditions including obesity. Hospital admission can be prolonged and the course complicated by multi-organ failure. Specific preventative strategies including social distancing measures and vaccination schedules are needed for people with DS.

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EP402
Bariatric Surgery in Type 1 Diabetes patients: a single centre study
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Background
Bariatric surgery significantly aids weight loss, improves glycaemic control and/or induces remission in Type 2 Diabetes patients. However, the impact of bariatric surgery in Type 1 diabetes (T1D) patients is less well-understood. With an increasing prevalence of obesity within the T1D population, it is important to identify whether bariatric surgery improves glycaemic control and prevents future complications.

Aim
To evaluate the effect on BMI, excess weight loss, Hba1c and insulin requirements over the course of a year following bariatric surgery, in patients with T1D in a large bariatric centre.

Methods
Between 2016-2020, 647 patients underwent bariatric surgery at Royal Berkshire Hospital, UK; 6 (0.9%, 83% female, mean age 49 years) had T1D and were retrospectively identified. The bariatric surgery type, BMI, HbA1c, basal insulin (BI) requirements and excess weight loss at time of referral, 6 and 12 months post-operatively were recorded. Information on short-acting insulin doses was not collected due to data inconsistencies.

Results
The majority of patients underwent a Roux-en-Y gastric bypass (n = 5) compared to gastric sleeve gastrectomy (n = 1). A sustained improvement in BMI was noted post-operatively, (-10 kg/m² at 6 months and -14 kg/m² at 12 months). A mean excess weight loss of 53.4% and 74.8% was achieved at 6 and 12 months, respectively. There was a reduction in mean daily BI requirement overall, with a 60% reduction in insulin noted at 6 months and 50% reduction at 12 months (37.8 units at referral vs 16.2 units at 6 months vs 19.2 units at 12 months post-operatively). HbA1c decreased at 6 months (mean -6 mmol/mol [-11 to +2 mmol/mol]) but this was not sustained at 12 months post-op compared to time of referral (mean -1 mmol/mol [-13 to +2 mmol/mol]).

Conclusion
Bariatric surgery resulted in a sustained improvement in excess weight loss and BMI in patients with T1D. Improvement in daily insulin requirements were noted, particularly in the short-term. However, the reduction in insulin requirements did not correspond with a reduction in HbA1c, with only short-term benefits seen. The majority of our patients had well-controlled diabetes at referral and improvement in glycaemic control was not the primary reason for surgery. The small number of patients and short follow-up may preclude definitive conclusions on the benefit of bariatric surgery in glycaemic control and complications in T1D patients in the long-term.

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EP404
Diagnosis of sarcopenia using biompedance analysis
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Objective
To study the peculiarities of the composition in patients over 50 years old.

Materials and Methods: The study involved 130 adults aged 50 to 82 years. All subjects underwent complex examination, which included anthropometry (height, weight, body mass index (BMI)) and body composition analysis using Inbody 770 (Inbody Co.Ltd., Korea). Statistical processing of the results was performed using MedCalc Statistical software.

Results
Women’s age was 60[55.0;64.0] years, weight 74.5[66.3;85.2] kg, height 159[150.6;164.0] cm, BMI 29.4[25.0;33.8] kg/m². Body fat mass was
Impact of obesity on the development of respiratory abnormalities
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Introduction
Obesity exposes to multiple complications, including cardiovascular and metabolic ones. It can also cause respiratory problems, which are still insufficiently researched. The objective of this study was to detect respiratory abnormalities in a group of obese people followed in an obesity unit.

Methods
This was a descriptive and analytical cross-sectional study of 100 obese patients consulting at the human obesity research unit of the National Institute of Nutrition in Tunis. Each patient underwent a clinical examination (history, anthropometric parameters, eating habits, symptoms of obstructive sleep apnea syndrome) and a biological assessment.

Results
The average age of our patients was 45.08 ± 13.93 years, with a clear female predominance (88%). The average weight was 103.76 ± 17.9 kg. The average BMI was 38.95 ± 5.72 kg/m². The average waist circumference was 123.88 ± 13.13 cm and the average fat mass was 45.98 ± 12.22 kg. Sedentary lifestyle was noted in 60% of the study population. 44% of the subjects were overweight, 33% had class I obesity, 20% had class II obesity and 3% had class III obesity. The majority of our population (72%) had central obesity. Within this population, 5% had dyspnea, 65% had nocturnal snoring, 50% described daytime sleepiness and 31.3% experienced apnea during sleep. The analytical study showed a positive association between BMI and the onset of possible nocturnal snoring. On the other hand, no positive association was found between BMI and the following factors: dyspnea, daytime sleepiness and the onset of apnea during sleep.

Conclusions
The diagnosis of obstructive sleep apnea requires a systematic and early approach to clinical screening for respiratory disorders. Better accessibility to respiratory explorations would improve the quality of care in this population.

Diabetes and pancreatic cancer: what link?
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Introduction
Pancreatic cancer is one of the digestive system cancers whose prognosis has not been improved, both in terms of early diagnosis and prognosis, despite the progress in clinical, radiological and biological investigation. A significant number of patients present at the time of diagnosis of this cancer, or just before, a relatively recent onset diabetes. The link between diabetes and pancreatic cancer is established, but it is sometimes difficult to distinguish whether its occurrence is the cause or the consequence of diabetes. Hereby we report 4 observations.

Observation
The 1st case was a 64-year-old woman. The diagnosis of a metastatic bilipancreatic adenocarcinoma was discovered fortuitously on abdominal ultrasound. Palliative chemotherapy was indicated. Diabetes was discovered during the pre-chemotherapy workup with a blood glucose level of 5.5 g/l. She was on insulin therapy. The 2nd and 3rd cases: Male patients aged 57 and 71 years respectively, diabetic for 1 year and 3 months on Metformin. A pancreatic adenocarcinoma was discovered in front of weight loss and jaundice. Both of them were treated surgically and put on insulin therapy. The 4th case was a man of 84 years old hospitalized for inaugural diabetic ketosis with an altered general condition. During his hospitalization, he developed jaundice and developed diabetes associated with abdominal pain. Abdominal ultrasound revealed an extensive process at the head of the pancreas.

Discussion
The relationship between pancreatic carcinoma and diabetes has been shown in different studies, but whether it is a cause or a consequence of diabetes is not clear. Pancreatic tumors are three times higher in the diabetic population than in the general population. Pancreatic cancer presents problems that we do not know how to solve, especially the circumstances in which cancer should be sought in a patient with diabetes. In two of our observations diabetes preceded pancreatic cancer. The pathophysiological mechanisms of diabetes mellitus in these cases are multiple. At present, there is no systematic screening strategy for pancreatic cancer in diabetics. Particular attention should be paid to any diabetic patient with disturbances of the liver function.

Diabetes pregnancy: a high-risk pregnancy for the mother and the foetus. Good medical surveillance by a multidisciplinary team from the preconceptional period until delivery allows a significant reduction in fetomaternal complications. Patient education and information are an integral part of the management of diabetic pregnancy.

Discussion
The prognosis of pregnancy in diabetic women has improved considerably over the last few years in developed countries, thanks to better management, based on the planning of the pregnancy, justifying the use of reliable contraception, perfect glycaemic control even before conception, rigorous obstetrical, diabetic and neonatal monitoring, and the active participation of the patient. In the light of our study and its comparison with some data in the literature, we feel it is appropriate to emphasise a number of points: The importance of preconception management, in order to optimise glycaemic control before pregnancy, based on education and the implementation of insulin therapy techniques. Good management also requires the motivation of the diabetic woman who must collaborate with a multidisciplinary team. Facilitating access to material means for control and treatment is essential.

Discussion
Pregnancy in women with diabetes: A review of 100 cases
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Introduction
Pregnancy in diabetics is one of the most frequent forms of high-risk pregnancy. It requires diabetic-obstetric-neonatalatalogical collaboration. Its risks affect the fetomaternal prognosis in the short and long term. Materials and methods: The aim of our work is to establish the main difficulties in the management of diabetic pregnancy. This is a retrospective study of 100 pregnant diabetic patients followed at the maternity hospital of CHU IBN ROCID of CASABLANCA, for a period of 2 years. Results: The average age of the patients was 32 years. In 40% of the cases, it was a type I diabetes and 49% a type II diabetes. Gestational diabetes, on the other hand, represented only 11%. Gestational age at the time of the first consultation is on average 2 months, the monitoring rhythm is one consultation per month. Self-monitoring of blood glucose is performed in only 19% of cases. Diabetic pregnancy was complicated by foetal death in 14% of cases, macrosomia in 15% of cases, urinary or genital infection in 17% of cases, spontaneous abortion in 6% of cases and pregnancy toxemia in 1% of cases.

Discussion
The prognosis of pregnancy in diabetic women has improved considerably over the last few years in developed countries, thanks to better management, based on the planning of the pregnancy, justifying the use of reliable contraception, perfect glycaemic control even before conception, rigorous obstetrical, diabetic and neonatal monitoring, and the active participation of the patient. In the light of our study and its comparison with some data in the literature, we feel it is appropriate to emphasise a number of points: The importance of preconception management, in order to optimise glycaemic control before pregnancy, based on education and the implementation of insulin therapy techniques. Good management also requires the motivation of the diabetic woman who must collaborate with a multidisciplinary team. Facilitating access to material means for control and treatment is essential.

Discussion
Diabetic pregnancy is a high-risk pregnancy for the mother and the foetus. Good medical surveillance by a multidisciplinary team from the preconceptional period until delivery allows a significant reduction in fetomaternal complications. Patient education and information are an integral part of the management of diabetic pregnancy.

Discussion
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**EP408**

**Hypothyroidism and cardiovascular risk in type 2 diabetic’s patients**

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**Introduction**

Hypothyroidism is a frequent endocrinopathy in type 2 diabetes (T2D) which can influence the cardiovascular profile in these patients. Our aim was to study the relationship between hypothyroidism and the occurrence of cardiovascular events in patients with T2D.

**Method**

It is a retrospective study, including 184 T2D patients, conducted in the department C of the National Institute of Nutrition of Tunis during the year 2021.

**Results**

The average age of our patients was 61 ± 10 years, predominantly female 64.1%, with an average duration of diabetes of 14 +/- 8 years. The prevalence of hypothyroidism was 14%. Patients with diabetes and hypothyroidism were mostly female (72%), and more than half of the patients were older than 65 years. These patients had dyslipidemia in 84% of cases. Obesity and metabolic syndrome were present in 64% and 72% of patients respectively. The average body mass index was 31 ± 6 Kg/m². Hypothyroidism was significantly associated with macroangiopathy complications (P = 0.038) mainly coronary artery disease (P = 0.027). A significant association was also notified with renal failure (P = 0.046).

**Conclusion**

The coexistence of T2D and hypothyroidism predisposes to an increased cardiovascular and renal risk in type 2 diabetic’s patient. This highlights the importance of early detection of this pathology.

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**EP409**

Abstract withdrawn

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**EP410**

**To study the Diabetic Foot at risk using an A 60 second Foot Screening Tool and Risk classification based on the comprehensive foot examination in patients of diabetes - At a Tertiary care Center East India**

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**Introduction**

The aetiology of a diabetic foot ulcer is multifactorial. The three principal components that ascertain the likelihood of ulceration in a diabetic foot are peripheral neuropathy, repeated minor trauma and deformity. Aims: To find the prevalence of diabetes patients having the foot at risk using the Simplified 60-Second Diabetic Foot Screen tool (SSDFST).

**Materials and Methods**

This was a cross-sectional study comprising of 128 patients; a detailed history and examination including neurological and vascular assessment were performed attending a Tertiary Care Hospital. Patients were screened for the risk of diabetic foot using the SSDFST. The detection of loss of protective sensation (LOPS) using a simple 10-g monofilament test (10 g) M was highly predictive of subsequent ulceration had been reported by the Seattle Diabetic Foot Study. Foot at risk was correlated with demographic and clinical features. Data were analyzed using descriptive and inferential statistics, significant at P = 0.05.

**Results**

Our study showed that diabetes is a risk factor for diabetic foot ulcer. Of 128 patients; 92 (72%), 36 (28%) were male and female respectively. The mean duration of diabetes was 7.42 ± 6.23 years (range 1-27). The mean BMI, of the study population was 53.12 ± 10.997 years; 25.93 ± 4.464 kg/m² respectively. Out of 128 patients, 82(64%) were normal without any risk factor for diabetic foot, and 46 (36%) patients had at least one risk factor for the diabetic foot using SSDFST. About 36% of patients were combinedly qualified for the foot at risk into (category 1), 18% (14%) patients were classified into risk category 2 with LOPS + PAD and 22 (17%) into category 3 with a history of ulcer and/or amputation. The duration of diabetes, previous foot ulcer, deformity, absent pedal pulses, active ulcers, neuropathy, all these factors (P = 0.05) were significantly associated with neuropathy measured by 10 g M.

**Conclusions**

Our study revealed that one-third of our patients had at least one risk factor for the diabetic foot by using an SSDFST. About one-fifth of our patients had neuropathy detected by monofilaments. One-tenth of the study population were aware of proper foot care practice.

**Keywords**

Diabetic foot, Simplified 60-Second Diabetic Foot Screen tool (SSDFST, 10 gm monofilaments).

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**EP411**

**Cognitive decline and diabetes: what is the relationship?**

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**Introduction**

The number of elderly with cognitive decline has been increasing. Several studies have shown that diabetes is a risk factor for cognitive impairment. Chronic hyperglycemia is implicated, probably by promoting the development of cerebral microvascular disease but physiopathology is complicated.

**Methods**

The study involved thirty-seven diabetic patients hospitalized in the department C of National Institute of Nutrition and Food Technology of Tunis and who responded to the mini-mental status examination (MMSE) scale.

**Results**

We included in our study thirty-seven diabetic patients over 65 years old. The sex ratio (M/F) was 0.68. The mean age was 70.9 ± 3.5 years and the mean duration of diabetes was 15 ± 9.1 years. The mean HbA1C was 10.5 ± 2.3 and the mean BMI was 29 ± 6.9. We examined the frequency of cognitive impairment using the MMSE. An MMSE score of 26 or less was adopted as an indicator of cognitive impairment. The average MMSE score was 22 ± 6.5. The prevalence of cognitive impairment in our sample was 56.8%. The score declined with increasing age and long diabetes evolution. The cognitive impairment was associated with low level of education and the presence of hypertension and there were no significant association with the smoking.

**Conclusion**

Cognitive impairment is highly prevalent among the elderly. Subjects with disturbed glucose metabolism may be at risk of impaired cognitive function, as these disturbances can influence cognition through atherosclerosis, thrombosis and hypertension. That’s why, routine screening of cognition in older subjects with diabetes is recommended.

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**EP412**

**Retinal vein occlusion: let’s stay classic and don’t forget diabetes!**

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**Introduction**

Retinal vein occlusions (RVO) are a heterogeneous group of disorders characterized by impaired venous return from retinal circulation. RVO can be classified into branch retinal vein occlusion (BRVO), hemiretinal vein occlusion (HRVO), and central retinal vein occlusion (CRVO) depending on the site of the obstruction. Major risk factors for BRVO include systemic arterial hypertension, arteriosclerosis, and diabetes, although many associations have been reported including thrombophilia and inflammatory conditions such as Behcet disease.
Herein we report a BRVO in a young man in whom Behçet’s disease was suspected. Observation A non-smoking 36-year-old patient, type 1 diabetic for 14 years on insulin, with no other significant medical history, presented in ophthalmology department for a brutal decrease in unilateral visual acuity of the right eye. Admission examination found visual acuity 4/10 right, 10/10 left, with skin lesions on both legs. Fluorescein angiography showed BRVO in the right, with bilateral minimal diabetic retinopathy. OCT macula scan found significant macular edema in the right eye requiring intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF). Given the notion of recurrent mouth ulcers and nodular skin lesions, the patient was referred to internal medicine department for suspicion of Behçet’s disease. The admission examination found no erythema nodosum, no pseudofolliculitis, no oral or genital ulcer scars. There was no neurological manifestation, no uveitis. Dermatological examination found eruptive lesions on both legs made up of multiple confluent and circumferential erythematous and brownish macules. There were infiltrated erythematous purple inflammatory nodules on the posterolateral sides of leg, some varicosities and oedema. A skin biopsy showed non-specific necrotic remodeling of the hypodermis compatible with lipodermatosclerosis. Glycated haemoglobin (HbA1c) at 7.3%. Besides, blood count, ionogram, lipid and thyroid analyzes were normal. An exhaustive etiological investigation. As part of the etiological assessment, looking for Behçet’s disease, coagulopathy, or connectivitis, pathergy test was negative. HLA typing didn’t show HLA B27 or B51 antigen. In addition, anti-nuclear antibodies, anti-extractable nuclear antigen, anti-cyclic citrullinated peptides, cryoglobulinemia and antiphospholipid antibodies were all negative. In addition, thrombophilia investigation didn’t reveal any anomalies. Therefore, this episode was attributed to diabetes, which is already at the stage of degenerative complications (diabetic retinopathy), and the patient was referred to his ophthalmologist and endocrinologist for follow-up.

Conclusion Among the wide spectrum of RVO, diabetes remains one of the main causes. Until today, it still one of the leading causes of vision loss. So let’s stay classic and don’t forget diabetes!

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EP414
Prevalence of pre-diabetes and diabetes mellitus in polycystic ovarian syndrome (PCOS)
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Objective
To determine prevalence of pre-diabetes and diabetes mellitus in polycystic ovarian syndrome (PCOS).

Study Design
Cross sectional study. Non probability consecutive sampling was done.

Sample Size
The estimated sample size was 84 women with 95% confidence level and confidence limit of ±5%. Setting Outpatient departments of Medicine and Gynaecology & Obstetrics at a tertiary care hospital of Quetta, Pakistan. Period: January 2021 to October 2021.

Methodology
All women of age 18-40 years who fulfilled the Rotterdam criteria of PCOS were included. Those having fasting blood sugar (FBS) ≥ 126 mg/dl or 2 hour blood sugar ≥ 200 mg/dl on OGTT were said to have diabetes mellitus. Those having FBS between 100-125 mg/dl were said to have impaired fasting glucose (IFG) and those having 2 hour blood sugar between 141-199 mg/dl were said to have impaired glucose tolerance (IGT). Their age, BMI and Oral glucose tolerance test (OGTT) results were documented in the proforma. For analysis SPSS version 20 was used.

Results
The mean age in our study was 29.12 ± 6.39 years and mean BMI was 30.49 ± 4.83 kg/m². A screening OGTT revealed that 7.1% of PCOS individuals have type 2 diabetes mellitus and 30.9% had pre-diabetes (IFG, IGT).

Conclusion
The prevalence of pre-diabetes and diabetes is high in PCOS, the main risk factor is increased BMI. Prevention and education should be undertaken in such individuals to avoid future complications. Key words: PCOS, Diabetes Mellitus, Developing Country

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EP413
The association of serum magnesium and risk of morbidity and mortality in patients admitted to the intensive care unit: A stratified analysis based on COVID-19 infection classification
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Objective
To investigate the association between magnesium levels and mortality and the length of ICU hospitalization in patients without COVID-19 infection status.

Methods and patients
A total of 69 patients admitted to the ICU of Shahid Mohammadi Hospital were included in the study. The mean age was 52.56 ± 16.43 years. Out of 69 patients, 18 patients (26.1%) died during hospitalization, and 24 patients (34.8%) required mechanical ventilation. The prevalence of COVID-19 infection was 39.1% (27 patients). Our results showed that there is no difference in serum magnesium in patients based on mortality status. Also, no difference was found in magnesium levels in patients based on most of the morbidities status; however, the magnesium level of patients with kidney failure was significantly higher than patients without kidney failure (P < 0.05). Based on the COVID-19 infection classification, there was only a positive correlation between Hypomagnesemia and the length of ICU hospitalization in patients without COVID-19 (P < 0.05).

Conclusion
Our findings showed no difference in magnesium levels of patients based on mortality status. Based on morbidities status, patients with kidney failure had higher serum magnesium than those without kidney failure. Also, our results showed no difference in magnesium levels of critically ill patients based on COVID-19 infection status.

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EP415
Flash glucose monitoring in patients with type 1 diabetes
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Objective
Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Our objective was to describe the characteristics of these patients and their glycemic control expressed as HbA1c and times in range.

Methods and patients
Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM1 between 14 and 18 years. Results
95 patients included. Mean age: 16.64 ± 1.25 years, with a mean DM evolution time of 6.46 ± 3.93 years. 47.4% women. Mean HbA1c 7.81 ± 1.77%. FGM metrics: 54.17 ± 21.25% time in range, 23.61 ± 9.72% time between 180-250 mg/dl, 17.05 ± 18.26% time above 250 mg/dl, 4.21 ± 0.93% time between 54-70 mg/dl, 1.06 ± 2.21% time below 54 mg/dl. Glycemic CV 38.14 ± 4.74%. Classically, patients with a HbA1c below 7% were described as well-controlled patients. 32.6% of patients in our series achieved this target. Nowadays, among users of FGM, those categorized as well-controlled patients have to achieve a good glucose control in our patients.

Conclusion
- In our series, there are more patients categorized as well-controlled using HbA1c < 7% (32.6%) than using the FGM metrics (9.5%). - FMI has revealed that using HbA1c is not enough to achieve a good glucose control in our patients.

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EP416
Lipid profile and deep vein thrombosis
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Introduction
Homocysteine is an intermediate sulfur amino acid in the metabolic pathways of cysteine production from methionine, which is increasingly involved in various pathological processes (arterial thrombosis, depression, schizophrenia, dementia). We are interested in the course of our work to study its implication on the lipid balance in patients with venous thrombosis.

Materials and methods
This is an observational case-control study, comparing 47 healthy control subjects with 47 patients admitted to the internal medicine department for the management of deep vein thrombosis confirmed by radiological examination. These two groups are matched by age, sex and body mass index. The homocysteine assay was done by an enzymatic method. The determination of total cholesterol and triglycerides was carried out according to an enzymo-colorimetric method. The HDLc assay was performed using an endpoint enzymatic solubilization method.

Results
The mean age of patients and controls was 40.8 ± 10.5 years with extremes of 18 and 59 years. The two groups consisted of 27 men (57.5%) and 20 women (42.5%) with a sex ratio of 1.35. Cholesterolemia did not show a significant difference (P = 0.63) between the group of patients (mean ± SD 4.33 ± 10 mmol/l) and controls (4.73 ± 9.9 mmol/l). The triglyceridemia did not show a significant difference (P = 0.78) between the group of patients (mean 1.42 ± 0.56 mmol/l) and controls (mean of 1.26 ± 0.6 mmol/l). HDLc was significantly (P < 0.001) lower in patients (mean 1 ± 0.25 mmol/l) compared to controls (mean 1.33 ± 0.3 mmol/l). Homocysteine was significantly (P < 0.001) higher in diseased subjects (mean 17.42 ± 5 mmol/l) compared to control subjects (mean 9.41 ± 3.1 mmol/l). Statistical analysis showed that homocysteine correlated positively with LDLc (P = 0.002; r = 0.392) and negatively with HDLc (P = 0.002; r = -0.392).

Conclusion
Homocysteine is a sulfur amino acid involved in many disease processes: this can be partly explained by the effect on lipid metabolism with a decrease in HDLc and an increase in LDLc with their toxic cellular effects.

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EP417
Prevalence of metabolic syndrome and its correlates in young PCOS women in South India
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Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women, affecting approximately 5% to 8% of premenopausal women. Insulin resistance is believed to be a key pathophysiologic factor and increases the risk of associated metabolic syndrome (MetSyn) and diabetes. We looked at the prevalence of insulin resistance in young women with PCOS from South India. The data is derived from a larger study of polycystic amenorrheic women looking at endotheal progenitor cell response to a glucose challenge.

Methods
The study population included 39 women with anovulatory cycles and polycystic ovaries on USG. The control group were 20 age and BMI matched healthy volunteers, with normal menstrual cycles. Fasting and postprandial glycemic, lipids, insulin and hormonal measurements were compared between the two groups. Categorical variables and proportion estimates were evaluated for statistically significant difference (P < 0.05) using student’s t-test and chi-square test as appropriate.

Results
As defined by the NCEP ATP III criteria, 41% (15 out of 36) of the young PCOS women (average age 22.5 ± 4.7 years) had metabolic syndrome compared to none (0/40) in the control group (average age 22.3 ± 3.7 years). Both the groups were matched with respect to BMI, and waist hip ratio. Only the mean waist circumference was significantly higher (96.6 ± 12.8 cm vs 90 ± 9.9 cms, P = 0.004849) in the PCOS women compared to control population. Both insulin resistance and insulin secretion parameters were significantly higher in the euglycemic PCOS as compared to the control group. The insulin resistance was estimated by the HOMA IR (2.94 ± 2.01 in PCOS vs 1.65 ± 0.58 in the control, P value 0.0005) and insulin secretion by the HOMA-β values (150.2 ± 56.86 in PCOS vs 110.9 ± 29.0 in control group, P value 0.001). The strongest predictor of the presence of metabolic syndrome was the waist circumference (r value 0.64), followed by the HOMA IR (r value 0.66).

Conclusions
In this study, the prevalence of MetSyn was significantly higher in young women with PCOS compared to control group. Waist circumference and HOMA IR are strong predictors of MetSyn. MetSyn is also associated with a higher HOMA-β value in the PCOS women. The high prevalence of insulin resistance and MetSyn drives home the need to screen more aggressively for the metabolic syndrome and insulin resistance in young women with PCOS.

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EP418
New-onset diabetes after transplantation (NODAT), A case report
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New-onset diabetes after transplantation (NODAT) is a serious complication after a solid organ transplantation. It has been reported to occur in 4% to 25% of renal transplant recipients, 2.5% to 25% of liver transplant recipients, 40% to 60% of hepatitis C virus (HCV) infection and 2% to 53% of all solid organ transplantations. The diagnosis is performed using unmodified criteria for diagnosing diabetes in the general population and risk factors are the commonly recognized factors for developing diabetes: obesity, diabetes family history, dyslipidemias, etc. Recent studies suggest that hyperglycemia is associated with an increased risk of hepatitis C virus-related fibrosis development and glycemic control may reduce the risk and severity of recurrence. In addition, it is well known that liver function plays an essential role in glycemic metabolism. That’s why it is important to be aware of this bidirectional relation to decrease morbidity and mortality and preserve quality of life. In this report, we describe a NODAT case after liver transplantation whose hyperglycemic state could have preceded a worsening of HCV infection. A 42 years-old woman affected by HCV infection and cirrhosis underwent liver transplantation. After the surgery, she started a posttransplant immunosuppressive treatment (prednison). Initially her glycemic control was excellent, but five years later she asked her doctor complaining of polyuria and polydipsia. Her endocrinologist performed a blood test that showed a high glycosylated hemoglobin (HbA1c) level (11.6%) and quickly started basal insulin therapy. The study showed a normal C-peptide and negative GAD antibodies, her weight was 70 kg and she had not another diabetes risk factors. Throughout the following years, because of suboptimal control, it was necessary to add a short-acting insulin in the mayor meal (basal-plus insulin regimen) and after one year it was necessary to add insulin also in the other meals (basal-bolus regimen). HbA1c levels decreased to 7%, but some months later the patient suffered a HCV infection recurrence with stage 4 fibrosis. The Digestive System Unit quickly started Sirolius, a direct-acting antiviral agent. Then, the patient started to lose weight and a year after that she had lost 12 kg. Some months later, the patient achieved sutained virological response and insulin sensitivity improved, allowing to decrease insulin therapy until it was withdrawn. In the long run, HCV infection can lead to cirrhosis, hepatocarcinoma and death in some patients. Physicians should be aware of the importance of NODAT and addressing insulin resistance to improve disease prognosis.

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EP419
Latent autoimmune diabetes in adults revealed by graves’ disease
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Introduction
LADA (Latent Autoimmune Diabetes in Adults), is defined by the association of diabetes after 30 years, the presence of antibodies against pancreatic beta cells and the non-use of insulin therapy within 6 months of diagnosis. Graves’ disease is the first cause of hyperthyroidism associating thyrotoxicosis, goiter and exophthalmos with a prevalence 5 times higher in women.

Case report
37-year-old female patient with no notable history, labeled type 2 diabetes, put on oral antidiabetics with good clinical and biological evolution. One (1) year later faced with a glycaemic imbalance, weight loss amounting to 20 kg (Patient was overweight with BMI at 28 kg/m²) and signs of thyrotoxicosis without
among the criteria of good glycemic control, TIR is the least achieved in our series of patients, more than a third of them (35.6%) don’t present with adequate glycemic control. The frequency of thyroid autoimmunity in LADA varies in the literature between 20 et 30%. In the cases of patients without goiter or orbitopathy (like our patient), the dosage of TSH receptor antibodies (TRAb) or scintigraphy are useful to confirm the diagnosis of Graves’ disease. This work highlights the association of LADA and Graves’ disease suggesting an autoimmune polyendocrinopathy type 2.

Conclusion
In any patient with autoimmune disease, regular monitoring is indicated to detect the outbreak of a possible autoimmune polyendocrinopathy.

References

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EP420
Flash glucose monitoring in DM1: Our experience in a secondary referral hospital
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Objective
Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Our objective was to describe the characteristics of patients in a secondary referral hospital and their glycemic control expressed as FGM targets.

Methods and patients
Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM1 referred to a secondary care center in Montilla (Córdoba).

Results
101 patients included. Mean age: 42.38 ± 15.63 years, with a mean DM evolution time of 19.46 ± 12.94 years. 44.6% women. Mean HbA1c 7.75 ± 1.13%. FGM metrics: 56.57 ± 18.58% time in range, 23.5 ± 10.74% time between 180-250 mg/dl, 15.87 ± 17.05% time above 250 mg/dl, 3.90 ± 4.50% time between 54-70 mg/dl, 0.84 ± 1.90% time below 54 mg/dl. Glycemic CV 37.31 ± 7.32%. Among users of FGM, those categorized as well-controlled patients have to fulfill the following criteria: TIR ≥ 70%, TAR ≤ 25%, TBR ≤ 4% with a CV ≤ 36% as long as ≥ 70% of glucose data is obtained. In 64.4% of our patients ≥70% of glucose data was registered with FGM. In this subgroup 10.8% of patients fulfilled well-controlled criteria. The reason why patients did not achieve the criteria of adequate control is shown in table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fulfill criteria</th>
<th>%</th>
<th>Not fulfill criteria</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIR</td>
<td>14</td>
<td>21.5</td>
<td>51</td>
<td>78.5</td>
</tr>
<tr>
<td>TAR</td>
<td>18</td>
<td>27.7</td>
<td>47</td>
<td>72.3</td>
</tr>
<tr>
<td>TBR</td>
<td>41</td>
<td>63.1</td>
<td>24</td>
<td>36.9</td>
</tr>
<tr>
<td>CV</td>
<td>28</td>
<td>43.1</td>
<td>37</td>
<td>56.9</td>
</tr>
</tbody>
</table>

Conclusion
- In our series of patients, more than a third of them (35.6%) don’t present with enough FGM data. &8nbsp; endemic;esp;Out of patients with enough FGM data, only 10.8% patients of them achieve a good control if we use FGM criteria for adequate glycemic control.
- Among the criteria of good glycemic control, TIR is the least achieved in our patients (21.5%), whereas adequate TBR was the most achieved criterium (63.1%).

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Dietary rules in type 2 diabetic patients: degree of compliance and determining factors

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Introduction
Nutraion is a cornerstone of the adequate management of Type 2 diabetes mellitus (T2DM). The aims of our work are to evaluate the degree of observance of dietary rules in T2DM patients, and the factors that influence this observance.

Methods
Cross-sectional study including 84 type 2 diabetic patients followed up in the outpatient endocrinology department of Taher Sfar university hospital from September to November 2021. The data was collected in face-to-face interviews with patients.

Results
The average age was 59 ± 12 years, with a male predominance (58% of cases). The mean duration of diabetes was 9.4 ± 6.4 years. The mean HbA1c was 9.9 ± 2.4. Compliance to dietary recommendations was reported by less than half of patients (46% of respondents). Taking meals based on a dietary plan was reported in 15% of patients, having 3 meals plan per day in 88% of cases, with a regular meal time in 84% of cases, and all these factors were significantly associated to a better glycemic control (P < 10^-3). Cutting down sweets and sugary was reported in 57%, and fried food and fat intake in 71% of cases and both were significantly associated to a better glycemic control (P < 10^-3 and P = 0.04 respectively). Men and women were comparable in the degree of application of dietary rules. Besides, urban residents had better diabetic practice than rural residents. Barriers for adherence to dietary recommendations were: cultural background and communal network in 86% of cases, poor self-discipline and lack of motivation in 70% of cases, poor dietary knowledge and lack of education in 67% of cases, financial constraints in 51% of cases, lack of awareness in 33% of cases, lack of self-control in 21% of cases, fear of hypoglycemia in 19% of cases and eating outside home (in work) in 9% of cases.

Conclusion
Dietary compliance in T2DM patients is still far below the objectives. It is determined by several factors, in particular dietetic education which proves to be insufficient. Through the mutual efforts, health-care professionals can help their patients in achieving health goals by individualizing their nutrition interventions.

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Correlation of body mass index with random blood sugar levels in rural Indians – a hospital based study

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Background
Obesity is the most important modifiable risk factor in the pathogenesis of type 2 diabetes. Prevalence of diabetes is increasing in India, possibly due to a rise in obesity and changing lifestyles with nutrition transition. Body mass index (BMI) is the primary marker of obesity. Many studies have shown a positive correlation between BMI and random blood sugar (RBS) levels.

Aim
The main objective was to determine the correlation between BMI and RBS of patients in rural India.

Materials and Methods
310 patients from age 30 to 85 years who visited our hospital in rural India from January 10.2021 to February 27.2021 were included in this study. Random blood glucose was estimated using the glucose oxidase method using venous sample. BMI was calculated using standard formula using patients weight in kilograms (kg) and height (m²). Using this, the patients were categorized as underweight (<18.5 kg/m²), normal or lean BMI (18.5–22.9 kg/m²), overweight (23.0 –24.9 kg/m²) and obese (≥25 kg/m²) based on the revised consensus guidelines for India. One way ANOVA, post hoc Tukey test and Pearson’s correlation test were used to analyse the data.

Conclusions
Statistical analysis showed positive correlation between BMI and RBS. As BMI increased, there was rise in RBS with P = 0.001. Comparison of RBS with BMI using one way ANOVA test showed that the mean value of RBS in Obese individuals (165.92) is highest followed by overweight (143.36), normal or lean BMI (137.07) least in underweight individuals (124.34). This difference was statistically significant with a test value of 5.636 and p value of 0.001.

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EP426

Association of fasting plasma glucose levels with wake-up timings in diabetic patients in India

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Background

The median sleep time per night has been declining in the world consistently over last 5 decades. The timing of sleep is distinct characteristic of sleep patterns that may impact metabolic disease risk independent of sleep duration, possibly through the effects of circadian rhythms on metabolism. The sleep and wake up timings are driven by both endogenous circadian rhythms that regulate sleep propensity, energy homeostasis and metabolism as well as by sociocultural factors that influence behaviour. As diabetes mellitus carries a high risk of cardiovascular-related mortality, the impact of sleep deprivation on glucose regulation suggests a mechanism whereby short sleep time might increase mortality.

Aim

Aim of our study was to determine the association of wake-up timings with fasting plasma glucose levels in rural Indians.

Materials and Methods

512 diabetic patients between age group 25 years to 75 years who visited our hospital in rural India from September 11, 2020 to June 15, 2021 were studied. Sleep timings and wake up timings were noted. Fasting plasma glucose levels were obtained by venepuncture after an overnight fast of at least 8 hours and blood glucose estimation done by the hexokinase method. One way ANOVA and post hoc Tukey test were used for analysis.

Results

We found that fasting plasma glucose was significantly higher in patients who wake up after 0700 hours compared with patients who wake up early before 0600 hours. This difference was statistically significant with P value of less than 0.001. Furthermore, fasting plasma glucose values were significantly less (better) in the patients who wake up before 0500 hours.

Conclusions

Our study supports that waking up early (before 0600 hours) in the morning can lead to better fasting glucose levels compared to those who wake up after 0700 hours. One possible explanation for these associations is circadian disruption, which occurs when different endogenous circadian rhythms are not synchronized with one another and/or with the external world. Circadian disruption could occur when the timing of volitional behaviours, including sleeping and eating, are not aligned with the endogenous circadian rhythms of associated physiological processes, such as sleep propensity, insulin sensitivity, or glucose metabolism. Waking up early provides more time to do physical activity and also for recreational purpose which leads to better fasting blood glucose levels. Further research is necessary to determine whether sleep and wake up timings do in fact lead to alterations in glucose metabolism.

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EP427

The role of deferoxamine (DFO) in insulin resistance and diabetes

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Iron also plays an important role in many physiological processes, including redox balance, inflammation, and metabolism. It is reported perturbation of iron (Fe) homeostasis has also been associated with metabolic diseases. Iron reduction, with iron chelator, has preventive effects in cardiovascular remodeling and obesity. On the other hand, deferoxamine (DFO) increases hypoxia and collagen production in the kidney. Thus, the effects of DFO on metabolic disease remains controversial. As a result, we investigated the effects of DFO on obesity, inflammation, insulin resistance, and diabetes in db/db mice models with type 2 diabetes. An in vivo study was performed on 7-week-old db/db mice. Mice were treated with DFO (100 mg/kg) or placebo every other day for 16 weeks. After treatment, an intraperitoneal glucose tolerance test and immunohistochemical examinations were performed. Fasting insulin and serum lipid levels were measured at the end of the study. Also, genes involved in inflammation and lipid metabolism were analyzed by real-time PCR. The DFO treated mice showed improved obesity, insulin resistance, and decreased levels of plasma inflammatory cytokines, total cholesterol, free fatty acid, and triglycerides. Fasting glucose in DFO group was also reduced by DFO treatment. Immunoblot analysis shows transferrin receptor 1 (TIR1) levels were increased in skeletal muscles of db/db mice models with type 2 diabetes. But DFO treatment decreased transferrin receptor 1 (TIR1) levels in skeletal muscles. DFO treatment also attenuated inflammatory cytokines and lipid deposition in the liver. Therefore, we consider the fine tuning of iron levels through DFO treatment as highly suggestive for preventing and/or treating insulin resistance and diabetes.

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EP428

Assessment of hypoglycemic properties of extracts from some medicinal plants in the experimental diabetes model

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Phytotherapy is the integral part of the combined treatment for diabetes mellitus. A large number of plants possessing hypoglycemic activity are described in the literature, but only small part of them is in use. Hypoglycemic effect of medicinal plants is preconditioned by the wide spectrum of compounds with biological activity in their composition. Flowers of carthamus (Carlina tinctoria) and leaves of celery (Apium graveolens) are known to possess a number of therapeutic effects, and in combination, bioactive compounds are known to amplify each other’s effects. In this connection, we have studied hypoglycemic activity of aqueous extracts of carthamus flowers and celery leaves, as well as the mixture of their extracts in rats with alloxan diabetes. The extracts were administered intragastically for 2 weeks. The experimental animals were divided into 5 groups. Intact animals were included into the 1st group, the 2nd groups consisted of animals with alloxan diabetes (alloxan controls), the 3rd one included those administered with carthamus flowers, the 4th group consisted of those administered with celery leaves; animals with alloxan diabetes administered with the mixture of carthamus flowers and celery leaves (1:1) were included into the 5th one. Our findings demonstrated the reduction in the blood glucose of all animals with experimental diabetes after a course administration of the extracts, as compared to the alloxan controls. Thus, blood glucose in rats with alloxan diabetes was reduced to 13.5 mmol/l. Following the course administration of the extracts, the blood glucose in animals similarly reduced reaching the normal parameters. Hypoglycemic effect of the extracts under study increased in this order: celery extract, carthamus-celery mixture and carthamus extract.

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EP429

Patient with pancreatic diabetes and insulin pump

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Introduction

Pancreatic diabetes is a special category of diabetes due to diseases of the exocrine pancreas, characterized by both insulin and glucagon deficiency and clinically could be very challenging to control. We present a case of a woman with pancreatic diabetes treated with sensor augmented pump therapy after undergoing total pancreatectomy for a nonfunctional pancreatic neuroendocrine tumor (NET).

Presentation

A sixty-one years old woman underwent two years ago total pancreatectomy for a non-functioning neuroendocrine tumor. Consequently she developed pancreatic diabetes and was treated with a basal - bolus insulin regime. Her diabetes was poorly controlled despite all efforts due to severe, frequent and sudden hypoglycemic attacks, affecting her quality of life. Her HbA1c was 8.5% and
her Time in Range (TIR) was 28%, Time above range (TAR) 56%, Time below range (TBR) 16%, Glucose management Indicator (GMI) 8.5%, Glucose Variability (GV) 34.1% and Average Glucose (AG) 233 mg/dl. To achieve a better management of her diabetes, a sensor augmented pump (SAP) therapy was initiated and she was greatly improved (TIR 60%, TAR 40%, TBR 0%, GMI 7.5%, GV 30.6% and AG 173 mg/dl) and hypoglycemia was not a problem any more. Conclusion:Treating patients with pancreatic diabetes could be very challenging. Sensor augmented pump therapy can greatly improve their glycemic control, but most of all their quality of life.

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EP430
Low serum epidermal growth factor level is associated with lack of diabetic control in type 2 diabetes mellitus in diabetic patients in Jordan
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Background
The worldwide type 2 diabetes mellitus (T2DM) prevalence is increasing dramatically. Inflammation is involved in the pathogenesis of T2DM and development of insulin resistance. Lack of diabetic control is associated with alterations in the endocrine milieu and various health sequelae’s. The aim of this research was to assess if uncontrolled T2DM is associated with increased serum levels of inflammatory cytokines and growth factors when compared with controlled T2DM in diabetic patients in Jordan.

Methods
A single institution, cross sectional study design was used in this research. One hundred and ten patients with controlled DM (HbA<1c<7%), and 105 age-, gender- and body mass index–matched patient with uncontrolled T2DM (HbA<1c>7%) were recruited from the internal medicine clinic in King Abdullah University Hospital in Jordan. An antibody membrane array was used to evaluate the difference in serum levels of inflammatory cytokines, followed by enzyme-linked immunosorbent assay to confirm the results.

Results
Fasting blood glucose, serum insulin, triglyceride and HOMA-IR were significantly higher in the uncontrolled T2DM group (P<0.01). Antibody membrane array showed that epidermal growth factor (EGF) is lower in the uncontrolled T2DM, and this was confirmed by ELISA (158.77 vs 111.7 + 82.7 pg/ml, P=0.002). The binary logistic model was used to predict the likelihood of being uncontrolled diabetic based on EGF levels. After controlling for age, gender, and BMI, EGF was statistically associated with diabetes control; lower EGF levels predicted uncontrolled diabetes.

Conclusion
Our data identify a novel link between serum EGF levels and the status of lower EGF levels predicted uncontrolled diabetes. After controlling for age, gender, and BMI, likelihood of being uncontrolled diabetic based on EGF levels. This was confirmed by ELISA (158.77 vs 111.7 + 82.7 pg/ml, P=0.002). The binary logistic model was used to predict the likelihood of being uncontrolled diabetic based on EGF levels. After controlling for age, gender, and BMI, EGF was statistically associated with diabetes control; lower EGF levels predicted uncontrolled diabetes.

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EP431
Body composition and insulin resistance in type 1 Diabetes Mellitus
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Introduction
DM 1 is proposed as a condition of accelerated muscle aging and mitochondrial dysfunction as a common link regulating muscle deterioration in aging and DM 1. Loss of muscle mass is associated with insulin resistance, metabolic syndrome and cardiovascular complications.

Objectives
To analyze body composition and metabolic variables related to insulin resistance in overweight/obese patients with DM1.

Material and Methods
Observational, cross-sectional study in patients with DM1 followed up in the Diabetes Clinic of the Hospital Universitario San Cecilio, Granada. Weight (kg) and height (m) were determined and BMI (kg/m²) was calculated. The recruited individuals were classified according to BMI > or < 25. Demographic variables (age in years), metabolic variables (years of disease, insulin sensitivity factor - FSI- and glycosylated hemoglobin determined by analysis (HbA1c)) and body composition (measurement with AKERN® biocompendiometry of fat-free mass (FFM) in%, skeletal muscle mass (SMM) in kg. Calculation of skeletal muscle mass index (SMMI) in kg/m²). Results
Forty persons with DM1 were included. 48% had BMI > 25, mean age 43±15 years and suboptimal glycemic control in both groups (BMI <25: 7.3±1.2 vs BMI > 25: 7.8±1.1, P=0.21).

Conclusions
In persons with DM 1 and overweight or obesity, parameters related to less muscle mass and higher insulin requirements are detected, a context associated with insulin resistance. It could be important to establish strategies aimed at maintaining a healthy weight (muscular strength and resistance exercise intake together with a Mediterranean pattern diet avoiding excess calories and optimizing the insulin therapy dose) to reinforce muscular behavior and increase insulin sensitivity, especially in diabetics with more years of evolution with the aim of avoiding metabolic deterioration.

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EP432
Metabolic impact of flash glucose monitoring system in patients with type 1 diabetes mellitus
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Introduction
Adequate glycemic control is essential in the diabetes prognosis. It has been described that the use of glucose monitor systems leads to an improvement in different metabolic parameters as well as facilitating decision making. Material and methods
Retrospective observational study to evaluate the metabolic impact of flash sensor implantation in a cohort of patients with DM1 of Virgen de Valme University Hospital of Seville. All patients with implantation of the glucose monitoring system in the period 1/1/2020 to 3/31/2020 were included. Subsequently, different metabolic parameters were compared at baseline and at 3, 6 and 12 months after implantation. SPSS program was used for statistical analysis.

Results
154 patients (46.7% men and 53.3% women) have been analyzed. Mean age 40.3±1.02 years. MDI treatment 87.3% vs CSII 12.7%. Previous HbA1c mean to the sensor was 8.03±1.35%, with a sustained reduction observed at 12 months (8.03±1.35% vs 7.68±0.101%; P=0.036). Number of capillary controls before sensor was 3.57±0.25, with an increase in sensor scans at 12 months (3.57±0.23 vs 10.62±0.69; P=0.000). Coefficient of variation before sensor was 47.15±2.38, with a decrease observed at 12 months (47.15±2.08 vs 37.66±0.63%; P=0.000). Percentage of time in range before sensor was 13.83±1.26%, with a decrease observed at 12 months (13.83±1.26% vs 5.36±0.49%; P=0.000). Percentage of time in range before sensor was 48.8±2.38, with an increase observed at 12 months (48.8±2.38 vs 59.58±1.48; P=0.001). Percentage of hyperglycemia before sensor was 38.08±2.54, with a decrease observed at 12 months (38.08±2.54 vs 35.06±1.6; P=0.043).

Conclusions
- The implantation of the sensor has shown, as in the literature, improvement in metabolic control in terms of HbA1c, number of controls, coefficient of variation, hypoglycemia time and time in range.
- Some parameters showed initial improvement but attenuated over time.

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EP433

Why do diabetic patients fail to break the fast in hypoglycaemia? About 58 cases

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Introduction
Ramadan fasting is associated with an increased risk of hypoglycaemia in diabetics.

Purpose of the study
To assess the prevalence of diabetic patients who are unable to break the fast in the event of hypoglycaemia.

Method
Descriptive prospective study, including diabetic patients followed in the Endocrinology department of the CHU Ibn Rochd in Casablanca from April to June 2021.

Results
Our study included 58 type 2 diabetic patients, all authorized to fast according to the DAR 2021 risk score. The average age was 57.4 years. Most patients were on sulfonylureas (51.7%). All our patients received pre-Ramadan education on the need to break the fast in the face of any hypoglycaemia. Among the patients observing the fast, 24% presented hypoglycaemia, of which 28% did not break the fast. Hypoglycaemia occurred more frequently in patients on combination insulin and oral agents (OADs) (57%) compared to OADs alone (28%). This reluctance was explained by the occurrence of mild hypoglycaemia close to the time of breaking the fast in 57% of patients.

Conclusion
Despite the pre-Ramadan education of diabetics on the need to break the fast in the face of hypoglycaemia, there is a worrying prevalence of patients who are unable to break it.

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EP434

Management of diabetic patients during the Ramadan fast: application of international recommendations in clinical practice About 91 cases

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Introduction
Fasting during the month of Ramadan is a religious rite. Fasting is not without risks in diabetic patients. Several recommendations and consensus of experts have recently made it possible to establish proposals to optimize the management of diabetics during Ramadan, and to specify the authorized population for this sacred practice.

Purpose of the study
To assess the prevalence of type 2 diabetics authorized to fast according to the DAR 2021 recommendations and to compare it with that of the old IDF 2016 classification.

Method
Descriptive prospective study, including diabetics type 2 wishing to fast, followed in the endocrinology and metabolic diseases department of the CHU Ibn Rochd in Casablanca from April to June 2021.

Results
Our study included 91 type 2 diabetic patients with an average age of 58.7 years. The average duration of diabetes was 9.5 years. The average HbA1c was 8.1%, 42% of our patients were on insulin, 43% were on sulfonylureas (SIH). In order to compare the recommendations, we classified our patients into 3 groups: group 1: Authorized to fast by the 2 classifications (35.2%) and group 2: Not authorized according to the 2 classifications (35.2%) and group 3: 39.5% authorized fasting only by DAR. Among the group 3, 27.7% were on insulin therapy, 33.4% on SIH. Acute complications, mainly hypoglycaemia, were observed in 44.5% of these patients.

Conclusion
The latest DAR 2021 recommendations allow a very large diabetic population to fast in Ramadan compared to the old classification. Waiting for more cautious recommendations, the fasting decision must be adapted to each patient, even when the risk score is reassuring.

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EP435

Dietary survey in diabetic patients during Ramadan

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Introduction
Ramadan is considered a sacred period during which Muslims practice fasting from sunset until dawn changing the rhythm of life and eating habits. The objective of this study is to evaluate diabetics diet during and after the holy month.

Patients and methods
Descriptive cross-sectional study, including diabetic patients, seen during the month of Ramadan, conducted at the Department of Diabetology and Endocrinology of the CHU Ibn Rochd of Casablanca. Data collection was done by interrogation, followed by an assessment of dietary intake by a 24-hour dietary survey conducted during and after Ramadan.

Results
A total of 74 patients were included, of which 51.35% were female. The mean age was 55.9 years. All patients were type 2 diabetics with a mean duration of 13.7 years and a mean HbA1c of 9.7%. Insulin-treated patients represented 81.08%. Only 24.3% of our patients have fasted. During Ramadan, the total daily caloric intake was lower in the fasting group than in the non fasting group (1658.70 kcal/d versus 1860.41 kcal/d). Among the fasting group, carbohydrate consumption was higher than among the non-fasting group during Ramadan with respectively 52.35% versus 46.59% but fat consumption was higher among the non-fasting group. Fiber and water consumption was lower during Ramadan. The diet of the fasting group during Ramadan was inadequate while that of non-fasters was excessive in liquids, putting them at risk of complications.

Conclusion
The change in lifestyle during the month of Ramadan influences the dietary practices of diabetic patients which can lead to an inadequate diet hence the interest of a nutritional education program before Ramadan.

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EP436

Insulinoma with Poland Syndrome

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23-year-old scaffolder, fit and well, presented several times to A&E with episodes of fitting which comprised of an energy surge followed by typical neuroglycopenic and autonomic signs of hypoglycaemia. He was only found to be hypoglycaemic after a severe episode where paramedics were called to his home and discovered his blood sugars to be 1.3 mmol/l with a serum insulin was measurable. His symptoms were moderately relieved by eating a combination of sugary food like honey and a starchy carbohydrate. Insulinomas are the most common cause of hypoglycaemia as a result of hyperinsulinism, though only occurring in 1–4 persons per million [1]. They commonly present with autonomic symptoms such as sweating, tremor and palpitations and neuroglycopenic symptoms which include disorientation, behavioural and personality changes, visual disturbances, seizure, and coma. He had multiple presentation to emergency department with shoulder dislocation, Computed Tomography (CT) imaging demonstrated absence of the right pectoralis muscle indicative of Poland syndrome. Poland Syndrome (PS), occurring only in 1 in 20000 new-borns, typically presents with missing or underdeveloped muscles on one side of the body, resulting in abnormalities that can affect the chest, breast, shoulder, arm, and hand. The extent and severity of the abnormalities vary among affected

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Units</th>
<th>Reference Range</th>
</tr>
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<tbody>
<tr>
<td>Plasma glucose (fasting)</td>
<td>1.8</td>
<td>mmol/l</td>
<td>4.1 – 6.1</td>
</tr>
<tr>
<td>Serum C-Peptide</td>
<td>6.12</td>
<td>Pmol/l</td>
<td>298 – 2350</td>
</tr>
<tr>
<td>Serum Insulin</td>
<td>4.9</td>
<td>mU/l</td>
<td>4.4 – 26.0</td>
</tr>
</tbody>
</table>

Test Results Units Reference

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individuals. Currently the aetiology of PS is unknown though likely to be genetic. Various syndromic and metabolic potential causes of hyperinsulinism hypoglycaemia have been found, one of which may be due to a sporadic mutation in the UCM A gene, causing 10p13-14 duplication in Poland Syndrome. This case is the first reported case of insulinoma as the case of hyperinsulinism along with Poland Syndrome both of which are rare and unique clinical presentations in themselves. Hyperinsulinism/Insulinomas can present with normal bloods and ECG once symptoms have passed. There is an association between Poland Syndrome and Hyperinsulinism, this link can help in earlier diagnosis/ruling out of one another.

Conclusions
Electrolytic metabolism.

achievements: no episodes of hypoglycemia were recorded; the HbA1C level was mmol/l. After additional examination the patient with DI was diagnosed with DM.

A major cause of morbidity is post COVID-19 complications. The symptoms of carbohydrate dysfunction can be due to has relationship with coronavirus disease. In patients with chronic disorders after SARS-CoV-2 infection, aggravation of pre-existing symptoms has also been noticed. Diabetes insipidus (DI) may be at risk of dysnatremia when developing respiratory complications of COVID-19. Particularly, the combination of two or more concurrent disorder is a major problem in patient treatment. Especially when one of the diseases is a predictor of another. This notify complicates the diagnosis but also prolongs the duration of treatment, sometimes complicating an algorithm of management and reduces its effectiveness. Thus considering the above mentioned facts, we would like to focus your attention on such comorbidities as post COVID-19 complication: diabetes mellitus (DM) in patient with DI, and give a sense of this problem on the basis of clinical case study. A 69-year-old female with a past medical history of DI diagnosed five years ago treated with nasip spray desmopressin (10 μg intranasal twice daily) after COVID-19 pneumonia who later manifested DM. She was diagnosed with COVID-19 infection with nasopharyngeal reverse transcriptase polymerase reaction (RT-PCR) at an outpatient clinic 60 days ago. IgG against SARS-CoV-2 was positive. After two month for the treatment of COVID-19 pneumonia the patient complaining of polydipsia, polyuria and nocturia during the previous month. Laboratory examinations showed abnormally increased blood sodium (serum sodium -156 mmol/l) and chloride (serum chloride - 115 mmol/l) and decreased urine osmolality and specific gravity of 1.006. Thyroid function tests were normal. The level of glycosylated hemoglobin (HbA<sub>1C</sub>) was 7.0%, blood sugar levels ranged from 7.6 to 19.0 mmol/l. After additional examination the patient with DI was diagnosed with DM. The patient was prescribed treatment with metformin at a daily dose of 1500 mg during the meal to correct carbohydrate metabolism and added doses of desmopressin (20 μg intranasal twice daily). After 3 months, the therapy resulted in patient’s improvement of the general conditions and compensation of DM was achieved: no episodes of hypoglycaemia were recorded; the HbA1C level was 6.4%; glycemia levels ranged from 5.4 to 8.0 mmol/l; and normalization of electrolytic metabolism.

Conclusions
Further studies are needed to clarify the link between COVID-19 and DM in patient with DI, to provide the optimal management.

Introduction
In recent decades, metabolic diseases have continued to increase. Several investigations concerning the origin of these diseases such as dyslipidemia, hypercholesterolemia, diabetes, etc., have been elucidated. These pathologies have been attributed to lifestyles and mainly to diet. Obesity is a serious metabolic and energy disorder, which has become a real major public health problem.

Materials and methods
We were interested in studying the effect of a high-fat diet on liver function, as well as the effect of the extract on rats receiving a hyperlipidemic diet. The variations in liver toxicity parameters in the different groups were highlighted by the study of biochemical parameters and confirmed by the study of liver histology.

Results
Under our experimental conditions, the obese had a significant elevation of serum levels of AST, ALT, LDF and CK of 32%, 31%, 43% and 22%, respectively. While, administration of the extract to the obese improved all indices of liver toxicity. Histological sections of the livers of rats subjected to a hyperlipidemic diet for 42 days showed the appearance of lipid droplets which correspond to a deposit of fat in the hepatocytes. Whereas, CNSF and orlistat exerted a protective effect against the development of non-alcoholic hepatic steatosis in HFD-rats, objectified by a notable decrease in lipid vacuolations.

Conclusion
Finally, we noted that the result of these positive effects of the CNSF studied on hepatic toxicity was translated by restoring effects of the histological organizations of the liver, making them comparable with those of normal controls. This confirms the important role of this natural product in the fight against oxidative stress and the prevention of hyperlipidemia.

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EP439
Time restricted feeding 16/8 improves metabolic parameters and fatty liver in obese mice
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Obesity is a major health problem that is crucial in the pathogenesis of diabetes mellitus, cardiovascular diseases, and some types of cancer. Intermittent fasting is an eating pattern in which periods of fasting, lasting from 12 up to 36h, are alternated with periods of eating. Time restricted feeding (TRF) 16/8 is a type of intermittent fasting that is being used to lose weight and for treating metabolic disorders. Several studies in humans have shown a slight effect of TRF on body weight but more consistent effects on metabolic parameters. However, the molecular mechanisms by which these effects occur are poorly understood. We aimed to investigate if TRF 16/8 in mice reproduced the metabolic effects observed in human and tested if TRF 16/8 reduces inflammation in obese mice. We used C57BL/6J mice under a high fat diet for 12 weeks (60%KCal in fat) to develop obesity associated with glucose intolerance and fatty liver. Then we exposed the animals to TRF 16/8 (feeding in active phase) for 6 weeks. We found that TRF decreases body weight without changes in epididymal or subcutaneous fat, it reduces fasting glycemia, improves glucose tolerance, decreases liver weight, and decreases gut epithelial permeability. In addition, TRF increases blood ketone bodies, in particular 1-hydroxybutyrate (BHB). These results show that 6 weeks of TRF are enough to produce metabolic improvements in obese mice. Since obesity is characterized by a low-grade inflammatory state and BHB may have anti-inflammatory effects, we propose that BHB induced by TRF has anti-inflammatory effects in the brain and periphery that explain why TRF improves metabolic parameters in obese mice.

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EP440
Metabolic syndrome in mediterranean patients with mental illness
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Introduction
Metabolic Syndrome (MeS) represents a cluster of vascular risk factors related to insulin resistance such as abdominal obesity, hypertension, and glucose and lipid dysregulations. Multiple studies suggest an increasing metabolic risk in psychiatric patients.
Prevalence and Risk Factors for Diabetic Lower Limb Amputation

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Introduction
Olive oil is the most representative food of the traditional Mediterranean Diet (MedDiet) that, besides having high-monounsaturated fatty acids content, contains other minor components with biological properties. Olive oil as a food, and the MedDiet as a food pattern are associated with a decreased risk of cardiovascular disease, obesity and diabetes mellitus. The aim of this study was to determine the relationship between adherence to the Mediterranean Diet and vascular complications among diabetic patients.

Methods
It was a prospective cross-sectional study conducted over a three-month period including patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes. We completed a 14-Item MedDiet adherence screener in face-to-face interview with the participant to assess dietary habits. Three categories of adherence to the MedDiet were identified (low ≤5, median 6-9, high ≥10 points of the 14-item questionnaire).

Results
The study enrolled 109 patients, 48% were males and 52% were females. The average age of the cohort was 53.7 years ± 17.9 years. 78.7% of the patients were running type 2 diabetes. Of them, 57.4% had dyslipidemia and 68% were overweight or obese. High Blood Pressure was found in 47.2% of cases. The capillary blood glucose and glycated hemoglobin were respectively around 12.41 mmol/l and 10.55%. Diabetic patients with low, median or high adherence to the MedDiet represent 11%, 64%, and 25% respectively. Low HDL cholesterol and type 2 diabetes. We completed a 14-Item MedDiet adherence screener in face-to-face interview with the participant to assess dietary habits. Three categories of adherence to the MedDiet were identified (low ≤5, median 6-9, high ≥10 points of the 14-item questionnaire).

Conclusions
We found an inverse significant relationship between the adherence to MedDiet and nephropathy ($P = 0.02$, $r = -0.15$), chronic peripheral artery occlusive disease ($P = 0.034$, $r = -0.21$), coronary artery disease ($P = 0.046$, $r = -0.2$) and body mass index ($P = 0.049$, $r = -0.15$). However, there wasn’t association with retinopathy ($P = 0.9$) or diabetic peripheral neuropathy ($P = 0.32$).

DOF: 10.1530/endoabs.81.EP444
Prevalence of early postpartum glucose intolerance in Spanish women with gestational diabetes mellitus

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García Orcoyen Hospital, Estella, Spain

Introduction
Women with gestational diabetes mellitus (GDM) have an increased risk for developing glucose intolerance in postpartum. The aim of our study was to describe the general characteristics of pregnant women with GDM and to assess the prevalence of glucose intolerance in early postpartum by postpartum oral glucose tolerance test (ppOGTT).

Methods
Retrospective study from January 2017 to December 2020 including patients with GDM followed at endocrinology department of García Orcoyen Hospital in Estella (Spain). Relevant data of pregnancy and postpartum were recorded. Diagnosis of GDM was performed using the two-step strategy at 24–28th week of gestation. Early pregnancy screening was performed in women at increased risk of undiagnosed diabetes, defined by the American Diabetes Association (ADA). After delivery, a ppOGTT was performed, and prediabetes and type 2 diabetes were diagnosed according to the ADA criteria.

Results
A total of 84 women with GDM were included. The mean age was 33.7 ± 5.1 years (21 to 47 years), 42.2% were caucasian and family history of diabetes was found in 48.8% of them. 36.9% of women were primiparous (n = 31) and 23/53 women with previous pregnancies had history of GDM. Mean pregestational BMI was 28.2 kg/m² ± 6.2 (19 to 49). GDM was diagnosed in the 1st trimester in 20 women, in the 2nd trimester in 63 women and in the 3rd trimester in 1 woman. During pregnancy, insulin therapy was required in 44% women. The average maternal weight gain was 8.2 ± 5.0 kg. 14.3% of fetus were above the 90th percentile and 4.8% newborns were macrosomia. After delivery, 58.3% of women (n = 49) performed the ppOGTT at 17 weeks postpartum, with the following Results: 33 women had a normal response; 14 women had prediabetes (8 had impaired fasting glycaemia, 3 had impaired glucose tolerance and 3 women had a combination of both) and 2 women had type 2 diabetes criteria.

Conclusion
The proportion of women with GDM who underwent postpartum glucose testing is low due to high prevalence of loss of follow up after delivery. One-third of women who underwent ppOGTT after delivery had glucose intolerance.

DOI: 10.1530/endoabs.81.EP446
Sudden deafness revealing type 2 diabetes: a case report

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Introduction
Sudden idiopathic deafness is often a diagnosis of elimination. It is defined by an isolated sensorineural hearing loss (sensorineural deafness) unilateral and without obvious etiology but a vascular hypothesis is plausible. We report in this context a case of unilateral sudden hearing loss revealing type 2 diabetes (T2DM).

Observation
This is a 40-year-old man, sedentary, with no particular pathological history, a 20-pack/year smoker and occasional alcoholic, who presented with sudden deafness justifying his hospitalization in an otorhinolaryngology department. The clinical examination revealed a blood pressure of 130/80 mmHg, a body mass index of 10 BMI, a normal glucose tolerance test (GTT) and normal serum triglycerides (1.7 mmol/l) and cholesterol (4.2 mmol/l).

Audiometric examination confirmed sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and neurological examination confirming sensorineural hearing loss.

Discussion
In Georgia the first lockdown measure prevented spread of COVID-19 was introduced in March 2020. This resulted in disruption of patients care especially those with chronic condition including diabetes. The worsening of diabetes control in these patient is explained by lack of exercise, weight gain and poor diet and probably poor compliance. The patients in this study reported anxiety and stress due uncertainty of COVID-19 pandemic and probably this contributed to worsening HbA1C. HbA1C in 75.6% of these patients deteriorated compared to 24.4% whose diabetes control improved. COVID-19 pandemic has helped healthcare professional to be more flexible and innovative in managing patients with diabetes and other chronic conditions.

DOI: 10.1530/endoabs.81.EP448

How to position Sodium Glucose cotransporter-2 inhibitors in the management of Diabetes in acromegalic patients? Another point of view

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Context
Diabetes mellitus represents one of the most frequent metabolic comorbidities and occurs in 30% to 40% of patients with acromegaly. Patients with acromegaly develop insulin resistance due to GH excess, and in those with longstanding disease, insulin deficiency may occur. Moreover, the use of second-generation somatostatin receptor ligands (SRLs) pasireotide might contribute to the increased development in new-onset diabetes and the worsening of hyperglycemia. Management of type 2 diabetes (T2DM) has been revolutionized since the introduction of sodium-glucose cotransporter 2 inhibitors (SGLT2i) with their beneficial protective cardiovascular and renal effects in patients with and without diabetes. The current treatment recommendations for diabetes management in acromegaly are similar to the general population. However, the use of incretin-based therapy such as glucagon-like peptide-1 (GLP-1) agonist and dipeptidyl peptidase-4 (DPP-4) inhibitors are more considered as second-line treatment modalities after metformin in patients with diabetes and acromegaly while the use of SGLT2i class is a less recommended option due to increased risk of diabetic ketoacidosis (DKA) in patients with acromegaly.

Our recommendations are based on our experience with the use of SGLT2i in clinical practice in this subgroup of patients and the recently available published data.

Evidence synthesis
Acromegaly disease activity should be considered one of the important criteria for the management of diabetes in this subgroup of patients when considering treatment with SGLT2i. This criterion is driven by the fact that DKA was the initial manifestation in unrecognized active acromegaly according to recently published data.

Our recommendations are based on our experience with the use of SGLT2i in clinical practice in this subgroup of patients and the recently available published data.

Discussion
EASD, and ESC guidelines for patients with controlled acromegaly - defined as age-sex normalized IGF-1 levels, random GH < 1.4 µg/liter, nadir GH after OGTT <0.4 µg/liter- that was achieved postoperatively with or without pharmacological treatment such as SSAs, GH receptor antagonist and dopamine agonists as monotherapy or in combination. For patients with active acromegaly treatment with incretin-based therapy as second-line therapy is more favorable, in such cases, the use of SGLT2i is less recommended due to increased tendency for DKA.

Conclusions
We recommend a more liberal strategy in using SGLT2i among patients with controlled acromegaly and diabetes. However, for patients with active acromegaly incetin-based therapy is more favorable.

DOI: 10.1530/endoabs.81.EP450

Diabetes mellitus represents one of the most frequent metabolic comorbidities and occurs in 30% to 40% of patients with acromegaly. Patients with acromegaly develop insulin resistance due to GH excess, and in those with longstanding disease, insulin deficiency may occur. Moreover, the use of second-generation somatostatin receptor ligands (SRLs) pasireotide might contribute to the increased development in new-onset diabetes and the worsening of hyperglycemia. Management of type 2 diabetes (T2DM) has been revolutionized since the introduction of sodium-glucose cotransporter 2 inhibitors (SGLT2i) with their beneficial protective cardiovascular and renal effects in patients with and without diabetes. The current treatment recommendations for diabetes management in acromegaly are similar to the general population. However, the use of incretin-based therapy such as glucagon-like peptide-1 (GLP-1) agonist and dipeptidyl peptidase-4 (DPP-4) inhibitors are more considered as second-line treatment modalities after metformin in patients with diabetes and acromegaly while the use of SGLT2i class is a less recommended option due to increased risk of diabetic ketoacidosis (DKA) in patients with acromegaly.

Our recommendations are based on our experience with the use of SGLT2i in clinical practice in this subgroup of patients and the recently available published data.

Evidence synthesis
Acromegaly disease activity should be considered one of the important criteria for the management of diabetes in this subgroup of patients when considering treatment with SGLT2i. This criterion is driven by the fact that DKA was the initial manifestation in unrecognized active acromegaly according to recently published data.

Our recommendations are based on our experience with the use of SGLT2i in clinical practice in this subgroup of patients and the recently available published data.

Discussion
EASD, and ESC guidelines for patients with controlled acromegaly - defined as age-sex normalized IGF-1 levels, random GH < 1.4 µg/liter, nadir GH after OGTT <0.4 µg/liter- that was achieved postoperatively with or without pharmacological treatment such as SSAs, GH receptor antagonist and dopamine agonists as monotherapy or in combination. For patients with active acromegaly treatment with incretin-based therapy as second-line therapy is more favorable, in such cases, the use of SGLT2i is less recommended due to increased tendency for DKA.

Conclusions
We recommend a more liberal strategy in using SGLT2i among patients with controlled acromegaly and diabetes. However, for patients with active acromegaly incetin-based therapy is more favorable.

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EP451
Metabolic syndrome in Cushing’s syndrome
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Introduction
Metabolic disorders are a relevant cause of morbidity and disability in patients with Cushing’s syndrome (CS) even after a successful treatment. The aim of our study was to assess the prevalence of metabolic syndrome in our CS patients, as central obesity, dyslipidemia, diabetes, and hypertension, and to discuss the main adverse effects of CS on metabolism and emphasize the importance of long-term monitoring and treatment of these complications.

Patients and Methods
It’s a retrospective and descriptive review of thirty-four patients records presenting Cushing’s syndrome. They were divided according to waist circumference, lipid, glucose and tension profiles, before and after treatment.

Results
45% of our patients had dysglycemia, 30% had dyslipidemia, and 23% had arterial hypertension with a pathological waist circumference, a mean age of 29.3 years old, and a female predominance. A decrease of this disorders after surgery or medical treatment were also noted.

Conclusion
Glucocorticoid excess leads to increased dysglycemia, dyslipidemia, visceral adiposity, and hypertension, which together delineate the metabolic syndrome, and increase cardiovascular morbidity and mortality. Treatment modalities and rapidity of controlling hypercortisolism is of paramount importance and have varied impacts on metabolic disorders.

Keywords
Cushing’s syndrome; Metabolic syndrome; Dysglycemia; Dyslipidemia; Hypertension; Obesity.

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EP453
"The prognostic efficiency of the N-terminal fragment of the Brain natriuretic peptide in the diagnosis of chronic heart failure in patients with type 2 diabetes"
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The purpose of the study is to study the prognostic role of NT-proBNP in patients with diabetes mellitus type 2 associated chronic heart failure (CHF). Material and research methods
For the period 2015-2021, 185 patients were identified as an object of study, and 185 patients based on the materials of their preparations into therapeutic and prophylactic institutions of Andijan from 30 years and older. Patients were distributed to 3 groups: 1 Group are patients with DM 2 type + CHF - 65 patients, 2 Group are patients with DM 2 type without CHF - 60 patients, 3 Group - these are patients with CHF without DM 2 type - 60 patients. Patients were fulfilled with general, biochemical, hormonal, genetic blood tests, as well as ECG, ECHC and other instrumental research.

Results
The average values of NT-proBNP were significantly different in all groups and at the same time they were significantly higher in the group of patients with DM 2 type + CHF compared with the parameters of the patients with insolated CHF. We selected median levels of NT-proBNP in increasing NT-proBNP trends ranging from 125 to 250 pg/ml, from 250 to 500 pg/ml and above 500 pg/ml.

Conclusions
Increasing the concentration of NT-proBNP in all patients of DM 2 with CHF, as well as the high sensitivity and specificity of the test dough, the value of this marker for the diagnosis of CHF in patients with a 2-type diagnosis. The dynamics of their concentration, mainly NT-proBNP, can help in assessing the effectiveness of the therapy and the need for dose of drugs.

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EP452
"Characteristics of cerebral hemodynamics in patients with type 2 diabetes on program hemodialysis"
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The goal is to study the changes in the parameters of cerebral hemodynamics in patients with diabetes mellitus of type 2 receiving program hemodialysis. Material and methods of research
We have been viewed and surveyed in just a period from January 1, 2019 to June 1, 2021 g - 117 patients suffering from type 2 diabetes mellitus, with chronic kidney insufficiency V stage on program hemodialysis. Of these, women were 58, men - 62. The average age of men amounted to 67 ± 4.2 years, and the average age of women is 64 ± 5.6 years. 20 patients of the relevant age amounted to a group of control. The number of hemodialysis sessions in patients varied from 2 to 162. All patients were carried out by all studies that included generally crystal biochemical, hormonal blood tests, an ultrasound of internal organs, dopplerography of the main arteries of the head, consulting narrow specialists.

Results
It was revealed that as the degree of the degree of brain ischemia decreased and the linear blood flow rate in all the main arteries of the head were decreased: carotid artery, internal carotid artery, vertebral artery on both sides ( P <0.05, <0.001). At the same time, differences in the LSQ from healthy individuals were significant. The most often stenosis of the lumen of the vessels of the magician met in patients with 3 groups, while they most often observed multiple stenosis of vessels.

Conclusions
1) Doppler of the main arteries of the head is informative to determine the forecast of brain ischemia in patients with type 2 diabetes with chronic kidney disease. 2) Linear blood flow rate was reduced in all groups of patients with type 2 diabetes with chronic kidney disease.

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EP454
"Hormonal characteristic of patients with diabetes mellitus 2 types of associated chronic heart failure"
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The purpose of the study is to study the clinical and hormonal features of diabetes mellitus 2 (DM) associated chronic heart failure (CHF).

Material and research methods of study
For the period 2015-2021, 185 patients were identified as an object of study, and 185 patients based on the materials of their preparations into therapeutic and prophylactic institutions of Andijan from 30 years and older. Patients were distributed to 3 groups: 1 gr. are patients with DM 2 type + CHF - 65 patients,2 gr. are patients w/DM 2 type without CHF - 60 patients, 3 gr - these are patients with CHF without DM 2 type - 60 patients. Patients were fulfilled with general, biochemical, hormonal, genetic blood tests, as well as ECG, ECHC and other instrumental research.

Results
The average values of the N-terminal fragment of the Brain natriuretic peptide (NT-proBNP) were reliably different in all groups, and at the same time they were significantly higher in the group of patients with DM 2 + CHF compared with the parameters of patients with insolated CXN. In the study of the aldosterone, elevated average values were found in all groups, in patients with CHF, the indicators are reliable higher than in the group of patients with DM 2 type, in the group of patients with DM 2, in combination with CHF, the indicators were the highest, reliably distinguish from indicators of patients with DM 2 type and unreliable in comparison with the CHF Group. Renin levels in groups were significantly higher than the upper limit of the norm lying. However, it should be noted that in the DM 2 + CHF group, the indicators statistically significantly exceeded the indicators in the first two groups.
Conclusions
1. Chronic hyperglycemia and activation of RAAS are pathogenic factors that are aggravated by chronic heart failure in patients with 2-type diabetes.
2. Increasing the concentration of NTproBNP in all patients of the 2-type diabetes with concomitant CHF, as well as high sensitivity and specificity of the test proves the value of this marker for the diagnosis of CHF.

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EP455
"The Level of awareness of the risk of developing coronary heart disease of patients with type 2 diabetes mellitus complicated by cardio-renal syndrome"  
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The purpose of the study is to study the Level of awareness of the risk of developing coronary heart disease (CHD) of patients with type 2 diabetes mellitus complicated by 4 type cardio-renal syndrome.

Material and methods
We examined in total for the period from October 1, 2021 to December 1, 2021 - 25 patients suffering from type 2 diabetes mellitus with chronic renal disease (CRD) and chronic cardiac insufficiency (CCIR). The average age of 33.3% of patients was within 50-59 years, and in 46.7% - from 60 to 69 years. The research included: 1) general clinical (study of endocrine, neurological status, anthropometry, height (sm), weight (kg), BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio 2) instrumental (ECG, roentgen of thorax, ultrasound of internal organs 3) biochemical tests (Hb1AC, glycemic profile, urea, creatinine, lipid spectrum, coaguogram),4) hormonal blood tests (insulin, C-peptide etc.)

Results
When patients learned about the risk of CHD: before the diagnosis of DM 2 is 20%, in the process of investigation the diagnosis of DM 2 - 6.7%, shortly after the DM 2 was revealed - 20%, a few years after the DM 2 was identified in 40%, when the diagnosis of cerebro-vascular disease (CVD) is 6.7%, does not know - 6.7%. The risk levels of the development of the heart complications (HC) were the following: low -20%, average - 35%, more average - 27%, high - 13%, below average - 7%. Among the suffering diseases were: arterial hypertension - 53.3%, arrhythmia -40%, kidney disease -13.7%, stroke -6.7%.

Conclusion
1 of the 3 respondents suffering from the DM 2 rated their level of risk of developing CVD low, while diabetes a history of already high risk of CVD. 40% of the respondents received information on the risk of the development of the CVD several years after the diagnosis of the diagnosis of the DM 2. All respondents talked with the attending physician about the DM 2 and the risk of CVD. Nevertheless, at the time of the survey, all of them had CVD.

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EP456
Plasmalogens levels are associated with the severity of diabetic neuropathy  
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Backgrounds
Diabetes mellitus is a complex disease accompanied by the development of complications. In addition to the classic hyperglycemia and dyslipidemia, a number of other factors are involved in the pathogenesis of complications. Plasmalogens disturbances participate in nerve tissue degeneration.

Materials and methods
In 76 people with DM2 plasma and erythrocytes membranes plasmalogens measured and compared according to diabetic neuropathy.

Results
Blood plasma plasmalogens and erythrocytes membranes plasmalogens level shown decreased in patients with DM2 in compare with people without diabetes. When results analysed according to severity of diabetic neuropathy Blood plasma and erythrocytes membranes plasmalogens levels showed linkage. Blood plasma plasmalogens level were significantly differs between the groups and shown in 2.4 and 3.1 times lower in DN1 and DN2 groups. Whereas erythrocytes membranes plasmalogens were more lower and showed lowering in DN1 groups in 3.6 times and DN2 groups in 4.2 times.

Conclusion
Blood plasma and erythrocytes membranes plasmalogens have linkage with severity of DN and involved into pathogenesis of neuropathy by neurodegeneration.

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EP457
Lipid metabolism in patients with type 1 diabetes mellitus accompanied by ischemic heart disease  
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Cardio-vascular disorders (CVD), ischemic heart disease (IHD) and myocardial infarction (MI) heading the line are the main cause of death among patients with diabetes mellitus (DM). DM has been proved to be an essential risk factor for IHD and MI to be instrumental in regarding all patients as belonging to the CVD high risk group. Dysfunction of adipocytes, insulin resistance, hyperinsulinemia, hyperglycemia and dyslipidemia seen in DM are the triggers for the cascade of hemodynamic and neuro-humoral responses underlying the atherosclerotic damages of vessels of various location with clinical manifestation in the form of IHD. The work was initiated to study lipid metabolism parameters in patients with the IHD- accompanied type 1 diabetes mellitus.

Materials and methods
We examined 10 patients with type 1 DM and 14 patients with type 1DM and IHD. 12 donors were included in the control group. Concentrations of lipids, triglycerides (TG), total cholesterol (TC) and high density lipoproteins (HDP) cholesterol were analyzed in all groups.

Results and discussion
Significant increase in concentrations of total lipids and TC could be seen in all patients being more pronounced in the IHD-accompanied type 1 DM. Concentrations of total lipids in patients with the accompanied pathology were the highest (11.42 ± 0.61 versus 5.2 ± 0.33 g/l in the controls). Total cholesterol concentrations were approximately equal in all groups of patients to be 226.0 ± 11.3 mg% in patients with type 1 DM and 223.0 ± 11.8 mg% in those with DM and IHD (∆P < 0.05) while the concentrations of TG and HDL cholesterol changed by presence of IHD. The most pronounced changes in the serum TG concentrations could be seen in patients with IHD-accompanied type 1 DM (232.8 ± 26.0 mg%), as compared to those in patients with DM but not IHD (211.3 ± 14.3 mg%/P < 0.05) and the controls (137.6 ± 1.9 mg%). The reduction in HDL cholesterol could be seen both in patients with type 1 DM (36.3 ± 2.26 mg%, P < 0.05) and those with the pathology-accompanied disease (33.9 ± 1.8 mg%, P < 0.001) to significantly differ from the parameters in the controls (59.7 ± 0.8 mg%). Thus, the increase in concentrations of total cholesterol, TC, TG paralleling reduction in HDL cholesterol could be seen characteristic of patients with type 1 DM. IHD was demonstrated to be the confounding factor for DM course due to metabolic and pro-atherogenic changes, as well as formation of risk factors, to name arterial hypertension, obesity and dyslipidemia.

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EP458
Are diabetes mellitus and parkinson’s disease linked?: a case report  
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Introduction
Parkinson’s disease is considered the most common chronic neurodegenerative disease that often affects the elderly, rarely the young. Meanwhile, Diabetes mellitus is the most common chronic metabolic disease. Because of the increase
in the prevalence of diabetes and neuro-vegetative diseases, we can wonder about the relationship between the two diseases. We report the case of a patient with type 2 diabetes mellitus associated with young onset Parkinson’s disease.

Case
A 44-year-old female patient, has been followed for type 2 diabetes mellitus for 5 years under Metformin and insulin with a history of Parkinson disease diagnosed 2 years ago in front of resting tremor, slowness of movements and muscular rigidity. She was put on L-Dopa with favorable clinical evolution.

Discussion & conclusion
The possibility of a relationship between Parkinson’s disease and T2DM has been well studied. A few epidemiological studies have shown that diabetes is a major risk factor that accelerates the deterioration of motor function or cognitive status. T2DM shares some common pathogenic traits with PD. For example, high levels of immune cells, cytokines and chemokines have been described in perineal islets of patients with T2DM, while microglia activation seems to play a central role in PD progression. Similarly, the role of mitochondrial dysfunctions and oxidative stress in both T2DM and PD is now well established.

Results
We collected 48 patients: 18 men and 30 women. The majority have type 2 diabetes (79%). For the type 1 diabetic group, the mean age was 35.2 ± 10 years and the mean glycated hemoglobin (HbA1c) level was 9 ± 1%. The mean age of type 2 diabetes (T2DM) was 65.7 ± 8.4 years and the mean HbA1c level was 10.7 ± 1.5%. Almost the half of T2D patients (49%) had diabetic retinopathy. It was minimal, moderate and proliferative in 35%, 18% and 47% of the cases, respectively. In type 1 diabetes (T1DM), retinopathy was observed in 70% of patients. In this case, minimal, moderate and proliferative retinopathy were found in 58%, 28% and 14% of the cases, respectively. Diabetic nephropathy was present in 47% of T2DM and in 10% of T1DM. Peripheral neuropathy was mentioned in 26% of T2DM and in 10% of T1DM. For the T2DM group, macroangiopathy affected 39% of hospitalized patients: 21% had coronary artery disease, 13% had chronic arterial occlusive disease of the lower extremities and 5% had a history of ischemic stroke. We did not found similar anomalies in the T1DM group. In the present data, no significant correlation was observed between the onset of chronic diabetic complications and the HbA1c level or age of diabetes (P = NS).

Conclusion
The prevalence of diabetes-related complications is increasing but often underestimated. Early screening of these complications may allow a better management.

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EP459
An inaugural diabetic ketoacidosis revealed by Fournier’s gangrene
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Introduction
Fournier’s gangrene (FG) is a rare but life-threatening disease. Although originally thought to be an idiopathic process, FG has been shown to have a predilection for patients with diabetes, HIV, alcoholism and other immunocompromised states. We report the case of a patient who presented an inaugural diabetic ketoacidosis revealed by Fournier’s gangrene

Observation
A 38-year-old male patient with a smoking history, presented to the emergency department for intense perineal pain associated with a fever. The physical assessment had revealed a tachycardia of 120 bpm, blood pressure 110/60 mmHg, a high respiratory rate 24 per minute & a temperature of 39°C. The perineum was swollen and necrotic. An abdominal CT scan was performed which showed air bubbles at the perineal area extended to the retroperitoneal space and to the scrotal region. In the other hand the biological assessment was in favor of an elevated plasma glucose level of 4 g/l, metabolic acidosis and urine ketones. C-reactive protein level was at 235 mg/l.

Discussion & conclusion
Fournier’s gangrene is a fulminant form of infective necrotizing fasciitis of the genital, perineal and perianal regions, which commonly affects men, but can also occur in women and children. Diagnosis should be prompt with early surgical intervention, along with antibiotics and good supportive care. Progressive management of diabetic and immunosuppressed patients with perineal infections is of extreme importance to prevent the development of the condition in the first place as this condition in the presence of such comorbidities is associated with high mortality.

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EP460
Long-term diabetes complications
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Introduction
Diabetic neuropathy (DN) is the most common complication of diabetes affecting up to 50% of patients with type 2 diabetes. Carotid to femoral pulse wave velocity (cPWV) is an independent cardiovascular marker of morbidity and mortality and is considered the gold standard in the assessment of arterial stiffness. The aim of

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic retinopathy (DR) was found in 24.1% of the patients. Among them 26.7% had proliferative DR. cPWV > 10 m/s was found in 95% of the patients with DR. In this group, cPWV was at 15.34 ± 2.94 m/s VS 13.10 ± 2.56 m/s in patients without diabetic retinopathy (P < 0.001). Moreover, in patients with DR, we did not find a correlation between cPWV and the stage of the retinopathy (P = 0.108).

Conclusion
Arterial stiffness is often increased in type 2 diabetes. And it is more increased in the presence of retinopathy. Microvascular disorders of the retina including DR were associated with cardiovascular disease, highlighting the relationship between microvascular abnormalities and atherosclerosis specifically and arterial stiffness overall.

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EP461
Correlation between pulse wave velocity and retinopathy in type 2 diabetes
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Introduction
Diabetic retinopathy (DR) is a serious complication of diabetes that affects 50% of patients with type 2 diabetes. It represents the first cause of blindness. The aim of this study was to examine the relationship between diabetic retinopathy and arterial stiffness.

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic retinopathy (DR) was found in 24.1% of the patients. Among them 26.7% had proliferative DR. cPWV > 10 m/s was found in 95% of the patients with DR. In this group, cPWV was at 15.34 ± 2.94 m/s VS 13.10 ± 2.56 m/s in patients without diabetic retinopathy (P < 0.001). Moreover, in patients with DR, we did not find a correlation between cPWV and the stage of the retinopathy (P = 0.108).

Conclusion
Arterial stiffness is often increased in type 2 diabetes. And it is more increased in the presence of retinopathy. Microvascular disorders of the retina including DR were associated with cardiovascular disease, highlighting the relationship between microvascular abnormalities and atherosclerosis specifically and arterial stiffness overall.

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EP462
Correlation between pulse wave velocity and neuropathy in type 2 diabetes
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Introduction
Diabetic neuropathy (DN) is the most common complication of diabetes affecting up to 50% of patients with type 2 diabetes. Carotid to femoral pulse wave velocity (cPWV) is an independent cardiovascular marker of morbidity and mortality and is considered the gold standard in the assessment of arterial stiffness. The aim of

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic retinopathy (DR) was found in 24.1% of the patients. Among them 26.7% had proliferative DR. cPWV > 10 m/s was found in 95% of the patients with DR. In this group, cPWV was at 15.34 ± 2.94 m/s VS 13.10 ± 2.56 m/s in patients without diabetic retinopathy (P < 0.001). Moreover, in patients with DR, we did not find a correlation between cPWV and the stage of the retinopathy (P = 0.108).

Conclusion
Arterial stiffness is often increased in type 2 diabetes. And it is more increased in the presence of retinopathy. Microvascular disorders of the retina including DR were associated with cardiovascular disease, highlighting the relationship between microvascular abnormalities and atherosclerosis specifically and arterial stiffness overall.

DOI: 10.1530/endoabs.81.EP461
this study is to examine the relationship between diabetic neuropathy and arterial stiffness. Methods We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPiPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic neuropathy (DN) was found in 27.7% of the patients. CPiPWV > 10 m/s was found in 94.2% of the patients with DN. In this group, cPiPWV was at 14.56 ± 2.99 m/s VS 13.29 ± 2.68 m/s in patients without DN (P = 0.001).

Conclusion
This study shows that arterial stiffness is higher in type 2 diabetic patients with diabetic neuropathy than in those without diabetic neuropathy. Indeed, increased aortic stiffness can directly damage microcirculation, including vasa nervorum, by increasing the transmission of larger and harmful pulsatile pressure waves due to loss of normal aortic buffer function. More importantly, diabetic neuropathy has been shown to be a major risk factor for cardiovascular disease. Thus, diabetic neuropathy and macroangiopathy might have common pathogenic mechanisms.

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EP463
Correlation between pulse wave velocity and hypertension in type 2 diabetes
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Introduction
People with high blood pressure have a greater risk of developing diabetes, and people with diabetes also have an increased risk of high blood pressure. These two associated pathologies can increase cardiovascular risks and cause other repercussions such as arterial stiffness. The aim of this study is to examine the relationship between pulse wave velocity and hypertension in type 2 diabetes.

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPiPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. The mean systolic blood pressure was at 138.9 ± 17.2 mmHg and the mean diastolic blood pressure was at 78.7 ± 9.8 mmHg. High blood pressure was found in 54.2% of the patients. Among them 33.3% had a controlled blood pressure under treatment. In this group, cPiPWV was at 14.66 ± 2.83 m/s VS 12.43 ± 2.29 m/s in patients without hypertension (P < 0.001). Moreover, the presence of arterial stiffness multiples by 8 the risk of hypertension (Odds Ratio = 8).

Conclusion
Both diabetes and hypertension are known to be causes for arterial stiffness and their association increases more this risk. Therefore a well-controlled blood pressure and glycemric level is necessary to slow down this process.

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EP464
Predicting factors of insulin requirement in gestational diabetes mellitus
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Background
The management of gestational diabetes mellitus (GDM) is based on nutrition therapy associated to insulin therapy in second intention if glycemic targets are not achieved. The aim of this study was to assess predictive factors of insulin requirement in a group of pregnant women with GDM.

Methods
We conducted a retrospective study at the Outpatient Department and functional explorations, in the National Institute of Nutrition of Tunis, between April and June 2021. Clinical and biological data were collected from medical observation results.

Results
The study included 110 pregnant women with GDM. Mean age of patients was 33.4 ± 5 years. Diagnosis of GDM was based on pathological 75 g oral glucose tolerance test (OGTT) in 60% of patients and pathological fasting blood glucose in 40%, with a mean term of discovery of 22.75 ± 7.55 weeks of gestation. Nearly to one-third (33.6%) of the patients required initiation of insulin therapy. The mean term of insulin therapy instauration was 27.27 ± 5.55 weeks of gestation with a mean time between diagnosis of GDM and insulin therapy of 4.76 ± 3.94 weeks. Insulin therapy was initiated during the first week of follow-up in 16.6%. Insulin therapy was initiated with short-acting insulin, NPH insulin and basal bolus pattern in 54.1%, 13.5% and 32.4% of cases respectively. Univariate analysis showed a significant association between level of education (P = 0.031), sedentarity (P = 0.013) and the need for insulin therapy. Glicated hemoglobin (Alc) was higher in women with insulin therapy (P = 0.018). We did not find a statistically significant association between insulin use and history of GDM, early discovery of GDM, maternal age, and fasting blood glucose. Multivariate analysis showed that predictive factors for insulin therapy were Alc (OR= 4.34) and personal history of miscarriages (OR = 3.67).

Conclusion
Pregnant women who develop gestational diabetes treated with insulin are at increased risk of developing type 2 diabetes in the future. That’s why postpartum management is essential based on long-term screening and diabetes prevention strategies.

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EP465
Are type 2 diabetic insulin-requiring elderly satisfied?
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Introduction
Glycemic control in elderly diabetics is a challenge. Treatment Satisfaction reflects this control. Objectives To assess insulin treatment satisfaction and to determine the factors associated with insulin treatment satisfaction among type 2 diabetic elderly.

Methods
A cross-sectional study on 86 type 2 diabetic insulin dependent elderly recruited from the outpatient endocrinology consultation during June and July 2021. We applied the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and geriatric assessment scores.

Results
Three quarters of the patients were satisfied with the insulin therapy. Satisfied patients had significantly less history of hospitalization and more regular follow-up. Diabetic neuropathy medications were significantly less taken by satisfied patients. The number of daily insulin injections was significantly higher among unsatisfied patients. Diabetic foot was significantly more frequent among unsatisfied patients. Satisfied patients had significantly less history of hospitalization and more regular follow-up. Diabetic neuropathy medications were significantly less taken by satisfied patients.

Conclusions
Risk factors for patients’ insulin dissatisfaction should be detected early and managed appropriately to improve patients’satisfaction and consequently their well-being.

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EP466
Insulin analogs: do patients know their treatment advantages and modalities?
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Introduction
In Tunisia, the prescription of insulin analogs is increasingly « automatic » by practitioners, convinced by this treatment superiority over human insulin in diabetes management. The aim of our study is to determine whether the analogs prescription modalities and advantages are known by the patients, and to assess the factors associated with this knowledge.

Patient and Methods
We conducted a retrospective study including 65 diabetic patients attending the National Institute of Nutrition and on insulin analogs. Information was extracted from medical record and patients interviews.

Results
Fourteen patients had type 1 diabetes, and 51 had type 2 diabetes. Prescription of analogs (primary or switch from human insulin) was the doctor initiative in 86.2% of cases, and was the patients’ in 13.8%. The motivation of this prescription (ie advantages over human insulin) was explained to the patients by the practician in 60.7% of cases. In 58.5% of cases, the patients knew that analogs are more flexible, 49.2 knew that analogs cause less hypoglycemia, and 10.8% that its injection (insulin pen, solely available to analogs in Tunisia) was less painful than syringe. The percentage knowing the fast analog latency and action duration were respectively 74.2% and 48.5%. There was a statistically significant association between the patient knowledge about hypoglycemia risks and the doctors explanations ($P = 0.00$). This knowledge was associated with a better diabetes management: less hypoglycemia ($P < 0.001$) a better HbA1C. ($9.62$ vs $8.81$, $P = 0.019$), 98.5% of patients manifested their satisfaction with analogs and their desire to keep their prescription.

Conclusion
A substantial proportion of diabetics on analogs didn’t know their advantages and characteristics. This ignorance was partly due to lack of communication with their doctors. Improving this knowledge will lead to a better management of this treatment, and will help to have a better glycemic control.

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EP467
Metformin adherence and its impact on diabetes control
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Introduction
Metformin is the first-line treatment of type 2 diabetes mellitus. Poor adherence can be lead to poor glycemic control. The aim of our study was to determine the level of metformin adherence and its link with glycemic control in type 2 diabetic patients.

Methods
We performed a cross-sectional study including 273 patients with type 2 diabetes taking metformin for at least three years. We assessed metformin adherence using the Girerd questionnaire in its Tunisian version. The level of adherence was considered good, medium or poor. Diabetes was considered controlled when HbA1C was less than 7%.

Results
The mean age was 60 ± 18.22 years. Mean duration of metformin treatment was 10 ± 5.5 years, with extremes ranging from 3 to 40 years. Mean HbA1c was 8.7 ± 1.8% with extremes ranging from 5.6% to 15.7%. The diabetes was controlled in 18.3% of patients. The compliance was good in 7.3% of patients, medium in 48% of patients and poor in 44.7% of patients. When comparing mean HbA1c in all three adherence categories, there was a near statistically significant difference between the three categories ($P = 0.058$). HbA1c was higher in patients with poor treatment adherence compared to patients with good or medium level of adherence (8.98 ± 1.96% vs 8.46 ± 1.7%, $P = 0.02$). Duration of diabetes was lower in patients with poor adherence (9.7 years vs 11.1 years, $P = 0.045$).

Conclusion
Poor adherence to metformin treatment is frequent in type 2 diabetic patients. It is associated with a poorer glycemic control and should be targeted in therapeutic education programs.

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EP468
Painful fat necrosis as a consequence of insulin application - an unsolvable problem?
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We report a case of 39-year-old female presented with painful, scaling skin lesions on insulin application sites. She was diagnosed with type 1 diabetes mellitus (T1DM) at the age of 21 years and treated with intensified conventional insulin therapy. Three months before hospital admission, she suddenly started to feel pain at insulin injection sites, followed by oval subcutaneous deposits and skin ulcer in the further course. Identical local changes repeated after subcutaneous use of every available type of both human insulin and insulin analog. Patient past medical history was significant for surgically treated cervical cancer, cervical disc herniation and unilateral hip replacement due to femoral head osteonecrosis. On physical examination, multiple skin lesions in a form of scabs with maximal diameter of 7 mm, were present in bilateral upper arm and anterior abdominal region, and along the thighs. Her insulin injection technique was observed and estimated as adequate. Clinical, biochemistry and radiological assessment was performed as the biopsy of skin lesions. An insulin pump was inserted, but after a few days the same changes occurred at the site of catheter application. She is currently being treated with insulin parenterally.

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EP469
Impact of COVID-19 lockdown on glycemic control in diabetic patients hospitalized in emergency months
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Introduction
The global pandemic spread of SARScov2 has led to a heavy medical and socio-economic toll since December 2019. Patients suffering from chronic diseases were particularly affected during the lockdown period due to difficulties in accessing care. The aim of our study was to evaluate the impact of the 2-month lockdown introduced in Tunisia in March 2020 on diabetic patients’ glycemic control.

Materials and methods
Retrospective study involving 54 diabetic patients hospitalized through the emergency room in June 2020, one month after lockdown, in the diabetology department “A” at the National Institute of Nutrition in Tunis. Glycemic control, lipid balance as well as microvascular complications of diabetes were noted for each patient before and after lockdown (in January 2020 and June 2020).

Results
Median age was 54.72 years [20-87 years]. The sex ratio (M/F) was 0.5, 74% of patients had type 2 diabetes and 26% had type 1 diabetes. Median diabetes duration was 15.5 years [2-38 years]. 20.37% of patients were on oral antidiabetic drugs (ADO), 59.26% were on insulin, and 20.37% were on a combination of insulin and ADO. 53.7% were hypertensive and 66.66% had dyslipidemia. Patients were hospitalized for unbalanced insulin-deficient diabetes in 59.27%, for switching to insulin in 20.37%, diabetic ketoacidosis in 16.66% and for unstable type 1 diabetes with severe hypoglycemia in 3.7%. Average fasting blood glucose increased from 9.35 mmol/l before lockdown to 13.24 mmol/l ($P < 10^{-5}$). Mean HbA1C value of lockdown (10.92%) was much higher than of pre lockdown (8.5%), ($P < 10^{-5}$), 3.7% of patients had developed mild nonproliferative retinopathy and 1.85% saw their pre-existing retinopathies worsen. 18.52% of patients had worsened their 24-hour microalbuminuria and developed at least moderate renal impairment. Worsening of LDL cholesterol levels was observed in 38.88% of patients. The main diabetes complications aggravating factors found were non-compliance with hypogenic-dietary measures during the lockdown period (83.33%), as well as non-compliance and non-availability of medications related to patients’ absenteeism at the consultation (61.11%).

Conclusion
COVID-19 lockdown was associated with a deterioration in glycemic control and diabetes complications mainly due to non-adherence to the diet and lack of access to care.

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EP470
Mitochondrial diabetes: from diabetes to syndrome
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Anamnesis
We report the case of a 54-year-old man who consulted for weight loss. He had been diagnosed with diabetes more than 20 years ago with good glycemic control (currently HbA1c 6.9%), no obesity, hypertension, or dyslipidemia. A history of chronic pancreatitis and reinitis pigmentosa with eyelid ptosis. He maintains regular treatment with metformin, sitagliptin, repaglinide, ASA, Kreon and Pregabalin.

Complementary test
In reference to the chief complaint, there had not been any changes in his eating habits, his glycemic control was in range, there were not abnormalities in CT scans, abdominal ultrasound, and faecal occults blood test. Subsequently, he was admitted for constitutional syndrome, and an echecodoppy was requested where a hypoechogenic lesion measuring 28x27 mm was observed in the head of the pancreas with FNA showing signs of cytological atypia. A radical pancreaticoduodenectomy was performed with a diagnosis of pancreatic adenocarcinoma with areas of squamous differentiation (G3pT4 N0, Mx). During hospitalisation the patient presented palpitations, with paroxysmal EKG conduction with right bundle branch block, and a permanent pacemaker was implanted.

Discussion
We assessed the different clinical profile and discussed a mitochondrial disease known as Kearns-Sayres Syndrome. It starts in childhood with a classic triad of palpebral ptosis, reinitis pigmentosa and progressive external ophthalmoplegia, associated with sensorineural deafness, myopathies (progressive neuralgic pain and generalised muscle weakness), cardiac conduction disturbances, CNS involvement (cerebellar, Nursing, Greek weakness, etc.), digestive disorders (pancreatitis, diarrhea, etc.), and endocrinopathies (diabetes, delayed puberty...) and kidney failure. The aetiology of diabetes is due to an A3243g mutation affecting the mitochondrial MTTL1 gene. This gene encodes Leucine transfer RNA, which results in an attenuation of cytosolic ADP/ATP levels, resulting in a resetting of the glucose sensor in the pancreatic B-cell, producing less insulin. There is a high clinical variability based on the percentage of mutated DNA. In the beginning, usually under 40 years of age, there is insulin reserve, but it usually progresses to insulin dependence and treatment with metformin is not recommended due to the risk of lactic acidosis.

Conclusion
Our patient underwent a muscle biopsy, which was positive for specific alterations of fibres with mitochondrial proliferation.

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EP471
Correlation of knowledge and self-care with glycemic control in people with diabetes
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Introduction
Diabetes mellitus (DM) is a disease that shows a rapid increase over the recent years and is a major cause of morbidity and mortality. Thus new ways of prevention and treatment are needed and constantly being developed. As a lifelong challenge, DM is likely to affect one’s life in a variety of ways. It requires daily planning and decision making. Self-care is a vital component of the disease.

Knowledge consists of information about the disease and its management, which makes people with DM capable to carry out self-care activities. Knowledge about DM, its course and its treatment how all of these factor work together are prerequisites for a sufficient level of self-care.

Aim
The aim of this study was to investigate the relationship between knowledge and self-care of people with DM in accordance with their glycemic control.

Materials and Methods
This is a cross-sectional study with a sample of 98 people with type 1 and type 2 DM, aged 18-50 years old. A convenience sample was used, and the data were collected through anonymous questionnaires.

Results
The average score of people’s knowledge regarding the diabetes disease showed a good level of knowledge. The results showed a moderate level of knowledge of the participants in insulin use. People with better knowledge of insulin use, younger people, people with lower body mass index, and people with shorter duration of diabetes appeared to have better level of knowledge in physical activity. Regarding the level of care of the lower extremities, a moderate level of care was observed. The average overall medication score showed a fairly good level of compliance with the treatment. It was also found that the average overall nutrition score was relatively good. In terms of physical activity, it was found that the average overall score was low, which indicates a low level of physical activity of the participants.

Conclusion
These results indicate the need to improve education of people with diabetes, in subjects related to the disease in order to enhance their capacity for self-care. Factors that have been shown to influence both the level of knowledge and the self-care activities need to be considered in the individualized diabetes education education.

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EP472
Abstract withdrawn

EP473
Oral health related behavior and knowledge in adults with diabetes: a questionnaire study
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Diabetes is a common disease with concomitant oral manifestations that impact dental care.

Purpose
To investigate oral health awareness, oral hygiene and behavior in adults with diabetes.

Subjects and methods
This study involved interviews with a sample of 30 patients with diabetes type 2 followed in the C department of the National Institute of Nutrition in Tunis using a questionnaire study on oral health behavior and awareness.

Results
The mean age of our patients was 53 ± 7 years, with a sex ratio M/F = 0.43. The average duration of diabetes was 10 ± 8 years. The majority of respondents (59.4%) visited a dentist once a year, but oral care varied: 67.2% reported brushing at least once a day, whereas only 4.3% flossed daily. Awareness of oral health risks was limited, only 22% of the participants answered correctly about oral health knowledge items related to diabetes and 74.1% had never received any oral health advice related to their diabetes.

Conclusions
Many adults with diabetes have poor awareness of oral care and health complications associated with diabetes, and are receiving limited advice. Health professionals should take the opportunity to educate patients with diabetes and to promote proper oral health behaviors.

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EP474
Daytime sleepiness in patients with diabetes
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Excessive daytime sleepiness (EDS) is commonly considered a cardinal sign of sleep apnea; however, the mechanism underlying the association is unclear.
Purpose
The purpose of this study is to investigate the daytime sleepiness in patients with diabetes.

Methods
Participants were 30 adults with type 2 diabetes (T2DM) followed in the C department of the National Institute of Nutrition in Tunis. Subjective sleepiness was assessed using the Epworth Sleepiness Scale (ESS).

Results
The mean age of our patients was 60 ± 11 years, with a sex ratio M/F = 0.48. The average duration of diabetes was 17 ± 4 years. Obesity was present in 83.4% of patients. The mean glycated hemoglobin was 10.8% and the frequency of hypertension was 73%. This study showed that most patients (43.2%) presented a mild daytime sleepiness. People who scored highly on the ESS (4.9%) were more likely to have poor glycemic and blood pressure control and a higher body mass index than those with lower scores (34.1 vs 31.8 kg/m²).

Conclusions
Sleep abnormalities and daytime sleepiness are frequent in T2DM and it is associated with decreased diabetes self-management. We suggest that diabetic patient should be more thoroughly investigated for symptoms of daytime sleepiness.

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EP475
Prophylactic gonadectomy in a young phenotypic female with turner syndrome 45.X/46.XY mosaicism: a case report
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Introduction
Turner syndrome is a chromosomal disorder that affects an estimated 1/2500 female live births. An estimated subset of 6-12% of all Turner Syndrome patients will be a mosaic with Y-chromosomal elements. It is recognized that a Turner female possessing Y chromosome material has an increased risk of developing gonadoblastoma, a precursor to dysgerminoma. Consequently guidelines recommend prophylactic gonadectomy in Turner females.

Observation
We present the case of a 17-year-old female, followed for mosaic turner syndrome, who underwent prophylactic gonadectomy. Patient was followed for 4 years, the diagnosis was initially suspected in front of a failure to thrive, presence of Nevi on the face, and primary amenorrhea. Karyotype study was ordered and revealed a mosaic pattern of 46,X/45,XY—70% of the cells containing Y chromosome material. The clinical examination finds the stigmata of the classic Turner Syndrome, wide neck with a low hairline, a high palate and a bradymetacarpus. An exploratory laparoscopy performed showed bilateral ovarian strips. Prophylactic gonadectomy was organized, by laparoscopy. The post-operative follow-up was simple, with anaphath, bilateral ganadic dygenesis without signs of malignancy.

Conclusion
Early gonadectomy has been recommended in mosaic Turner females with Y-chromosomal material as a consequence of high risk of gonadoblastoma in infants as early as 5 months old.

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EP476
Globoid cell leukodystrophy: case report and literature review
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Krabbe disease, also known as globoid cell leukodystrophy, is an autonomic recessive genetic disorder caused by GALC mutations. GALC gene codes for galactosylceramidase, which is a lysosomal enzyme. This disorder can occur during early childhood, between the ages of 1 and 8 years old (later onset form) or during adulthood; its prevalence is estimated at 1/100 000. Nevertheless, in most cases, this disorder occurs during childhood. With this case report, our aim is to attempt to describe both clinical features and evolution of this rare defect. A 5-year-old non-consanguineous female with a good psychomotor development has been showing psychomotor regression including generalised hypotonia, loss of both speech and walking since age 3. This patient no dysmorphism and no organomegaly and she had no fever. Genetic testing revealed the presence of a compound heterozygote mutation in GALC gene—c.865G>C and c.195G>C confirming diagnosis of globoid cell leukodystrophy. Both parents received genetic counselling in order to determine the risk of reiteration and to offer prenatal diagnosis in case of any future pregnancy. Regarding patients with later onset globoid cell leukodystrophy (occurrence between 1 and 8 years of age), as is the case we are currently reporting, initial symptoms usually include eating difficulties and irritability. Then hypertonic episodes including myoclonic seizures occur in association with development regression. During the final stage of this disorder, hypotonia, blindness and deafness appear. Diagnosis can be established based on reduced galactosylceramidase enzymatic activity or by genetic testing for mutations in GALC gene. Death usually occurs 2 to 5 years after initial symptoms begin. For patients with either early childhood or later onset forms of this disorder, the only therapeutic option is hematopoietic stem cell transplantation which slows down development of this disease. These facts provide new light on the need for genetic counselling in order to provide pre-symptomatic diagnosis in at-risk relatives. Furthermore, reporting of new cases will help to better unravel the phenotype-genotype correlation of GALC gene variants.

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EP478
Metabolic and hemodynamic disorders in obese patients with true and pseudo-resistant hypertension
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Objective to conduct a comparative assessment between metabolic and hemodynamic parameters in obese patients with true and pseudo-resistant (due to different causes) hypertension.

Materials and methods
The study included 302 patients with uncontrolled hypertension and obesity. Initial treatment efficacy was assessed 3 months after dual therapy was administered. Those patients who did not reach target blood pressure (BP) in dual therapy were transferred to triple therapy. Among patients who received triple therapy, 60 people did not reach target BP (they received the fourth drug spironolactone). All patients were additionally examined 6 months after the initiation of antihypertensive therapy.

Results
A comparative assessment of office BP, ambulatory BP monitoring (ABPM) and home self-measurement of BP was carried out between non-resistant and resistant patients: at the initial stage of enrolling patients, there was no significant difference in BP levels between non-resistant and subsequently resistant patients; after 3 months of follow-up (after prescribing double fixed combinations), there was a significant difference in the indicators of both office and out-of-office BP in resistant and non-resistant patients; despite the achievement of target BP levels after 6 months of therapy (double or triple fixed combinations in non-resistant patients and triple therapy + spironolactone in resistant patients), in the presence of resistance, both office, home and most ABPM indicators were significantly higher in non-resistant patients. If at the stage of enrolling patients into the study and 3 months after the start of therapy there was no significant difference in BP levels between patients with true and pseudo-resistance, then after 6 months of antihypertensive therapy, patients with true resistance had significantly higher levels of office systolic BP (SBP, P < 0.01) and 24 h average SBP according to ABPM data (P < 0.05) compared with pseudo-resistant patients. Obese patients with pseudo-resistance had also significantly lower body mass index (BMI) and low-density lipoprotein cholesterol (LDL-cholesterol, P < 0.05) as well as higher levels of aldosterone and SBP (P < 0.05) compared with pseudo-resistant patients.

Conclusions
Even when target BP levels in antihypertensive therapy are achieved, obese resistant patients are characterized by higher levels of office and out-of-office BP, compared with non-resistant patients. Compared with pseudo-resistance, the presence of true resistance in obesity is associated with higher SBP and aldosterone levels, as well as lower BMI and LDL-cholesterol.

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EP479
A new rehabilitation complex for muscle strength deficit correction and movement disorders in case of obesity
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Aim
The Aim of the study was evaluation of effectiveness a new complex included aerobic and physical training, kinesiohydrotherapy, balance therapy on changes in muscle strength and movement disorders in patients with obesity.

Materials and methods
The study group included 40 patients aged 58 [53;66] y.o. with a BMI ≥ 30 kg/m2. The control group included 40 people aged 57 [54;63] y.o. with BMI,2.30 kg/m2. Study methods included anthropometry, functional tests, and dynamometry.

Results
In research it was a significant decrease in body weight (from 106.03 [83;145] to 102.8 [80;141] kg), BMI (from 39.2 [30;12;49.1] to 38.1 [29,4;46.7] kg/m2), decreased WC (from 109 [105;125.8] to 107 [98.8 12] cm), HC (from 127 [112;139.8] to 121 [109;5;133.5] cm), decreased pain syndrome (from 5 [3;7] to 2.5 [1;4.75] points), increased arm strength (in right arm from 20 [14.25;34] to 30 [19;42], in left arm from 19.5 [14.25;29.5] to 22 [18,30;75] daN). Conditioning and coordination abilities improved significantly in the main group according to the functional tests: "Up and go test" (from 7.9 [7;1;8.9] to 7.4 [6;5.8;3] sec, 1, back muscle strength (from 5[5;5] to 5[5;5]), static and dynamic abdominal muscle endurance (from 12.04 [9.47;17.13] to 16.07 [10;69;27.7] sec. and from 31[21;37.25] to 39 [29.5;46.5] sec, and back and from 14.94 [5.8775;22.205] to 18.41 [9.745;31.335] times and from 8 [5;14] to 10 [8;23], times, respectively); Fukuda test scores (from 65 [56;76.75] to 72 [61;82] rep), One leg standing test (from 13.9 [5.38;32.15] to 18.61 [8.6125;38.1575] sec. for the left) and closed eyes (from 3.45 [2.16;6.38] to 3.975 [2.71;5.82] seconds for the right and from 4.12 [1.38;6.1] to 4.31 [2.16;8.13] seconds for the left).

Conclusions
A new complex including aerobic and strength training, kinesiohydrotherapy, and balance therapy showed significant effects on body weight reduction, body volume reduction, and muscle strength improvement in obese patients. A new integrated method results in a longer maintenance of the achieved effect when controlling the long-term results after 3 months and 1 year compared with the group that received only the 2-component program.

Keywords
obesity, kinesiohydrotherapy, balance, rehabilitation, coordination training, muscle strength.

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EP480
Age aspects and body mass index in patients with toxic hepatitis
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Background
Over the last year the social consequences of obesity has become significant, with weight-based stigmatization and prejudiced common outcomes. Toxic hepatitis is one of those diseases that has obese as comorbidity in different age groups. The pervasiveness of prejudice toward obese in patients with toxic hepatitis makes it imperative that scientists have access to valid and reliable measures to assess weight bias.

Objectives
Age groups structuring and examination of patients with toxic hepatitis for obesity detection as one of the hepatic fibrogenesis triggers.

Methods
124 patients with toxic liver disease were examined. The body mass index (BMI, Kettle index) was calculated using anthropometric indicators. For all our patients BMI was interpreted using standard weight status categories (classification of BMI adopted by the WHO (1997). The value of BMI in the range of 18.5-24.9 kg/m² should be considered optimal - normal or healthy weight; reduced BMI or underweight ≥ 18.5; overweight ≥ 25.0-29.9; obesity I degree - 30,0-34,9; obesity II degree - 35,0-39,9; grade II obesity - ≥ 40 kg / m²). The age standards were interpreted using adopted by the WHO/Europe, according to which the young age is 25-44, the average age - 44-60, the older age - 60-75, the elderly age - 75-90, people aged 90 and over considered as long-lived. However, it should be noted that the last age category among the examined patients was not presented.

Results
The examination revealed that the following changes were observed in BMI: 52.8% of patients were with normal weight, 39% were overweight, obesity I degree was detected in 8.1% of patients. Age structuring of BMI is given in the table.

| Characteristic | Young age | Average age | Elderly age | Old age |
|---------------|-----------|-------------|-------------|
| n = 8(%)      | n = 56(%) | n = 52 (%)  | n = 7(%)    |
| BMI kg/m²     | 1(12.5)   | 22(39.3)    | 23(44.2)    | 2(28.6) |
| 18.5-24.9     | 31(55.4)  | 4(7.2)      | 3(42.9)     |
| BMI kg/m²     | 1(12.5)   | 22(39.3)    | 23(44.2)    | 2(28.6) |
| 25,0-29,9     | 3(5.4)    | 5(9.6)      | 2(28.6)     |
| BMI kg/m²     | 30,0-34,9 |            |             |         |

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Conclusions
Obesity of varying degrees was found in 47.2% of patients with toxic hepatitis in all age groups. The most numerous was group of average age (n = 56), the smallest in number was group of old age patients (n = 7). These data should be taken into account when choosing and prescribing adequate treatment, nutrition should always be considered among physicians in the liver and obesity fields, who have an important role to play in improving the quality of life for so many individuals affected by these pathologies.

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EP481
Prevalence of non alcoholic fatty liver disease and fibrosis in morbidly obese patients undergoing bariatric surgery
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Background
Patients undergoing bariatric surgery have a higher prevalence of non alcoholic fatty liver disease (NAFLD) than the general population; however, its assessment and the accurate staging of fibrosis are often complicated because noninvasive tests are not very accurate in patients with morbid obesity, and liver biopsy cannot be performed as a routine exam.

Aim
The aim of this study was to determine the prevalence of non alcoholic fatty liver disease and fibrosis in patients undergoing bariatric surgery.

Methods
This is a monocentric prospective descriptive study including 40 morbidly obese patients before bariatric surgery. NAFLD was diagnosed by ultrasound and alterations in liver enzyme levels (aspartate aminotransferase (ASAT), alanine aminotransferase(ALAT) and yGlutamylTransferase (yGT)). Fibrosis score used was the fibrosis-4 (FIB-4) index.

Results
The mean age was 38.18 ± 10.03 years, 35 (87.5%) were females, mean body mass index (BMI) was 47.13 ± 7.73 kg/m² and mean waist circumference was 134.64 ± 20.39 cm. Mean triglyceride level was 1.8 ± 1.67 mmol/l [0.41-7.67].

Mean serum levels of liver enzymes ASAT, ALAT and yGT were respectively 25.29 ± 12.11 UI/l [10-54], 26.82 ± 14 UI/l [14-58] and 28.11 ± 15.6 UI/l [8-55].

Mean 25 OH vitamin D level was 17.02 ± 13.61 ng/ml [8.1-64.8]. Ultrasound was abnormal in 26 patients (65%). NAFLD was associated with triglyceride levels (P = 0.034). However, age (P = 0.5), body mass index (P = 0.44), hypertension (P = 0.7), diabetes (P = 0.4), ASAT levels (P = 0.4), ALAT levels (P = 0.1), ASAT/ALAT (P = 0.053) and yGT levels (P = 0.4) and Vitamin D levels (P = 0.05) were not associated with NAFLD. Mean FIB-4 index was 0.74 [0.19-3.76]. Of the study population, 92.1% of patients had a FIB-4 index < 1.3. 5.3% had a FIB-4 index between 1.4 and 2.67. 2.6% of patients had a FIB-4 index > 2.67. FIB-4 index > 1.3 was associated with ALAT levels (P = 0.005), vitamin D levels (P = 0.038) and yGT (P = 0.03). However, no association was found with ASAT levels (P = 0.1), yGT (P = 0.3), homa2-insulin resistance (P = 0.9), age (P = 0.3), BMI (P = 0.56) and waist circumference (P = 0.4).

Conclusion
Vitamin D status were associated with NAFLD and advanced fibrosis in morbidly obese patients. Therefore, routine screening of 25OH vitamin D deficiency have important therapeutic implications in this population. FIB-4 index ruled out advanced fibrosis in most of our study cases.

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EP483
Hypoglycemia after gastric bypass
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Introduction
Today, approximately 33% of the world population is either overweight or obese. National Health and Nutrition Examination Survey (NHANES) results show that, when 20 years and older American adults are examined, it is seen that 33% of them are overweight, 35.7% of them are obese, and 6.3% of them are morbidly obese (1). Roux-en-Y gastric bypass is a restrictive and malabsorptive combined method and is a complicated operation. Cases of endogenous hyperinsulinemic hypoglycemia developing an average of 5-6 years after the operation have been reported (2). We aimed to present a case of severe hypoglycemia after Roux-en-Y gastric bypass.

Case
A 27-year-old female patient had a sleeve gastrectomy in 2015 and a Roux-en-Y gastric bypass operation in 2018. She lost 76 kg after the operation. His hypoglycemia started one year after Roux-en-Y gastric bypass. The patient, who has tremors, sweating, and palpitations, especially 2-4 hours after the meal, states that his capillary blood sugar is 24 mg/dl. Therefore, the patient sometimes applied to the emergency room. The patient was interned at Bursa Uludagu University in 2019. At the 15th hour of the 72-hour fasting test, blood glucose was: 20 mg/dl Insulin: 19.2 pmol/l c-peptide: 7 ng/ml. At the 2nd hour of the mixed meal test, blood glucose was 47 mg/dl while insulin: was 43.4 pmol/l.

Computed tomography (CT) was performed on the patient. The pancreas was normal in CT. Islet abnormalities after Roux-en-Y gastric bypass surgery were considered in the patient. The patient received acarbose and metformin treatments for three months, but to no avail. Then liraglutide was started. After a month, the controlled hypoglycemia continued, and isoptin and acarbose were added to his treatment. However, the patient’s complaints continued. Therefore, octreotide LAR 20 mg was started. The patient whose hypoglycemias years improved is being followed up.

Conclusion
It is necessary to be careful about hypoglycemia developing after Roux-en-Y gastric bypass. Also, we should consider the long-term results of bariatric surgery.

EP482
The effect of laparoscopic mini-gastric bypass on the compensation of carbohydrate metabolism in patients with morbid obesity and type 2 diabetes
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Objective
Sustained weight loss is a highly effective strategy to treat and prevent the development of type 2 diabetes (T2D). Bariatric surgery leads to significant weight loss, which ensures the achievement of remission of diabetes mellitus and other obesity-related comorbidities.

Aim
The aim of this study was to estimate glycemic profile of patients with morbid obesity and T2D after laparoscopic mini-gastric bypass (LMBG).

Methods
We conducted a retrospective study of obese patients admitted to the Endocrinology Research Center between February 2019 and December 2020. We included 45 adults (41 women and 4 men, median age 57.3 years) with diabetes mellitus type 2 (median duration of disease 8 years, 3 newly diagnosed) and morbid obesity (BMI > 40 kg/m²). Anthropometric (BMI) and metabolic (fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), C-peptide) parameters were determined before surgery and at 6, 12 months after. Statistical analysis was performed with the use of Statistics v. 13.3 (TBSCO Software Inc., Palo Alto, CA, USA). Data is presented by medians and interquartile ranges (Median, (25;75)).

There were carried out a comparative analysis of three dependent groups for quantitative data using the Friedman criterion, pairwise comparison of groups for quantitative data using the Wilcoxon criterion. The initial critical level of significance in testing statistical hypotheses was assumed to be 0.05.

Results
In the studied group the baseline median BMI was 51 kg/m² (44.3; 55.6), FPG 7.4 mmol/l (6.6; 9.0), HbA1c 7.2% (6.5; 8.5), C-peptide 4.5 ng/ml (4.3; 5.1). 6 months after LMBG the median BMI was 38.6 kg/m² (35.5; 42.1), FPG 5.3 mmol/l (4.9; 6.2), HbA1c 5.5% (5.3; 6.2), C-peptide 2.5 ng/ml (2.3; 3.9); 1 year after LMBG 31.6 kg/m² (28.6; 34.2), FPG 4.9 mmol/l (4.4; 5.3), HbA1c 5.7% (5.1; 5.9); C-peptide 2.2 ng/ml (1.9; 3.2). Comparing three groups differences in HbA1c levels were revealed (n = 11, P < 0.001). Difference between groups of 6 and 12 months after LMBG (n = 10, P > 0.05) was significantly less than before LMBG and 6 months after (n = 23, P < 0.001), before and 12 month after LMBG (n = 18, P < 0.001) in further pairwise comparison.

Conclusion
Weight loss was accompanied by a significant improvement of carbohydrate metabolism. A more pronounced decrease in body weight and improvement of metabolic parameters were observed in the first 6 months after surgery.

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This article discusses the assessment of quality of life, psychological state and anxiety-depressive disorders in patients with metabolic syndrome. It is known that the prevalence of metabolic syndrome in different countries is about 30% and varies from included criteria. The problem of the quality of life of obese and overweight patients is relevant and socially significant.

**Research Methods**

The authors present the results of a study of 70 patients with MS and 36 apparently healthy volunteers who do not have concomitant diseases and are not obese. The study was conducted on the basis of the clinic of the Federal Research Center. Patients were examined, anthropometric parameters were determined (waist circumference, body weight) with an assessment of the quality of life (SF-36 questionnaire). The level of anxiety and depression was determined by the hospital anxiety and depression scale HADS.

**Results**

Analysis of the results revealed that most of the quality of life indicators were significantly different in patients with metabolic syndrome relative to the control group. Thus, the indicators of the level of QoL are significantly higher in healthy individuals than in patients with obesity. Differences in all groups are significant \((P \leq 0.05)\). It was found that the average level of parameters “physical functioning” decreased by 19.2% \((P < 0.05)\), “role functioning” by 34.2% \((P < 0.05)\), “general health” by 14.7% \((P < 0.05)\), “vitality” by 16% \((P < 0.05)\), “emotional functioning” by 53.1% \((P < 0.05)\). The assessment of the level of anxiety and depression in patients with MS corresponded to the subclinically expressed level, and the level of depression exceeded the control group by 19%. The level of QoL in patients with obesity is significantly lower than in healthy individuals.

**Conclusion**

Assessment of the quality of life of patients with obesity and overweight is one of the most important factors in the integrative assessment of the condition of such patients. I would like to note that the higher the patient’s body weight, the lower his physical condition and the more pronounced concomitant diseases. Patients with MS are characterized by a decrease in quality of life indicators, subclinically expressed anxiety-depression. Patients require correction of psychological disorders, which will reduce the level of anxiety and depressive disorders, which will further improve the quality of life.

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Background
In Pathogenesis of Neurodegeneration in Diabetes Mellitus (DM) addition to insulin resistance, glycemic control and blood plasma lipid levels existing other mechanisms were proposed. We investigated plasma insulin level in patients according to severity of diabetic neuropathy.

Materials and methods
In 32 people with DM2 glyceria, HbA1c, blood plasma insulin, blood total cholesterol, triglycerides, Low Density Lipoproteins (LDLP) levels were measured and compared regarding to DN severity by stages in DN1 and DN2 groups.

Results
People with DN1 and DN2 have the same age and disease duration. Glyceria and HbA1c level were also comparable between groups. Although, body weight and BMI (in 1.32 times), blood total cholesterol (in 1.3 times), triglycerides (in 1.32 times), LDLP (in 1.4 times) levels were significantly higher in DN2 group than DN1, blood plasma insulin was higher in DN2 group and suggested about involvement of insulin resistance into pathogenesis of DN. However, people in DN2 group used metformin with combination of sulfonylurias, whereas DN1 group mostly used metformin for lowering blood sugar.

Conclusion
DM2 patients with severe DN have higher BMI, blood lipids and plasma insulin level. Plasma insulin level has a linkage with DN severity in DM2 and play a role in the development of neurodegeneration.

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EP488
Salvage nephrectomy for a severe acute emphysematous pyelonephritis with septic shock: a case report
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Introduction
Emphysematous pyelonephritis is associated with high mortality rate. It is seen in patients with a long-standing diabetes. We report a case of a women presenting a septic shock following a severe acute right emphysematous pyelonephritis and requiring salvage nephrectomy.

Case report
A 52-year-old female presented fever with right flank pain. She had a long history of uncontrolled diabetes. Physical examination revealed a with high fever (39°) with tender right loin. Basic investigations reported high blood sugar (33 mmol/l) and leukocytosis (109/l) and thrombocytopenia (85109/l). kidney, ureter, and bladder (KUB) X-ray revealed no significant abnormality. Ultrasonography showed a right kidney with hydronephrosis upon a 8 mm lumbar ureteral calculus. Left kidney was normal. The diagnosis of acute obstructive right pyelonephritis has been established and antibiotherapy using cefotaxime, amikacin injection and insulin has been immediately started. A double J stent has been also inserted to the removed kidney. The removed kidney was gangrenous. She had an uneventful recovery during 5 days in intensive care unit. She received imipenem for 21 days. She had an uneventful recovery during 5 days in intensive care unit. She received imipenem for 21 days.

Renal and tests and CBC normalized. Blood sugar became normal with insulin.

Conclusion
Emphysematous pyelonephritis occurs mostly in patients with diabetes and a predilection for females. It has a high fatality rate. Therefore, aggressive medical with early surgical intervention is recommended.

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EP489
Pteosis and type 1 diabetes: fortuitous association?
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Introduction
Diabetes is the cause of ophthalmological complications that are all the more severe when the balance of diabetes is precarious. Among the non-retinal ocular targets of diabetes is damage to the optic nerve. The diagnosis of diabetic mononeuropathy should only be made after excluding other causes of neuropathy.

Observation
We report the case of a patient referred to our service for equilibration of diabetes. This is a 59-year-old patient, type 1 diabetic for 30 years, coronary stent 6 years ago. In addition, the patient presents a pteosis of the right eye which appeared two weeks ago. As part of the exploration of this symptomatology, a brain scan and a brain MRI were requested. The scan came back with no abnormalities. MRI showed moderate thickening of the optic nerve consistent with optic neuritis. The etiological investigation was continued by serological, enzymological and immunological tests. CMV and HIV serologies were negative. The antiglantin converting enzyme level was normal. Polymorphonuclear anti-cytoplasm antibodies and native anti-DNA antibodies also came back negative. On biology, he had a fasting blood sugar level of 25.1 mmol/l and a glycated hemoglobin of 12.9%. The patient was on insulin therapy. The evolution was marked by the normalization of the glycemic figures after one week of hospitalization.

Conclusions
Optimal glycemic control reduces the risk of diabetic retinopathy but also of the occurrence of other ocular pathologies, in particular oculomotor damage and damage to the optic nerve responsible for reduced visual acuity.

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Sulphonylureas induced hypoglycemia: a neglected cause of focal encephalopathy
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Introduction
Sulphonylureas (SU) are an effective therapy for type 2 diabetes (T2DM). As insulin secretagogues, hypoglycemia is a potential adverse effect. Hypoglycemia may cause neuroglycopenic brain injury, which can mimetize stroke and infections of the central nervous system.

Case Report
The authors report the case of an autonomous 71 year-old woman, with medical history of hyperension and T2DM, treated with enalapril and glisazide, that was admitted in the Emergency Room after being found unresponsive at home. The first medical evaluation revealed: GCS 14, hypertension (172/85mmHg) and capillary blood glucose of 28 mg/dl. Complete neurological exam showed left hemiparesis and apasia, being stroke the most probable diagnosis. Patient was admitted to the Neurology floor. No ischemic lesion or hemorrhage were found in two separate cerebral MRIs. All other exams were normal, including: holer, cardiac ultrasound, carotid doppler, EEG and lumbar puncture. Blood workup was unremarkable, without signs of infection or inflammatory disease. A1C hemoglobin was 5.7%. All symptoms and deficits remitted after SU discontinuation. After excluding differential diagnosis, it was assumed the diagnosis of neuroglycopenia with focal neurological deficits caused by treatment with SU.

Conclusion
Nowadays, with the development of new antidiabetic drugs, the use of SU has been reduced. The risk of SU induced hypoglycemia is relevant, mainly in the elderly. Cognitive and mental impairment are the most frequent symptoms of hypoglycemia. In rare cases, hypoglycemic encephalopathy with focal deficits may occur. Being a reversible cause of injury, its peremptory diagnosis is relevant.

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EP492
Diabetic muscle infarction: a case study
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Introduction
Diabetic muscle infarction (DMI) is a rare complication of long-standing, poorly controlled diabetes, and it’s more common in patients with micro-vascular complications. Herein, we present a case of DMI occurring in patient on hemodialysis.

Case presentation
A 44-year-old man on maintenance hemodialysis presented with an acutely painful and swelling in his left calf. He had a 21-year history of poorly controlled type 1 diabetes, with micro-vascular complications (neuropathy and retinopathy). On physical examination: his skin was pale, his temperature was 37°C, his heart rate was 80 beats per minute and his blood pressure was 150/80 mmHg. His left calf was swollen and tender with no edema or inflammatory signs. Biochemical findings showed: C-reactive protein (CRP) 42 mg/l, CPK 179 IU/l (39-308) and LDH 382 IU/l (140-280). A Doppler ultrasound showed no sign of deep vein thrombosis, but demonstrated edema of the superficial tissues which prompted the practice of an MRI showing thickening of the lateral gastrocnemius muscle with edema. It is the seat of a lack of enhancement extending over 3 cm with the interposition of a few fibers of marked enhancement. The thickening and muscle edema was more important in the posterior compartment of the leg. It also showed edematous infiltration of fascia and subcutaneous cellulitis without significant enhancement and minimal fatty degeneration of the different muscle compartments of the leg. The patient was put on analgesics and activity restriction in the acute phase followed by gradual mobilization.

Conclusion
Diabetic muscle infarction is a rare and under-reported condition that should be suspected in any diabetic dialysis patient who develops a painful, swollen muscle.

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iron deficiency anemia, hypocalcemia and poor glycemic control (A <ce:inf> c</ce:inf> = 10.19%). The foot surgery removed the affected soft tissue including the 4th metatarsal joint of the left foot. Under antibiotic therapy with Clindamycin (i.v) and Ciprofloxacin, α-lipoic acid, benfotamine, aspirin, atorvastatin, cilostazol and iron substitution, the clinical evolution was slowly favorable. The plaque culture was negative, possible in the context of prior Amoxicillin Clavulanate administration before hospital admission. Given his clinical presentation, a Cardiosy evaluation was performed, which confirmed the CAN diagnosis. In order to decrease the number of the symptomatic orthostatic episodes, 0.1 mg/day of Fludrocortisone was initiated under 24 h BP monitoring. The therapeutic education with emphasis on carbs ingestion, blood glucose self-monitoring and foot care was resumed.

Conclusions
This case illustrates typically the negative impact of peripheral and clinical CAN association on the quality of life (QoL). Unfortunately, the poor prognosis in this case relies mostly in the lack of adherence to the medical therapy and foot care.

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EP495
The prevalence of diabetic peripheral neuropathy among the futsal players participating in the DiaEuro 2017 Championship
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Objectives
To assess the prevalence of diabetic peripheral neuropathy (DPN) among futsal players participating in the 2017 edition of the European Futsal Championship for people with diabetes (DiaEuro).

Methods
In this cross-sectional study were included 94 amateur/professional futsal player, from 9 European countries. The evaluation was made based on the data extracted from the standard medical certificate completed by each player’s diabetologist. The official participation criteria were: age ≥ 18 years old, a diagnosis of diabetes and no other severe comorbidities that could contraindicate this type of sport.

Results
Of 94 subjects, 90 (95.74%) had type 1 diabetes, 3 (3.19%) had type 2 diabetes, and one player had type 3c diabetes secondary to chronic pancreatitis. 3 players were on oral medication, one was on diet therapy and 90 players (95.74%) were under insulin treatment as follows: 78 (82.97%) on a basal bolus regimen and 12 (12.76%) on insulin pump. Regarding the diabetes microvascular complication, 2 (2.12%) individuals were diagnosed with DPN and 3 (3.19%) with retinopathy and 6 (4.31%). Furthermore, only one subject out of the 2 with DPN received treatment with alpha-lipoic acid for his condition.

Conclusions
In our analysis of 94 amateur/professional futsal players with diabetes, we found a prevalence of 2.12% of DPN.

Parameter | Interval (min-max) | Mean | STDEV
---|---|---|---
Age (years) | 18 - 65 | 27.74 | ±8.23
Diabetes duration (years)* | 1 - 39 | 12.21 | ±7.34
Last A1c (%)* | 5.3 -10.5 | 7.31 | ±0.99

The general characteristics of the study population; *Data were available for 91 subjects; STDEV = standard deviation; A1c = glycated hemoglobin

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EP496
Metabolic complications of obese Tunisian adults
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Introduction
Obesity is a major health problem through its numerous complications especially metabolic complications associated with cardiovascular risk. The aim of our work was to describe the clinico-metabolic profile of obese Tunisian adults.

Methods
This was a descriptive cross-sectional study involved 174 obese patients who consulted between July and December 2020 at the Obesity Unit of the National Institute of Nutrition in Tunis.

Results
The average age was 45.21 ± 13.88 years with a female predominance of 75.3%. All patients were obese with an average BMI of 40.2 ± 7 kg/m². Obesity was visceral in 100% of cases with a mean waist circumference of 121.05 ± 14.4 cm (men 123.93 ± 14.01 cm vs women 120.11 ± 14.45 cm). Arterial hypertension was noted in 47.13% of our population of which 15.85% were not known hypertensive. Dyslipidemia was found in 54.6% of cases of which 45.26% were unknown. Carbohydrate tolerance disorders was found in 67.81% of cases (2.12% prediabetes; 24-71% diabetes and 5.17% unknown diabetes). Hyperuricemia was found in 33.3% of cases. Endocrinopathies were symptomatic. Waist circumference Was significantly correlated with BMI (r = 0.62, P < 0.001)). As was triglycerides (r = 0.16; P = 0.039).

Conclusion
In our study metabolic disorders were of incidental discovery in many patients. Their treatment must be specific, it should not be limited to weight loss, and the early detection of these abnormalities and their management will improve the cardiovascular prognosis of patients.

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EP497
Metabolic profile of morbid obesity compared to moderate and severe obesity: What particularities?
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Introduction
The prevalence of obesity is increasing in the world. It constitutes a major risk factor associated with diabetes, hypertension, dyslipidemia and cardiovascular diseases. The aim of our work is to compare the metabolic profile of morbid obesity with that of moderate to severe obesity.

Patients and methods
It is a Retrospective, descriptive and analytical study, including 63 obese patients, followed at the endocrinology, diabetology and nutrition department of the CHU Mohamed VI Ouja. The patients were divided into two groups: Group 1 (G1: moderate to severe obesity): 37 cases (BMI: 30 to 40 kg/m²), Group 2 (G2: morbid obesity): 26 cases (BMI ≥ 40 kg/m²). Collected data were analysed using SPSS V24 software.

Results
The mean age of the patients was 30.5 ± 16.9 years in G1 and 39.8 ± 12.5 years in G2. A female predominance was noted in the 2 groups with a Sex-ratio F/M (G1): 5.08 (P = 0.001), as was triglycerides (G1: 1.99 ± 1.24 mg/dl vs G2: 2.29 ± 1.54 mg/dl, P = 0.005). The prevalence of diabetes was higher in G2 compared to G1 (69.2% vs 48.6%) but without significant difference (P = 0.085). The prevalence of dyslipidemia was higher in G1 (32.4%) compared to the group having morbid obesity (26.9%) with a highly significant difference (P = 0.008).

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Discussion/Conclusion
Obesity is an excess of body fat with harmful consequences for health. It has been defined as a disease by the World Health Organization since 1997 in view of its epidemic dimensions and its somatic, psychological and socio-economic repercussions. The main metabolic complications of obesity are associated with the phenomenon of insulin resistance and are included in the metabolic syndrome. Several studies suggest that despite a greater accumulation of fat, morbid obesity is not characterized by a more deleterious metabolic profile than moderate and severe obesity. The results of our study are also in line with those of the literature, which show that the severity of obesity is not significantly correlated with metabolic risk.

Keywords
Morbid obesity, moderate and severe obesity, metabolic profile

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EP498
How to treat severe obesity due to binge eating in children?
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Introduction
As the incidence of pediatric obesity is gaining pandemic levels, with children and teenagers developing obesity complications similar to the adult population, a rapid evaluation and treatment is necessary. We present such a case.

Case report
A 12-year-old male with a medical history of binge eating, treated by Topiramate, since the age of 11 and 3rd degree obesity, complicated with JNC stage II hypertension, NASH and dyslipidemia was referred to our clinic for nutritional assessment and treatment. He was referred by a colleague endocrinologist that evaluated his obesity for endocrinological causes, which were excluded. The clinical examination: Showed normal pubertal Tanner stage (P1G2), BMI 37.3 kg/m², height of 155 cm (75th centile), 51.4% fat, 205% obesity degree from the 95th centile, normal muscle mass of 23.7 kg, BP 150/90 mmHg and a waist circumference of 120 cm.

Laboratory
Dyslipidemia with HDL = 30 mg/dl, TG = 133 mg/dl, insulin resistance HOMA-IR: 6, blood glucose = 82.5 mg/dl, an inflammatory status with a VSH=21, fibrinogen = 357, 25-OH vitamin D of 17 ng/ml, TSH of 2.71, normal salivary cortisol, IGFI, FSH, LH < 0.3, testosterone of 0.16 nmol/l and a prolactin of 295 mcU/ml. The abdominal ultrasound showed liver steatosis. The basal metabolic rate (indirect calorimetry) - low of 1600 kcal (85%), correlated with the low muscle mass. The cardiologist consult found normal ECG, JNC stage II hypertension, septal left ventricular hypertrophy and indicated treatment with Lisinopril 10 mg per day. We began a hypocaloric Mediterranean diet (400 calories daily deficit), moderate physical activity (45-60 minutes), low sodium intake, but the patient didn’t lose weight for the first month of nutritional monitoring, so Liraglutide was introduced, with a 0.6 mg/day regimen, with dose titration every 2 weeks to avoid adverse effects, to a dose of 2.4 mg per day. He received Omega 3(2000 mcg) and 2000 UI vitamin D per day. After 1 month of diet and Lipaglutide, the binge eating improved, he lost 2% of body fat and the BP normalized. Also, the eating disorder improved.

Conclusion
The lipid profile of the obese is highly atherogenic. It is distinguished by a variety of lipid abnormalities dominated by elevated LDL-cholesterol, total cholesterol and triglycerides with hyper-HDLemia justifying their early management in order to improve their cardiovascular prognosis.

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EP499
Lipid profile of the obese: about 100 cases
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Obesity is a major public health problem. It is a privileged provider of a constellation of metabolic abnormalities, particularly lipids, increasing the risk of morbidity and mortality and hampering the quality of life of the obese.

Material and methods
We conducted a prospective study on 100 obese patients recruited at the Human Obesity Research Unit at the National Institute of Nutrition in Tunis. Our patients benefited from an assay of fasting insulinemia and a complete lipid profile including the assay of cholesterol, triglycerides, HDL-cholesterol with calculation of LDL-cholesterol and non-HDL-cholesterol.

Results and Statistical Analysis
The average age of our population is 37 ± 10.8 years. The average BMI is 38 ± 6.7 kg/m² with extremes of 30 and 67 kg/m². Mean fasting insulinemia is 24.7 ± 20.1 μU/ml with extremes of 5.3 and 146 μU/ml. One-third of obese people have high fasting insulin levels. Hypertriglyceridemia is noted in 19% of obese patients, 29% of obese people have hypercholesterolemia. More than a quarter of obese people (27%) have low LDL-cholesterol levels below 1.03 mmol/l (0.4 g/l). On the other hand, 14% of patients have an HDL-cholesterol level greater than or equal to 1.55 mmol/l (0.6 g/l). The average non-HDL-cholesterol is 3.35 ± 0.9 mmol/l (1.3 ± 0.36 g/l). The average LDL-cholesterol of 2.81 ± 0.85 mmol/l (1.09 ± 0.33 g/l) with extremes of 1 and 6 mmol/l (0.39 and 2.32 g/l). HyperLDLemia was discovered in 29.3% of obese patients. The duration of evolution of obesity is positively and significantly correlated with the elevation of cholesterolemia (P = 0.001), LDL-cholesterol (P = 0.002) and non-HDL-cholesterol (P = 0.001). The rise in fasting insulinemia is positively and statistically correlated with the rise in cholesterolemia (P = 0.001), LDL-cholesterol (P < 10–3), non-HDL-cholesterol (P < 10–3). A negative and statistically significant correlation was also noted between fasting insulinemia and HDL-cholesterol (P = 0.02).

Conclusion
The lipid profile of the obese is highly atherogenic. It is distinguished by a variety of lipid abnormalities dominated by elevated LDL-cholesterol, total cholesterol and triglycerides with hyper-HDLemia justifying their early management in order to improve their cardiovascular prognosis.

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Assessment of depression in diabetics with erectile dysfunction (ED): 37 cases

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Introduction

Diabetes is a disease that can slowly be. Among its complications, erectile dysfunction can appear. Be careful, these problems can be warning signs. These problems can be warning signs, especially cardiovascular, but they also have significant psychological retention.

Materials and methods

Prospective study on 37 diabetic patients collegiate in the department of Endocrinology CHU Hedi Chaker Sfax Tunisia. All patients are assessed for erectile function by the International Index (IIEF) 5 and screened for depression using the Beck Scale (BDI).

Results

The majority of our hospitalized patients (80.5%) were between 45 and 70 years old. As well as 60.25% of diabetics had diabetes evolving for more than 10 years. The mean blood glucose at young was 18 mmol/l with HbA1c at 9%. Only 20% had a normal sex life. Erectile dysfunction is found in 72% of cases; it is severe in 8% of patients, moderate in 12% of cases, mild to moderate in 22% of cases and mild in 30% of cases. Concerns are all the more frequent as the diabetic disease is old, and especially poorly controlled. 77% of poorly controlled diabetics are subject to erectile disorders against 64% for those whose pathology is under control. According to the Beck Scale (BDI), 54% of our patients had experienced a feeling of sadness, of which 14% were unable to cope.

Conclusion

When the chronic complications of diabetes are already present, almost 75% of patients also have erectile dysfunction. A consequence that alters the quality of life. Only 25% of nurses are interested in the psychological side of diabetics with erectile dysfunction, of which 70% encourage them to consult a psychiatric hospital.

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Obesity and lifestyles related to diabetes during COVID-19 pandemic

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Diabetes is mainly a consequence of the lifestyle of the current population, characterized by an increase in obesity, sedentarism and a highly caloric diet, added to which is an ageing population. Prevention and its treatment consist in following an adequate diet, practising physical exercise regularly and maintaining normal weight, factors which are achieved through the adoption of healthy lifestyles. However, weight loss remains a problematic issue among diabetics, mainly due to the fact that the diabetic individual neither understands nor incorporates the need for significant alterations in his lifestyle. The current COVID-19 pandemic has drawn, once again, our attention to the problem of obesity. This study depicts the analysis of residents in a neighbourhood in greater Porto, Portugal. The data collection derived from the answers of a questionnaire highlighted the existence of various factors that contribute to the development of obesity over a long period of time, being behavioural patterns one of the most impactful causes as they are related to our lifestyle. Repeated lockdowns were responsible for a decrease in the practice of physical activity and changes in the eating habits of the Portuguese population in general, resulting in an increase in the consumption of fizzy drinks, fried and fast food, processed meals, frequent intake of food and, consequently, weight gain. The present pandemic has also contributed to a rise in a sedentary behaviour exemplified by prolonged periods of time spent watching TV or on other technological gadgets (cell phone, laptop, etc.), attending online classes and working from home, aspects which increase the risk of obesity and diabetes. Smoking, the lack of physical activity and a poor diet also add to the increase in weight and poor glycaemic control. There are, however, lifestyle alteration programs which include a variety of procedures to overcome obstacles regarding weight loss. In fact, significant changes in lifestyle appear to be associated with a greater weight loss e better glycaemic control.

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Inadequate iodine intake in lactating women in the inland area of norway

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Background

Many studies in Norway have found inadequate iodine status in pregnant and lactating women, but no studies have been undertaken in a random, population-based sample. Globally, the main strategy to eliminate iodine deficiency is iodization of salt. However, this is not compulsory in Norway, where the current legislation only permits iodization up to 5 mg per gram of salt. To reach the Nordic Nutrition Recommendation (NNR) of 200 μg/day iodine, supplements are recommended to lactating women who do not cover their needs through food sources. In Norway, the main iodine sources in the diet are milk and lean seafood. A study in 130 lactating women in 2018 revealed that mild-to-moderate iodine deficiency was common in the inland area of Norway. Considering the importance of iodine for infant development, more information on iodine status in lactating women is needed.

Objective

This study aimed to evaluate iodine status and intake in a random sample of lactating women and their infants in the inland area of Norway.

Methods

From April 2020 to October 2021, 366 mother-infant pairs were recruited in a cross-sectional study through public health care centers. Urine samples from the mothers and their infants, and breast milk samples were collected for analysis of iodine concentration. Data on habitual and recent iodine intake was collected using food frequency questionnaire (FFQ) and 2 x 24-h dietary recall (24HR), respectively.

Results

Urinary iodine concentration (UIC), breast milk iodine concentration (BMIC) and data from FFQ are pending analyses. Recent use of iodine-containing supplements was reported by 30.1% of the women. Including supplements, the estimated 24 h median (IQR) iodine intake was 125 (70.8, 233.45) μg/day. Excluding supplements, the 24 h median (IQR) iodine intake was 100.1 (65.05, 161.5) μg/day. According to the 24 HR, the food sources that contributed the most to the iodine intake were milk and dairy products, carbonated mineral water from a specific water source in Larvik (Norway), lean fish, whey cheese and eggs. More than two-thirds of the 24HR (68.2%) had an estimated iodine amount below the NNR recommendation for lactating women.

Conclusion

We found inadequate iodine intake in lactating women in the inland area of Norway. Milk, lean fish, eggs, and a specific type of carbonated mineral water were important iodine sources in the diet. The study indicates that a large proportion of lactating women in Norway may need iodine-containing supplements due to a low dietary iodine intake.

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Metabolic burden in mediterranean patients with schizophrenia and psychotic disorders

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Introduction

Mortality among patients with schizophrenia and psychotic disorders (SAPD) is two to threefold higher than in the general population and is widely attributed to cardiovascular and metabolic morbidity.

Objectives

We aim to highlight the metabolic profile of Mediterranean patients diagnosed with SAPD.

Methods

We conducted a descriptive and analytical cross-sectional study involving 55 patients who attended the psychiatry department at Gabes regional hospital, Tunisia, from 2019 to 2020. SAPD were diagnosed according to the DSM-5. MetS was defined based on the 2005 IDF criteria.

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Results
The mean age was 46.8 ± 11.1 years with a male predominance (74.5%). The majority were single (54.5%), from rural areas (52.7%), low-educational background (65.5%), and low-socioeconomic status households (74.5%). Addictive behaviors were reported in 49.1% mainly tobacco (45.5%). Suicidal behavior was noticed in 9.1%. Schizophrenia and schizoaffective disorder were the leading diseases in 72.8% and 16.4%, respectively. Obesity was the most common metabolic comorbidity in 30.9%. Dyslipidemia, diabetes, and hypertension were recorded in 20.0%, 14.5%, and 1.8%, respectively. The prevalence of MetS was 29.1%. MetS was significantly associated with female gender (P = 0.046) and atypical antipsychotics prescription (P = 0.018).

Conclusions
Patients with SAPD are five times more prone to develop MetS than healthy patients. Increased insulin resistance was substantiated in antipsychotic-naive patients. Besides common genetic predispositions to both MetS and schizophrenia suggested by some researchers, this population often has a poor lifestyle, little physical activity, and an unhealthy diet. That could be partially related to negative symptoms of psychotic disorders and drug-induced sedation. Second-generation antipsychotics seem to increase the risk of insulin resistance, obesity, and diabetes by the antagonism at serotonin 5-HT2c receptors.

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EP505
Hepatic steatosis and cardiovascular risk in type 2 diabetes
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Introduction
Non-alcoholic fatty liver disease (NAFLD), is a frequent cause of chronic liver disease and is widely associated with metabolic syndrome. When associated with diabetes, it can increase the risk of cardiovascular events. The aim of this study is to evaluate the relationship between hepatic steatosis and the occurrence of cardiovascular events in patients with type 2 diabetes.

Method
It is a retrospective study, including 184 type 2 diabetic patients, conducted in the department C of the National Institute of Nutrition of Tunis during the year 2021. The diagnosis of hepatic steatosis was retained by an abdominal ultrasound.

Results
Our population was composed of 66 men and 118 women. The mean age of the patients was 61 ± 10 years, and the average duration of diabetes was 13 ± 8 years. The prevalence of NAFLD was 29.3%. A clear female predominance was noted in patients with NAFLD (77.8%). Diabetic patients with NAFLD had dyslipidemia in 88.9%. The majority of patients had poorly controlled diabetes with a mean HbA1C of 10.4 ± 2%. The average body mass index of these patients was 35 ± 5 kg/m². Hepatic steatosis is positively correlated with coronary artery disease (P = 0.016) and high blood pressure (P = 0.000). Moreover, a significant association was noted with hyperuricemia (P = 0.021) and obesity (P = 0.000).

Conclusion
The coexistence of type 2 diabetes and NAFLD increases the occurrence of cardiovascular events and disturbs the glycemic balance of diabetic patients, which underlines the importance of screening for this hepatopathy.

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EP506
Clinical and biochemical outcomes of sodium-glucose co-transporter-2 (SGLT2) inhibitors in type 2 diabetes mellitus patients as a fourth oral anti diabetic medicine
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Objectives
To evaluate the clinical and biochemical effects of (SGLT2) inhibitors as a fourth oral anti-diabetic drug in patients with type 2 diabetes mellitus (T2DM).

Patients (Materials) and Methods
In a tertiary hospital in Karachi, Pakistan, a retrospective assessment of patient medical records was conducted from January 1, 2017 to December 31, 2020. A total of 100 patients (mean age [Standard Deviation]: 53.8 [9.63] years) with poorly controlled T2DM were included. Data was collected before the SGLT-2 inhibitor was added, as well as three and six months after the medication was started. Weight, Body Mass Index, blood pressure (BP), Hba1c, SGPT, and Creatinine were measured at the start and during the study.

Results
There was a significant reduction in Hba1c (P-value < 0.001) with (Mean Reduction [Standard Deviation]) of 0.81[1.02] % at 3 months and 1.07[1.11] % at 6 months. Weight (P-value < 0.001) with (Mean [SD]) of 1.83[2.32] kg at 3 and 4.02[5.04] kg at 6 months, BMI with 0.69[0.95] kg/m² at 3 months and 2.13[3.41] kg/m² at 6 months of follow up. Systolic Blood Pressure showed significant reduction (P-value < 0.05) of 5[1.75] mmHg at 3 months and 6[1.38] mmHg at 6 months. Mild variation in creatinine and SGPT was also noted.

Conclusions
SGLT-2 is a safe and effective oral anti-diabetic medicine that can help individuals with diabetes who are currently using glucose-lowering or anti-diabetic medications. These medications can be used as an alternative to injectable insulin for people who do not want to use it, and they can help diabetic patients stick to their regimen.

Key words: type 2 diabetes mellitus, SGLT-2 Inhibitors, T2DM, Weight loss

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EP507
Verapamil can be used as a type 2 diabetes mellitus saviour and stopping the need for insulin in uncontrolled type 2 diabetes mellitus
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Introduction
Diabetes mellitus is not just a disease as it is already known, the matter is more complicated, and it is considered as an assembly of metabolic defects with end result of hyperglycemia. verapamil can decrease the expression of thioredoxin-interacting protein (TXNIP), which is recognized as an important factor in pancreatic beta cells, verapamil could enhance beta cell mass and function.

Materials and methods
160 type 2 diabetes mellitus and hypertensive patients into 2 parallel groups. Each group had 80 patients, 50 males and 30 females. All patients were monitored in a private clinic. All the patients Lied between 30-60 years old. All patients are on maximum doses of glimepiride, sitagliptin, metformin and empagliflozin but are uncontrolled on this combination with hba1c more than 8. The first group received verapamil 240 mg as substitute or added to the present hypertension therapy for 6 months. The second group was still on hypertensive therapy but received lantus 20 units added to the oral therapy. We measured hba1c and c-peptide levels in the 2 groups at the start of the trial and after 6 months of the trial.

Results
The results show a statistically significant difference in hba1c in group 1 patients before and after 6 months of treatment with verapamil With P value less than 0.0001. The results show statistically significant difference in hba1c in group 2 patients with P value less than 0.0001. The results show significant differences in c-peptide levels in group 1 patients before and after 6 months of treatment of verapamil. The results show non-significant differences in c-peptide levels in group 2 patients before and after 6 months treatment of basal insulin with b value 0.9822. The results show significant difference in hba1c after 6 months of treatment of verapamil vs. basal insulin with b value less than 0.0001. Results also show that verapamil can increase c-peptide levels after 6 months of treatment.

Conclusion
Verapamil could be used as a type 2 diabetes saviour by increasing beta cell mass and function.

Key words: type 2 diabetes mellitus, verapamil, (TXNIP), beta cells

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Therapeutic optimization of type 2 diabetes: what role of the pharmacist?  
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Introduction  
Type 2 diabetes is a chronic disease whose management is characterized by the complexity of its therapeutic axes (methods of taking, storage of drugs, adverse effects, compliance with treatment, etc.), which requires the patient to be well informed to avoid the onset of complications. Faced with this issue, the pharmacist could make a real contribution.  
Goal  
The objective of this work was to assess what role the pharmacist could play in the therapeutic optimization of type 2 diabetes.  
Materials and methods  
We conducted a descriptive study in patients with type 2 diabetes over a period of 03 months. We used a questionnaire comprising 04 parts: knowledge of antidiabetic drugs, assessment of compliance (Morisky’s questionnaire), drug iatrogenism and treatment monitoring.  
Results  
The study was carried out on 60 patients. Analysis of the results showed that 36.6% of patients on insulin did not master the injection technique, 51.7% did not know how to store the drugs and 40% were poor observers.  
In addition, 66.7% exhibited adverse effects, 25% exhibited at least one drug interaction and 26.7% did not master the technique of self-monitoring of blood glucose.  
Discussion  
Our study revealed the existence of several gaps in these patients in terms of knowledge and good and proper use of their treatment and monitoring of their disease. This emphasizes the need for pharmacist involvement in therapeutic education programs for these patients in order to optimize their therapeutic management.  
Keywords  
type 2 diabetes, anti-diabetic drugs, pharmacist, compliance, therapeutic education.

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Is Semaglutide superior than Liraglutide in patients with type 2 diabetes on insulin therapy - case presentation  
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Type 2 diabetes (T2DM) is a chronic and progressive disease associated with microvascular and macrovascular complications leading to increased morbidity and mortality. Insulin remains the cornerstone therapy for longer-duration T2DM and b-cell failure. Glucagon-like peptide-1 receptor agonists are a class of multifactorial T2DM medications that have been shown to improve numerous risk factors for diabetes-related complications, including glycemic control, reduction in body weight and a low risk of hypoglycemia. Improvements in glycemic control confer a reduced risk of long-term diabetes-related complications. We reported here a case that provides the efficacy and safety of once-weekly semaglutide vs once daily GLP-1 RA in obese patient with T2DM inadequately controlled on insulin therapy (Insulin Aspart +OADs). Improvements in glycemic control were greater with once-weekly semaglutide 1 mg than with once-daily liraglutide 1.8 mg, resulting in a longer time to treatment intensification with insulin therapy. Together with lifestyle modifications and physical activity we achieved better glycemic control without severe or blood glucose-confirmed symptomatic hypoglycemia (plasma glucose level below 3.1 mmol/L), HbA1c, FPG, and body weight in patient who is receiving insulin therapy. Also with this therapy we achieved reduction in his lipoprotein metabolism because he could not tolerate any statins. Overall, the case presented here summarized the benefit of once-weekly semaglutide 1.0 mg as an add-on to insulin therapy as the most efficacious GLP-1 RA in terms of further reductions in HbA1c, body weight, BMI in patient with T2DM, insulin therapy and GLP-1RA injections. The reasons for switching to semaglutide from liraglutide included a need to reduce HbA1c or weight further, decreased frequency of administration and cardiovascular protection.  
Keywords: Type 2 diabetes, obesity insulin therapy, GLP 1 RAs, lifestyle modifications

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A weight loss of 20 kg on liraglutide  
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Introduction  
Liraglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist, approved for the treatment of adult patients with type 2 diabetes mellitus of a particular interest in the significant improvement of glycaemic, systolic blood pressure and lipid control with their impact on weight, making it possible to avoid this infernal spiral of weight gain-increased insulin resistance.  
Observation  
55-year-old female patient, known diabetic for 10 years, put on metformin 2 g. Before liraglutide: the patient had grade 2 obesity (Weight = 102 kg, BMI = 37.5 kg/m²). HbA1c = 8.4%. Total cholesterol = 2 g/l, LDL = 1.4 g/l, HDL = 0.36 g/l. After 18 months of liraglutide 1.8 mg/j and metformin 2 g: weight loss of 20 kg (weight = 82 kg, BMI = 29 kg/m²). HbA1c = 6.5%. Total cholesterol = 1.5 g/l, LDL = 0.8 g/l, HDL = 0.42 g/l  
Discussion  
Incretins are digestive tract hormones secreted in response to oral carbohydrate intake. They stimulate the secretion of insulin, inhibit that of glucagon, slow down gastric emptying and increase satiety, thus allowing weight loss. These molecules have pleiotropic effects enriching current therapy, with associated weight loss, allowing better control of diabetes. We report in this case a significant weight loss with an improvement of glycaemic and lipid control without any episode of hypoglycemia.  
Conclusion  
At a time of epidemics of chronic diseases such as obesity associated with type 2 diabetes, recent therapeutic options focusing on several targets are emerging, such as GLP-1 analogues.

References  

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Association between cortisol/DHEA-S ratio and inflammatory indicators in patients with non-functioning adrenal incidentalomas  
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Introduction  
It is well known that DHEA and DHEA-S has and impact on lipid metabolism, cardiovascular system and others. De Castro et al. showed that cortisol/DHEA-S ratio was an independent predictor of long-term mortality in patients with sepsis. Chronic inflammation is an important factor in cardiovascular diseases development that reduce quality and life expectancy. CVDs are more common in patients with adrenal incidentaloma than in general population. Literature data on the cortisol/DHEA-S ratio are contradictory, there are no scientific studies in the group of patients with endocrinopathies, including adrenal incidentalomas.
Aim
The aim of the study was to evaluate inflammation indicators – old one: insulin, CRP and new one: PLR (platelet-lymphocyte ratio), MPVLR (MPV-to-lymphocyte ratio), NLR (neutrophil-lymphocyte ratio), SII (systemic immune-inflammation index) in group of patients with non-functioning adrenal incidentalomas.

Material and methods
The study included 150 patients with non-functioning adrenal incidentalomas hospitalized in Endocrinology City Hospital in Piekary in 2016-2019. The exclusion criteria were mainly: other adrenal disorders (e.g. secreting adrenal adenomas, overactive adrenal cortex), decompenesated diabetes defined as HBA1C%>7, kidney failure as GFR<60 ml/min/1,73 m² liver failure as bilirubin>2 µmol/l, INR>1.5 and albumins<3.5 g/dl, severe inflammation, treated cancer disease. Morphology parameters, cortisol and DHEA-S concentration (taken from the patient’s medical record) were used to calculate inflammatory indicators and cortisol/DHEA-S ratio, CRP and insulin concentration was also taken from medical record.

Results
Most of the respondents (n = 150) were women (72.67%). The median age was 62 years in women, 66 years in men (P=0.00), cortisol concentration at 8 a.m. was 278.62 nmol/l in women, 320 nmol/l in men (P=0.00), DHEA-S was 78.3 µg/dl in women, 102.5 µg/dl in men (P<0.05), CRP was 1.69 in women, 1.5 g/l in men (P>0.05), MPVLR 5.33, in women, 5.32 in men (P=0.00). There was negative correlation observed (r<0.05) between cortisol/DHEA-S ratio and: CRP (r=-0.21), insulin (r=-0.18), There was no significant correlation (P>0.05) demonstrated between analyzed cortisol/DHEA-S ratio and new inflammation indicators: MPVLR, SII, PLR, NLR.

Conclusion
There was an association between cortisol/DHEA-S ratio and old inflammation indicators but not between cortisol/DHEA-S ratio and new ones in studied group of patients with non-functioning adrenal incidentalomas. There is a necessity to enlarge the studied group to confirm obtained results.

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EP512
Omega 6 and 3 intake in depressive patients
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Background
Several studies show a relation between the lack of omega 6 and 3 and the development of depression. On the other hand, there is a modification in the food behaviors in case of depression which can lead to the persistance of symptoms so the intake of omega 6 and 3 should be assessed for every depressive patient.

Methods
50 patients with depression were involved in our study. They were recruited from outpatient department in a psychiatric hospital Razi. The severity of depressive symptoms were assessed by HADS and PHQ9. A food history coupled with the frequency of consumption of foods rich in alpha-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid were carried out in order to assess the typical eating habits of patients. Food quantity was estimated using a photographic manual in order to assess food portions and quantification of intakes. The estimate of the daily intakes of EPA (eicosapentaenoic acid), DHA (docosahexaenoic acid) and alpha-linolenic acid (GA:CH:3) was made manually based on data from the table of food composition (CQUAL, 2016). We compared the intakes of our population compared to the ANC’s of the general adult population.

Results
The mean age of the population is 45 year old. There were 34 women for 16 men. The average BMI was 28.2 Kg/m². The study of consumption shows lipids intake about 36% of total energy intake (TEI). The monounsaturated fatty acid about 15.62% of TEI and poly unsaturated fatty acid 11.62 % of TEI. The intake was unsuficient for 46% of population for linolenic acid, 86% for EPA, 76% for DHA, 38% for omega 3 and 16% for omega 6. According to HAD more is the intake in omega 3 and linoleic acid less are the severity of symptoms (P=0.03 and 0.002) and according to PHQ9 score the depression was more severe if the intake of linoleic acids was low (P=0.04).

Conclusions
The omega 3 and 6 intake are important to assess to improve patient symptoms and ensure faster healing.

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EP513
Nutritional status in patients with heart failure and its relation with cardiac function
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Background
Heart failure (HF) has a rising incidence and is one of the most prevalent diseases worldwide. Serum NT-proBNP and systolic ejection fraction correlate with the severity and prognosis of this condition. The nutritional evaluation of patients with HF, who usually have normal weight, overweight or obesity, has acquired a novel approach due to the incorporation of novel techniques (bioelectrical impedance, nutritional ultrasonography), and functional tests.

Objective
To evaluate the relation between nutritional parameters (bioimpedance, adipose and muscle ultrasound) and clinical outcomes. in patients with HF

Methods
Patients with at least one hospital admission during the previous year were included. Anthropometric, biochemical, ultrasound, cardiac and functional tests were collected. Statistical analysis was performed with SSPS v.24.

Results
Thirty-eight patients (72.2% males; 44.4% with type 2 diabetes) were included; 36.2% presented at least one episode of acute myocardial infarction; mean systolic ejection fraction measured by echocardiogram was 37.35%. During the previous 12 months, 39.5% of patients required more than one admission due to HF, with a mean length of stay in hospital of 5 days. In our cohort, the incidence of overweight/obesity and malnutrition reached 75% and 58.3% respectively. Decreased phase angle (<5.5) was observed in 60% of the patients. Fat and lean mass measured by bioelectrical impedance correlated with systolic ejection fraction (P<0.05). This cardiac biomarker also showed a positive correlation with the adipose tissue measured in rectus femoris nutritional ultrasonography (Spearman’s r <0.384; p<0.05). Serum NT-proBNP levels correlated with body cell mass (BCM) measured by bioelectrical impedance, calf circumference, albumin, prealbumin and LDL cholesterol levels (p<0.05).

Conclusions
Nutritional and cardiac parameters are correlated in patients with HF. Routine nutritional evaluation and early nutrition intervention, if required, should be implemented in order to improve the clinical outcome in these patients. Prospective, interventional studies should be performed.

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EP514
25(OH)D vitamin D status and anthropometric parameters among patients hospitalized in geriatric department
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Introduction
Vitamin D deficiency is observed across all age groups and both sexes. Moreover vitamin D deficiency is common in elderly especially among elderly patients. Elderly people are prone to develop of vitamin D deficiency caused by various factors such as decreased dietary intake, impaired intestinal absorption, reduced sunlight exposure, impaired skin synthesis as well as impaired hydroxylation in the liver and kidneys. Vitamin D deficiency may lead to rickets, osteoporosis,
ostegomalacia and furthermore increase the risk of cardiovascular diseases, type 2 diabetes, mental illness and many others.

**Aim**

We have set out to investigate status of vitamin D among patients over 60 years hospitalized at the geriatric department.

**Material and methods**

The study was carried out with 422 patients. From the study was excluded patients with marked physical and/or mental impairment, liver disorders, decompensated thyroid disorders, cancer, as well as people using medications such as glucocorticosteroids or and using of vitamin D supplement. Finally to the study was included 242 patients (172 females, 70 males). All patients provided consent before included to the study. Venous blood samples were collected after overnight fasting. The serum level of 25-hydroxyvitamin D (ng/ml) was measured by enzyme-linked immunosorbent assay (ELISA). Anthropometric parameters and body impedance analysis were measure on the morning.

**Results**

The mean serum 25(OH) vitamin D concentration among total patients was 14.88 ± 5.95 ng/ml, among women group was 14.41 ± 6.19 ng/ml, among men group was 16.06 ± 5.16 ng/ml. The mean serum 25(OH) vitamin D concentration was higher among patients aged 60-74 years in comparison to patients aged 75 years and over (16.24 ± 6.18 ng/ml vs 14.22 ± 5.73 ng/ml, *P* = 0.0120). Most of elderly patients 79.8% (n = 193) had vitamin D deficiency defined as 25(OH)D ≤ 20.0 ng/ml. Suboptimal vitamin D concentration (≥ 20.0-30.0 ng/ml) was observed in 19.0% (n = 46) study group and adequate of vitamin D concentration (≥ 30.0 ng/ml) was observed in 1.2% (n = 3) patients. The mean value of BMI was 28.15 ± 5.50 kg/m² (men 27.52 ± 4.76 kg/m²; women 28.41 ± 5.77 kg/m²), mean of body fat in % was 33.56 ± 9.59 (man 26.93 ± 7.86; women 36.26 ± 8.93) mean of muscle mass in kg was 43.30 ± 8.25 (man 42.57 ± 6.63; women 39.57 ± 5.45). Vitamin D concentration was 14.84 ± 5.50 ng/ml among obese patients (BMI ≥ 30.0 kg/m²), 15.32 ± 6.00 ng/ml among overweight patients (BMI 25.0-29.0 kg/m²) and 4.00 ± 6.00 ng/ml among patients with normal weight (18.5-24.9 kg/m²), *P* = 0.3480.

**Conclusion**

Vitamin D was observed in geriatric patients irrespective of age, gender and body mass. Proper vitamin D supplementation should be recommended in this group of people.

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**EP515**

Diabetes, a sign of diabetes: A case report

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**Introduction**

Diabetes mellitus is the leading cause of neuropathy worldwide. Non-retinal diabetic complications including oculomotor damage represent 1 to 3% of ocular manifestations of diabetes. The affected oculomotor nerves are essentially the external oculomotor nerve (VI), the common oculomotor nerve (III), and more rarely, the pathetic nerve (IV).

**Observation**

We report the case of a patient referred to our department for additional management of recently discovered diabetes. This is a 44-year-old patient with a history of Buerger’s disease with amputation of both right toes. The clinical examination showed binocular diplopia with left horizontal myastigmus and damage to the external oculomotor nerve VI on the left. As part of the exploration of this diplopia, a CT scanner and an angioscanner were performed. They were normal and showed no signs of an ischemic stroke. A cerebral MRI and a lumbar puncture were strictly normal. On biology, we found a fasting blood sugar at 7 mmol/l and a glycated hemoglobin at 8.9%. The patient started diet and metformin. The evolution was marked by the progressive remission of diplopia after glycemic control after six weeks.

**Conclusions**

Our observation illustrates the interest of screening for diabetes in the face of damage to the oculomotor nerves. The evolution is favorable spontaneously after few weeks, but the recurrence on the same side or on the contralateral side is possible.

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**EP516**

Treatment Induced Neuropathy in Diabetes: Case Report

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**Introduction**

Treatment-induced neuropathy of diabetes (TIND) is a small fibre neuropathy precipitated by rapid correction of chronic hyperglycemia.

**Methods**

We report two patients who developed TIND after rapid improvement of glycaemic control.

**Results**

21-year-old gentleman, underlying type 2 DM diagnosed since 2017. He was not compliant to insulin therapy and defaulted follow up. His Hba1c ranged from 16.6%-19%. In July 2020, he was admitted for diabetic ketoacidosis and dengue fever. He was discharged with basal bolus insulin. Within a month after discharge, he experienced severe lower limb paresthesia. The pain worsened at night and affected his sleep. On examination, he had increased pinprick sensation over bilateral lower limb dermatomes. His Hba1c was reduced markedly to 8.9%. His urine biochemistry revealed proteinuria. He was started on Gabapentin and Vitamin B1, B6 and B12. His insulin dose was reduced. A month later, his neuropathic symptoms had much improved. His subsequent neurological examination revealed reduced pinprick sensation at gloves and stocking distribution. Nerve conduction study (NCS) revealed symmetrical length dependent sensory motor predominantly axonal polyneuropathy, suggestive of diabetic neuropathy. 36-year-old lady, diagnosed with type 2 DM since 2016 and was started on Sitagliptin/Metformin. Nevertheless, she defaulted her follow up and medication. In September 2020, she was admitted for diabetic ketoacidosis with Hba1c > 14%. She was discharged with basal bolus insulin. During follow up, she complained of severe lower limb pain since discharge, with pin and needle sensation, worsened at night. Her neurological examinations were unremarkable. Her biochemistry revealed proteinuria. She was commenced on Gabapentin and Amitriptyline. One month later, her neuropathic symptoms improved markedly. NCS showed symmetrical length dependent sensory motor axonal polyneuropathy, suggestive of diabetic neuropathy.

**Conclusion**

These 2 cases highlight the importance of early detection and timely management of this distressing and potentially debilitating condition. The condition may be prevented by gradual titration of glycaemic control treatment, especially in long standing poorly controlled diabetic patients.

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**EP517**

Trigger finger complicating diabetes: a case report

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**Introduction**

Trigger finger is a stenosing tenosynovitis in which constriction of the tendon sheath is associated with the presence of a nodule on the flexor tendon of the finger. This is an often unrecognised complication in the diabetic patient. We report the case of a diabetic patient with a complication of trigger finger.

**Observation**

A 35 year old female patient, known to be diabetic for 10 years and treated with a basal-bolus insulin therapy regimen. Her evolutionary profile is marked by several episodes of ketoacidosis decompensation. Her diabetes is complicated by chronic renal disease at the stage of proteinuria, and proliferating diabetic retinopathy. The clinical examination found limited mobility in flexion and extension of the fourth finger of the right hand, with a palpable nodule on the flexor tendon of the finger. Biological findings: Hba1c: 9%, renal function and lipid profile were correct. The patient had unbalanced diabetes complicated by microangiopathy and a trigger finger. The therapeutic management is based first on glycemic control and therapeutic education then we proposed corticosteroid injections, with a good evolution.

**Discussion**

Trigger finger is an often unrecognised tenosynovitis in the diabetic patient. It can occur during flexion or extension. The nodule is palpable on the flexor tendon of the affected finger. In diabetes, trigger finger occur in 4-10% of cases, and their occurrence is correlated with the length of time the patient has had diabetes, but not with its control. In a study of young insulin-dependent diabetic patients, this symptom was noted in 5% of patients and no controls.Treatment is based on
Correlation between pulse wave velocity and nephropathy in type 2 diabetes
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Introduction
Nephropathy is a kidney complication that affects up to 50% of people with diabetes during their lifetime. Diabetes is the first cause of kidney failure. The aim of this study was to examine the relationship between diabetic nephropathy (DN) and arterial stiffness.

Methods
We conducted a prospective study including 249 diabetic patients without macroangiopathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cPWV).

Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic nephropathy (DN) was found in 34.5% of the patients. The mean microalbuminuria was 48.58 ± 86.67 mg/g of creatinuria. CIPWV > 10 m/s was found in 90.5% of the patients with DN. And the mean microalbuminuria in patients with CIPWV > 10 m/s was 52.36 ± 90.17 mg/g of creatinuria. In this group, cIPWV was at 14.38 ± 2.70 m/s VS 13.25 ± 2.81 m/s in patients without DN (P=0.002). We did not find a correlation between cIPWV and the stage of the nephropathy. Moreover, the presence of arterial stiffness multiplies by 5 the risk of diabetic nephropathy (Odds Ratio = 5).

Conclusion
This study shows that arterial stiffness is higher in type 2 diabetic patients with diabetic nephropathy than in those without diabetic nephropathy. Indeed, an elevated microalbuminuria is a marker of arterial stiffness in the general population and in the diabetic and hypertensive population. Several studies have investigated the relationship between arterial stiffness in type 2 diabetes, but there is little information regarding the relationship between cIPWV and microalbuminuria.

Material and methods
We examined in total for the period from January 1, 2018 to January 1, 2021 - 90 patients suffering from type 2 diabetes mellitus with chronic renal failure (CRF) on programmed hemodialysis.

Results
We analyzed 90 cases of grade 5 diabetic nephropathy who were on programmed hemodialysis. Of these, women -43, men -47. The obtained results also confirm the literature data that patients with type 2 diabetes mellitus have low quality of life indicators before programmed hemodialysis. According to the degree of chronic brain ischemia (CBI), patients were divided into 3 groups: 1 gr. - 36 (40.0%) patients with diabetic nephropathy (DN) 5 stage with CBI 1 degree; 2 gr. - 32 (35.5%) patients with DN 5 stage with CBI 2 degree; 3 gr. - 22 (24.4%) patients with DN 5 stage with CBI 3 degrees. A reliable difference between the mean values of S100 in the blood in patients 2 and 3 groups compared with the rate indicators was detected. In addition, in 2 and 3 groups of patients revealed direct correlation with the quality of life in 3 questionnaires - WHOQOL-BREF, MMSE test and Hamilton depression scales.

Conclusions
Assessing the quality of life using the WHOQOL-BREF scale, determining the level of anxiety and depression, as well as the MMSE test must act as the criteria for the clinical and functional severity of the state and the effectiveness of the treatment of therapy in patients with CRF in the conditions of therapy with various methods.

Obesity and diabetes mellitus as predictors of adverse course of COVID-19 infection
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According to WHO epidemiological data, there are more than 650 million obese people in the world, the medical and social significance of which is determined by the development and aggravation of insulin resistance. Accumulation of experience in the treatment of patients with COVID-19 infection has demonstrated that obesity and diabetes mellitus are important risk factors affecting the clinical severity of inflammatory disease - for impaired function of β-cells along with a cytokine storm and the release of contrainsulohormones. The aim of the study was to identify phenotypic parameters that affect the prognosis of the course of COVID-19 infection by analyzing data on the features of the manifestation and course of the disease in patients with endocrine and metabolic risks.

Results and discussion
The main group consisted of 15 patients with confirmed COVID-19 infection, a history of type 1 or type 2 diabetes mellitus, or increased fasting glycemia (more than 5.5 mmol/l in capillary blood and 6.1 mmol/l in venous blood) and/or any hyperglycemia (more than 11.1 mmol/l). Comparison group - patients with confirmed COVID-19 infection without dysglycemia. All patients had a severe course of the disease, requiring transfer to the intensive care unit and resuscitation.

Results and discussion
The main group consisted of 7 (47%) men and 8 (53%) women. It was found that in the main group BMI (31.6 (29.0–33.8) vs. 26.0 (24.0–31.0), U = 60, P = 0.045) and the number of days of hospitalization (17, 6 (14.0–21.1) vs. 14.4 (10.0–18.0), U = 67, P = 0.035) is significantly higher than in the control group, which confirms overweight and obesity as risk factor for adverse course of COVID-19. Patients with DM have a low percentage of lymphocytes (18.48 (19.0–27.0) vs. 29.0 (16.2–37%) U = 51, P = 0.042) and a level of leukocytes (4.6 (3.4–7.9) vs. 5.9 (4.9–9.0) * 10^9/l, U = 68, P = 0.035), increased levels of C-reactive protein (62.5 (27.0–120.0) vs. 41.0 (22.5–59.0) mg/l, U = 69, P = 0.045), procalcitonin (0.14 (0.1–0.2) vs. 0.1 (0.08–0.11) ng/ml, U = 65, P = 0.05) and IL-6 (38.4 (19.0–70.0) vs. 15.0 (9.0–39.0) pg/ml, U = 53, P = 0.04) compared with patients without diabetes. In the main group of patients, hyperglycemia was first detected in 61.1% of patients, which may indicate COVID-19 as a significant risk factor for the manifestation of DM.

Conclusions
Patients with diabetes have a worse prognosis for COVID-19 due to a complex of associated conditions that increase the risk.
**EP521**

**India epidemiological mapping study- attempt at early screening - early intervention**

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Background

Hypertension is the most important chronic condition leading to cardiovascular complications in India. Lack of awareness and epidemiological data is the reason for inertia for primordial, primary and secondary prevention. Education, region epidemiological mapping and early screening and intervention can help benefit the population in terms of cardiovascular morbidity and mortality.

Aims & Objectives

To gather, analyze and intervene a large population for early screening, primary and secondary prevention for hypertension.

Patients/Materials & Methods

A team of doctors, nurse, educator and MSW gathered together to understand the prevalence and the incidence of diabetes and Hypertension at rural and sub-urban areas under 9 consultants at different geographical areas of India. Collection of anthropometric data and medical history along with education of the population was done. Further analysis and follow up with Lab parameters was advised to those with newly detected hypertension. They consulted those with pre-existing and uncontrolled hypertension and the therapy was up titrated at the consultant’s discretion. Screened population was from 30 to 88 years of age.

Results

No. of sites: 9 Population screened: 346 Male- 189; Female: 157. Median Age: 46 Newly detected Hypertension: 66 Pre-existing Hypertension: 142 Undetected HTN is more common in females, Rural area and those with T2DM.

Discussion & Conclusion

Hypertension is Far More prevalent than what it seems in Indian Population, the need is to emphasize screening amongst those found at more risk of having undetected hypertension. Also healthcare workers should focus more emphasis on educating those with undetected HTN so that they can get themselves screened early and get treated. As this subset of patient often go undetected and suffer long-term consequences.

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**EP522**

**Gut microbiota genera regarding carbohydrate metabolism status and GLP-1 treatment**

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Introduction and Objective

The composition of human gut microbiota is an emerging field of research and is currently regarded as pathophysiologically linked to obesity. However, we still lack a thorough understanding of what constitutes health and disease in this subject. We present herein a descriptive study of the gut microbiota composition among Spanish morbidly obese subjects, clustered regarding the carbohydrate metabolism status (CHMS) displayed.

Methods

Stool samples were collected from type II-III obese subjects to perform metagenomic analysis of the intestinal bacterial community. This analysis was realized by the Sequencing and Bioinformatics Service of the Foundation for the Promotion of Health and Biomedical Research of Valencia Region, according to their own protocol. To compare the differences in the relative abundance (RA) of taxa between groups, we employed SPSS v22 and performed the Wilcoxon rank sum test.

Results

Stool samples were obtained from 56 obese subjects (64% women) of 48.1(± 9.8) years old and BMI 45.6 (± 6.6) kg/m². 22 subjects presented a normal CHMS, 15 had prediabetes and 19 suffered diabetes mellitus (DM). When comparing the microbiota composition regarding the CHMS, no differences were found in the Shannon nor Chao1 alpha-diversity indexes. At phylum level, no differences were detected either in the RA of Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria nor Verrucomicrobia. At genus level, subjects with a normal CHMS presented higher RA of Faecalibacterium (p = 0.032) and Clostridium (p = 0.026) and lower of Escherichia (p = 0.038), with no differences in Akkermansia. Among DM patients, 15 were treated with a GLP-1 agonist (GLP-1A), compared to the rest of the participants, these subjects displayed higher RA of the phylum Proteobacteria (p = 0.044), higher RA of the genera Parabacteroides (p = 0.034) and Escherichia (p = 0.002), and lower RA of Clostridium (p = 0.007). In the DM subgroup, patients treated with GLP-1A displayed higher RA of Bacteroides spp. (p = 0.027) and lower of Prevotella spp. (p = 0.009) than the rest of diabetic subjects.

Conclusions

In this small study performed in severely obese subjects, significant differences were found in the RA of the genera Faecalibacterium, Clostridium, Escherichia, Bacteroides and Prevotella in regards of the CHMS and the use of GLP-1A.

Further research is needed to ascertain whether a pathophysiological relationship between these phenomena exists.

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**EP523**

**HbA1c evaluation predicting hyperglycaemia and avoiding morbidity in steroid initiation**

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Introduction

Steroids can precipitate significant hyperglycaemia and Diabetes Mellitus in vulnerable populations including DM, pre-DM and the elderly. Steroid risks include deterioration in DM, glucose toxicity, HONK and HHS. This may be avoided by a simple screening HbA1c, which could prompt a ‘safeguard algorithm’ for the patients including instruction in glucose monitoring. The ‘at risk’ cohort is identified, and a surveillance regime is implemented.

Methods

We conducted a pilot study, assessing the prevalence of HbA1c screening pre-steroids commencement. This was a prospective study, identifying all patients (medical, surgical and oncological admissions/inpatients) in the BSH Cork, commencing oral steroids from July 19 – August 1, 2021. We reviewed if any had HbA1c screening within the preceding three months.

Results

Of all inpatients, 49 were commenced on steroids. 8/49 (16%) patients had an HbA1c measurement pre-treatment, ranging from 45-134 mmol/mol.

Discussion

The results highlight low level HbA1c testing pre steroids. 94% of steroid induced hyperglycemia develops within 48 hours of initiation (1), when most patients are still inpatients. 41/49 patients were not tested and are at risk for steroid induced hyperglycaemia. Of those tested, all were in ‘at-risk category’ (HbA1c ≥ 42mmol/mol). This may suggest a limitation in our study, in so far as, all those tested may have been known to be hyperglycaemic and the true screening value may be lower. Nonetheless, a simple HbA1c will identify those ‘at-risk’ for targeted glucose monitoring on steroids, ideally in hospital. This may minimize the risk of readmission and morbidity with HONK/HHS.


**EP524**

**Insulin resistance: in type 1 diabetes**

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Introduction

Insulin resistance is one of the characteristic abnormalities of type 2 diabetes. Recently it has been recognized that type 1 diabetes may also present with insulin
resistance of varying intensity. We report a case of insulin resistance in a patient with type 1 diabetes. Observation The patient was 23 years old, with a history of type 1 diabetes since the age of 20, with positive antibodies against GAD (glutamate acid decarboxylase), revealed by a cardinal syndrome with inaugural ketosis on discovery under high dose insulin: mixtard30 (70IU at 08:00 - 30IU at 12:00 - 64IU at 20:00) and Actrapid: (5IU at 08:00 - 38IU at 12:00 - 34IU at 20:00), no diabetic heredity. The admission examination revealed a stable conscious patient with hyperglycemia between 2.53 and 3.2 g/l, systolic pressure at 132 mmHg, body mass index (BMI) at 22 kg/m² with a waist circumference (WC) of 77 cm. Biology showed normal transaminases: ALT 38IU/L, ASAT 33IU/L, GGT 12IU/L, total cholesterol 1.67 g/l, LDL 1.28 g/l, HDL 0.61 g/l, Triglycerides 1.36 g/l, management consisted of an introduction of oral antidiabetic drugs: metformin 2 g, empagliflozin 10 mg/d, in combination with insulin. The evolution was marked by the improvement of the glycemic figures with reduction of the doses of insulin, currently under: mixtard30: (24UI at 08:00-24UI at 20 h) metformine 2g/d and jardiance 10 mg/d.

Discussion Insulin resistance is mainly related to type 2 diabetes. Recently it has been recognized that type 1 diabetes may also present insulin resistance of variable intensity. The pathophysiology of this insulin resistance is not known. Hypotheses have been put forward, notably a deficit in muscle oxidative phosphorylation. In our case, the high doses of insulin and the chronic imbalance despite the respect of the injections and the dietary rules pushed us to evoke insulin resistance. The improvement of the glycemic figures after the setting on ADO in particular metformin and the recourse to lesser doses of insulin reinforced our diagnosis. Insulin resistance remains rare in type 1 diabetics and the pathophysiological mechanisms have not yet been elucidated, but it should be considered when faced with profiles of type 1 diabetics who remain in chronic imbalance under very high doses of insulin.

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EP526 Does the initial daily insulin dose vary with the amount of glycated hemoglobin Zeineb Zennini, Wissal Ghamgui, Dai Raia, Rihab Yamoun, Amal Salem, Safina Abudita, Imen Hedfi, Chaïma Jamai, Yosra Hitra & Faïka Ben Mani National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Introduction Insulin therapy remains a treatment of last resort for type 2 diabetic patients with uncontrolled diabetes with oral antidiabetic. The aim of this study was to find a correlation between the initial dose of insulin and the glycated hemoglobin (A1c) level.

Methods We conducted a cross sectional study. We included 63 patients with type 2 diabetes hospitalized for a switching to insulin in the C department of diabetology and nutrition at the National Nutrition Institute in Tunis, during 3 months. We correlate the initial daily insulin dose and the A1c level using the Spearman test.

Results The mean age of patients was 58.75 ± 12.4 years, 43% were men and 57% were women. The average duration of diabetes was 9.27 ± 6 years. We found a statistically significant correlation between the initial daily insulin dose and the A1c level (r = 0.66; P = 0.000).

Conclusion Our results showed a positive correlation between A1c level and initial insulin dose, which encourages us to consider insulin treatment in time to avoid the need for high doses and to minimize side effects.

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EP527 Effective treatment of allergy to the insulin excipient meta-cresol with desensitization therapy in type 1 diabetes mellitus: a case report

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Introduction Insulin allergy is a clinical challenge in the management of type 1 diabetes mellitus since there is no other therapeutic alternative. The specific cause of insulin allergy can be related to insulin itself or to additives including zinc, protamine and meta-cresol. The manifestations range from localized reactions to systemic severe anaphylaxis. We here present the case of a generalized allergy to insulin excipient meta-cresol, in a type 1 diabetic patient successfully handled by desensitization therapy.

Case-presentation A 35 years old female with a medical history of seasonal allergic sinusitis and type 1 diabetes mellitus for 4 years on insulin glargine and insulin aspart, presented to our department for the development of generalized urticaria, erythema and pruritus. Symptoms started since diabetes diagnosis, but the intensity and frequency of these reactions increased recently. Symptoms occur 10-30 minutes after insulin injection. Antihistamine treatment improves partially the condition. The allergic reaction persisted with the other types of insulin (regular human insulin, NPH-insulin, detemir, glulisine). Immunological evaluations revealed negative results for specific immunoglobulin E to latex and protamine. Anti-human insulin IgE antibodies (CAP) were inferior to 0.1 kU/l. Skin prick testing revealed a hypersensitivity to all types of insulin stated above. Because the patient had an allergic reaction to all available insulin and meta-cresol was the only excipient common to all tested insulin types, a presumed allergy to the excipient meta-cresol was diagnosed. We started desensitization therapy to glargine following Joselyn Rojas’s protocol using subcutaneous insulin injection with simultaneous intravenous regular insulin infusion associated to premedication with corticosteroid and H1 antagonist. Subsequently, we conducted desensitization to aspart insulin adopting Fusun
Erdelen's protocol. Seen 1 month later, the patient didn’t require antihistamines anymore with tremendous allergic symptoms relief.

Conclusion

Allergy to insulin excipient meta-cresol in a type 1 diabetic is unusual and represents a substantial challenge warranting a stepwise approach to be diagnosed and managed. Specific immunotherapy should be considered as a key treatment option.

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EP528

Should the Fracture Risk Assessment tool be used without Bone Mineral Density in elderly patients having type 2 diabetes mellitus? Malak Belkhiri1, Boubaker Fadia1, Hosoda Ben Salem1, Mouna Brahem2, Houssein Mokrani1, Alaaya Wafa1, Znourtour Baha1, Mohamed Yousse2 & Sfar Mohamed Habib1

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Introduction

Osteoporosis and diabetes are two chronic diseases with increasing prevalences, particularly among elderly. Their coexistence results in socio-economic burdens. Clinical and paraclinical assessment for fracture risk among diabetic elderly patients are necessary to implement in clinical practice. Appropriate tools should be determined and tested.

Objective

To assess comorbidities and fracture risk in elderly patients having type 2 diabetes mellitus (T2DM).

Methods

A cross-sectional study was conducted between December 2020 and January 2021 among 31 patients having type 2 diabetes and aged over 65 years in the department of Endocrinology at the UHC Taher Sfar in Mahdia, Tunisia. Patients with risk factors for secondary osteoporosis weren’t included. Fracture risk of the population study patients was assessed using the FRAX tool.

Results

Our population study included 16 women and 15 men having T2DM. The mean age was calculated at 69.5 ± 4.5 years. The most frequent comorbidities encountered were: overweight (26 patients), dyslipidemia (23 patients), hypertension (20 patients), osteoarthritis (21 patients), and history of (previous fracture(s)) (8 patients). The median of A1c was situated at 9.73%. The median duration of diabetes was of 14.7 years (1–30 years). Twenty seven patients were treated with anti-diabetic agents presenting a potential hypoglycemic risk. Chronic complications of T2DM were found among 28 patients. Bone Mineral Density (BMD) results showed osteopenia in 13 cases (41.9%) and osteoporosis in 3 (9.7%). Without including BMD, the Fracture risk of the population study patients assessed using the FRAX was estimated at 11.09%. Without including BMD, the Fracture risk of the population study patients was assessed using the FRAX tool.

Conclusion

Osteoporosis should probably be considered as a complication of diabetes rather than a comorbidity to encourage clinicians to prevent bone demineralisation and risk of falls leading to fracture specially among elderly patients. Appropriate tools should be used to detect osteopenia, osteoporosis and fracture risk among diabetic patients, since having usually an associated metabolic syndrome. BMD was reported by studies underestimating osteoporosis among T2DM. FRAX tool should probably be used without including BMD to better estimate the risk of fractures the elderly diabetic population. Other collated essays are needed and testing of new appropriate tools seems relevant.

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EP530

Degenerative complications of diabetes during the switch to insulin

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Introduction

Type 2 diabetes is a chronic, silent disease. Patients with diabetes could experience complications during the evolution of their disease. We studied the presence of degenerative complications during the initiation of insulin.

Methods

Cross-sectional study including a group of patients with type 2 diabetes requiring a switch to insulin, hospitalized at the A department of Diabetology and Nutrition in the National Institute of Nutrition of Tunis between July 2021 and December 2021. The data was collected by consulting medical records.

Results

We included 50 patients with type 2 diabetes hospitalized for a switch to insulin, 44% were men, 56% were women, with an average age of 51 years, the average duration of diabetes was 6 years, 10% had diabetes for less than a year. We found that 32% of the patients had diabetic retinopathy, 18% had diabetic nephropathy, 40% had diabetic neuropathy, 10% had a history of stroke, 2% had a history of transient ischemic attack, 20% had a myocardial disease, 4% suffered from chronic obliterator arterial disease of the lower limbs.

Conclusion

In our study degenerative complications were present during the initiation of insulin. This could be explained by the therapeutic inertia in type 2 diabetes. The switch to insulin when indicated is necessary to prevent degenerative complications of diabetes.

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EP531
Type 1 diabetes, metabolic syndrome and cardiovascular risk
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Introduction
Metabolic syndrome (MS) is responsible for the increased cardiovascular risk in type 2 diabetes, but few studies have looked at the metabolic syndrome in type 1 diabetes. The aim of this study is to evaluate the prevalence of microvascular and macrovascular complications and evaluate the cardiovascular risk among patients with T1DM associated with metabolic syndrome.

Materials and Methods
Retrospective study which included 36 type 1 diabetics, hospitalized in the diabetology endocrinology department CHU Hedi Chaker in Sfax, with a metabolic syndrome from 1997 to 2018. MetS was defined according to the NCEP-ATP III criteria.

Results
The average age of our patients was 53 years (extremes: 26-80), a female predominant is noted (21 men vs 15 women) with a sex ratio of H/F 14. Diabetes duration average was 15 years. Metabolic syndrome occurred after an average duration of diabetes of 13.7 years (E: 1-35). HTA was present in 21 patients (58.3%). The mean BMI was 26 kg/m², 19.7% of patients were obese. The average waist circumference was 95.5 cm. an android distribution of fat was present in 3 women. The mean total cholesterol level was 7 mmol/L, that of triglycerides was 3.3 mmol/L. Hypertriglyceridemia was present in 7 cases. The mean HDL cholesterol level was 0.6 g/L. HypoHDLemia was present in 20 patients (55.6%). The mean BMI was 26 kg/m², 19.7% of patients were obese. The average waist circumference was 95.5 cm. The mean total cholesterol level was 7 mmol/L, that of triglycerides was 3.3 mmol/L. Hypertriglyceridemia was present in 17 cases. The mean HDL cholesterol level was 0.6 g/L. HypoHDLemia was present in 20 cases. The DM consisted of 3 criteria in 22 cases, 4 criteria in 11 cases and 5 criteria in 3 cases. In the majority of cases, it was the combination of dyslipidemia, HTA plus diabetes (80%). Therapeutically, the average dose of insulin used was 0.8 IU/kg/day (0.2-1.4). The combination of an insulin sensitizer was required in 3 cases. Hepatic steatosis was present in 8 cases. Microvascular complications were present in all patients with retinopathy (74%) and nephropathy (86%). Macrovascular complications, such as coronary insufficiency, were present in 20% of cases. The Cardiovascular risk is very high in all patients.

Conclusion
The prevalence of metabolic syndrome during type 1 diabetes is increasing. Its presence indicates an increased risk for micro- and macrovascular complications. A comprehensive management including lifestyle modification might reduce their risk of micro and macrovascular complications in adults with T1DM and MetS.

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EP532
A case of idiopathic postprandial syndrome in a middle-aged nigerian woman
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Introduction
Not much has been reported about Idiopathic Postprandial syndrome, especially in Africa. Many cases are often wrongly diagnosed as reactive hypoglycemia. Idiopathic postprandial syndrome refers to signs and symptoms of hypoglycemia in the absence of low blood sugar occurring after meals and is of unknown cause.

Clinical case
We report a case of Idiopathic Postprandial Syndrome in a 44-year old woman living in Nigeria. We present a 44-year-old woman who had been having recurrent hypoglycemic symptoms, which included dizziness, body weakness, lightheadedness, restlessness, headaches, and fatigue after she eats a meal (Post-prandial) for a year. Blood glucose is normal during episodes, and extensive examinations and investigations yielded no other cause.

Discussion
Idiopathic postprandial syndrome (IPS) is a condition in which an individual experiences symptoms of hypoglycemia without having biochemical evidence. The major difference between idiopathic postprandial syndrome (IPS) and hypoglycemia is that IPS may present with only symptoms of low blood sugar without the other components of Whipple’s triad. These symptoms usually occur within a few hours of eating and the exact cause is not known. Managing the possible identified triggers, dietary modification and the use of alpha-glucosidase inhibitors have been seen to improve the condition. Much work still needs to be done to identify the exact etiology of the syndrome.

Keywords: Postprandial syndrome, hypoglycemia, idiopathic postprandial, adrenergic symptoms, Whipple’s triad

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EP533
Effect of a high calorie diet on the ileum histology of Psammomys Obesus
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Obesity is associated with low-grade systemic inflammation, indeed the production of pro-inflammatory cytokines by mesenteric adipose tissue has been implicated in the pathogenesis of inflammatory diseases of the small intestine: duodenum, jejunum and ileum. This is the main site of intestinal inflammation. The objective of this work is to study the effect of a high calorie diet on the histology of the ileum in Psammomys obesus. The animals were captured in the area of Beni Abbès, in the Algerian Sahara. 11 Psammomys obesus were divided into two groups, a control group (n = 5) fed with the halophyte plant containing (0.4 Kcal/g), and the second group (n = 6) subjected to a high calorie diet (3.85kcal/g) for 12 weeks. A part of the ileum was fixed in brown’s solution and was sliced at 3 mm thickness then stained with masson trichrome. Our results show that the high calorie diet induced significant increase on body weight gain compared to control group. Histological analysis shows an increase in muscularis thickness in high calorie diet group compared to the control one. Furthermore in the submucosa we observed the presence of fat cells and lymphoid infiltration in high calorie diet group, we also observed fibrosis in conjunctive tissue. These results show that our animal could be a model of inflammation and nutrient-induced fibrosis of the ileum. We conclude that a high calorie diet induces inflammatory lesions in ileum that may affect enterocarcinoid cells involved in the control of feeding and metabolic pathways related to obesity.

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EP534
Esophagogastroduodenoscopy Findings in a group of morbidly obese patients undergoing bariatric surgery
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Background
Studies of morbid obese patients undergoing bariatric surgery (BS) have revealed that obesity is related with an increased prevalence of endoscopic and histologic gastritis. Performing esophagogastroduodenoscopy (EGD) prior to BS allows the detection and treatment of Helicobacter pylori (H.pylori) infection which is considered to be limiting access to bariatric surgery.

Aim
The aim of this study was to determine the prevalence of gastric lesions and Helicobacter pylori (Hp) infection in a group of morbidly obese patients referred for endoscopy prior to bariatric surgery.

Methods
This is a monocentric prospective descriptive study including 40 morbidly obese patients undergoing EGD before BS. Preoperative data included Age, gender, BMI, comorbidities, upper digestive symptoms, EGD findings and H.pylori infection assessed during a histopathological examination.

Results
EGD was performed in 40 patients. Only 30 patients underwent bariatric surgery:79.3% had sleeve gastrectomy and 21.4% had bypass surgery. The mean age was 39.49 ± 8.41 years, 35(85.7%) were females, with a mean body mass index of 48.39 ± 7.03 kg/m². Of the study population,42.9% had hypertension,
20% had type 2 diabetes, 28.6% had dyslipidemia, 8.6% had hypothyroidism, 65.7% had obstructive sleep apnea syndrome, 14.3% had hypochromic microcytic anemia and 28.6% had vitamin D deficiency. The overall upper digestive symptoms prevalence was 48.5%, with the most frequent being gastroesophageal reflux disease (37.1%), followed by constipation (11.4%). Regarding endoscopic findings, 45.5% presented no endoscopic lesions. Pathological findings were detected in 61.1% of asymptomatic patients. Of the study population, 35.5% presented hyperemic gastropathy, 18.5% erosive gastropathy, 15.6% had hiatus hernia, 21.9% had peptic ulcers and 16.1% had cardiac beanie. No patient had duodenal or gastric ulcer. On histopathological examination, 40.7% presented no lesions, 59.3% (n=24) had chronic antral gastritis and no patient had intestinal metaplasia or dysplasia. H.pylori was present in 20 (50%) patients. All patients with H. pylori infection had chronic gastritis of variable severity. There was no significant association between H.pylori infection and age (P=0.8), gender (P=0.6), BMI (P=0.38), hypochromic microcytic anemia (P=0.1), vitamin D deficiency (P=0.67).

Conclusion
EGD with histological analysis plays an important role in the pre-surgical evaluation in BS, with a high rate of pathological findings in asymptomatic patients.

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EP535
Prevalence of metabolic syndrome in obese children and adolescents
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Introduction
The metabolic syndrome is a major public health problem. Its prevalence is constantly increasing, especially in children and adolescents. Our objective was to determine the prevalence of metabolic syndrome in a population of obese children and adolescents.

Method
This is a descriptive cross-sectional study including 47 children and adolescents recruited at the obesity unit of the National Institute of Nutrition in Tunis. Each patient underwent anthropometric measurements, clinical examination, metabolic and hormonal assessment.

Results
The mean age of the population was 14.04 ± 2.55 years. Females were predominant in 57.4% of cases. The mean body mass index (BMI) was 34.34 [20.27-46.28] kg/m². All patients had abdominal obesity with a mean waist circumference of 111.93 ± 12.47 cm. The mean HOMA index was 9.03 ± 4.97. Type 2 diabetes and hypertension were present in 21% and 8.5% of obese patients respectively. Hypertriglyceridemia was found in 13.3% of cases. Almost two thirds of the patients (64.4%) had hypertension and more than one third had impaired glucose tolerance (40.4%). Hyperuricemia was noted in 18 patients (35.6%). Almost half of our sample (48.9%) had a metabolic syndrome. This syndrome was found in 15 girls (57.7%) and 7 boys (36.8%) but without significant difference (P=0.17). It was positively correlated with age and BMI but not significantly (P=0.26 and P=0.44 respectively). Metabolic syndrome was independent of uricemia (P=0.7). It was positively and significantly correlated with the HOMA index (P=0.015).

Conclusion
The metabolic syndrome was frequent in our population justifying prevention, screening and early and adequate management of obesity, from childhood, in order to decrease the risk of metabolic and cardiovascular complications.

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EP536
The role of hypothalamus mediators in energy imbalance.
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Obesity is considered a chronic metabolic disease that occurs at any age. Regulation of body weight in the body is carried out through complex interaction of a complex of interrelated systems that control the body’s energy system. Energy imbalance is the cause of obesity and overweight, in which the supply of energy from food exceeds the energy needs of the body. Obesity is closely related to impaired appetite regulation, and hypothalamus is a key place of neural regulation of food consumption. The nucleus of the hypothalamus is connected and interdependent on receiving, integrating and sending hunger signals to regulate appetite.

Purpose of The Study
To identify markers of food behaviour.

Materials and Methods
The screening was carried out to identify eating disorders in 200 men and women aged 18 to 35 years with overweight and obesity and to check the effects of Orexin A and Neuropeptide Y markers. A questionnaire and questionnaires were conducted with over 200 people aged 18 to 35 years. Questionnaires were for abnormal eating habits and hidden depression (Zung Anxiety Rating Scale-ZARS). Anthropometry is measured by waist circumference, hip circumference, body mass index, weight, height. Based on the results of the collected data, were divided three groups: People with obesity; People with overweight; Control group of healthy people.

Results
Of the 200 analysed persons, 86% had eating disorders. Of these, 60% of eating disorders were associated with childhood. According to the result ZARS: Normal condition was about 37%, mild depressive disorder 20%, moderate depressive disorder 25% and 18% of people suffered from severe depressive disorder without knowing it. First group of people with obesity had eating disorders, moderate and severe depressive disorder, second group was overweight with mild depressive disorder. According to laboratory data, the first group had the lowest concentration of Orexin A and Neuropeptide Y in blood serum.

Conclusion
Overweight and obesity are the first signal of many diseases. Prevention and detection of these problems will avert various illnesses, including type 2 diabetes. Obesity aetiology is associated with eating disorders which leads to anxiety conditions and signal transmission of the orexinergic system of the hypothalamus.

Keywords: obesity, energy imbalance, hypothalamus, orexin A, neuropeptide Y.

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EP537
Biochemical parameters in laboratory diagnostics of metabolic syndrome
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MS is defined by a combination of abnormalities, such as obesity, arterial hypertension, elevated blood sugar and cholesterol levels, type 2 diabetes mellitus and is not a disease, but represents a group of risk factors that often occur together, increasing the likelihood of severe disease. It is well known that the main reasons for the increase in the incidence of MS is a decrease in physical activity with a high-calorie diet.

The aim of the study
Assessment of biochemical parameters in the pathogenesis of MS.

Materials and methods
70 MS patients and 45 practically healthy volunteers were examined at the clinic of the Research Institute of MPS. The glucose level was determined by the glucose oxidant method, lipid profile assessment, the use of standard test systems. Insulin was determined by enzyme immunoassay using the DRG test system. All study participants signed an informed consent approved by the ethics committee of the Federal Research Center. Statistical data processing was carried out using the application packages ‘Statistica for Windows 8.0’.

Results
The main diagnostic criterion for MS is abdominal obesity, it is important to find out the cause of obesity, which may be associated, for example, with diseases of the endocrine system, in combination with a number of additional symptoms confirmed by tests. It is known that insulin resistance is one of the most important links in the pathogenesis of MS, and the calculated coefficient HOMA-IR was used to assess it. This coefficient is of the greatest diagnostic value and has received wide practical application at the present time. The calculation of HOMA-IR revealed an almost 2-fold increase in this indicator in patients with MS (P<0.05), which is a predictor of the risk of developing vascular and diabetic complications. The level of NEFA in patients with MS was increased in 97% of cases and was almost 2 times higher than the normal values. Also, in patients with...
EP538

Vologda’s Regional Diabetes Center - equal care for everyone

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Vologda is situated in the North-Western region of Russian Federation. It is mostly rural – about 30% of population lives in remote villages. One can compare Vologda’s region with Greece – same amount of land area (approximately 140000 m²), but the population density is 10 times less (8 per km² and 85 per km² respectively). The Vologda region population is approximately 1151000, the amount of Diabetes patients is 42 000 (3.7% of overall population). The territory is divided into 28 subregions with endocrine care available in 5 subregions. That is why there is an issue of equal access to specialized care for people with diabetes. Vologda’s Regional Diabetes Center was established in 2016. Diabetes center is armed with Diabomile on which multidisciplinary team (consisted of Endocrinologist, Cardiologist, Neurologist, Ophthalmologist, Podiatrist and nurse-educator) reaches every part of the region. 50000 consultations were made by multidisciplinary team. During the consultation patients treatment plan, diet and physical activity are revised. Special attention is paid to the detection of Diabetes complications. Center specialists are cooperating with the main Vologda’s, Moscow and Saint Petersburg’s hospitals. The Diabetes registry is maintained by general practitioners and endocrinologists. Before the Center opening the data about Diabetes patients in the region was scarce and inconsistent. Thanks to the multidisciplinary team every bit of data acquired is included into Diabetes registry now, which led to better understanding of prevalence, morbidity and mortality, complications and Diabetes drugs distribution throughout the region. The results of data processing are clearly indicating the improvement of medical quality. There is a great improvement in Diabetes compensation – 15% of patients have 1% reduction in HbA1c level per year. Type 2 Diabetes Mellitus patients’ life expectancy has increased from 72 to 74 years (Vologda region total population average -70.7 years). The percentage of patients treated with insulin is about 23%, the proportion of insulin analogues – 90%. 78% of type 2 Diabetes Mellitus patients have metformin as monotherapy or as a part of combination therapy. Consistent with current guidelines the main emphasis is on life quality improvement and avoiding cardiovascular mortality using SGLT2 inhibitors and GLP-1 agonists.

In the COVID-19 era there is an urgent need for switching to online visits. The most important future direction for Center is partial shift to online consultations. In order to achieve this goal a special application is being developed.

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EP539

High prevalence of pre-diabetes and diabetes in asymptomatic patients attending an endocrine clinic in a tertiary care institute in Colombo.

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Background and Objectives

The prevalence of pre-diabetes and diabetes has risen exponentially in the recent past. Though the symptomatic patients frequently undergo testing for the diagnosis of the disease, asymptomatic individuals are not routinely subjected to diagnostic testing. Thus, data on asymptomatic people are still lacking. We have studied the prevalence of pre-diabetes and diabetes in asymptomatic subjects attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.

Methods

A descriptive cross sectional study was conducted from January to August 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting non diabetic patients aged more than 40 years, attending the clinic for other endocrine diseases. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. Pre-diabetes or diabetes was diagnosed according to the ADA-2020 diagnostic criteria.

Results

The study enrolled hundred and nine patients. The mean age was 53.9 years (range 40-76) and 90.8% were females. The mean weight was 62.1 (SD = 11.3) kg and BMI was 26.6 (SD = 4.6) kg/m². Forty six percent had a family history of first degree relative being affected with type 2 diabetes. All the patients were asymptomatic of classic symptoms of hyperglycemia. Patients were evaluated with fasting blood glucose levels and HbA1c values. Forty nine patients (45%) were diagnosed with diabetes or pre-diabetes with either one or both values being impaired range. Out of 10 patients with type 2 diabetes and 43 patients (39.4%) were diagnosed with pre-diabetes. Out of the patients diagnosed with pre-diabetes and diabetes (n=49), sixty four percent did not had a family history of first degree relative being affected with type 2 diabetes. Out of the pre-diabetes and diabetes patients 32% had their BMI < 25 kg/m².

Conclusions

The prevalence of pre-diabetes and diabetes are much higher than expected in asymptomatic individuals. Hence, the likely patients should be regularly screened to diagnose asymptomatic phase of the disease. This is important as the prevalence has escalated in the immediate past, and diagnosing and treating early will improve long term outcome of the disease. Further large scale studies including community studies are needed to recognize the current prevalence and the rising trend both in urban and rural regions.

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EP540

The Evaluation of the quality of life questionnaire of patients with autoimmune polyglandular type 2 syndrome

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The purpose of the study is to assess the quality of life of patients with autoimmune polyglandular type 2 syndrome using the questionnaire. Material and research methods

Under our observation there were the following 2 groups of patients: 1 gr. - patients with PAI with AIT (primary adrenal insufficiency and autoimmune thyroid) - 25 patients, 2 gr. - PAI with DM 1 (type 1 diabetes mellitus type 1 - 30 patients, as well as 20 healthy persons of the appropriate age and gender. The study used generally crystal and clinical and biochemical methods of research, hormonal blood tests (TSH, free thyroxine, antibodies to TPO, cortisol), immunological studies (antibodies to thyroid gland, to the pancreas, to adrenal glands), and instrumental research methods (ECG, ultrasound of internal organs, thyroid gland, genitl organs, neuropsychological, radiographic - MSCT of adrenal glands, statistical techniques, as well as the quality of life of patients with ADDIQOL. AddoQol consists of 30 questions with the estimate of each question in 6 points. At the same time, the patient must be selected in each question 1 answer: ‘Yes’ or ‘no’. If the patient is gaining more than 15 points with the answer ‘Yes’, then this indicates a low quality of life [1].

Research results

The assessment of the quality of life (QoL) on the AddIQOL questionnaire showed that the middle score of patients of 1 group was 18 ± 0.95, and in healthy - 2.35 ± 0.54 (P <0.05). The average score in patients 2 groups amounted to 19.6 ± 1.06 (P <0.05).

Conclusions

QoL patients in patients with APS 2 type of both groups has significantly lagging behind QoL in healthy faces.

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**EP541**

**Rickettsiosis in diabetics: a Case Report**

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**Introduction**

Rickettsiosis diseases are infectious, re-emerging, polyvalent, potentially fatal diseases that are widespread worldwide. These diseases are caused by strict intracellular bacteria with a Gram-negative stain associated with arthropods, mainly ticks, but also lice, fleas and other mites. In diabetics, adequate and early management is essential given the risk of developing malignant Mediterranean spotted fever.

**Observation**

We report the case of a 69-year-old patient, known to be type 2 diabetic for 13 years, well balanced on 1 g/d of metformin (HBA1C at 6.9%) and who consulted for a fever associated with a generalized rash evolving since 1 week with intense myalgia and asthenia. Clinical examination revealed a maculopapular rash and a pressure ulcer spot. Laboratory workup demonstrated thrombocytopenia, lymphopenia, inflammatory syndrome with elevated CRP, hepatic cytolysis and glycemic imbalance. The treatment consisted of antibiotic therapy and insulin therapy with good clinical and biological progress.

**Discussion and conclusion**

The diabetic subject can present a polymorphic clinical picture of rickettsioses associating an infectious syndrome which is sometimes severe, a skin rash and a disturbance of the biological assessment with thrombocytopenia and hepatic cytolysis as the case of our patient. This observation underscores the value of early and adequate management in diabetics in order to avoid multisystem involvement that can be life-threatening.

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**EP542**

**Leo-Burger’s disease: a rare cause of gangrene in diabetics**

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**Introduction**

Leo Burger’s thromboangiitis obliterans ‘TALB’ is a rare inflammatory, segmental and occlusive disease affecting small and medium-sized arteries and the veins of the extremities of the limbs. It is more common in males and its major aggravating factor is smoking.

**Observation**

We present the case of a 66-year-old patient with a history of chronic smoking at a rate of 25 packs per year, known type 2 diabetic for 10 years, well balanced under hygienic-dietetic measures alone (HBA1C = 6.5 %) without degenerative complications and who consults for necrosis of the right big toe associated with plantar clasification and right plantar erythema. Clinical examination revealed acute right distal ischemia of the right lower limb with ablation of the distal pulses on the right and gangrene in the right big toe. The inflammatory, lipid and hemostasis assessment as well as the immunological assessment and viral serologies (HIV, HCV, and HBV) are negative. Vascular imaging shows an occlusion of the right superior popliteal artery. The patient underwent a femoropopliteal bypass with strict discharge and local care combining cleanings and excision of necrotic tissue. Amputation of the right big toe is indicated. Psychological and medical support is in place to obtain smoking cessation.

**Discussion and conclusion**

The diagnosis of TALB is a diagnosis of elimination evoked in the absence of specific markers and identified etiological factors and which must be considered in the well-balanced diabetic patient with chronic smoking hence the interest of a careful discharge and local care combining cleanings and excision of necrotic tissue. Amputation of the right big toe is indicated. Psychological and medical support is in place to obtain smoking cessation.

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**EP543**

**Type 1 diabetes in autoimmune polyendocrinopathy**

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**Introduction**

Type 1 diabetes is accompanied by a high frequency of autoimmune diseases. The aim of this study is to determine the different epidemiological, clinical, immunological and therapeutic aspects of Type 1 Diabetes in Autoimmune Polyendocrinopathy and to analyze the results obtained.

**Patients and methods**

This is a retrospective study of 44 patients with type 1 diabetes, suffering from Autoimmune Polyendocrinopathy and followed in the Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition the CHU Mohammed VI or in the consultation dedicated to type 1 diabetes.

**Results**

A total of 44 patients were included in the study. Of these patients, 32 females and 12 males. The average age at the discovery of type 1 diabetes was 12.77 ± 6.26 years. Only one patient had type 1 APS associating chronic mucocutaneous candidiasis, hypoparathyroidism, adrenal insufficiency, exocrine pancreatic insufficiency and type 1 diabetes. A APS type II was found in 14 patients, 2 of whom had Schmidt syndrome. 17 patients had APS type 3: 15 patients had Hashimoto’s disease and type 1 diabetes, 1 patient had Hashimoto’s disease, celiac disease and type 1 diabetes, only one patient had Graves-Basedow disease associated with diabetes type 1, 12 patients had a APS type 4 associating type 1 diabetes and celiac disease. Therapeutic management is based on replacement therapy, synthetic antithyroid drugs, gluten-free diet with education and monitoring of patients and their family members.

**Discussion**

APS-1, or APECED syndrome, is the rarest of the autoimmune polyendocrinopathy. The discovery of the syndrome dates back to 1929, when Torpe and Handley described the association of hypoparathyroidism and chronic candidiasis. Type 2 autoimmune polyendocrinopathy is the most frequent: it mainly affects the adrenal cortex, the endocrine pancreas, the thyroid, the ovary, the anterior pituitary, possibly associated with digestive disorders (Biermer’s disease, celiac disease), cutaneous (vitiligo, alopecia areata), rheumatological (rheumatoid arthritis). PAI 3 is a rare disease defined by the association of autoimmune dysthyroidism with type 1 diabetes, celiac disease, vitiligo or other autoimmune disease, in the absence of adenocortical involvement and hypoparathyroidism according to the Neufeld classification. Autoimmune polyendocrinopathy type 4 is a diagnosis of elimination, which associates at least two of the organ-specific autoimmune endocrine syndromes that cannot be attributed to APS2 or APS 3 .

**Conclusion**

In any patient with autoimmune disease, regular follow-up is indicated in order to detect the outbreak of possible Autoimmune Polyendocrinopathy Syndrome.

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**EP544**

**Hospitalization in a diabetes unit**

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**Introduction**

Diabetes is a chronic disease. Its management may require frequent hospitalization. The aim of our study was to determine hospitalization reasons in the diabetic department of The National Institute of Nutrition of Tunis. Method It was a prospective study conducted in the department of diabetology in the National Institute of Nutrition in Tunis for three months. The study was carried out on the medical records of hospitalized patients. Results We included 90 patients with diabetes with a sex ratio (M/F) of 0.7 and a mean age of 51.7 ± 17.7 years. The majority were type 2 diabetics (72%). The mean age of diabetes was 12,7 ± 8.8 years [0;34]. Smoking concerned 11% of patients. A history of hospitalization in the department was found in 36% of the cases. Chronic diabetic imbalance was the most frequent reason of hospitalization (72%): the initiation of insulin therapy was necessary in 35% of the cases. Emergency hospitalization was indicated in 22% of patients with diabetes and it was correlated significantly with type 1 diabetes (P=0.004) among whom 11% were hospitalized for diabetic ketois and 11% for severe hypoglycemia. Among hospitalized women with diabetes, 6% were pregnant. The average length of hospital stay was 5.2 ± 2.4 days [2;15]. Hypertension, dyslipidemia, dysthyroid, obesity and coronary artery
**EP545**

**Pegylated Interferon induced Latent Autoimmune Diabetes Mellitus of Adults (LADA) in acute setting is not uncommon**

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**Introduction**

Type 1 diabetes Mellitus/latent Autoimmune Diabetes of Adults (LADA). It’s recommended that pre-treatment HbA1c levels, number of anti-GAD antibody, and anti-nuclear antibodies are tested. This case highlights causal relationship between Pegylated interferon-alpha and Type 1 diabetes mellitus. Pegylated interferon-alpha therapy may be associated with onset of Diabetes mellitus, which can be acute, slow or fulminant.

**Case Report**

A 50-year-old male presented with a 3-week history of polyuria, polydipsia and weight loss. Following review by his General Practitioner he was found to have an elevated serum glucose (55.4 mmol/l). Inpatient treatment with intravenous fluids was given alongside initiation of Metformin and Gliclazide. Further investigations revealed HbA1c 170 mmol/l and positive Anti-GAD antibody titer, confirming a diagnosis of LADA, therefore, Insulin detemir was commenced and Gliclazide was stopped. He has polycythemia Vera being treated with peginterferon alfa-2a 135 mg fortnightly, and a history of ischemic heart disease, stroke and an implantable cardioverter-defibrillator. He was taking peginterferon alpha-2a for 4 years prior to diagnosis of LADA.

**Discussion**

Polycythaemia Vera is a myeloproliferative disorder with Pegylated interferon-alpha as possible treatment option. Pegylated interferon-alpha therapy may be associated with onset of Diabetes mellitus, which can be acute, slow or fulminant. In our case, LADA presented 4 years after initiation of treatment. The pathogenesis of pegylated induced autoimmune diabetes is unclear. It has been proposed that pegylated interferon may shift the Th1/Th2 balance to a Th1-predominant state, resulting in an induction of Th1-type cytokines which leads to an accelerated destruction of β-cells within the pancreas as demonstrated by Murine models. Additional studies have reported high levels of anti-GAD antibodies in patients a few months after initiation of pegylated interferon treatment.

**Conclusion**

This case highlights causal relationship between Pegylated interferon-alpha and Type 1 autoimmune diabetes/LADA. It’s recommended that pre-treatment HbA1c is measured alongside regular serum glucose and GAD antibodies during course of treatment with Pegylated Interferon-alpha to ensure timely diagnosis and management of diabetes.

**EP547**

**Familial hypercholesterolemia: a case report**

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**Introduction**

Familial hypercholesterolemia is an autosomal dominant genetic disease linked to a mutation in 3 genes involved in the catabolism of LDL particles. It is characterized by an exclusive increase in low-density lipoproteins (LDL). It is associated with a high risk of premature cardiovascular complications. We report the case of a patient with familial hypercholesterolemia.

**Case**

44-year-old patient, From a first-degree consanguineous marriage, with a history of: hypertension under treatment, deaths at an early age as well as hypercholesterolemia in the family. Her history of the disease dates back to the age of 7 years with the appearance of cutaneous xanthomas and xanthelasma. The diagnosis of hypercholesterolemia was retained following family screening at the age of 33 years, treated with Rosuvastatin 40 mg. The evolution was marked by the development of severe coronary artery disease requiring double coronary bypass surgery. Clinical examination found tendon and skin xanthomas and xanthelasma. The biological work-up showed LDL-C: 5.41 g/l, HDL-C: 0.34 g/l, triglycerides (Tg): 0.88 g, total cholesterol (TC): 5.93 g/l, Lipoprotein electrophoresis (LPE) found: clear appearance, LDL: 83.3%, HDL: 12.5%, VLDL: 4.2%, ApoB measuring: 3.14 g/l. The diagnosis of familial hypercholesterolemia was retained.

**Observation**

We report the case of Miss A.M., 24 years old, admitted for exploration of hyperandrogenism. Anamnesis: the patient reported polyuropolydipsic syndrome and the notion of weight gain without eating disorder and a total of 25 kg in 6 months. This period is also marked by the onset of amenorrhea, increased body and facial hair, increased pigmentation of skin, increased sweating and alopecia. Upon presentation to the Endocrine clinic, examination of the patient revealed:

- Severe hirsutism scored at 34 according to the Ferriman and Galloway score, associated with acne and seborrhea
- Obese without male musculature
- Acanthosis nigricans was positive at the flexor surfaces, neck, axillae, cubital fossae the base of the neck.
- Buffalo hump

Investigations showed:

- Follicle stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) are within normal limits. She had normal estradiol level, and testosterone level of 0.5 mg/l, 4 androsten-dione and 17 OHP within the standards. Low-dose dexamethasone suppression test returned to negative at 0.35 mg/dl, 2 normal 24-hour urinary free cortisol (UFC), UFC the first at 31.85 mg/24 h, the second at 42 mg/24 h and salivary cortisol was normal level of 0.6 ng/ml. Ultrasound of the pelvis revealed that the left ovary measured 18.8 cm3 with several anechoic cystic formations, number > 10 of infracentimetric size. The right ovary measured 13.7 cm3 in volume, seat of several anechoic cystic formations number > 10 of infracentimetric size concluding to an aspect in favor of a bilateral ovarian dystrophy. The metabolic impact assessment showed hypertriglyceridemia level of 2.02 g/l and diabetes with an HBA1c 6.8%. From a therapeutic, the patient was started hygiene and dietary measures with metformin for her blood sugar, and to help in enhancing the peripheral insulin action., cyproterone acetate associated with ethinyl estradiol.

**Discussion**

The HAIR-AN syndrome is one of the most underdiagnosed clinical entities in endocrinology. The reason for this is that women with hyperandrogenism are not usually screened for insulin resistance and acanthosis nigricans. It probably accounts for 1%-3% of women with hyperandrogenism. Barbieri and Ryan have described the salient features of this syndrome.

**Conclusion**

The HAIR-AN syndrome can cause profound psychological distress manifested by morbidity, depression and a sense of worthlessness which may require long-term psychological support.
hypercholesterolemia in the patient was retained: in view of the family history of the first-degree relative with early coronary disease, the personal history of early coronary disease, the presence of tendinous xanthomas, and the LDL-C level above 3.3 g/l according to the Dutch Lipid Clinic Network Score. The workup showed multiple bilateral atherosclerotic plaques in the carotid arteries and in the arteries of the lower limbs. The management of the patient consisted of a reinforcement of hygienic and dietary measures, with a combination of Rosuvastatin 40 mg per day, Ezetimib 10 mg per day and IPCSK9. The genetic study is essential but not available in Morocco, a cascade screening is proposed in her family.

Discussion & Conclusion

Familial hypercholesterolemia is often underdiagnosed and undertreated. The diagnosis is made according to the Dutch Lipid Clinic Score, which takes into account LDL c levels, personal and/or family history of cardiovascular disease and clinical signs of dyslipidemia. Early diagnosis is important to treat the disease as early as possible and prevent cardiovascular complications.

Acknowledgement

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Table 1

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
<th>p value</th>
<th>Mean change</th>
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<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>8.3</td>
<td>2.2</td>
<td>7.3 to 9.2</td>
<td>0.081 ns</td>
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<tr>
<td>Follow up</td>
<td>7.8</td>
<td>2.3</td>
<td>7.0 to 9.0</td>
<td>0.05 ns</td>
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<td>LDL (mg/dl)</td>
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<tr>
<td>Baseline</td>
<td>134.8</td>
<td>39.3</td>
<td>101.0 to 178.9</td>
<td>0.01 ns</td>
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<tr>
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<td>128.2</td>
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<td>104.0 to 152.4</td>
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<tr>
<td>Baseline</td>
<td>1.19</td>
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<td>1.08 to 1.30</td>
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<tr>
<td>Follow up</td>
<td>1.27</td>
<td>0.13</td>
<td>1.11 to 1.43</td>
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<td>0.12</td>
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<td>0.91 to 1.13</td>
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<tr>
<td>Baseline</td>
<td>1.09</td>
<td>0.25</td>
<td>0.91 to 1.27</td>
<td>0.08 ns</td>
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<td>0.64</td>
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<td>Baseline</td>
<td>9.52</td>
<td>5.72</td>
<td>7.1 to 12.0</td>
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<td>5.25</td>
<td>5.8 to 10.7</td>
<td>0.06 ns</td>
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</table>

Introduction

We explored utility of ankle-brachial index (ABI), toe brachial index (TBI), Albumin Creatinine Ratio (ACR), Low Density Lipoprotein Cholesterol (LDL-C) in context with change in HbA1c

Methods

We conducted an observational study in 25 T2DM on standard care in real world setting

Results

The mean follow up (months) was 19.2 (±6, range 12). The mean age (years) was 57 (±12, 95% CI 52 to 63). Initially 36% (9/25) had HbA1c < 7% which increased by 16% with an addition of four patients with HbA1c < 7%, 52% (13/25). Additional four patients achieved LDL-C < 100 mg/dl, 72% (18/25) increase to 88% (22/25). Initially, TBI Left was within range (0.5-0.75) in 80% of patients (2/25) which increased to 16% (4/25). ACR was unchanged with < 30 in 80% of patients (20/25). There was a decrease in the number of patients with target range of ABI- right and left from 80% (20/25) to 68% (17/25) and 72% (18/25) to 68% (17/25) patients, respectively. There was no significant correlation between the change in HbA1c and change in LDL (r = -0.14, 95% CI -0.51 to 0.26, P = 0.47 ns), ABI- right (r = -0.18, 95% CI -0.54 to 0.22, P = 0.36 ns), ABI- left (r = 0.25, 95% CI 0.13 to 0.59, P = 0.21 ns), TBI- right (r = -0.14, 95% CI -0.15 to 0.26, P = 0.48 ns), TBI- left (r = -0.32, 95% CI -0.63 to 0.08, P = 0.11 ns), ACR (r = 0.06, 95% CI -0.34 to 0.44, P = 0.77 ns). Table: Change in markers

Conclusion

The change in HbA1c was independent of the change in the markers of peripheral arterial disease and nephropathy. The results need corroborate with larger studies.

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**EP551**

**Dopplerography and neurormarker BDNF indicators correlation in patients with diabetic neuropathy at the later complications stage**

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The purpose of the study is to study the correlation bond indicators of ultrasonic doppler and neurormarker BDNF in blood in patients with diabetes mellitus type 2 (DM 2) with diabetic neuropathy at the later complications stage

Material and methods

A study was conducted 215 patients with DM 2, of which 160 persons suffering from diabetic neuropathy (DNP) in the late complications stage. The following groups of patients were formed: 1 gr. - patients with DM2 type without DNP - 55 patients, 2 gr. - Patients of the DNP in the stage of late complications - 160 patients. In the study, the patients were subjected to clinical and biochemical methods of the study (Glycemia, HBA1C, Alt, Ast, Bilirubin, Urea, Creatine, BDNF, etc.), as well as instrumental examination methods - ECG, Electro-neuromyography, Doppler Vessels of the lower extremities, etc.

Research results

Revealed significant correlations of BDNF levels and a number of laboratory and instrumental indicators. A correlation bond with a level of HBA1C and doppler indicators in both groups of patients was detected. In this case, the connection with the glycemia on an empty stomach was unreliable. All the above data indicate the need for timely adequate conservative therapy of chronic wound defects of the lower limbs in patients with DM 2, developing the prevention measures for their recurrence and organizing long-term observation of patients with high risk of development of this complication of diabetes.

Conclusions

The correlation relationship with a level of glycated hemoglobin, blood flow rate in the femoral artery, in the leg, the pulsation index in the tibial artery and the index of resistance in the femoral artery

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**EP552**

**‘The Echocardiography data of patients with type 2 diabetes mellitus complicated by cardio-renal syndrome’**

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The purpose of the study is to study the Echocardiography dataof patients with type 2 diabetes mellitus complicated by 4 type cardio-renal syndrome

Material and methods

We examined in total for the period from October 1, 2021 to December 1, 2021 - 25 patients suffering from type 2 diabetes mellitus with chronic renal disease (CRD) and chronic cardiac insufficiency (CCR). The research methods included: 1) general clinical (study of endocrine, neurological status, anthropometry) 2) instrumental (ECG, roentgen of thorax, ultrasound of internal organs 3) biochemical tests (Hb1AC, glycemic profile, urea, creatinine, lipid spectrum, coagulogram),4) hormonal blood tests (insulin, C-peptide etc.)

Results

We analyzed 25 patients with type 2 diabetes mellitus complicated by chronic renal disease III and chronic heart insufficiency (CHI). Of these, women -13, men -12. Biochemical blood tests have shown that urea and creatinine were reliably elevated in all patients. The Echocardiography investigation showed dysfunction of left ventricle and cardiomyopathy. According to the classification of cardio-renal syndrome, we distributed patients to 2 groups: 1 group – 15 patients with 2 type of cardio-renal syndrome. 2 group with 4 type of cardio-renal syndrome.

Conclusions

In the diagnosis of cardio-renal syndrome, the assessment of the indicators of central hemodynamics plays an important role. Patients with type 2 diabetes mellitus complicated by cardio-renal syndrome have dysfunction of left ventricle and cardiomyopathy

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**EP553**

**‘The results of the Echo-cardiographic investigations in patients with diabetic foot syndrome and chronic heart failure’**

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The purpose of the study is to study the echo-cardiographic disorders in patients with diabetic foot syndrome (DFS) and chronic heart failure (CHF)

Material and methods

The study was conducted in 62 patients with SDS treated in the department of surgical diseases and civil defense of the Andijan State Medical Institute in 2019 - 2021. The following groups of patients were formed: 1 gr - patients with DM 2 Type and the neuroichemic form of DFS and HSN-31 patients, 2 groups - patients with diabetes mellitus type 2 (DM 2 Type) and neuroichemic DFS form without CHF -31 patients, 3 gr. - A group of control, 20 healthy persons of the appropriate age and gender. All 50 patients were exposed to surgical treatment. In a study, patients were subjected to clinical and biochemical methods of research, functional tests, as well as instrumental methods of examination, doppler vascular vascular methods, bacteriological analysis of separated from the wound, as well as statistical techniques.

Results

In the 1st group of patients, the average value of the fraction of the left ventricle emissions (LVE) were in the range of 41.5 ± 2.2 compared with the 2nd group of 56.3 ± 3% (P<0.001). The indexed finite-systolic volume of LV was reduced only in patients 1 of the group (43 ± 8 ml/m against 57 ± 9 in 2 groups; P<0.05). The value of the anterograde shock volume was also reliably below in 1 group of patients (39 ± 9 vs 49 ± 11 ml in 2 group: P<0.05). Cardiac output and the heart rate were also reliably reduced in 1 group (4.4 ± 0.5 vs 5.7 ± 0.6 l/min; P<0.05 and 1.23 ± 0.26 vs 1.72 ± 0.29 l/m 2; P<0.005, respectively).

Conclusions

In patients with diabetic foot syndrome and chronic heart failure reliable decrease in echo-cardiographic indicators was revealed.

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**EP554**

**‘The Hemodynamic indicators in patients with diabetic foot syndrome and chronic heart failure’**

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The purpose of the study is to study the Hemodynamic indicators in patients with diabetic foot syndrome (DFS) and chronic heart failure (CHF)

Material and methods

The study was conducted in 62 patients with SDS treated in the department of surgical diseases and civil defense of the Andijan State Medical Institute in 2019 - 2021. The following groups of patients were formed: 1 gr - patients with DM 2 Type and the neuroichemic form of DFS and HSN-31 patients, 2 groups - patients with diabetes mellitus type 2 (DM 2 Type) and neuroichemic DFS form without CHF -31 patients, 3 gr. - A group of control, 20 healthy persons of the appropriate age and gender. All 50 patients were exposed to surgical treatment. In a study, patients were subjected to clinical and biochemical methods of research, functional tests, as well as instrumental methods of examination, doppler vascular vascular methods, bacteriological analysis of separated from the wound, as well as statistical techniques.

Results

In the 1st group of patients, the average central systolic pressure was significantly higher (168/90 ± 7.2 mm hg. in comparison with the 2nd group of 126.3 ± 3.6; (P<0.001). Peripheral blood pressure was increased only in patients 1 groups (162/99 ± 4.2 mm hg. against 118/66 ± 3.6 mm hg in group 2; P<0.05). The value of the daily blood pressure was also reliably higher in 1 group of patients (171/98 ± 4.3 vs 129/82 ± 11.2 mm. In 2 groups; P<0.05).
Conclusions
In patients with the syndrome of the diabetic foot of the neuro-ischemic form with chronic heart failure, reliable deterioration of hemodynamic indicators was revealed.

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EP555

‘Biochemical indicators in patients with type 2 diabetes mellitus in hemodialysis’

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The purpose of the study is to study biochemical indicators in patients with type 2 diabetes in hemodialysis

Material and methods
The study was carried out in 30 patients with type 2 diabetes mellitus (DM 2) treated in the Diabetic Nephropathy Department 2019 - 2021. Healthy volunteers (n = 20) amounted to a control group. The paper included general-clinical, clinical and biochemical, hormonal, immunological methods of blood testing, as well as instrumental methods of investigation – ultrasound of internal organs, ECG, ECHO-ECG, indicators of the quality of life of patients (questionnaire), as well as statistical techniques.

Results
We analyzed 30 patients with type 2 diabetes mellitus, complicated by chronic kidney disease CKD V degree and receiving hemodialysis. Of these, women -12, men -18. The average age of patients amounted to 56.3/675 years, respectively, among men and women. Biochemical blood tests have shown that urea and creatinin were reliably increased in all patients of the group, while in the control group they were within the normal range (P<0.05). The average pulmonary filtration rate in these patients was less than 20 ml/min/1.73 m², which indicated the need for substantive renal therapy.

Conclusions
In patients with DM 2 associated with the CKD, the average temperature of the glomerular filtration rate in these patients was less than 20 ml/min/1.73 m², which indicated the need for substitution renal therapy.

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EP556

‘The renal dysfunction indicators of the patients with severe complications of diabetic foot syndrome (ulcer, gangrene, amputation) and chronic kidney disease’

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Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, of Diabetic Foot Syndrome, Tashkent, Uzbekistan

The purpose of the study is to study the results of the biochemical investigation of the patients with diabetic foot syndrome and chronic kidney disease (CKD).

Material and research methods
A study was conducted 60 patients with diabetes mellitus type 2 (DM 2) with diabetic foot syndrome (DFS) in the late complications stage associated with chronic kidney disease. All observed patients will be divided into 3 groups:

1 gr. - 20 patients with DFS, complicated by ulcers, gangrene and amputation in combination with CKD 4-5 stages without hemodialysis
2 gr. - 20 patients with DFS, complicated by ulcers, gangrene and amputation in combination with CKD 4-5 stages without hemodialysis
3 gr. - 20 patients with DFS, complicated by gangrene and amputation, without CKD.

A group of control will be 20 healthy faces. The investigation methods included biochemical (bilirubin, lipid spectrum, ALT, AST, blood sugar, HbA1C, urea, creatinine, etc) and instrumental (ECG, MRI of feet, Dopplerography of the legs vessels, ultrasound of the internal organs, etc)

Results
Patients with 1 and 2 groups have revealed a reliable increase in urea levels and creatinine in the blood. The average of the blood urea in group 1 reached 15.6 mmol/l, in the second 26.5 mmol/l, in group 3 - 3.4 mmol/l (normally 2.1 - 8, 2 mmol/l). The average blood creatinine values were 167, 82 mmol/l in group 1, 186, 7 mmol/l in 2 groups and 35.6 mmol/l in 3 groups in men (normally 77-127 in men and 44-96 mmol/l in women). The average value of creatinine in women group reached 101, 4 mcmol/l, in group 2 - 126.7 mcmol/l and in group 3 - 49 mcmol/l. The value of the HbA1C achieved in groups of values 9, 2%, 10, 4% and 10, 6%, respectively.

Conclusions
In patients with diabetic foot syndrome and CKD IV-V st. without hemodialysis, reliably worse indicators were revealed in comparison with patients with DFS and CKD IV-V st without hemodialysis and patients with DFS without CKD.

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EP558
Characteristics of dyslipidemia in a group of patients with diabetes
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1Tunisian Institute of Nutrition, The Day Hospital Department, Tunis, Tunisia

Objective
Dyslipidemia represents an added factor of cardiovascular risk for patients with diabetes. The objective of this work was to study the characteristics of dyslipidemia in a group of patients with diabetes.

Methods
Cross-sectional study including a group of patients with diabetes associated with dyslipidemia, during a period of 6 months, admitted in the day hospital unit of the National Institute of Nutrition of Tunis. The data was collected by consulting medical records.

Results
We included 58 patients with an average age of 57 ± 11 years and a female predominance (69%). The average duration of diabetes was 14 ± 7 years. Patients were on insulin therapy in 84% of cases. Mean glycated hemoglobin (HbA1c) was 9.4 ± 1%. Arterial hypertension, dysthyroidism, coronary artery disease and renal failure were found in 62%, 13%, 14% and 4% of cases respectively. Pure hypercholesterolemia was noted in 58% of patients while 42% had mixed dyslipidemia. Mean cholesterol level was 4.6 ± 1 mmol/l, mean triglyceridemia was 1.5 ± 0.6 mmol/l. The average HDL-cholesterol level was 1 ± 0.2 mmol/l. Mean LDL-cholesterol was 1.1 ± 0.3 mmol/l.

Conclusion
Lipid abnormalities are frequent in diabetes, hence the importance of systematic screening and adequate therapeutic management in order to improve cardiovascular prognosis.

DOI: 10.1530/endoabs.81.EP558

EP559
Treatment adherence in Type 2 Diabetes: Experimental study research project
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Summaries
Treatment adherence in Type 2 Diabetes: Experimental study research project
Diabetes is a metabolic disease brought about by high levels of glucose in the blood over a long period of time. It’s a disease which shows an increasing incidence, mainly in developed countries. When untreated, diabetes can cause several acute complications, such as ketonuria, hyperglycemic hyperosmolar state or even death. Prevention and treatment consist in maintaining adequate eating habits, doing physical activity regularly and keeping a normal weight. The development of type 2 diabetes prevention projects in the community is regarded as a significant opportunity of promoting health, whereby health professionals play a vital role in its implementation. This project is integrated in “Doctoral Program in Metabolism – Clinic and Experimental” and its aim is to evaluate the efficiency of a Therapeutical Education Program in the treatment adherence in Type 2 diabetes carriers. An experimental, quantitative study is going to be conducted among individuals with Type 2 diabetes, who are being followed by health professionals at a university hospital located in Porto, Portugal. The population will be submitted to randomization and separated into experimental and control groups. Randomization will be done through random number selection per site. The evaluation of results will be carried out by responding to a questionnaire entitled “Treatment adherence in diabetes”, both prior and posterior to the implementation of the program. It is expected that the results garnered from the questionnaire will prove that the adoption of Therapeutical Education Programs by the population will improve the rates of treatment adherence in diabetes.

DOI: 10.1530/endoabs.81.EP559

EP560
Long-term-high-fat/high-carbohydrate-diet-induced subcutaneous adipose tissue inflammation in gerbil model (Gerbillus tarabuli)
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Obesity results from an imbalance between energy intake and expenditure. The WHO has considered it as a chronic disease which is associated with many complications, such as insulin resistance, metabolic syndrome, etc. It is defined as an abnormal or excessive accumulation of body fat that can harm health. The distribution of this fat (visceral and subcutaneous), the size of the adipocytes and the inflammatory state of the adipose tissue are of great importance in the progression of this disease. The objective of this work is to study the effect of a long-term high-fat/high-carbohydrate diet (HFHC) on the subcutaneous adipose tissue histology of the gerbil. Gerbillus tarabuli, nocturnal desert rodents, is native to North Africa (south western Algeria). Our study involved 12 animal divided into 2 groups. Control group: gerbils received a natural diet (carrots and lettuce) and HFHC group: experimental animals were fed a high-fat/high-carbohydrate diet (barley, dried date and butter). After 20 weeks, gerbils were decapitated, their body weight measured, and subcutaneous adipose tissues were fixed in 10 % formalin solution for 24 h, dehydrated in graded ethanol, embedded in paraffin and stained with hematoxylin-eosin for microscopic observation. Our results show a significant increase in the final body mass induced by the HFHC diet. The histological examination revealed changes in the structure of subcutaneous adipose tissue (expansion, inflammation, and fibrosis) in HFHC group. Indeed HFHC diet increased both the accumulation of macrophages in visceral adipose tissue and in subcutaneous adipose tissue with the presence of significant vascularization and connective tissue deposition in the latter. Thus, we suggest that adipose tissue remodeling can affect all adipose tissues in the gerbil model submitted to long-term HFHC diet.

DOI: 10.1530/endoabs.81.EP560

EP561
Source of folic acid in obesity patients in the Odessa region (Ukraine)
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Introduction
Obesity is known to be a disease of civilization. Both genetic and environmental factors play a role in the development of obesity. In the vast majority of cases, the main factor is eating disorders and hypodynamy. The modern human exceeds daily food demand mainly due to saturated fats and refined carbohydrates, with lack of fibre and vitamin. We decided to test the source of folic acid, because this vitamin is part of the folate cycle as a coenzyme to reduce homocysteine levels. At high levels of homocystein, the risk of cardiovascular disease, stroke, Alzheimer’s disease and osteoporosis increases. Cardiovascular diseases are the main cause of death in Ukraine. The goal of the work is to study the source of folic acid depending on the body mass index in the inhabitants of the Odessa region.

Methods
Fifty-six persons (16 men and 40 women) aged from 20 to 65 living in the Odessa region were examined. Height, weight, and BMI were measured. Folic acid was determined with an immunochemical method with electrochemiluminescent detection of the test system Cobas 6000; Roche Diagnostics (Switzerland). The survey of inhabitants of the Odessa region had a deficiency of this vitamin. In the obesity group, the rate was 32 per cent. Folic acid deficiency can be nutritional (insufficient use of deciduous green and/or abuse of coffee) or genetically induced (folate cycle polymorphism), and further research is needed, with the development of deficit correction techniques.

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Cardio-metabolic profile of morbidity obesity compared to moderate and severe obesity

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Introduction
Obesity is the disease of modern society whose prevalence continues to increase. The aim of this study was to compare the cardio-metabolic profile of morbidity obesity with that of moderate to severe obesity.

Methods
It was a retrospective study conducted at the obesity unit of the national institute of nutrition in Tunis including 174 obese patients. We divided the population into two groups. Group 1 (G1) with morbidity obesity including 83 patients and group 2 (G2) with moderate to severe obesity including 91 patients. Morbid obesity is defined by a BMI ≥ 40 kg/m² and moderate to severe obesity is defined by a BMI between 30-39.9 kg/m².

Results
The mean age of our patients was 42.22 years in G1 and 47.93 years in G2 (P=0.006). A female predominance was noted in both groups, sex ratio M/F (G1): 0.18 and (G2): 0.49. A significant association was found between female gender and moderate obesity (P=0.008). The study of the metabolic profile did not find any significant difference in the prevalence of diabetes between the two groups but dyslipidemia was higher in G2 (P=0.024). The mean waist circumference was higher in the morbidly obese group (127.7 cm VS 114.99 cm) (P<0.001). No significant difference was found between the biological parameters of the two groups. Regarding cardiovascular complications, there was no significant difference between the two groups in the prevalence of heart failure, hypertension, and stroke. Joint complications such as gonalgia and low back pain were higher in G1 (P=0.015). Sedentary lifestyle was higher in the morbidity obese group (69.88% vs. 51.65%) with a significant difference between the two groups (P=0.014). The prevalence of eating disorders (the presence of at least one disorder) was higher in G1 (89.16% vs 74.73%) (P=0.014).

Conclusion
Our study showed that despite higher body fat, morbidity obesity is not characterized by a more severe cardio-metabolic profile compared to moderate and severe obesity.

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Diabetic ketoacidosis in pregnant women with type 1 DM and Covid 19

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Introduction
Diabetes is a recognized risk factor for the development of complications in COVID-19 infection, with an increased incidence of ketoacidosis observed in patients admitted to hospital.

Case Reports
We present the case of a patient with type 1 DM complicated by diabetic retinopathy and unplanned pregnancy (pregestational Hba1c 9.1%). In follow-up during pregnancy: progression of retinopathy and fetal renal pyeloectasia in morphological ultrasound at 20 weeks, Hba1c second trimester 6.8%. Consultation in the Obstetrics Emergency Room of a 29+4 week pregnant woman due to emetic symptoms of 3 days of evolution, showing ketocidosis (fasting plasma glucose 287 mg/dl, pH 7.11 bicarbonate 5.7 mmol/l and ketonuria), and starting intravenous insulin and fluid therapy. In case of suspicion of COVID-19 contact, PCR Sars-CoV-2 is performed, which is positive. Cardiographic record (CTG) on admission: pattern according to gestational age and adequate fetal HR, limited variability in some section that recovers spontaneously. No sustained decelerations. Non-dynamic. Free Style Libre (previous 14 days): average glucose 155 mg/dl, GMI 7.0%, CVG 41.7%, time on target 65%, above target 29%. Although the patient did not present respiratory symptoms or vital compromise, it was decided to admit her to the intensive care for treatment and monitoring of ketocidosis and obstetric control with continuous CTG. At 24 h, uterine dynamics is evident in the CTG, for which she receives tocolytic treatment with atosiban to inhibit contractions, magnesium sulfate and betamethasone for fetal lung maturation and a slight worsening of glycemic control. After intensifying intravenous insulin therapy, optimal fasting plasma glucose levels for pregnancy were achieved, but refractoriness in the control of ketoacidosis and intermittent oral tolerance prevented withdrawal of the insulin perfusion. On the 11th day of admission (current gestation of 31 +1 weeks) there was evidence of CTG, loss of fetal well-being and uterine dynamics, deciding to carry out an urgent cesarean section that proceeded without complications. After this, correction of ketoacidosis and improvement of oral tolerance were achieved, with withdrawal of intravenous insulin therapy and transfer to a conventional ward without complications.

Conclusions
We present this case emphasizing the importance of multidisciplinary management of diabetic ketoacidosis during pregnancy and the role that COVID-19 infection may have played.

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Endocrine-Related Cancer

Clinical features and survival outcomes of patients with ectopic Cushing’s syndrome: a single-center study

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Objective
To analyze long-term treatment outcomes and to determine prognostic factors affecting the survival of patients with ECS.

Materials and methods
Retrospective, observational study on 147 patients (88 women, 59 men) with ECS diagnosed between 1990 and 2021. Various imaging studies were performed on all patients to find the source of ACTH producing neuroendocrine tumor (NET). Multivariable analysis was performed using a Cox proportional hazards model to define the independent prognostic factors.

Results
The median age at diagnosis was 40 years [28;54], 89 patients (60.5%) had bronchial (bronchial NET, 15 (10,2%) - thymic carcinoid, 5 - pancreatic NET, 6 - pheochromocytoma, 1 - cecum NET, 1 - appendix carcinoid tumor, 1 - mediulary thyroid cancer and 29 (19,7%) patients had an occult NET. Mean time to diagnosis was 31 months, 11 patients (7,5%) had a cyclic course of disease. The most common complications in the active stage of disease were arterial hypertension (83,7%), osteoporosis with low-energy fractures (60%), type 2 DM (56,5%), cardiovascular disease (52,4%). The median follow-up period of patients was 36 months [11;75] with a maximum follow-up of 379 months. To the present date, the primary tumor was removed in 94 (63,9%) patients. Regional and distant metastases were revealed in 32 (21,8%). At the time of last observation, 62 patients (66%) had achieved stable remission, 12 (12,8%) had relapsed and received treatment with somatostatin analogs (n=9) or octreotide (n=2), and 38 patients (75,9%) had died from multiple organ failure (n=22), pulmonary embolism (n=5), sudden cardiac death (n=2), acute cerebrovascular accident (n=2), COVID-19 (n=3), complications of surgery (n=2), hip fracture (n=1), unknown cause (n=1). Bilateral adrenalectomy was performed on 45 patients (30,6%); due to occult tumor in 16 patients and incurable stage of disease in 29 patients. Multivariate analysis revealed that negative predictive factors for survival were: age ≥ 51 years at diagnosis, P<0.001 (HR 5,513 (2,286–13,293)), localization of NET in the pancreas, P=0.013 (HR 5,771 (1,473–23,176)), occult tumors, P=0,006 (HR 3,670 (1,461–9,216)) and LNSC ≥108,4 nmol/l, P=0,009 (HR 4,205 (1,433–12,334)). Bronchial NET, P=0,006 (HR 0,272 (0,109–0,684)) was a positive predictor of survival.

Conclusion
The survival rate of ECS is up to 75% over a mean follow-up of 36 months in spite of severe multiple complications associated with hypercortisolism. The severity of hypercortisolism, NET localization and occult tumors are negative factors associated with high mortality. Consequently, more aggressive treatment of

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hypercortisolism is potentially beneficial for survival in patients with extremely high LNSC.

Aim

A retrospective study, using the MD-Clone interface, including data from the electronic medical records of all cancer patients treated with checkpoint inhibitors between January 2015 and January 2021.

Results

Among 3384 patients treated with immunotherapy during the study period, a statistically significant increase in glucose levels was observed after the initiation of immunotherapy [mean of maximum glucose levels during the month before immunotherapy 132.3 ± 55.8 mg/dl vs 139.8 ± 64.6 mg/dl in the month after immunotherapy (P-Value < 0.001)]. Glycemic dysregulation was significant among patients treated with glucocorticoids as part of an anti-ecdemic regimen in protocols combining chemotherapy and immunotherapy or managing immune-related adverse events (n = 2168). Mean of maximal glucose level was 136.4 ± 59 mg/dl during the month before immunotherapy and 145.6 ± 68 mg/dl one month after immunotherapy (P < 0.001). Among patients who were not treated with glucocorticoids (n = 1216), glycemic dysregulation was not found to be significant.

Conclusions

Concomitant glucocorticoid therapy is the primary determinant of post-immunotherapy hyperglycemia. Evaluation of the possibility of a distinct, reversible, autoimmune damage to beta cells would require a prospective study with a dynamic assessment of the beta-cell reserve.

DOI: 10.1530/endoabs.81.EP564
Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary autosomal dominant tumor syndrome caused by inactivating mutations of the tumor suppressor gene MEN1 which encodes the protein menin. It is characterized by the occurrence of tumors involving two or more endocrine glands, primarily parathyroid, enteropancreatic, and anterior pituitary, as well as non-endocrine neoplasms. Glucagonomas occur in fewer than 3% of patients with MEN1, causing hyperglycemia, skin rash (neuroectodermal migratory erythema), weight loss, anemia, and stomatitis.

Case report
In March 2019 a 35-year-old Pakistani woman underwent surgical removal of 2 overactive parathyroid glands causing primary hyperparathyroidism diagnosed after a pelvic fracture and the identification of brown tumors. After surgery, she was lost at follow-up. In August 2020, she was admitted to Emergency Department for fever, weight loss, and new-onset diabetes mellitus causing polyuria and polydipsia without ketocidosis. Glucagon was at the upper limits of normal (252 pg/ml) and abdominal MRI revealed a neuroendocrine tumor (10 mm in the pancreatic tail) and left adrenal adenoma, confirmed by a 68Ga-DOTATOC-PET, that showed 4 areas of abnormal uptake in the pancreatic tail, body, and head, and in left adrenal gland. Duodenopancreaticoenterectomy and left adrenalectomy were performed; histological examination revealed the presence of multiple well-differentiated G1 neuroendocrine tumors (Ki67 <3%) with intensive positive IIC for glucagon, and adrenal adenoma. The post-surgical period was complicated by cava vein thrombosis, typical of glucagonoma, and endocarditis. The study of other endocrine glands showed the persistence of primary hyperparathyroidism due to hyperplasia of the remnant parathyroid glands confirmed by Sesta-MIBI-scintigraphy; pituitary function and MRI were normal. Dermatological investigation showed cutaneous collagenomas. Genomic testing identified a novel loss-of-function MEN1 heterozygous pathogenic variant c.703T>G;p.Cys235Arg in exon 4. The patient was monitored by MRI, 68Ga-DOTATOC-PET, and FDG-PET and no significant abnormal uptakes have been identified until now, however, she developed skin lesions suspected for neuroectodermal migratory erythema and she is in a close follow-up. Genetic inheritance is under investigation.

Conclusion
The clinical behavior of MEN1 depends on histological features of the tumors, the type, and degree of hormone hypersecretion and the risk of tumor recurrence. Some authors described a potential genotype-phenotype correlation, but this link remains debated. Current clinical guidelines recommend that index case and their relatives should be included in a screening program to reduce morbidity and mortality. Our case of a new pathogenetic mutation associated with glucagonoma underlines the need for a closer follow-up and surveillance with an interdisciplinary approach.

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keep fasting plasma glucose in range. Abdominal CT with intravenous iodinated contrast in basal phase evidenced a 12x15 mm hypodense lesion in the tail of the pancreas with enhancement in the portal phase suggestive of insulinoma. Given clinical and radiological suspicion of insulinoma and given the impossibility of suspending intravenous glucose fluid, treatment with diazoxide was considered. Initially presents good tolerance and evolution, with progressive reduction of the requirements of intravenous glucose. However, after 6 days of treatment, he develops picture of pruritic skin lesions that do not disappear on pressure compatible with erythroderma. Evaluated by allergy service confirming allergy to diazoxide, started treatment with steroids. Consequently, the treatment was discontinued, being the evolution of the lesions favorable. In the absence of a medical therapeutic alternative, finally required surgical treatment. Distal pancreatectomy with a pathological result of a low-grade neuroendocrine tumor compatible with insulinoma. After surgery, he maintains excellent glycemic control, without hypoglycemia. Nonetheless, the patient presented a torpid postoperative period (acute renal failure, cavitary pneumonia with therapeutic bronchoscopy, respiratory failure with invasive mechanical ventilation) and she finally died.

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Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM diagnosis at initial evaluation</td>
<td>13(48%)</td>
</tr>
<tr>
<td>BM diagnosis during follow-up</td>
<td>14(52%)</td>
</tr>
<tr>
<td>Time until BM appearance (months)</td>
<td>151(78-234)</td>
</tr>
<tr>
<td>Thyroglobulin at diagnosis, after thyroidectomy (ng/ml)</td>
<td>1000(195-7743)</td>
</tr>
<tr>
<td>T 1-2</td>
<td>8(30%)</td>
</tr>
<tr>
<td>3-4</td>
<td>14(51%)</td>
</tr>
<tr>
<td>N1</td>
<td>9(33%)</td>
</tr>
<tr>
<td>Multiple BM</td>
<td>22(81.5%)</td>
</tr>
<tr>
<td>BM location</td>
<td></td>
</tr>
<tr>
<td>Spine</td>
<td>20(74%)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>10(37%)</td>
</tr>
<tr>
<td>Cranial</td>
<td>5(18%)</td>
</tr>
<tr>
<td>Rib cage</td>
<td>4(15%)</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>3(11%)</td>
</tr>
<tr>
<td>Lower limbs</td>
<td>4(15%)</td>
</tr>
<tr>
<td>Metastases in other locations</td>
<td>19(70.3%)</td>
</tr>
<tr>
<td>Skeleton-related events</td>
<td></td>
</tr>
<tr>
<td>Bone fractures</td>
<td>7(26%)</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>7(26%)</td>
</tr>
<tr>
<td>Pain</td>
<td>10(37%)</td>
</tr>
<tr>
<td>Treatment with I131</td>
<td>19(70.4%)</td>
</tr>
<tr>
<td>I131 Uptake in BM</td>
<td>10(37%)</td>
</tr>
<tr>
<td>Antiresorptive treatment</td>
<td></td>
</tr>
<tr>
<td>BM surgery</td>
<td>4(15%)</td>
</tr>
<tr>
<td>Palliative radiation therapy</td>
<td>9(33%)</td>
</tr>
<tr>
<td>Treatment with Tyrosine-kinase inhibitors</td>
<td>7(26%)</td>
</tr>
</tbody>
</table>

Results
N = 27. Women = 17(63%). Follicular carcinoma = 13(48%). Follow-up time (months) = 72(34-222). Age at diagnosis = 62(55-73). Exitus = 18(66.7%). Survival at 1 and 5 years was 68.5% and 43.5% respectively. No independent risk factors for increased risk of death were found.

Conclusions
In our case series, 5-year survival was slightly lower than that reported in the scientific literature. This may be due to the fact that 48% presented with BM in the initial evaluation, although it has not been possible to prove it given the low number of cases. No other prognostic factors were found, possibly for the same reason.

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EP572
Clinical case of ACTH ectopic syndrome associated with small cell lung cancer (SCLC)
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Introduction
Ectopic Cushing’s syndrome (ECS) is a rare disease caused by ACTH secretion by extrapituitary neuroendocrine tumors, characterized by high mortality. Despite the clinical sings of Cushing’s syndrome, difficult access to reliable clinical examinations, leads to a delay in diagnosis and the choice of optimal treatment tactics. Small-cell lung cancer patients with ECS have a very poor prognosis.

Case report
A 35-year-old woman was hospitalized in the endocrinology department with complaints of dry mouth, thirst, hypertension (up to 170/100 mmHg). The patient also had signs of heart failure due to concomitant congenital heart disease, diabetes mellitus type 2 (T2DM) and obesity. During the year, she was repeatedly examined due to the presence of clinical manifestations of Cushing’s syndrome. Physical examination: centrapetal obesity with fat deposits around the face, neck and upper back. BMI = 41.8 kg/m², hyperpigmentation in the neck, axillary and inguinal region, reddish-blue stretch marks on the arms, abdomen, buttoks. Laboratory evaluation revealed high levels of ACTH in the blood – 229.3 pg/ml (reference 7.2-63.3), and cortisol in daily urine 3600.8 µg/24 h (normal 58 - 403), and a decrease in potassium levels to 1.1 mmol/l, fasting glucose - 12 - 21 mmol/l. CT scan of the thoracic segment revealed a dense focus of the X segment of the right lung, metastatic character is not excluded. Abdominal CT revealed hyperplasia of both adrenal glands, multiple liver formations. PET-CT (18F-fluorodeoxyglucose): metabolically inactive formation of the lower lobe of the right lung, multiple metabolically inactive hypodense liver formations, moderately pronounced splenomegaly. The tumor marker Pro Gastrin Releasing Peptide (ProGRP) in blood was significantly increased - up to 5000 pg/ml (reference 0-46), which can increase in small cell lung cancer. Somatostatin analogues and stereoidogenesis blockers (Ketoconazole) were used to treat the disease, but cortisol levels did not decrease. The primary tumor during life could not be identified, death occurred due to lung and cardiovascular failure. The histological examination at post-mortem autopsy revealed the lung neuroendocrine tumor with signs of malignancy and multiple metastatic lesions of the liver.

Conclusion
Despite the availability of modern imaging diagnostic methods, the search for the primary focus and the treatment of ACTH-ectopic syndrome present considerable difficulties and often require long-term follow-up and an interdisciplinary approach. Although the prognosis for this type of tumor is unfavorable, timely diagnosis using lung tissue tumor markers and PET could help clarify the diagnosis at an earlier stage of the process.

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EP573
Postoperative prediction of tumor recurrence in patients with non-functional pancreatic neuroendocrine tumors
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Introduction
Pancreatic neuroendocrine tumors (pNETs) are a heterogeneous group of various treatment options depending on grading, staging, and presence of symptoms related to hormonal secretion. Their incidence significantly increased over the past decade and nowadays constitutes 30% of all NETs of the gastrointestinal tract. Despite the evidence of a different malignancy potential of pNETs G2, postoperative management is the same in all patients.

Aim
The purpose of the study was to determine possible predictors of postoperative tumor recurrence in patients with nonfunctional pNET G2.

Materials and methods
We identified 165 patients diagnosed with pancreatic neuroendocrine tumors. 47 of them with locally advanced or metastatic pNET G2 were included in the study.

Results
Recurrence occurred in 37.93% of patients operated with intention to treat, with the mean time to progression equaling about 2 years. In this group based on preoperative CT examinations, the average largest dimension of the tumor was estimated to be over twice bigger in comparison to patients with no recurrence (46.71 mm vs 22.89 mm), which was confirmed by postoperative histopathological examination (36.83 mm vs 34.36 mm). In over 80% of patients with disease relapse, the average largest dimension of tumor equaled 25 mm or more, whereas in the group without relapse only 55.65% of patients had lesions of this size. Ki-67 varies significantly (metastatic 8.8% vs disease recurrence 6.78% vs no recurrence 5.15%). Both progression and recurrence were associated with the primary location of the tumor in the pancreatic tail. Interestingly, about 50% of patients were symptomatic in all three groups.

Conclusions
Based on the analyzed material it seems that lesions with the largest dimension equaling 25 mm or more and a higher Ki-67 may be a predictor of the disease recurrence. Patients’ complaints, important for the management of disease, seem to be unrelated to the possible pNET G2 relapse. The unequivocal confirmation of these findings requires further observation.

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EP574
Pregnadiene-structures coupled with anti-inflammatory moieties as inhibitors of the 5α-reductase activity
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Proliferative inflammatory atrophy and prostatic intrapelvic neoplasia are the first signs of prostate cancer. This inflammatory etiology, together with the infiltration of immune cells, could lead to the binding of the cytokines with cancer cells, forming a population that could initiate tumor growth. [1] Androgens also play an essential role in prostate tumor growth, as is well documented. [2] Androgen deprivation therapy is currently the gold standard for hormone-sensitive metastatic prostate cancer patients. [3] These data have inspired researchers to improve therapy for this disease. Previously, our group prepared a new series of hybrid compounds based on a 5,16-pregnadiene scaffold linked to anti-inflammatory drugs. These derivatives showed important antiproliferative properties. [4] In the present study, we identified the effect of 5,16-pregnadiene derivatives bound to anti-inflammatory drugs (M1-5) as inhibitors of the 5α-reductase enzyme activity. This enzyme has been recognized as responsible for forming intraprostatic dihydrotestosterone from testosterone. Dihydrotosterone has also been associated with prostate cell proliferation [5], so blocking this enzyme and preventing prostate inflammation could improve therapies for this disease. Derivatives of M1-5 were tested as inhibitors of 5α-reductase activity by incubating radiolabeled testosterone in the presence or absence of these compounds. A fraction of the human prostate membrane and NADPH were added to this medium. Subsequently, the compounds formed were separated and identified by thin-layer chromatography. Compounds M1-3 and M5 inhibited in vitro formation of dihydrotestosterone, with the highest activity for M1-2, with IC₅₀ values of 24.2 and 0.26 μM, respectively. However, M3 and M5 showed IC₅₀ values too much higher, 15.8 and 6.06 μM, than M1-2, respectively, and M4 no-displayed activity. Previously, our group demonstrated the inhibitory effect of 5,16-pregnadiene on 5α-reductase activity [6]. Thus, 5,16 pregnadiene effects was completely diminished by indomethacin moiety attached to this compound, as shown in the M4 derivative.

Reference List

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EP575
Somatostatin analogues in the treatment of metastatic paraganglioma
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Introduction
Paraganglioma (PGL) is a neuroendocrine tumor derived from extra adrenal autonomic paraganglia with a germinal mutation rate of 30%. Metastatic paraganglioma (MPGL) can only be predicted after evidence of secondary lesions and it can occur in up to 50% of cases. Clinical course is remarkably variable, but 5-year overall survival is generally around 50%. Treatment options include surgical resection, chemotherapy, radiotherapy, and 123I-MIBG. Being a neuroendocrine tumor, PGL usually express somatostatin receptors but somatostatin analogues have been seldomly used in metastatic PGL and its efficacy is not well demonstrated.

Case study
We present a 45yr female patient with a 1-month history of right thoracic pain associated with hemolobar back pain and upper limb paresthesia. Thoracic CT identified a 6 cm lesion on the right lung apex, with extensive invasion of posterior thoracic wall, D1 and D2 vertebral bodies and vertebral canal. Urinary normetanephrine was markedly increased (7719 pg/ml, RR <600). Tissue biopsy allowed the diagnosis of aggressive PGL with Ki-67 of 15%. PET ⁶⁸Ga-DOTANOC was unremarkable except for the previously known lesion. After alfafa-blockade, surgery was performed and then followed by ¹²³I-MIBG (200 mCi). Post-treatment scintigraphy and PET ⁶⁸Ga-DOTANOC identified residual tumor without distant metastasis. After 4 years of loss of follow-up, symptoms returned, and a new ¹³¹I-MIBG scintigraphy and PET ⁹⁰Ga-DOTANOC identified a 7 cm thoracic lesion and additional bone lesions on multiple vertebræ and iliac bone. The patient underwent a second surgical procedure but had tumor progression 4 months later. Stereotaxic radiotherapy with 49 gray was then given. However, the following PET ⁹⁰Ga-DOTANOC showed new metastatic bone lesions and so we decided to start lanreotide 120 mg every 28 days. After 6 months, all previously known lesions were stable but a new slightly increased uptake was seen at the pleura. So that, we increased lanreotide frequency to every 3 weeks. Since then, 18 months have passed with no evidence of disease progression and she is still on this treatment regimen.

Discussion
To date, metastatic PGL can only be cured by surgical resection. Chemotherapy, radiotherapy and ¹²³I-MIBG are used for disease control. Most recently, peptide receptor radionuclide therapy has shown promising results. Somatostatin analogues such as lanreotide are currently used on gastroenteropancreatic neuroendocrine tumors but its role in PGL treatment is still unclear. This case suggests there is a role of somatostatin analogues in the treatment of metastatic PGL.

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EP576
Panhypopituitary diabetes insipidus due to metastatic breast cancer
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We report the case of a 36 years old female, with personal history of breast cancer, treated with neoadjuvant chemotherapy, breast resection and then chemotherapy and radiation therapy 2 years ago. She was continuously monitored by her oncologist, disease free for over a year, with recent CT scan that showed no particular lesions suggestive for secondary disease. Meanwhile, she got pregnant and delivered at term a healthy baby. She was admitted 3 months postpartum with intense headache, weight loss, fatigability and low blood pressure. She mentioned hydric intake of aproximate 6 l/day and similar diuresis during pregnancy. No visual field defects were found at the neurological examination. The initial blood tests revealed panhypopituitarism and central diabetes insipidus and adequate substitution was started. Her blood pressure normalized, but headache persisted without response to pain medication. The magnetic resonance imaging was suggestive for pituitary metastasis and cytologic evaluation of CSF obtained by lumbar puncture was inconclusive. Transsphenoidal surgery was performed and histopatologic exam confirmed a metastatic carcinoma.

Discussion
Although rare, metastatic pituitary spread should always be taken into consideration in a patient with personal history of malignancies and signs and symptoms suggestive of pituitary involvement. Breast cancer is the most likely source of pituitary metastasis in women, while in men lung cancer is usually encountered. Hematogenous tumor spread explains why neurohypophysis is first affected, with early development of polyuria-polydipsia syndrome and diabetes insipidus that precedes anterior pituitary deficiencies. Once diagnosis is made, treatment is difficult and implies correct substitution of hypopituitarism, surgical removal of pituitary lesion, systemic chemotherapy and radiation therapy.

Conclusion
Pituitary metastasis is a rare cause of hypopituitarism and diabetes insipidus associated with a poor prognosis and a median survival rate after diagnosis of 10 months.

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EP577
Novel steroidal derivatives preventing prostate dihydrotestosterone synthesis
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It is well-known that the increase of intraprostatic levels of 5α-dihydrotestosterone is related to the development of prostatic pathologies such as benign prostatic hyperplasia and prostate cancer. So finasteride and dutasteride-based therapies are much used to improve these diseases. These drugs are potent inhibitors of the enzyme 5α-reductase, which is found in the androgen-dependent tissues. This enzyme is responsible for converting testosterone into dihydrotestosterone in these tissues. This study aimed to identify the effect of new pregnane (2-8) analogs as inhibitors of 5α-reductase activity. The action of these steroidal derivatives was compared with that of finasteride. Two different experiments were performed: in vivo and in vitro. In in vitro experiments, we separately incubated derivatives 2-8 in the presence of radiolabeled testosterone, a membrane fraction of the human prostate as a source of 5α-reductase and NADPH. In addition, products 2-8 were also evaluated in testosterone-treated neutered male hamsters. After six days of treatment, the hamsters were sacrificed, and the weight of the prostate as determined for the reference compound finasteride (IC50

At the same time, testosterone plus finasteride treatment effectively decreased the weight of this gland. In conclusion, derivatives 2-8 were more potent than finasteride to blockade in vitro dihydrotestosterone formation. Nevertheless, their lack of efficacy for decreasing the weight of the prostate could be explained based on the pharmacokinetic processes undergoing these steroids.

Table 1. A series of pregnane derivatives (2-3) with a 17-N-cyclohexylcarboxamide residue (5-8) were evaluated as blockers of 5α-reductase type 2 (SRD2A) activity. The figure shows the 50% (IC50 value) inhibition of enzyme produced by 14C

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EP578
Genetic novelty in MEN1: about a tunisian family
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Introduction
Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary syndrome that should be considered when different endocrine tumors are associated in an individual or familial context. We report the observation of a Tunisian family, two sisters and a brother.

Observations
Patient 1: a 31 years old female, followed for multinodular goiter, was hospitalized for a left maxillary tumefaction associated with headache and blurred vision. Investigations concluded to a maxillary epulis complicating a primary hyperparathyroidism (PHP). A macroprolactinoma was also diagnosed. The epulis completely regressed after parathyroidectomy. Patient 2: a 48 years old female, was followed for asymptomatic hypercalcemia due to a PHP. The investigations showed multiple parathyroid adenomas wrongly taken radiologically and macroscopically as nodular thyroid tissue. The screening for further lesions of MEN 1 was negative. Patient 3: a 41 years old male was followed for multinodular goiter. PHP was revealed by recurrent bilateral renal lithiasis. He underwent a total thyroidectomy with removal of the hyperfunctioning adenoma on parathyroid scintigraphy. A persistent hypercalcemia was objectified indicating a reoperation. The screening for further lesions of MEN1 was negative. The genetic

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study of this family identified a new missense mutation, not described in the literature, at exon4 of the MEN1 gene in the heterozygous state.

Conclusion
Recent studies have shown that specific clinical manifestations may affect one family more than the other. Intra-familial correlations were shown to be significant only for pituitary, adrenal glands and thyroids. For this family, PH was the constant lesion.

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EP579
Bilateral localization of Leydig tumor in the testicles: Case Report
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1 Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco; 2 Ibn Rochd University Hospital, Mohamed VI Oncology Center, Casablanca, Morocco

Testicular cancer represents 1% of male tumors. The bilateral testicular tumors are very rare (1 to 2% of cases), with a histological predominance of 90–95% of germ cell tumors. The objectives of this case report are to describe the clinical, paraclinical, and the management of a rare neoplastic disease of the testicle, the bilateral Leydig tumor of the testicles. It is a 57-year-old patient with a family history of different neoplasms, including ovarian and breast cancer in siblings, and followed since the age of 51 for a Leydig tumor of the testicle, revealed by an indolent testicular mass of the right testicle, without any clinical signs of endocrine disorders. Ultrasound scrotal found a 30 mm left testicular hypoechoic nodule, testis law without particularity. The tumor markers and hormonal explorations were normal. Extension report without anomaly. A right orchectomy was performed. 3 years later, he presented a second localization of a Leydig tumor in the left testicle, also treated by orchidectomy. No adjuvant treatment (radio or chemotherapy) was indicated. A hormone replacement therapy was also established. Currently, the patient is followed in the oncogenetic consultation, for the identification a possible hereditary predisposition of neoplasms. The Leydig cell tumors of the testicles are typically characterized by the association of a tumor testicular and clinical and biological endocrine signs. The typical manifestations in adult include a secondary feminization. But in 10% of case, the clinical presentation is limited to the testicular mass and only the histology confirms the diagnostic. The diagnosis of the Leydigoma is histological but there is no clear limit between tumor benign and malignant, therefore, orchiectomy is the standard treatment and it is only the absence of long-term metastases that will confirm the benignity, prolonged monitoring is essential.

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EP580
Solitary fibrous tumors of the pleura with Doege-Potter syndrome: a case report
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CHU IBN Sina, Department of Thoracic Surgery, Rabat, Morocco

Background
Solitary fibrous tumor of the pleura is a rare primary intrathoracic tumor that arises from mesenchymal tissue. Hypoglycemia associated Solitary fibrous tumor of the pleura is referred to as the Doege-Potter syndrome and is caused by inappropriate secretion of an insulin-like growth factor IL.

Case presentation
We report 70-year-old women with no particular medical history, who present a right chest pain for 1 year with fatigue. The clinical examination revealed diminished breath sounds in right lung fields, and dullness to percussion. The Lab test showed non-insulin mediated hypoglycemia. Hypoglycemia was managed firstly with corticosteroid therapy and frequent programmed nutritional intake. Scanning demonstrated a right large, well-circumscribed, homogeneous pleural mass. A transthoracic puncture was performed which came back inconclusive. Right posterolateral thoracotomy through the five intercostal space was performed for the resection of the tumor. The histopathologic examination confirmed the presence of malignant Solitary fibrous tumor of the pleura with free marginal resection. Removal of the mass solved the hypoglycemia. The patient was discharged on postoperative day 5.

DOI: 10.1530/endoabs.81.EP580

EP581
Localisation of insulinomas : the role of different imaging techniques
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Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction
The diagnosis of insulinomas is made biochemically. However, proper localization of insulinomas is essential before surgery. Therefore, we aimed to evaluate the role of different imaging techniques in the localization of insulinomas. Case series
This case series include 10 patients with biochemically proven insulinomas. The age, gender, results of MRI, CT, EUS, are shown in Table-1. In imaging investigations, abdominal ultrasonography (AU) was normal in the 4 patients it was performed on. Abdominal CT scan was performed in all patients and found a tumor in only 6 cases. Abdominal MRI was performed in 2 patients and found a tumor in 1 case. The tumor confirmed by MRI wasn’t found by other imaging means. Endoscopic ultrasound was performed in 6 patients, was normal in 2 cases and found a tumor in 4 cases. 3 tumors were only diagnosed with endoscopic ultrasound. CT scan and endoscopic ultrasound were enough to find the localization of insulinomas in 8 patients. No lesion was identified in 1 case. All the 9 patients with confirmed pancreatic lesion underwent surgery and a diagnosis of insulinoma was made in all patients by immunohisto pathological analysis. All these patients achieved cure after surgery.

Conclusion
The diagnosis of insulinoma is easily confirmed biochemically. The challenge remains in its localization as no imaging procedure was enough on its own to confirm the presence of a pancreatic lesion, confirming therefore the difficulty of pre-operative investigations.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender/Age</th>
<th>Presence of tumor on AS</th>
<th>Presence of tumor on CT</th>
<th>Presence of tumor on MRI</th>
<th>Presence of tumor on EUS</th>
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DOI: 10.1530/endoabs.81.EP581

EP582
A personalised approach to tracking circulating cell free tumour derived DNA in a patient with adenocortical carcinoma
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Introduction

Adrenocortical carcinoma (ACC) is rare, with an incidence of 0.5-2 cases per million. Although generally aggressive, prognosis is highly variable and difficult to predict. Unlike other malignancies, there are no biomarkers routinely available for use in patients with ACC to help guide management. Circulating cell free tumour derived DNA (cfDNA), the proportion of circulating cell free DNA (ctDNA) originating from tumour cells, is a liquid biopsy that is quickly gaining favour as a clinically useful and superior biomarker in oncology but is only in the early stages of being investigated in ACC.

Aims

To identify and track cfDNA in a 60 year old male patient with metastatic ACC using a precision, patient specific approach.

Materials and Methods

Blood samples were collected at 5 time points over 25 months and separated into plasma and leucocytes. Paired whole exome sequencing (WES) was performed on leucocyte extracted DNA and DNA extracted from formalin fixed paraffin embedded ACC tissue. The 2 sequences were then compared to identify tumour specific somatic mutations. These mutations were used in the design of a bespoke Ampliseq™ HD ctDNA assay. ctDNA was extracted from plasma and the bespoke assay used to detect cfDNA through targeted next generation sequencing.

Results

This patient had a 14.5 cm left adrenal mass with lymph node metastases at presentation. WES identified 83 tumour specific somatic mutations including a TP53 mutation. 22 of these mutations (including TP53) were chosen as targets for inclusion in the Ampliseq™ HD ctDNA panel assay. Pre-adrenalectomy, 9/22 variants were detected on cfDNA analysis with variant allele frequencies (VAF) of up to 1.16%. Post-operatively, ctDNA was initially undetectable. He was commenced on mitotane however imaging later demonstrated disease progression. cfDNA analysis at this point detected 3/22 variants with VAF up to 2.72%. He received radiotherapy for bone metastases and subsequent chemotherapy following which cfDNA was not detectable on samples 4 and 5. The TP53 mutation was not detectable at any time point.

Discussion

We have demonstrated that cfDNA can be detected and tracked in a patient with ACC, with ctDNA dynamics mirroring progression and response. Targeting multiple, personalised variants is methodologically key to successful cfDNA detection. Only targeting mutations common in ACC, for example in TP53, runs the risk of missing other variants present in cfDNA. Further development is required in assay design to improve sensitivity however cfDNA is a hopeful future biomarker for patients with ACC.

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EP584

Genes involved in chromatin-remodeling complex could alter the regulation of alternative splicing in lungNENs

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Lung neuroendocrine neoplasms (LungNENs) comprise a diverse group of rare tumors with a commonly difficult and late diagnosis, which often require complex management and treatment. The most frequently mutated genes in LungNENs have recently been identified, including known components of the chromatin-remodeling pathways such as MEN1, PSIP1 and ARIDIA, which are the subject of ongoing detailed studies. In contrast, other key regulatory mechanisms, particularly posttranscriptional processes linked to RNA regulation and downstream mechanisms involving RNA regulation, remain largely unexplored. Therefore, the main objective of this study was to gain further insight into the role of chromatin-remodeling genes in LungNENs by focusing not only on their mutations but also in their potential interactions with RNA biology. To this end, we used RNAseq data from two distinct cohorts, the first one included 20 lung atypical carcinoids (EGAS00001003699) and the second cohort included 30 typical and atypical carcinoids (SRP156394). To investigate the potential impact of dysregulation of the selected genes we used a biocomputational approach, which enables to explore the putative connections between the altered genes and other factors contributing to RNA processing, splicing and maturation. Interestingly, initial results already indicated that patients harboring mutations in genes of the chromatin-remodeling pathway also displayed a dramatic dysregulation in the expression levels of these same genes. Furthermore, a detailed examination of the association between the altered genes and particular changes in functional and gene enrichment categories revealed that the chromatin-remodeling machinery could likely modulate transcriptional activity, hence affecting crucial peripheral regulatory systems. Interestingly, samples presenting mutations in chromatin-remodeling pathway genes also showed different patterns in splicing-related genes, which may suggest a dysfunctional RNA processing. Altogether, our study supports the use of biocomputational approaches to discover new alterations in and relationships among regulatory systems, which could lead to the discovery of new biomarkers and therapeutic tools in LungNENs. Ongoing efforts are aimed at using functional assays with LungNEN cell models to better delineate these biocomputational outcomes.

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EP586
Nonpathogenic variants in genes involved in signalling pathways differ between MEN1 patients with different outcome of pancreatic tumours
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Background
Although it is well-known that single pathogenic variants in the gene MEN1 are responsible for the development of multiple endocrine neoplasia type 1 (MEN1), the outcome of the disease in individual patients cannot be deduced from known genetic factors, the clinical picture of other family members, nor environmental data. Encouraged by publications suggesting a possible role of the genetic background in MEN1 outcome, we performed a study that aimed at searching for pathways or biological processes in which genetic variants are identified, that might clarify the different phenotypes in MEN1 patients.

Materials and methods
The exomes of MEN1 patients with confirmed pathogenic genetic variants in MEN1 were sequenced on an Illumina HiSeq platform. The results served for two analyses: (1) lack or presence of pancreatic tumour, and (2) insulinoma or non-insulinoma pancreatic tumour. For each analysis, three patient pairs were available. Genetic analyses were based on genes with non-synonymous exonic, splice-site, 5’UTR and 3’UTR variants identified in patients with the given clinical phenotype under investigation. The identified genes were interpreted for their function, gene ontology annotations, interactions, and pathways.

Results
(1) The genes identified in MEN1 patients with vs those without pancreatic tumours were annotated primarily to be involved in metabolic processes, cellular component organization or biogenesis, and biological regulation. Annotation of the individual genes included pancreas development, enterocyte differentiation, cytoplasmic ribosomal proteins, and vitamin metabolic process. After adding interactions, the most significantly enriched pathways were BMP signalling and regulation and TGF-beta signalling pathway.
(2) In insulinoma- vs non-insulinoma-patients, biological process annotations primarily indicated genes involved in metabolic processes and cellular response to stimulus. Individual gene annotations included lipid metabolic process, response to chemical, regulation of hormone levels, insulin signalling, and secretion. Together with close interaction partners, the following pathways were enriched, among others: metabolism of lipids; oxidation by cytochrome P450; synthesis of IP2, IP, and Ins in the cytosol; transcription factor regulation in adipogenesis; vitamin D receptor pathway; cytoplasmic ribosomal proteins; and selenoamino acid metabolism.

Conclusions
Although the genetic background of MEN1 is well established, we identified inherited genetic variations that differed depending on the clinical outcomes and the outcome of the disease in individual patients cannot be deduced from known genetic factors, the clinical picture of other family members, nor environmental data. Encouraged by publications suggesting a possible role of the genetic background in MEN1 outcome, we performed a study that aimed at searching for pathways or biological processes in which genetic variants are identified, that might clarify the different phenotypes in MEN1 patients.

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EP587
Poor outcome of systemic therapy in secondary high-grade pancreatic neuroendocrine tumors
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Introduction
Longitudinal changes in pancreatic neuroendocrine tumor (panNET) cell proliferation correlate with fast disease progression and poor prognosis. The optimal treatment strategy for secondary panNET grade (G)3, that has progressed from a previous low- or intermediate-grade to high-grade panNET G3 is currently unknown.

Methods
This was a single center retrospective cohort study, aimed to characterize treatment patterns and outcomes among patients with secondary panNET-G3. Radiological responses were assessed utilizing the Response Evaluation Criteria in Solid Tumors version 1.1.

Results
A total of 22 patients were included and received a median of 2 (range 1-4) treatment lines in 14 different combinations. Median overall survival (OS) was 9 months (interquartile range (IQR): 4.25-17.5). For the 15 patients who received platinum-etoposide chemotherapy, median OS was 7.5 months (IQR: 3.75-10) and median progression-free survival (PFS) was 4 months (IQR: 2.5-5.5). The 15 patients who received conventional panNET therapies achieved a median OS of 8 months (IQR:5-16.75) and median PFS was 5.5 months (IQR:2.75-8.25). We observed one partial response on 177Lu DOTA-TATE therapy.

Conclusions
In conclusion, this hypothesis-generating study failed to identify any promising treatment alternatives for patients with secondary panNET-G3. This demonstrates the need for both improved biological understanding of this particular NET entity and for designing prospective studies to further assess its treatment in larger patient cohorts.

DOI: 10.1530/endoabs.81.EP587
Nonislet cell hypoglycemia (NICHT) is a rare complication of malignancy characterized by overproduction of incompletely processed IGF-2 and subsequent stimulation of insulin receptors and increased glucose utilization. We report a patient with pancreatic adenocarcinoma with neuroendocrine differentiation who presented with NICHT and paraneoplastic hypercalcemia. A 51-year-old male was admitted to the ER for altered mental status and confusion. His blood glucose was 27 mg/dl and serum potassium was 3.1 mEq/L; other investigations showed increased transaminase levels and normal thyroid function. His vital signs were normal and he was taking no medication. He was treated with a 30 ml bolus of 33% dextrose solution, intravenous KCl and continuous infusion of 10% dextrose solution at 100 ml/h, achieving normoglycemia. After stopping the dextrose infusion for 2 hours, his blood glucose levels dropped again to 22 mg/dl and blood samples were taken; insulin and c-peptide levels were undetectable, cortisol was 18.5 mg/dl and IGF-1 was 48 mg/l (53-201). A 1 mg glucagon stimulation test was performed and blood glucose raised to 63 mg/dl at 20 minutes. Whole body CT scan revealed a pancreatic mass measuring 14x12 cm with cystic component, pathological abdominal lymphnodes and numerous liver metastases; tumor biopsy revealed a poorly differentiated adenocarcinoma with neuroendocrine differentiation (synaptophysin +, CD56 -). A diagnosis of NICHT was made and he was started on 30 mg methylprednisolone BID, hyperglucidic diet and 10% dextrose infusion was continued. Despite these therapeutic measures, other severe hypoglycemic episodes occurred and he was started on 8 mg dexamethasone BID, because of its longer duration of action, with some benefit. On the fourth day, he experienced a hypercalcemic crisis (blood calcium levels 14.9 mg/dl); other exams showed phosphorus 1.8 mg/dl, normal 25 (OH) vitamin D and magnesium with suppressed PTH 15.3 pg/ml (14-65). Treatment of paraneoplastic hypercalcemia consisted of i.v. bisphosphonate infusion (zoledronic acid 4 mg) in addition to saline rehydration. In the next three days, calcium levels normalized and remained stable. A trial of octreotide was started in attempt to further reduce hypoglycemic events with no benefit. Unfortunately, the patient was not eligible for tumor debulking or chemotherapy and after seven days, he died due to multiorgan failure. This case report has shown that hypoglycemia in the setting of NICHT is difficult to manage and can be accompanied by other hormone secretery syndromes; longer acting glucocorticoids and increased carbohydrate intake may help reducing severity and frequency of hypoglycemic episodes.

Discussions

Even if it is a considerable overlap between hyperthecosis and PCOS making difficult to distinguish between these two conditions, testosterone levels are higher than the levels observed in PCOS and since this modified parameter is the single most important laboratory finding, imaging of the adrenal glands and ovaries must be performed. A complete medical history and full physical examination for virilisation are important hallmarks of diagnosis. Effective and timely treatment can reverse the cardio-metabolic consequences of hyperandrogenemia as well as clinical and biochemical outcomes.

References

1. "Sf. Spiridon" Clinical Emergency Hospital, Endocrinology Department, Iasi, Romania; 2Regional Institute of Oncology, Iasi, Romania; 3"Gir. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Introduction

Ovarian hyperthecosis (OH) is a rare condition, reported only in case reports and small case series and is characterized by severe hyperandrogenism leading to virilisation and insulin resistance. The term hyperthecosis refers to the presence of luteinized thecal cells within a hyperplastic ovarian stroma and the pathophysiology of this remains poorly understood. Despite the fact that hyperandrogenism is a relatively common clinical problem, severe hyperandrogenism causing virilisation is rare.

Case report

A 40-year-old Caucasian woman with a prior history of PCOS presented to our department with clinical signs of hyperandrogenism (hirsutism – Ferriman–Gallway score = 28, androgenic alopecia with temporal and anterior baldness, clitoromegaly and deepening of the voice). Menarche occurred at 14 years old with irregular menses and she reported secondary amenorrhea at the age of 30. She was known to have type 2 diabetes and hypertension. Clinical examination revealed acanthosis nigricans on armpits and groin, purple stretch marks on breasts and she was obese with body mass index of 34 kg/m² with moon face and buffalo hump. Hormonal profile demonstrated elevated total testosterone 4.11 nmol/l (0.29-1.67), with dehydroepiandrosterone sulfate 134.5 (60-337), 17-hydroxyprogesterone 1.82 ng/ml, low follicular stimulating hormone (FSH) 8.03 mIU/ml and luteinizing hormone (LH) 6.79 mIU/ml and a serum estradiol in the premenopausal range 53.9 ng/ml. The results of further diagnostic test were as follows: elevated urinary free cortisol 604.8 mg/24 h (9.5-148) but with normal cortisol in overnight demecolmehasone suppression test (1.32 mg/d). Thyroid function tests and prolactin were normal. Abdominal and pelvic CT scan indicated bilateral ovarian enlargement (right ovary: 36/50/55 mm and left ovary: 38/41/57 mm) with hypodense structure on unenhanced imaging showing mild contrast uptake. She underwent laparoscopic surgery with total hysterectomy and bilateral salpingooophorectomy. Anatomopathological examination confirmed diagnosis of OH describing ovarian cortex bilaterally expanded, with multiple follicular cysts in the superficial layer and scattered luteinized cells isolated or organized in small clusters.

Purpose

Pheochromocytomas (PCs) and paragangliomas (PGLs) are rare neuroendocrine tumors arising from chromaffin cells of the adrenal medulla and the sympathetic/parasympathetic neural ganglia, respectively. Metastatic PCs/PGLs occur in about 5-26% of cases. Their management and diagnosis still remain a challenge due to their heterogeneity, the absence of guidelines and the few prognostic tools.

Aim

The aim of this study was to describe clinical and genetic characteristics of a series of PCs/PGLs patients in a tertiary center as well as to evaluate their diagnostic and therapeutic approach.

Methods

Clinical data of 50 (30 females) patients (25 with PCs and 25 with PGLs) referred to the University Hospital of Laikon were retrospectively collected and analysed. Results

Patients’ follow-up ranged from 12 to 93 months (median: 31). The 84% of PCs and 36% of PGLs were functional. Genetic analysis was performed in 50% of the total included patients (n = 12/25 patients with PCs and n = 15/25 with PGLs) and was found positive in both blood and tissue analysis in 12 patients (9 with SDHID/B, 2 with RET and 1 with NF-1 mutation). Genetic mutations were twice as common in PGLs (15%) compared with PCs (7%). Median PASS was 5 (min-max:4-7) for PCs and GAPP 5 (min-max:2-11) for PGLs. Median Ki-67% index levels was 3 (min-max:1-18). In 96% of PCs surgery was the treatment of choice compared to 72% of PGLs. Metastatic disease (n = 9) or local recurrence (n = 5)
were found in 14/50 (28%) of patients; 25% of them with PCs and 26% with PGLs. Surgery was more often chosen (2nd line treatment) for PCs’ recurrence or metastasis (37%) compared to PGLs (16%) in which systemic treatments including chemotherapy (temozolomide), radiopetides, targeted treatment, radiotherapy or follow-up (watch and wait strategy) were applied. MSI/PD-L1 expression was negative in 10 tested samples (all metastatic or progressive) and thus immunotherapy was not considered. Survival rate was 98% during the follow-up. Median progression free survival was 36 months for patients with metastatic disease, and median overall survival 96 and 48 months in patients with PCs and PGLs respectively.

Conclusion
In our series, 44.4% of patients with PCs and PGLs were diagnosed with genetic mutations confirmed in both blood and tissue analysis whereas the frequency of patients with PGLs diagnosed with pathological mutations was double compared to patients with PCs. The 28% of our cases presented local recurrence or distant metastases; however MSI/PD-L1 analysis was negative and thus immunotherapy was not applicable.

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**EP591**

Atypical presentation of recurrence following previous resected Primary Parathyroid Carcinoma- dilemmas in follow up of this rare malignancy

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Introduction
Parathyroid cancer is a rare endocrine malignancy and constitutes 0.005% of all cancers. It can recur in 50% of cases. The first recurrence commonly occurs within 3 years of the original diagnosis. Hypercalcaemia is the main cause of morbidity and mortality. We present a case of a 62-year-old male patient who had an atypical lung nodule recurrence with normal calcium and PTH levels, six years following resection of a functioning parathyroid cancer.

Case Report
A 62-year-old male patient was referred to endocrinology due to hypercalcaemia post resection of adenocarcinoma of the rectum. Post-bowel surgery, his serum calcium levels ranged from 3.07 to 3.71 mmol/litre (2.10-2.60), serum PTH 16.1 pmol/litre (1.2-6.9), and vitamin D3 43.6 nmol/litre (<25). A parathyroid sestamibi scan revealed right superior parathyroid adenoma and an intrathyroidal mass suspicious of parathyroid tissue. He was monitored annually by endocrinologists and surgeons. This was done by checking his serum calcium, PTH, and ultrasound neck which all remained normal. Six years following the parathyroid surgery, he was found to have an enlarging lung nodule on surveillance imaging for his rectal cancer. A CT-guided lung biopsy confirmed a parathyroid cancer metastasis. A PET CT scan and ultrasound of the neck did not reveal any evidence of local recurrence. The lung nodule was resected which confirmed a parathyroid cancer metastasis.

Discussion/Conclusions
Long-term survival is possible with recurrence of parathyroid cancer and routine surveillance can identify early recurrence. However, there is no clear consensus guidance on the follow-up of patients with parathyroid cancer. The existing guidelines recommend regular surveillance of functioning parathyroid cancer by performing serum calcium, PTH, and ultrasound neck. Our case is atypical in that the patient did not have hypercalcaemia at the time of recurrence despite the originally resected functional parathyroid cancer. If surveillance imaging for rectal cancer had not been done, the lung nodule may not have been picked up in a timely manner. This case highlights the need for lifelong follow-up for parathyroid cancer patients. Current guidelines should be reviewed to include whole-body imaging modalities to pick up early distant recurrence. Our case also highlights that recurrence of functional parathyroid cancer might not present with hypercalcaemia.

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**EP592**

Pheochromocytoma associated with type 1 neurofibromatosis

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Introduction
Compared to normal population, patients with neurofibromatosis are at higher risk for the development of benign and malignant tumors. Pheochromocytomas are relatively rare in neurofibromatosis type 1 (NF1), and malignant ones are even rarer.

Aim of the presentation
Our aim was to report a malignant pheochromocytoma with multiple metastases in a patient with NF1.

Case report
A male patient aged 23 years old, with laparoscopically resected pheochromocytoma. He was investigated for headaches, flushing and palpitations. The diagnosis of pheochromocytoma was confirmed by elevated 24-hour urine levels of metanephrines and catecholamines. Computed Tomography Scan revealed a mass measuring 10 x 8, 2x 9.4 cm in the left adrenal gland and pulmonary metastases. The patient presented with classic clinical features of NF-1, café-au-lait spots and skin nodules. He was operated on and histological examination confirmed the diagnosis of pheochromocytoma with a Pash score of 9. After surgery, urinary catecholamines were high and there were diffuse pulmonary and liver metastases with Octreotide scan uptake. Somatostatin analogues and MBG therapy are being considered.

Conclusion
The association of a malignant pheochromocytoma with neurofibromatosis type 1 although very rare should be known as pheochromocytoma and its metastases may be totally asymptomatic as in the presented case.

Key-Words : Pheochromocytoma-neurofibromatosis-malignant-catecholamines

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**EP593**

An analysis of blood parameter changes in cushing’s syndrome - a population-based study

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Aim
Glucocorticoids play a significant role in inflammation and immune system disruption. Our study aimed to analyse different biochemical and blood count indices and serum inflammation-based scores in patients with all different causes of endogenous Cushing’s Syndrome (CS) in a well-defined population.

Methods
Clinical records of 35 patients diagnosed with CS between 2008 and 2020 at the only central national health service hospital in Malta, were retrospectively analysed. Detailed clinical and biochemical data were obtained for each patient. Correlation and receiver operator characteristics (ROC) curve analyses were used to establish a threshold value for different variables to predict malignant CS.

Results
Malignant cause of CS (ectopic CS and adrenocortical carcinoma) had statistically significant higher cortisol, size of the tumour and lower potassium at diagnosis (P<0.001). Additionally, malignant causes had a lower lymphocyte count (P=0.001) and eosinophil count (P=0.008), and a higher neutrophil-to-lymphocyte ratio (NLR) (P=0.001), systemic immune inflammation index (P=0.005) and a lower lymphocyte-to-monocyte ratio (LMR) (P<0.001). Using Spearman’s correlation, a positive correlation was noted between cortisol levels (baseline, post-ODST cortisol and 24-hour urinary cortisol) and pre-operative NLR whilst a negative correlation was observed with pre-operative LMR. Using ROC curve analysis to predict malignant cause of CS, a potassium level of < 3.05
was 75% sensitive and 100% specific (ROC-AUC 0.907, P = 0.001), a post-ODST cortisol level of > 841 nmol/l was 100% sensitive and 91% specific (ROC-AUC 0.981, P < 0.001), while a NLR ratio > 3.9 was 100% sensitive and 57.7% specific (ROC-AUC 0.885, P = 0.001).

Conclusion
Biochemical and blood count indices and serum inflammatory-based scores remarkably differ between benign and malignant causes of endogenous CS. Such indices can help predict the severity of disease and thus prognosis.

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**EP594**

New CDKN1b mutation in multiple endocrine neoplasia type 4 and brief literature review on clinical management.

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Background
The fourth type of Multiple Endocrine Neoplasia (MEN) is a rare variant of MEN presenting a MEN1-like phenotype and originating from a germline mutation in CDKN1B. However, due to the small number of cases documented in literature, the peculiar clinical features of MEN4 are still largely unknown, and clear indications about the clinical management of these patients are currently lacking.

In order to enlarge our knowledge on MEN4 and to better typify the clinical features of this syndrome, we present two more patients with a germline CDKN1B mutation developing MEN features and perform a review of the current literature about MEN4.

Case presentation
The first case is a man who was diagnosed with a metastatic islet G2-NET at the age of 34. Genetic analysis revealed the mutation p.119T (c.356T>G) of CDKN1B. This variant is of first description in literature in association to MEN4. The patient was screened for pituitary and parathyroid disease without any pathological findings. The second report is a 76-year-old woman with a multifocal pancreatic G1-NET. Genetic analysis identified the CDKN1B mutation c.482C>G (p.S161C). The variant is of first description in literature in association to MEN4. It is located into the C-terminal RhoA binding domain, potentially affecting cell motility. However, in silico analysis supports that this missense variant does not alter protein structure/function and it has been currently classified as a variant of uncertain significance. Pituitary and parathyroid function resulted normal as well.

Review of literature
To date, twenty-three different mutations of CDKN1B have been described in literature in association to MEN4, including fifty-seven carriers. Forty-two of these subjects developed at least one endocrine tumor, involvement of multiple endocrine organs was detected in seventeen of them. Primary hyperparathyroidism results the most frequent endocrine neoplasm (75%), followed by pituitary adenoma (=40%) and neuroendocrine tumors (=20%). In general, MEN 4 seems a variant with later onset, less penetrance, and milder clinical features than MEN1.

Conclusions
MEN4 patients might need a different and personalized approach in clinical management. For hyperparathyroidism, when recurrence and/or multiple parathyroid involvement appears to be rare, a less aggressive surgical approach than in MEN1 could be justified. Therefore, MEN4 carriers should be screened for neuroendocrine tumors and pituitary adenomas. Larger case series are still necessary to clarify the peculiar features of MEN4 and to establish a specific diagnostic and therapeutic standard.

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**EP595**

Severe psychosis: think of adrenocortical carcinoma

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Introduction
Adrenocortical carcinoma (AC) is a rare malignant endocrine tumor of the adrenal cortex. The psychiatric manifestations observed in AC are associated with a delayed diagnosis.

Case presentation
A 27-year-old woman with medical history of severe psychosis resistant to antipsychotic medications, was hospitalized in our unit for Cushing’s syndrome (CS). The physical examination revealed classical signs of CS. The Laboratory results showed 24-hour urinary free cortisol values higher than 4 times the upper limit of normal, elevated midnight serum cortisol at 86 ng/ml and no suppression of cortisol during a low-dose dexamethasone suppression. The presence of a plasma ACTH level < 3 pg/ml suggests ACTH-independent CS. Adrenal CT scan showed a 35*23 mm mass located in the left adrenal gland with an absolute washout of 28%. The patient underwent unilateral adrenalectomy. Histopathological analysis revealed adrenocortical carcinoma with a Weiss score of 4. The evolution was characterized by the improvement of psychiatric symptoms, hence the discontinuation of antipsychotic medications.

Discussion
AC is a rare malignant tumor. Its incidence is approximately 1 to 2 new cases per million per year. It occurs most often in adults between 40 and 50 years of age, with a female predominance. The prognosis is poor (five-year survival rate of less than 50%). The glucocorticoid hypersecretion observed in CS is accompanied by sleep disorders, thymic manifestations, especially depression, and cognitive disorders, but psychotic states are rare. Hypercortisolism modulates the response of the central nervous system through the activation of membrane channels, synaptic transmission of neurotransmitters (such as serotonin, glutamate and GABA), gene transcription, synaptic plasticity, neurogenesis and apoptosis. Excessive activation of the dopaminergic system is at the basis of the pathophysiology of manic symptoms, psychotic disorders and also some forms of depression.

Conclusion
Our case illustrates the importance of a good interrogation and a careful clinical examination in all patients presenting with a psychiatric illness, in order to eliminate an organic cause which can engage the vital prognosis.

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**EP596**

A case of asymptomatic Pheochromocytoma with high risk of malignancy

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Introduction
The classical triad of pheochromocytoma comprises paroxystic headache, palpitation, and diaphoresis. It is a common cause of secondary hypertension. Glycemic abnormalities are not rare. Hyperglycemia and diabetes can be the presenting features of pheochromocytoma. However, cases of hypoglycemia are also described. Malignant tumors account for about 10% of cases. The clinical and biochemical presentation of the tumour is usually helpful in the diagnosis.

Case description
In this report, we present a case of a 41-year-old man referred to the endocrinology department for asymptomatic hypoglycemia as an incidental finding on routine laboratory screening. There was no personal or family medical
history, and patient was not taking any medication. An insulinoma was initially suspected, and patient underwent abdominal magnetic resonance imaging. The latter revealed right 24 mm hypervascular adrenal mass and normal pancreatic parenchyma. The blood pressure was normal (110/60 mmHg). The laboratory showed an elevated level of chromogranin A (322 mg/L) (N: <100 mg/L) and elevated urinary metanephrines (814 mg/24 h, (N): 74-297) and normetanephrines (755 mg/24 h, (N): 105-354). The fasting insulin, glucose, and c-peptides were in normal range. PET CT showed a strong expression of the somatostatin receptors in right adrenal mass. On a non-contrast-enhanced computed tomographic (CT) scan, density of the lesion was 35 HU. On a contrast-enhanced CT, the value was 100 HU. At this stage, a pheochromocytoma was suspected. Surgical resection was performed. The pathology confirmed a pheochromocytoma. It was described as having a high risk of malignancy because of capsular invasion, presence of nuclear atypia, up to eight mitotic figures in 10 high-power fields (hpf), presence of atypical mitoses, and confluent nodules. There was no invasion of peri-adrenal fat, vascular, lymphatic, or peri-neural tissues. The genetic tests showed no mutation in the SDHI, RET, VHL, and NF1 genes. The urinary metanephrines and normetanephrines were in the normal range 2 months after the surgery.

Discussion
In conclusion, we present a case of pheochromocytoma in a patient with incidental asymptomatic hypoglycemia. Our case emphasizes that eight percent of patients with pheochromocytoma are completely asymptomatic. Histopathology results demonstrated a tumor with a high risk of malignancy because of the extensive capsular invasion. Nevertheless in literature, the only indicator of malignancy is the presence of distant metastases. Our case also highlights absence of reliable histopathologic methods to distinguish between benign and malignant tumors. However, certain histologic features are more common in malignancy, including extensive capsular invasion (as present in our patient), tumor necrosis, and vascular invasion.

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EP597
Levels to designate progressive increase in aggressiveness of medullary thyroid cancer depending on the identified mutations in the Republic of Belarus
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Background
The recommended method of initial testing for MEN2A is either a single or multi-tiered analysis to detect RET mutations in exon 8, 10, 11, 13, 14, 15, and 16. The aim of the study was to determine the relationship between the aggressiveness of the clinical course of MTC and identified mutations.

Materials and methods
The research is carried out of the program ‘To develop and implement effective technologies for the diagnostic detection and observation of patients with MEN2A.’ 32 patients with established medullary thyroid cancer (MTC), who underwent genetic testing, with the presence of pathogenic mutations of the RET proto-oncogene, were selected. The patients were divided into 3 groups depending on whether the mutation of the RET gene belongs to the highest, high, and medium risk levels.

Results
The number of carriers of the mutation of the highest risk level (16 exon M918T) was 2 people, which is 6.25% of the total. The median age at diagnosis is 28.7 years. At the time of diagnosis, the metastatic form of the disease was detected in 1 patient, which is 9.1%. After the treatment, remote recurrence of the disease was registered in 1 patient (9.1%), and local recurrence - in 2 patients, which is 18.2%. In 4 people (36.4%) pheochromocytoma was found. In 19 people, pathogenic mutations of the RET gene were identified, which are related to the level of moderate risk, which accounted for 59.37% of the total. Mutations in these patients are localized in exon 10. In this group of patients, MTC was diagnosed on average at the age of 41.1 years. The metastatic form of the disease at the time of diagnosis was not detected in this group. Local recurrence after the treatment was registered in 4 patients (21.05%), remote relapses in this group of patients were not registered. Pheochromocytoma was not detected in this group.

Conclusions
High-risk mutations are characterized by the earliest onset of the disease, as well as the most frequent presence of pheochromocytoma.

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EP598
Choroidal metastasis from follicular thyroid carcinoma: a case report
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Introduction
Choroidal metastases are among the most common malignant ocular tumors. In the majority of cases, their origin is pulmonary in men and mammary in women. We present a rare case of choroidal metastasis from a vesicular thyroid carcinoma.

Case presentation
A 35-year-old woman presented to our department complaining of progressive visual acuity reduction in the right eye. Six years previously, she was operated for vesicular carcinoma of the thyroid with pulmonary metastases, she was under iratherapy. The ocular examination of the right eye revealed best visual acuity to 1/20. Intraocular pressure was 12 mmHg. Fundus examination showed retinal detachment with the presence of an underlying yellow-orange mass. The left eye examination was normal. Ultrasound B-scans, optical coherence tomography, fluorescein angiography and magnetic resonance imaging made the diagnosis of choroidal metastasis from thyroid carcinoma. Chest X-ray and abdominal ultrasoundography were normal. Bone scintigraphy with iodine 131 showed increased uptake in the humerus and the femur, with no ocular or cerebral uptake. External radiotherapy in addition to iratherapy was proposed but refused by the patient. Then, she was lost of view. Five months later, she came back with red and sore right eye. The examination noted the increase in the size of the metastasis with extension of the retinal detachment and appearance of neovascular glaucoma. Iodine 131 scintigraphy showed ocular uptake of iodine, thus confirming the diagnosis. The iratherapy was resumed but the patient quickly died due to deterioration in her general condition.

Conclusion
Choroidal metastases secondary to vesicular thyroid carcinoma are very rare. There are few cases reported in the literature. This work describes an additional case. In all reported cases, there are bone and/or pulmonary metastases in association with choroidal metastases. Indeed, thyroid carcinomas most often metastasize to the lungs and bones. Other metastatic sites are rare and are seen in advanced stages of the disease with poor prognosis. Vesicular carcinomas of the thyroid are known to metastasize to unusual sites and are more aggressive than papillary carcinomas. The appearance of the choroidal metastasis in our patient constituted a severe evolutionary turning point of the disease.

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EP599
Co-secretary ACTH & Calcitonin tumor presented with refractory hypokalemia
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An 81-year-old ex-smoker presented to emergency with transient facial droop, slurring of speech and generalized weakness. He had a background of ischemic
Sporadic metastatic pancreatic neuroendocrine tumor in a young patient

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Background
Pancreatic neuroendocrine neoplasms (NEs) are rare tumors which can sometimes be diagnosed based on symptoms of hormone excess, but, more often, they are asymptomatic, and patients frequently present with metastatic disease. While they can occur in hereditary cancer syndromes such as multiple endocrine neoplasia type 1 (MEN1), von Hippel-Lindau (VHL), or neurofibromatosis (NF1), the majority of pancreatic NEs are sporadic.

Case report
We report the case of a 37-year-old male referred to a gastroenterology clinic for nonspecific gastrointestinal symptoms. Abdominal ultrasound reported a large hepatic mass, which was confirmed with an abdominal CT scan. This prompted an ultrasound-guided hepatic biopsy, which raised the suspicion of metastatic liver disease arising from a primary pancreatic NE. The diagnosis was confirmed with immunohistochemistry, which graded the tumor as a NET G2 based on a ki-67 of 5%, and thus the patient was referred to our department. Considering the patient’s young age, biochemistry screening for MEN1 was performed, but serum calcium, PTH, gastrin, insulin, IGF-1, and prolactin were normal, as were NEN-specific tumor markers. The patient also had no symptoms of hormone hypersecretion, no clinical features of VHL or NF1, and no remarkable family history. Somatostatin receptor SPECT/CT was performed, reporting a primary pancreatic NEN, with multiple metastases to the liver, abdominal lymph nodes and left adrenal gland, and portal vein invasion. The patient received monthly intramuscular lanreotide injections, in combination with a systemic chemotherapeutic regimen. However, owing to the unsatisfactory response of the treatment and the significant adverse reactions, the patient was recommended for Peptide Receptor Radionuclide Therapy (PRRT). Following five Lu-177-DOTATATE PRRT cycles, partial response was observed, and debulking surgery was being considered as the next therapeutic step.

Conclusions
Widespread metastatic disease is often reported in pancreatic NEs, frequently requiring multiple lines of treatment. As such, multidisciplinary teams play a pivotal role in the management of such complex cases, carefully balancing risks, benefits, the biology of the tumor, and patients’ wishes.

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EP602
Ectopic Cushing’s syndrome due to metastatic lung carcinoid presenting on a background of DIPNECH
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Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a relatively recent disease, frequently misdiagnosed. It is characterized as a generalized proliferation of pulmonary neuroendocrine cells and is recognized as a precursor lesion for pulmonary neuroendocrine tumors, although the risk of progression to malignancy is considered low. Here we report a patient with ectopic ACTH-dependent Cushing’s syndrome due to metastatic lung carcinoid tumors arising on a background of DIPNECH. A 73-year-old woman presented to the emergency department with 4 weeks of progressive lower limb edema, sudden onset of hypokalemia, refractory hypertension and de novo diabetes. She had basal cracks on auscultation and hepatomegaly on examination. Past medical history included controlled hypertension, obesity, dyslipidemia. She was being followed in Pulmonology for chronic cough and radiological findings suggestive of DIPNECH. A thoracic CT showed diffuse mosaic attenuation with multiple bilateral lung nodules, with the largest nodules measuring 8 mm. Biopsy of the pulmonary nodules demonstrated tumorlet/typical carcinoid tumor, with evidence of DIPNECH. Severe elevated GGT prompted a cholangio-MRI that showed heterogeneous/micronodular liver parenchyma suggestive of chronic liver disease. Liver biopsy demonstrated hepatic involvement by a well differentiated neuroendocrine neoplasia expressing chromogranin and synaptophysin with a proliferative index Ki67 < 2%, compatible with metastasis. The patient became increasingly confused and disoriented over the first days of hospitalization. In view of the clinical suspicion of endogenous hypercortisolism, screening for Cushing’s syndrome was performed. She had elevated morning and midnight plasma cortisol levels (58.0 and 83.4 μg/dL, respectively) markedly increased 24-hour urinary free cortisol (3648.0 μg/day) and morning serum ACTH (167.1 ng/l). High-dose dexamethasone suppression test revealed no suppression of urinary free cortisol. A PET-Ga-68-DOTATOC was obtained for the purpose of excluding ectopic ACTH-dependent Cushing’s syndrome and assessing for metastatic disease. A PET-CT showed bilateral lung nodules, with the largest nodules measuring 8mm. Biopsy of the pulmonary nodules demonstrated tumorlet/typical carcinoid tumor, with evidence of DIPNECH. Brain MRI showed a tumor remnant. Visual field was normal.

The peculiarity of our case stems from the fact that MEN1 was revealed at an advanced age by a non-functioning macroadenoma. That’s why it should not be overlooked in diagnosis. In addition early recognition, multidisciplinary management and life long follow up are crucial.

Discussion
MEN 1, a rare endocrine syndrome, is defined by the presence of 2 or more primary endocrine tumors mainly located at parathyroid glands, anterior pituitary and gastro-enteropancreatic (GEP) function. Mutations of the MEN1 gene are identified as responsible for the development of this syndrome. Primary hyperparathyroidism, the most common manifestation of MEN1, presents usually in the second to the fourth decade of life. Multiple glandular disease is typical of MEN1. The most common type of pituitary adenoma in MEN1 is a prolactinoma. Conversely, non-functioning adenoma are rare (5%). GEP, which are asymptomatic in 70% of cases, are the primary life-threatening manifestation of MEN1 due to their malignant potential.

Conclusion
The development of primary hyperparathyroidism at advanced age by a non-functioning macroadenoma represents a unique presentation in a MEN1 syndrome.

EP604
Metachronous germ cells and sex cords ovarian tumors in an adolescent girl: Hormone replacement therapy at what cost?
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Introduction
Gonadal tumors are rare in children. Because surgery is the primary treatment for ovarian tumors, ovarian salvage with fertility preservation and use of a minimally invasive surgical technique are important in children and adolescents. We report the case of an adolescent girl who was referred after bilateral annexectomy.

Case report
This is a 14-year-old girl who just had her first menses. She has been followed the last year for an ovarian tumor. She initially had a right annexectomy. The pathology examination concluded to a moderately differentiated Sertoli tumor of 11×13 mm. Two months later, she developed large ascites. Radiological explorations showed a mass of the remaining left ovary of 9×7 mm with peritoneal carcinosis classified as high risk stage IIC. After a multidisciplinary discussion about fertility, cryopreservation of the ovarian cortex and all other preservation techniques have been discussed but they are impossible due to the high risk of recurrence upon reintroduction of the ovarian tissue. The child received 2 lines of chemotherapy followed by a left annexectomy. The surgery was considered complete and the pathology examination concluded to an ovarian teratoma. Currently, the 16-year-old patient is castrated with complete remission and no tumor recurrence. Her major complaint was the regression of secondary sexual characteristics.

Discussion-Conclusion
In the absence of high-level evidence literature, the Expert Consensus regarding hormone replacement therapy was consulted (1). Overall, the options for hormonal treatment depend on possible hormone dependence and the risk of recurrence. For germine tumors, these treatments can be used. On the other hand, a certain caution has been adopted for tumors of the sexual cords.


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EP605

The combination of medullary thyroid carcinoma and sporadic clear cell renal cell carcinoma: coincidence or new syndrome? Ihssane Abidi, Kaoutar Rfiai, Hinde Mohamedelhassan Gharbi, University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco

Introduction

COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by an influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste. Its severity is highly variable, ranging from asymptomatic to severe or prolonged forms. We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.

Observation

This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium. She received the first dose of astrazeneca in July 2021, after 4 hours she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/l. As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 hours and there was no recurrence.

Discussion

COVID-19 vaccines are as well tolerated in neuromuscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations. Campesium can be seen with COVID-19 vaccines, and is generally benign and transient. The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.

Conclusion

The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be monitored to avoid complications, particularly neuromuscular ones.

References


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EP606

Multiple endocrine neoplasia type 2: About two Tunisian patients Mnif Fatma, Kawthar El Arbi, Abdelmouhaymen Missaoui, Faten Haj Kacén Akid, Wafa Belabel, Dhoïha Ben Salah, Nadia Charfi, Mouna Mnif1, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction

Multiple endocrine neoplasia type 2 (MEN2) is a rare inherited disease characterized by the occurrence of medullary thyroid cancer (MTC) either isolated or associated with pheochromocytoma, primary hyperparathyroidism (PHP), or typical morphological features. Thus, we report two cases.

Patient(1)

A 27-year-old female patient with a marfanoid appearance, had a histologically confirmed conjunctival and mucosal ganglioneuromatosis, bilateral composite phaeochromocytoma (pheochromocytoma and ganglioneuroma) with multifocal and metastatic MTC. MEN2b was strongly suspected. A genetic study showed the presence of a mutation in the exon 16 (codon, M918T), in the heterozygous state, which is the most frequently associated with the MEN2b phenotype.

Patient(2)

A 46-year-old female patient presented with a complete MEN2a panel: multifocal CMT, PHP and bilateral phaeochromocytoma. In addition, she had hyperpigmented indurated lesions on the upper back following intense pruritus. These lesions are reminiscent of cutaneous amyloid lichen (CAL), a rare clinical variant of 2A. The genetic study is ongoing.

Conclusion

As distinct from MEN1, each variant of MEN2 corresponds to a specific genetic mutation. It is possible to predict the patient’s phenotype from the genetic study.

EP607

Multiple endocrine neoplasia type 1: A puzzle that builds over the years Mnif Fatma1, Kawthar El Arbi1, Yosra Lajmi2, Asma Zargni1, Faten Haj Kacén Akid1, Handi Friki1, Dhoïha Ben Salah1, Nadia Charfi1, Mouna Mnif1, Nabila Rekik Majdoub1, Mouna Elleuch1, Hassen Kammoun1, Fatma Abdelhedi2 & Mohamed Abid1

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Introduction

Multiple endocrine neoplasia type 1 (MEN1) is a genetic disease that predisposes to the development of both hyperplastic and tumorous lesions of the endocrine glands, in particular parathyroid, pancreatic and pheochromocytoma. Thus we report our case.

Observation

An 18-year-old male patient was hospitalized for severe hypoglycemia mistakenly treated as epileptic seizures. The etiological investigation concluded to a benign multiple insulinomas, confirmed by the anatomopathological study. The patient was lost to follow-up and was re-hospitalized 11 years later for an intracranial hypertension related to a macro-prolactinoma of 7 cm of diameter. Prolactin level was 11300 µg/l. A MEN1 was suspected. The investigation of additional associated lesions revealed a primary hyperparathyroidism. The evolution was fatal with the death of the patient in a cerebral herniation. The genetic study was not performed.

Discussion

Parathyroid tumors are the first manifestation of MEN1 in over 85% of cases. Less than 15%, the first manifestation may be an insulinoma or prolactinoma, likewise our patient. The chronology of lesion onset could differ from patient to another. The clinical presentation is usually completed over time. Thus a continuous screening of the different lesions is necessary. For our patient, the discovery of a primary hyperparathyroidism as well as a prolactinoma 11 years later make it particular.

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EP608

Clinical case: MEN1 syndrome Ieva Meskinyte1, Saulė Cyrolyte1, Igne Strazdiene1, Egle Urbonaviciute1, Raimonda Klimaite1,2,3 & Neli Jakubonienė1,3

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Introduction

Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare, autosomal dominantly inherited syndrome that causes tumors of the endocrine glands [1]. This syndrome is most commonly associated with neuroendocrine tumors of the parathyroid glands, pituitary gland and pancreas [2].

Case

A 30-year-old woman was admitted to the Hospital of Lithuanian University of Health Sciences, Kaunas Clinics for unconsciousness and significant hypoglycaemia: 1.0 - 3.04 mmol/l. Anamnesis

In 2016, the patient was examined for infertility. Hyperprolactinemia was diagnosed. Head MRI was performed to detect pituitary microadenoma, treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis. For our patient, the discovery of a primary hyperparathyroidism as well as a prolactinoma 11 years later make it particular.

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After evaluating multiple endocrine pathologies (prolactinoma, hyperparathyroidism, hypoglycaemia), MEN1 syndrome was diagnosed with the following outcomes:
1) Microadenoma hypophysis – prolactinoma. Secondary infertility
3) Insulinoma. Hypoglycaemia.

Parathyroid Scintigraphy TC-MIBI + SPECT/CT: right and left parathyroid adenomas. Head MRI: 0.6x0.6 cm hypo-enhanced area on the left side of the adenohypophysis - pituitary microadenoma, without negative dynamics. Abdominal MRI: a possible neuroendocrine tumor - insulinoma in the body and tail of the pancreas. Genetic test: sequencing of 2-4 exons of the transcript encoded by the MEN1 gene was performed. A pathogenic change in the c.446-2A>T sequence was identified, and the diagnosis of MEN1 syndrome was confirmed. The patient underwent parathyroidadenomecctomy subtotal, laparoscopic surgery to remove insulinoma. An abdominal MRI was performed 6 months later and two new neuroendocrine tumors were identified in the pancreas. Confirmed during scintigraphy. The patient underwent reoperation. After 1 year, there were no signs of recurrence of insulinoma and hyperparathyroidism, test results were in normal ranges.

Conclusion
This clinical case reflects the classic manifestation of MEN1 syndrome with the typical target organs: the parathyroid glands, pancreas, and pituitary gland. In addition, secondary symptoms of these diseases were hyperparathyroidism, infertility, hypoglycaemia and osteoporosis. Multiple endocrine disorders should lead to a suspicion of a diagnosis of MEN1. Therefore, precise laboratory, imaging tests of the target organs and genetic tests should be performed.

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EP609
Diagnostic and evolutionary profiles of adrenocortical tumor, about 30 cases
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Adrenocortical tumor is a rare malignant tumor of adrenal location. With a poor prognosis that can be improved by rapid diagnosis and adequate early management, hence the importance to evoke this etiology in front of any atypical adrenal mass or any suggestive clinical or biological context. The objective of our modest work is to report through a retrospective study the profile of adrenocortical tumors treated in our service over a period of 13 years from 2007 to 2020. Thirty (30) patients were collected with a middle age of 45 years (27 to 74 years) with a slight female predominance of 60%. A family history of neoplasia was noted in 5 patients (16.66%) and breast neoplasia in a single patient. The most frequent mode of revelation is represented by abdominal pain observed in 56.66% of cases. Hypercortisolemia is found in 40% of cases. Morphologically, the size of the tumor varies from 66 to 180 cm with an average of 110 cm. At least one metastasis was found in 10 patients (33.33%), dominated by hepatic location. 50% of our patients benefited from surgical excision of the tumor and 6.66% underwent a biopsy only. 77% of our patients received adjuvant treatment with mitotane supplemented by chemotherapy in 30% of cases. Only two patients received adjuvant radiotherapy (6.66%). The evolution was marked by remission in 33.33% of cases with an average survival of 5 years and death noted in 50% of patients. In conclusion: Adrenal carcinoma can be seen at any age, by remission in 33.33% of cases with an average survival of 5 years and death occurred at a mean glucose level of 1.8 ± 0.62 mmol/l and at a mean insulin level of 18.9 ± 6.4 mU/l. The pancreatic lesion was identified on cross-sectional imaging in 6 cases and on endoscopic ultrasound in 3 cases. No lesion was identified in 1 case. The median tumor size was 1.9 ± 1.1 cm. Insulinoma was found in the pancreatic uncinate process in 2 cases; in the pancreas body in 4 cases and in the tail in 2 cases. Multiple insulinoma were found in 1 case and was associated to multiple endocrine neoplasia type 1. Surgical procedures included 2 enucleations and 7 pancreatic resections. Histologic findings concluded to benign endocrine tumors in all cases. All patients had resolution of symptoms after surgery. The median follow-up is 6 years to date.

Conclusion
This case highlights the difficulty of the radiological identification of small pancreatic lesions leading to a multitude of imaging investigations. Our experience also highlighted that the 111In-DTPA-octreotide uptake in pancreatic uncinate process may be physiological and its interpretation must, therefore, be cautious.

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EP610
Insulinoma with confusing imaging: a case report
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Introduction
Insulinoma is a rare pancreatic tumor. It is the most frequent cause of organic hypoglycemia due to endogenous hyperinsulinism.

Case report
A 55-year-old woman was admitted in our department for the management of a recurrent hypoglycemic coma. Endogenous hyperinsuliniic hypoglycemia was confirmed with a spontaneous hypoglycemia. Plasma blood glucose was 0.25 g/l concomitant to a high insulinemia of 31.5 μU/ml (≥ 3) and C-peptide level of 3,16 ng/ml (≥ 0.6) In imaging investigations, abdominal CT scan and endoscopic ultrasound were both normal. A complementary nuclear imaging by OctreoScan was performed and detected the presence of 2 pancreatic lesions: one in the uncinate process and the other in the tail. Abdominal MRI was performed and concluded to the presence of a unique lesion of the pancreas tail. Our patient was then proposed for surgery of the two insulinomas. Per-operative exploration concluded to the presence of a single corporal tumor mass of the pancreas of 1.5 cm. A left pancreatectomy was then performed. Our patient had resolution of symptoms after surgery. The follow-up is 6 months to date.

Conclusion
This case highlights the difficulty of the radiological identification of small pancreatic lesions leading to a multitude of imaging investigations. Our experience also highlighted that the 111In-DTPA-octreotide uptake in pancreatic uncinate process may be physiological and its interpretation must, therefore, be cautious.

DOI: 10.1530/endoabs.81.EP610
Introduction
Renal cell carcinoma (RCC) is the most common type of malignant renal tumors in adults. It is often difficult to detect it precociously since early-stage renal tumors are usually asymptomatic and non-palpable. We report a case of RCC revealed by acute adrenal insufficiency (AAI).

Case report
Mr. A.B, 46 years old, 30 pack-year smoker, with a medical history of gout treated with Allopurinol, was admitted to our department for acute adrenal insufficiency. The anamnesis revealed a significant weight loss, asthenia and melanodermia. The evolution was marked by acute abdominal pain with vomiting, leading the patient to consult our emergency department. A baseline blood sample revealed hypotension, hypokalemia and functional renal failure. The patient immediately received intravenous hydrocortisone hemisuccinate with hyperhydration. The diagnosis of primary AAI was confirmed by a low plasma cortisol level (99 nmol/l) in the face of high adrenocorticotropin hormone (ACTH) level (>2000 pg/ml). Adrenal computed tomography (CT) showed hypostrophic adrenal glands and a right corticomedullary renal mass (38*47*48 mm). Renal magnetic resonance imaging (MRI), performed for a better characterization of this mass, showed a right medio-renal tumor with a central necrotic zone and exophytic development, without signs of locoregional extension. A tumorectomy was performed. Anatomopathological examination revealed RCC.

Discussion
An AAI revealing a RCC has been reported in a few publications. In those cases, the adrenal insufficiency was related to bilateral adrenal metastases. However, in the present study medical imaging showed hypostrophic adrenal glands suggesting an auto-immune mechanism. Indeed, the increasing use of ultrasound, abdominal CT and more recently MRI has increased the diagnosis of renal cancers at a presymptomatic stage to nearly 70%.

Results
Of the 88 patients included in this report, 30 (34%) were males, 58 (66%) were females with a median age of 43.5 years (interquartile range 26-53.7). No more was found in 42 patients (47.7%). The other 46 patients (52.3%) had an underlying PPGL predisposing genetic mutations. The most commonly mutated gene was SDHB (11/88), followed by SDHD (8/88), RET (6/88) and SDHC (3/88). There was a tendency for more locally invasive and metastatic PPGL in the patients with underlying genetic alterations, especially SDHB mutations, but this did not reach statistical significance. Although the majority of patients achieved cure (60.5%), 26 patients (29.5%) had persistent/recurrent disease. There was no difference in the final outcome between those with underlying genetic mutations and those without mutations.

Conclusions
In this study, 52.6% of PPGL carry underlying genetic mutations. SDHB is the most commonly mutated and associated with higher risk of locally invasive and distant metastases. There is tendency towards locally invasive and distant metastases in those carrying underlying mutations but the final outcome was similar between those with and those without underlying mutations.

Frequency of CYP1B1 gene polymorphism in obese and non-obese women with hormone-dependent endometrial cancer

Aim
There is a significant link between the increased activity of estrogen and its metabolites in endometrial carcinogenesis. Polymorphisms of the gene involved in metabolism of estrogen can modulate risk for the development of endometrial cancer. CYP1B1 plays an important role in estrogen metabolism. In our study, the frequency of three CYP1B1 gene polymorphisms (4326 C>T, 4390 A>G and 355 G>T) were studied in obese and non-obese women with endometrioid endometrial carcinoma and healthy controls.

Methods
Genotype were determined in DNA from peripheral blood lymphocytes of 44 women with endometrial cancer and 47 healthy age-matched controls by restriction fragment length polymorphism polymerase chain reaction (RFLP-PCR).

Results
Polymorphism 4326 C>T was verified in 70.5% of women with endometrial carcinoma and 59.6% of healthy controls (P=0.277). In the group of women with endometrial cancer, polymorphism 4326 C>T was verified in 72.2% obese and 69.2% of non-obese women (P=0.831). Polymorphism 4390 A>G was verified in 38.6% of women with endometrial carcinoma and 34.0% of healthy controls (P=0.649). In the group of women with endometrial cancer, polymorphism 4390 A>G was verified in 27.8% obese and 46.2% of non-obese women (P=0.218). Polymorphism 355 G>T was verified in 43.2% of women with endometrial carcinoma and 59.6% of healthy controls (P=0.118). In the group of women with endometrial cancer, polymorphism 355 G>T was verified in 44.4% obese and 42.3% of non-obese women (P=0.888).

Conclusion
There was no statistically significant difference in the frequency of the CYP1B1 gene polymorphism in our group of women with endometrial carcinoma and healthy controls and in women with endometrial carcinoma regardless of their body mass index.
**EP616**

**Ectopic parathyroid adenoma of the recurrent laryngeal nerve (RLN) chain lymph node**

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**Introduction**

Parathyroid adenoma can be localized in an ectopic situation, especially at the mediastinal level. The localization at the level of the RLN chain lymph node has not been reported yet.

**Case presentation**

A 67-year-old woman without clinical signs of hyperparathyroidism, having undergone a left isthmolectomy for a thyroid nodule suspected of being malignant, with intraoperative discovery of lymphadenopathy of the left RLN chain lymph node. The anatomo-histopathological analysis revealed a follicular adenoma and for the lymphadenopathy a morphological appearance in favor of a parathyroid adenoma which was confirmed by immunohistochemistry. The preoperative work-up was unremarkable with a calcium level of 98 mg/l (84-102) and albuminemia at 44g/l (32-46) and phosphoreemia at 37 mg/l (23-47).

The diagnosis of non-functional ectopic parathyroid adenoma of the RLN chain lymph node was discovered incidentally on histological study.

**Conclusion**

This case illustrates an unusual location of a non-functional ectopic parathyroid adenoma of the RLN chain lymph node.

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**EP617**

**Metastatic medullary thyroid carcinoma with diagnostic and therapeutic challenges: a case report**

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**Introduction**

Medullary thyroid cancer (MTC) is a neuroendocrine tumor that arises from the parafollicular C-cells of the thyroid gland with a tendency to regional and distant metastases. It is a rare tumor, making up about 3% of all thyroid malignancies. MTC occurs in both heritable and sporadic forms, early diagnosis is important as it can improve treatment outcomes. We report a case of metastatic medullary thyroid cancer with both diagnostic and therapeutic challenges.

**Case presentation**

37-year-old man presented with anterior cervical mass. CT scan showed a cervico-medial mass measuring 29 x 56 x 66 mm, with calcitonin level at 1890 ng/l. The patient underwent total thyroidecomy, with removal of the mediastinal mass and cervical lymph nodes. The pathology revealed initially a poorly differentiated malignant tumor proliferation of thymic origin. Immuno-histochemistry was in favor of a neuroendocrine carcinoma. An anatomical-pathological re-reading revealed a medullary thyroid carcinoma aspect with secondary mediastinal location. One year later, the cervico-thoracic CT scan showed a retro clavicular mass of 31.3 mm x 26 mm x 20 mm, with intimate contact with the left common carotid artery, end intra-parenchymal micronodules measuring 4.4 mm and 4.2 mm, in favor of metastasis. The patient underwent an exeresis of the mass with surgical difficulty due to the intimate contact of the tumor with the cervical vascular axis. The patient was thereafter referred to medical oncology for systemic treatment.

**Discussion**

Distant metastases in MTC are observed at presentation in 7-23% of patients, they often affect multiple organs including lungs, bones and liver, and they are frequently associated with persistent disease in the neck. Calcitonin and carcinoembryonic antigen (CEA) with conventional radiographic modalities are widely used for the diagnosis, prognosis, and follow-up of MTC patients. In our case, the metastatic MTC was diagnosed with difficulty in the anatomo-pathological reading, with a loco-regional recurrence presenting a difficulty in the surgical management.

**Conclusion**

MTC is a rare disease with a high risk of not being cured by the initial treatment.

In cases of metastasis, the approach depends on the severity and rate of progression of disease. Metastatic MTC can be treated with limited surgical resection, or medical management with tyrosine kinase inhibitors (TKIs) or another agent.

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**EP618**

**Pro-inflammatory biomarkers in Papillary thyroid cancer**

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**Introduction**

Papillary thyroid carcinoma (PTC) is the most frequent endocrine malignancy. Apart from genetics, autoimmune disease may play an important role. Autoimmune thyroiditis is associated with an increased risk of PTC. Apart from genetics, autoimmunity has been implicated in its pathogenesis. In this context, we set out study the role of Pro-inflammatory cytokines in PTC in South Indian population.

**Material and methods**

This prospective case-control study was conducted on surgically managed PTC patients. Institutional ethical committee approval was obtained. Diagnosis of PTC was confirmed on imaging, fine needle aspiration cytology and histopathology. Exclusion criteria were subjects with any systemic or chronic inflammatory disease or any medication which interferes with the normal function of the hypothalamic-pituitary-gonadal axis. Serum samples were collected from 66 PTC subjects and 64 age matched healthy controls. Interleukin-6 (IL-6), Tumour necrosis factor-alpha (TNF-α) and high sensitive C reactive protein (hsCRP), lep levels were measured in all serum samples. Statistical analysis was performed by one way ANOVA with Dunnet’s test and Pearson correlation tests.

**Results**

The mean hsCRP level in PTC and controls were 18.4 ± 3.1 mg/ml and 5.5 ± 1.2 mg/ml respectively. The mean TNF-α level, IL-6 level and Leptin levels were 294 ± 30 pg/ml, 12.8 ± 4.5 pg/ml and 1.97 ± 0.7 ng/ml respectively. Serum hsCRP level in controls was 3.4 ± 1.6 mg/l. There was statistically significant difference of all the pro-inflammatory cytokines compared to controls (P value < 0.05) with negative correlation for leptin levels.

**Conclusions**

Our study shows raised titers of pro-inflammatory markers – IL-6, TNF-α and hsCRP, while reduced leptin levels correlated with PTC suggesting a contributory role. But, the exact immuno-modulatory role and pathogenetic mechanism needs more research.

**Key words:** Papillary thyroid cancer; Tumour necrosis factor; Interleukin-6; Auto-immunity; Leptin

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**EP619**

**The different faces of a long-lasting metastasized pancreatic neuro-endocrine tumor with calcitonin paraneoplastic secretion and cardiac carcinoid**

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**Introduction**

Besides medullary thyroid carcinoma (MTC), increased calcitonin serum concentrations may be due, rarely, to neuroendocrine tumour (NET) ectopic secretion, especially those of the foregut (pancreatic/lung). Patients with NETs and right-sided heart failure due to cardiac carcinoid have a worse prognosis than those presenting without.
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**EP621**

Medullary thyroid Cancer, an experience from a tertiary care hospital of a developing country

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Background

Medullary thyroid carcinoma is a rare type of thyroid cancer that is either sporadic or familial. It occasionally occurs alongside parathyroid hyperplasia and pheochromocytoma as part of MEN2A. Our aim was to study the presence and patterns of above mentioned characteristics of medullary thyroid carcinoma in our population.

Methodology

This is a retrospective study conducted in a tertiary care hospital of Pakistan in which data of medullary thyroid cancer over past 20 years was reviewed. Data from 32 patients was analyzed after fulfillment of the inclusion criteria. Their clinical, pathological, biochemical and treatment outcomes were recorded through retrospective review of their medical record files.

Results

The mean age of patients with medullary thyroid carcinoma (MTC) was 42.88 ± 2.67 in our study, with male to female ratio of 2:1. 68.8% of MTC patients were sporadic and 31.2% were familial in our study. 81.3% of patients presented with neck swelling, lymph nodes were palpable in 43.8% of patients and distant metastasis were present in 25% of the patients. The rates of metastasis were highest in bones followed by lungs and liver (12.5%, 9.4%, and 3.1% respectively). Histologically, the mean tumor size was 7.62 ± 3.64 with 8 (25%) having distant metastasis. Lymph node metastasis was present in 19 (59.3%) of the patients, out of which 16 had bilateral involvement. Over 50% of carcinomas in our study were unifocal, followed by bifocal (21.9%) and multifocal (9.4%). Mean pre-surgery calcitonin was 11225.7 ± 4043.57 which then decreased to a mean of 244.43 ± 113.48 post surgery. Mean pre-surgery CEA level was 25.08 ± 7.23 which then decreased to 0.0645 ± 0.044 post surgery. Hyperparathyroidism was found in two patients while pheochromocytoma was found in one patient only. Two patient were positive for RET gene mutations. Total thyroidectomy was done in 26 (81.2%) of the patients while one patient had subtotal thyroidectomy followed by complete thyroidectomy as initial FNAC was Bethesda category 3. Surgery was not performed in 5 patients due to distant metastasis or palliative intent. Chemotherapy was given only to one patient while XRT was performed in two patients.

Conclusion

Medullary thyroid carcinoma usually presents in fourth decade of life with male predominance and mostly sporadic occurrence. Total thyroidectomy with subsequent serial calcitonin and CEA levels thereafter are the mainstay of treatment and follow-up.

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**EP620**

A NEM 2A with mutation in a gene outside panel ROTERC

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Introduction

Multiple endocrine neoplasia type 2 is an inherited syndrome characterized by the characteristic combination of medullary thyroid cancer, pheochromocytoma and primary hyperparathyroidism. We report one case with phenotype-genotype mismatch.

Observation

Patient A. T is 45 years of age with a family history of thyroid bone marrow cancer (CMT) and sister brain cancer, father colon cancer, with no personal history of disease. A 60 mm long-axis left adrenaloma during a nephritic colic test with 4x normal urinary metanephrins. The diagnosis of primary hyperparathyroidism was raised in the presence of hypercalcemia: 2.9 mmol/l, Phosphoremia: 0.7 mmol/l and confirmed by normal PTH. The topographic assessment concluded a parathyroid adenoma and a multinodular goiter. The absence of medullary thyroid cancer (CMT) decreased the probability of NEM2A but this is still possible. The patient received a left adrenalectomy. A The genetic study did not reveal any pathogenic variant or VSI.

Discussion

The association of pheochromocytoma, hyperparathyroidism and multinodular goiter, as well as the family history of CMT and cerebral cancer in the sister and colon cancer in the father, suggested a mutation that does not belong to the ROTERCC panel. Our observation attested to the value of conducting a genetic study for personalized medical care of patients and for establishing genetic counseling for patients and their families.

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**EP622**

Refractory papillary thyroid carcinoma treated with sorafenib: an Algerian experience

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Introduction

5-10% of papillary thyroid carcinoma develop metastatic disease, of which about 60-70% will become refractory to radioactive iodine. Significant negative impact on the prognosis and an average life expectancy of 3 to 5 years.

Material and method

Since 2018, patients with refractory thyroid carcinoma and considered to be progressive according to the RECIST criteria have been treated with anti tyrosine Kinase type sorafenib.

9 patients treated: an anaplastic carcinoma, a medullary carcinoma and 7 differentiated carcinomas. 3 women/6 men, average age: 56 years old. Tumor regression was observed in 3 patients but stopped in 2 due to the onset of a serious side effect, with rebound phenomenon in one of them; lesion stability in 3 patients; disease progression leading to discontinuate the treatment in 3 patients.
Discussion
Refractory thyroid cancers are rare but responsible for the majority of cancer-related deaths. The use of kinase inhibitors has improved the outcome of these patients. On the other hand, in addition to their high cost, they have a notable toxicity, responsible of major side effects impairing the quality of life, for an uncertain response. Due to the complexity of these treatments, these patients are at best managed by multidisciplinary groups.

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EP623
Hungry bone syndrome in the post-operative management of severe primary hyperparathyroidism: a case report
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Introduction
Hungry bone syndrome (HBS) is a rare complication of parathyroidectomy for primary hyperparathyroidism. We report a case of HBS after parathyroid surgery for severe primary hyperparathyroidism.

Case presentation
A 46-year-old woman was admitted with generalized weakness and difficulty walking due to progressive worsening of low-back pain. Clinical examination revealed tachycardia at 110 bpm and chest deformity. Laboratory results revealed hypercalcemia at 185 mg/l and hypophosphatemia at 19 mg/l. The parathyroid hormone (PTH) concentration was at 4936 pg/ml (normal 15-65) and the alkaline phosphatase concentration reached 478 U/l (normal 40-150). Medical treatment was initiated with rehydration, forced diuresis and intravenous infusion of biphosphonates. Ultrasound of the neck and Sestamibi scan showed a localized adenoma. The parathyroidectomy was performed and anatomopathological examination confirmed parathyroid adenoma, weighing 4 g and measuring 3*2*0.6 cm. The postoperative period was characterized by prolonged hypercalcemia, hypophosphatemia and normal PTH levels, which was consistent with the diagnosis of HBS. The patient was discharged on high doses of calcium carbonate and alfacalcidol.

Discussion
HBS refers to the rapid, profound, and prolonged hypocalcaemia associated with hypophosphatemia and hypomagnesaemia, and is exacerbated by suppressed PTH levels, which follows parathyroidectomy in patients with severe primary hyperparathyroidism and preoperative high bone turnover. Although HBS does not have a consensus definition, most resources define it as profound hypocalcaemia of less than 8.4 mg/dl that persists for more than four days postoperatively. The severe hypocalcaemia is believed to be due to the greatly increased skeletal usage of calcium, thought to occur as a result of removal of the effect of high circulating parathyroid hormone (PTH) levels on bone, with immediate arrest of bone resorption in the face of continuing and enhanced bone formation. The duration of the HBS is the time taken to remineralise the skeleton, which is also mirrored by normalisation of bone turnover markers, by healing of radiological features of osteitis fibrosa cystica and brown tumours and by significant gains in bone mass. Treatment is aimed at replenishing the severe calcium deficit and at restoring normal bone turnover with the use of high doses of calcium and active metabolites or analogues of vitamin D.

Conclusion
HBS is relatively uncommon, but a serious side effect of parathyroidectomy. It can bring significant morbidity related to the consequences of hypocalcaemia in the case of patients in whom it is not recognized and corrected promptly.

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EP624
A rare case of gonadotropin independent precocious puberty in young child
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Introduction
Adrenocortical carcinoma (ACC) is a rare malignancy with overall incidence of 0.7–2.0 cases/million. It’s a rare & aggressive childhood cancer with a reported incidence of 0.2–0.3 new cases per 1 million. It has Bimodal distribution - at first decade - 85% functional & 5-6th decade of life 15-30% functional. Paediatric virilising adrenal tumours have a better prognosis after complete resection than in adults. Surgery is the mainstay of treatment. Even after complete resection, a high risk of recurrence of ACC remains, 2yrs 3months – 1st born male child brought by parents with complaints of appearance of pubic & axillary hair, enlargement of both breasts, accelerated height gain, increase in penile length without any increase in testicular size. On examination a palpable mass was noticed in right hypochondrium which was firm in consistency. A provisional diagnosis of Gonadotropin independent precocity (GIPP) due to adrenal mass lesion was made. Biochemical and Radiological evaluation was suggestive of Adrenocortical cancer. Subsequently child underwent Right adrenalectomy. Postop was uneventful and he was discharged on Day 6.

Discussion
Here is a male child with Premature development of axillary, pubic hair with features of androgenisation, Increase in penile length without Increase in testes size, with Bl/Gynecomastia, accelerated Ht gain, with palpable mass in RUQ which Implies -Precocious Puberty of Peripheral origin (Gonadotropin Independent) due to Adrenal neoplasm.

Conclusion
Though ACC is a rare cause of GIPP in paediatric age group, this entity should be considered in differential diagnosis.

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Environmental Endocrinology

EP625
The development of a GLP protocol for the measurement of 17β-estradiol and testosterone in the H295R steroidogenesis assay, Test No 456
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Regulators are concerned about the potential for environmental chemicals such as agrochemicals and their metabolites to perturb hormone systems. This has led to recommendations for the testing of potential endocrine disrupting chemicals. The Steroidogenesis H295R assay is an in vitro cell model used to investigate compound effects on steroid hormone biosynthesis, specifically 17β-estradiol (E2) and testosterone (T). The human H295R adrenocarcinoma cell line expresses genes that encode for all the key enzymes for steroidogenesis and thus forms one of the required OECD in vitro tests (TG456) for the assessment of potential endocrine disrupting chemicals. Although it is possible to assess hormone levels with ELISA we elected to perform the TG456 assay with LC-MS/MS hormone detection, avoiding the test item interference issues reported for immunoassay-based readouts. We describe herein the implementation of a robust GLP bioanalytical method for the detection of testosterone and 17β-estradiol in the steroidogenesis assay, to LLQ levels of 10 pg/ml for each hormone. This method has been used to correctly identify inducers and inhibitors of T and E2 production while remaining unresponsive to a negative chemical. We present the impact this has on assay performance with respect to the proficiency items and discuss the benefits of the optimised bioanalytical protocol on Test No 456 performance.

References
1. Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC)/No 1107/2009. European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC)Niklas Andersson, Maria Arena, Domenica Auteri, Stefania Barnaz, Elise Grignard, Aude Kienzler, Peter Lepper, Alfonso Maria Lostia, Sharon Mum, Juan Manuel Parra Morte, Francesca Pellizzato, Jose Tarazona, Andrea Terron and Sander Van der Linden DOI https://doi.org/10.2903/j.efsa.2018.5311

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EP626
Clinical and demographic analysis of the structure of telemedicine “doctor-patient” consultations of the Endocrinology Research Centre
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Rationale
The COVID-19 pandemic has accelerated the development of telemedicine technologies. Today there is evidence of the successful use of telemedicine in various areas of healthcare, particularly in endocrinology. At the same time, there is not enough information for efficient integration of telemedicine into the routine management of patients.

Aim
The aim of this work was a clinical and demographic analysis of “doctor-patient” telemedicine consultations (TMC) conducted at the Endocrinology Research Centre (Moscow, Russian Federation) in 2020-2021.

Materials and Methods
A cross-sectional, single-centre, retrospective study was conducted. The study included all patients who received at least one TMC at the Endocrinology Research Centre in 2020-2021. Clinical and demographic information was analyzed (gender, age, region of residence, disease code according to ICD-10). All patients signed an informed consent for the telemedicine consultation. The received data were processed using the Microsoft Office software.

Results
In 2020, 1548 TMC were held, in 2021 - 4180 TMC. Among adults, women predominated in the structure of TMC (83.86%), among children there is a tendency towards equivalent appeals for boys and girls (in 2021 - 45% and 55%, respectively). The median age of adult patients in 2021 was 38 years [31;53], among children - 11 years [7;14]. In 2020, residents of 74 regions of the Russian Federation applied for TMC, in 2021 - of 82 regions. There is a tendency for patients from the Central, Volga, Southern and North Caucasian federal districts to predominate in the structure of TMC. In the nosological structure of TMC among adults diseases of the thyroid gland (35.2%), parathyroid glands (6.8%), diabetes mellitus types 1 and 2 (5.8%), ovarian dysfunction (5.6%) and obesity (4.7%) predominated. In children, TMC the most frequent nosologies were type 1 diabetes mellitus (49.8%), thyroid diseases (13.9%), adrenogenital disorders (5%), and polyglandular dysfunction (4%).

Conclusion
TMC proved to be in demand in patients with a variety of endocrinopathies. It is important to analyze both the TMC market and the effectiveness of remote counseling for various nosologies in order to determine the place of telemedicine in the modern healthcare structure and introduce TMC into the system of clinical recommendations.

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EP627
Abstract Withdrawn
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EP628
Exposure to the endocrine disruptor cadmium alters human aortic endothelial cells homeostasis
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Cardiovascular diseases (CVDs) represent a complex and multifactorial issue that results from a combination of behavioural, genetic and environmental factors. Toxic metal contaminants, many of which act as endocrine disruptors (EDs), have been identified as potential risk factors for CVDs. Among EDs Cadmium (Cd), present both in cigarettes and in food, has been suggested to be cytotoxic on vascular endothelium, likely leading to blood pressure increase and vascular inflammation. We previously demonstrated that Cd exposure increased TNF-α, IL-6 and IL-8 mRNA in HUVEC. To further evaluate and characterize the potentially detrimental effect of Cd exposure on Endothelial cells. The effect of Cd exposure on the vascular system was evaluated by using a human in-vitro model for vascular endothelial cells, the human Aortic Endothelial Cells (HAEC). Firstly, we evaluated HAEC morphology after 24 h exposure to increasing Cd concentrations, ranging from 1 to 10 μM. Cd induced a collapse of cytoskeleton, with a toxic effect already evident upon treatment with 1 μM. The effect on cellular morphology was accompanied by a reduction of cell proliferation and an increase in cell death. In addition, the Bas/Becl2 ratio increased. Moreover, Cd affected the expression of pro-inflammatory cytokines, showing an increase of both IL-6 and IL-8 upon 5 and 10 μM Cd exposure, confirming our previous results obtained in HUVEC. Accordingly, a decrease of endothelial adhesion molecules, such as V-CAM and I-CAM, was observed. In conclusion, our results suggest that Cd exposure affects HAEC morphology and behaviour inducing cytotoxicity and apoptosis. In addition, already at low concentration, Cd exposure induces a pro-inflammatory state with production of pro-inflammatory cytokines and reduction of endothelial adhesion molecules, strongly suggesting that this heavy metal is able to alter endothelium homeostasis.

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EP629
Epidemiological characteristics and psychological distress of well-controlled endocrine outpatients from Crete, Greece during the COVID-19 Pandemic: preliminary results of the EPITOME study.
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Aim
To explore the epidemiological characteristics and symptoms of psychological distress of well-controlled endocrine patients without a diagnosis of a psychiatric disorder attending the Endocrine outpatient clinic of the University Hospital, Heraklion, Crete, Greece during the COVID-19 pandemic. Methods: Eighty-four patients participated by completing questionnaires about demographics, endocrine diagnosis, covid infection, preventive measures, vaccination status, source of support and lifestyle changes. Psychological distress was assessed by means of the Greek version of the DASS 21 questionnaire. Ethical approval was obtained by Institutional Review Board and all participants provided written informed consent.

Results
Patients’ mean age was 50.8 years; 76.2% were female, 68.7% married and 57.8% employed. Most common endocrinopathies were thyroid diseases, diabetes mellitus and pituitary disorders. Only two patients had been infected with COVID-19 and 31% were a close contact to a COVID-19 patient. The level of adherence to COVID-19 preventive measures was 96.4%, whereas 21.7% hesitated to visit a healthcare professional due to the fear of becoming infected. Sixty-four (77.1%) had at least one dose of the COVID-19 vaccine. The majority cited family as their supportive network (84.3%) followed by friends and neighbors (16.9%) and only 2.4% the social services. Forty-one reported changes at eating habits and thirty one had gained weight; twenty-three had decreased their physical activity and thirty-one dropped hobbies due to the pandemic. Approximately one in four reported sleep difficulties. The majority did not present symptoms of stress (71.43%), anxiety (80.52%) or depression (80.3%). Patients with chronic endocrine disease reported stress symptoms less frequently.

Conclusions: This is the first study in Crete, Greece regarding social parameters and psychological distress due to the COVID-19 pandemic in endocrine patients.
Our participants follow the recommended preventive measures and are mostly vaccinated. They would seek help from family and friends if required and do not rely on state-provided sources for support. Contrary to numerous studies indicating that depression and anxiety increased during the present pandemic, we found that our sample had low rates of moderate/severe anxiety/depression. We hypothesize that this is related to the well-controlled endocrine problems, and to protective factors such as marital status, employment, family support, as well as the vaccination status and compliance with preventive measures. This is an ongoing study with an aim to define whether different demographics and social parameters may influence levels of distress in this patient group and to develop strategies which may improve well-being during severe crises in endocrine patients.

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EP630
Comparison of perceived sufficiency of information, sources of information, worries about the pandemic and psychological distress between endocrinology patients and staff at the outpatient department of the university hospital, heraklion, crete: preliminary results of the EPITOME study

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Background
Psychological distress is elevated during pandemics such as the COVID-19 outbreak both in health care professionals and patients.

Aim
To compare worries about the COVID-19 pandemic, need and sources of information, and psychological distress between endocrinology patients and staff at an outpatient department of the University Hospital, Heraklion, Crete, Greece

Methods
One hundred and four patients and sixty members of staff completed questionnaires about demographics, need for information, sources of information, worries about the COVID-19 pandemic and the Greek version of the DASS-21 for psychological distress. Ethical approval was obtained by Institutional Review Board and all participants provided informed consent.

Results
Mean age of staff was 41.2 years and patients 50.6 years (<0.001), with predominance of women in both groups. The majority of both groups stated that they worried about the pandemic reporting a moderate degree of worry. Main worry was the risk of contagion and infection of their family, and this was more prevalent for staff (P<0.036). Regarding the need for information on a 5-item Likert scale (1: prefer having no more information than needed; 5: prefer as much information as possible) both groups reported moderate degrees of information needs. Regarding specific aspects of COVID-19 infection, staff was better informed about symptoms, prognosis, infection route, preventive measures (p, 0.001, 0.032, 0.001, 0.047 respectively) with no differences about information on treatment and the COVID-19 vaccine, compared to patients. Both groups preferred formal sources of information. Staff relied mainly on information by health professionals (P=0.006) whilst patients showed an additional preference for informal sources (P=0.022). There were no differences in stress and anxiety symptoms between the two groups, which showed low rates of both; few participants displayed moderate/high symptoms of depression, and these were mostly in the staff group (P=0.040).

Conclusions
The current study highlights differences between endocrine patients and staff regarding their main worry about the pandemic with staff being more worried about the safety of family/relatives likely due to their higher chance of exposure.

Although both groups were informed by formal sources, staff was more informed on most aspects of COVID-19, but this did not include treatment and the COVID-19 vaccine, perhaps due to the scarcity of studies. Among participants, staff reported more often moderate/severe symptoms of depression. These results are relevant when designing policies on information on pandemics and supportive measures for patients and staff in General Hospitals.

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EP631
Perception of training and job perspectives of the specialty of Endocrinology and Nutrition among final-year residents.

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Introduction
Medical specialization model in Spain is carried out through specialized health training, through the residency program. Residents are a key element for the proper functioning of today’s National Health System. The aim of the study is to analyze, by an anonymous survey, the opinion of three aspects among final-year residents in Endocrinology and Nutrition (E&N): self-assessment of the knowledge acquired, working prospects, and training consequences arising from the pandemic COVID-19.

Materials and methods
Cross-sectional observational study using a voluntary and anonymous online survey, shared among final-year national interns in the last year of the E&N program, carried out between June-July 2021. The survey consisted of 20 questions. The results were analyzed with the SPSS version 25 statistical program.

Results
Fifty-one responses were obtained, 66% of the residents, most of them from the central region of the country. Fifty-nine percent of the respondents were trained in tertiary hospitals with more than 800 beds compared to 41% who were trained in centers with between 200-800 beds. Overall perception of their knowledge was 7.8 out of 10, being diabetes and thyroid the best rated sections, followed by nutrition, pituitary, adrenal and finally lipids. Most external rotations were in thyroid and nutrition areas. A total of 96.1% residents, carried out some activity associated with COVID-19, with a training deterioration of 6.9 out of 10. 88.2% have cancelled their rotations and 74.5% have extended their working schedule. The average negative emotional impact was 7.3 out of 10. Most of them carry out research work, spending time out of their working day to do so. 80.4% would like to continue in their training hospital, remaining 45.1%. 56.7% have an employment contract of less than 6 months, most of them practicing Endocrinology.

Conclusion
The perception of the knowledge acquired during the training period is a ‘B’. Residents consider that the pandemic has led to a worsening of their training, generating a negative emotional impact. Employment outlook after completing the residency can be summarized as: temporality, practice of Endocrinology and hospital mobility.

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EP632
Bisphenol-A and Pentocholorophenol Sodium Levels in Patients with Acne Rosacea

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**EP633**

**Histology of the diffuse endocrine system of the lungs in ontogenesis and in pathological conditions in Uzbekistan**

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**Background**

The study of fundamental questions related to the analysis of recent advances in the field of cellular and molecular pathways involved in lung organogenesis provides a basis for understanding the pathogenesis of acute and chronic diseases of this organ. Cells of the diffuse endocrine system - apudocytes (APUD) absorb the precursors of biogenic amines introduced from the outside and subject them to decarboxylation with further formation of biogenic amines and peptide hormones. The APUD system also includes innervated clusters of endocriocyt - neuroepithelial bodies (NETs).

**Purpose**

Identification in a comparative aspect of the features of the structure of the endocrine apparatus of the APUD-system of the lungs during embryogenesis, as well as in the pathology of the organ caused by inflammatory processes. Material and methods. We studied histological prepartations of the lungs in human fetuses at 9-28 weeks of fetal development and full-term newborns.

**Results**

By the 11th week of their embryonic development, intrabronchial bronchi appear, the same picture is observed in fetuses of 12 and 13 weeks. Carlilaginous plates are found only in the walls of the lobar and segmental bronchi. In the lungs of fetuses of 9-10 weeks of development, endocrine cells in the epithelium of the bronchi and in the epithelial tubules are not found. Starting from 11 weeks, argyrophilic apudocytes and NET are detected in the large bronchi. In the tubular and alveolar stages of histogenesis, the number of endocrine structures increases, and it is especially significant in the distal parts of the bronchial tree. It should be noted that the branching of the bronchial tree is ahead of the development of the endocrine apparatus in it. Open-type cells are found in the proximal sections of the bronchial tree, while closed-type cells are found in the distal ones. Apudocytes and NETs are found in all children with inflammatory lung disease. Their number is much greater than in the lungs of children who died from diseases not related to the respiratory organs. Closed-type apudocytes are often found in the bronchial epithelium.

**Conclusions**

We found that open-type apudocytes appear in large bronchi during the development of the lungs, i.e., earlier generations of branching of the airways. Closed-type apudocytes are more characteristic of newly formed bronchial tubes. NETs during lung development appear later than apudocytes and are also more numerous in the developing small bronchi and respiratory region.

**EP634**

**Effect of nighttime melatonin intake on vitamin D levels**

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**Introduction**

Melatonin is involved in many physiological processes, including the regulation of circadian rhythms, sleep, antioxidant effect, aging, tumor growth, reproduction and bone formation. The latter function is also regulated by the metabolism of vitamin D. Our goal during this study is to detect a possible increase in vitamin D levels under the effect of exogenous melatonin.

**Participants and methods**

Different anthropometric parameters were collected (weight, height, body mass index, percentage of fat). The experimental protocol is carried out in a randomized clinical trial between an overnight intake (around 9 p.m.) of melatonin and double-blind placebo, once in the middle of the follicular phase and once in the middle of the luteal phase. The dose is determined at around 9 a.m. the next day, using an immuno-electro-chemiluminescence method on the Cobas 6000 analyser from Roche.

**Results**

Ten healthy young women between the ages of 20 and 23 were included in our study after obtaining their consent. The mean age of the participants was 21.63 ± 0.94 years. The average height of our patients was 165.72 ± 3.38 m. The average weight of our patients was 59.45 ± 3.5 kg. Vitamin D levels were significantly higher after taking melatonin (mean 13.6 ± 7.9 ng/ml) than after taking placebo (mean 12.68 ± 5.7 ng/ml) during the follicular phase (P = 0.001). Whereas, the increase in vitamin D with the intake of melatonin (mean of 15.8 ± 7.8 ng/ml) compared to the taking of placebo (mean of 14.6 ± 5.7 ng/ml) was not significant during the luteal phase (P = 0.7). In addition, there was no significant variation in vitamin D levels between the luteal phase and the follicular phase when taking placebo (P = 0.07) and when taking melatonin (P = 0.25).

**Conclusion**

Melatonin can regulate the metabolism of vitamin D. Indeed the vitamin D receptor can act as a nuclear receptor for melatonin. Further studies are essential to better explain the relationship between melatonin and vitamin D according to menstrual cycles.

**EP635**

**Recurrent hypoglycemia : looking for an unusual cause**

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Hypoglycemia in non-diabetic patients is a rare event, and autoimmune hypoglycemia with the presence of positive anti-insulin antibodies is even rarer. We report the case of a 15 years old non diabetic female patient, she was referred to our hospital for recurrent hypoglycemia for 2 weeks before admission to hospital, these are severe hypoglycemia with impaired consciousness. The first step was to eliminate the general causes and factitious hypoglycemia. Adrenal insufficiency was also ruled out. A 72-hour fasting test was performed and the peptide C assay (< 0.15 ng/ml), and Insulinemia (<1 mU/l) were not in favor of endogenous insulin secretion. Autoimmune origin was suspected. The dosage of anti-insulin antibodies was realized with a positive result of 0.7 (Normal: 0.4).

The patient was put on corticosteroid therapy with a regression of hypoglycemic episodes, pending the results of the anti-insulin antibodies after 2 months of corticosteroid therapy. The case of our patient illustrates the importance of an exhaustive exploration in the face of hypoglycemia and of thinking about the autoimmune cause, which remains rare, especially in non-diabetic patients. Keywords: Hypoglycemia-non-diabetic-autimmune-insulin.

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**EP636**

Di-Butyl-Phthalate (DBP) exposure impact on human masculine reproductive hormones. A review of literature

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Background

Phthalates are currently used in medical devices, adhesives as plasticizers. Masculine reproductive toxicity is the greatest concern associated with exposure, known as the “phthalate syndrome”. The European Chemicals Agency has recognized di-butyl-phthalate (DBP, CAS 84-74-2) as an endocrine disruptor with deleterious effects on reproductive hormones, with an estimated human intake of 0.84-5.22 μg/kg/day. Effects reported include the disruption of Sertoli and Leydig cells with decreased testicular production of androgens, known as the “testicular dysgenesis syndrome”. However, a quantitative relationship between DBP exposure and hormone levels is not available in the literature.

Objective

Review the scientific literature on DBP exposure measured as urinary metabolites, and corresponding reproductive hormone effects such as testosterone, in human adult men.

Methods

Four online scientific databases [PubMed, ISI Web of Science, Embase, Cochrane library] were searched in January 2022. The search criteria included English-language full text publications, human, adult men, serum testosterone total (TT) and testosterone free (fT) concentrations, urinary DBP metabolites concentrations (creatinine-adjusted values). Studies with n>100 participants were selected. Studies with a low score on qualitative assessment were excluded.

Results

Of the 329 search results, 11 toxicological studies met the inclusion criteria. Nine were cross-sectional studies conducted in East-Asia (4), Europe (4), North America (2), and Middle-East (1), and were conducted in the general population, occupational-exposed and fertility clinic population. The urinary DBP metabolites generally evaluated were mono-n-butyl-phthalate (MnBP) and mono-isobutyl-phthalate (MiBP). The phthalates are often used in mixtures depending on occupational-exposed and fertility clinic population. The urinary DBP metabolites generally evaluated were mono-n-butyl-phthalate (MnBP) and mono-isobutyl-phthalate (MiBP). The phthalates are often used in mixtures depending on

Conclusions

The review showed that the studies were incongruent and therefore, a significant correlation could not be established. However, the data suggest that adult men exposed to DBP are more likely to have altered testosterone levels. Future studies should explore possible relationships with luteinizing hormone, follicle-stimulating hormone, sex hormone binding globulin, estradiol and inhibit B in the current context.

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**EP637**

Vitamin D status in patients with adrenal tumors and previous COVID-19 infection

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Context

The current pandemic showed a great handling of the resources and research in order to find not only a way to cure but also to prevent and improve the course of the Covid-19 infection. Optimal vitamin D (VD) levels and treatment was seen as a potential aid due, in principal, to its immunomodulatory effect. The ACE-2 receptor is the key the virus uses for entering the body, but its location is not restricted to the lungs, it’s also found in the adrenal cortex. At that same level, we can find the vitamin D receptor. Romania, with its temperate climate, has a significant number of people with suboptimal levels of VD, especially during the winter season.

Objectives

To assess vitamin D status in patients with adrenal tumors who recovered from SARS-CoV-2 virus infection as compared with those without infection.

Materials and methods

Notes of 205 patients with adrenal tumors - inpatients in an Endocrine Clinic between August 2020 and August 2021 - were retrospectively reviewed. 48 patients (6M/42F) had had the COVID-19 infection - group 1, aged 57 ± 14 years, and 157 patients (30M/127F) without the infection - group 2, aged 54 ± 14 years. 25-OH-VD status, full adrenal workup and abdominal imaging were noted.

Regarding tumor secretion, 82.4% were non-functioning adrenal tumors. 25-OH-VD levels were measured by electrochemiluminescence and were classified as follows: optimal 30 ng/ml, insufficiency 10-30 ng/ml, deficiency <10 ng/ml.

Results

The mean value of 25-OH-VD was 27.1 ± 7.8 ng/ml for group 1 and 25.5 ± 10 ng/ml for group 2 (P-value = ns). Regarding VD supplementation, group 1 had 41.6%(20) patients without and 58.3%(28) with treatment and group 2 had 52.8%(83) patients without and 47.2%(24) patients with treatment. In group 1, 77% (36) had VD insufficiency and 26% (12) had optimal VD status, whereas in group 2, 67.6%(106) had insufficiency or deficiency and 32.4%(51) had optimal VD status. Evaluating group 1, 30 patients had VD levels measured before and after the infection, and in the latter case the VD levels were lower for 10 patients, higher for 11 patients and remained almost the same in 9 patients (±10% modification).

Conclusions

Patients with adrenal tumors and Covid-19 infection do not have lower levels of vitamin D compared to patients who didn’t go through infection.

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**EP638**

Contaminación del aire ambiente y función tiroidea en adultos españoles. Un estudio de base poblacional de ámbito nacional (estudio DivaEndo)

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Objective
Recent reports have suggested that air pollution may impact thyroid function, although the evidence is still scarce and inconclusive. In this study we evaluated the association of exposure to air pollutants to thyroid function parameters in a nationwide sample representative of the adult population of Spain.

Methods
The Di@bet.es study is a national, cross-sectional, population-based survey that was conducted in 2008-2010 using a random cluster sampling of the Spanish population. The present analyses included 3846 individuals, free of thyroid disease, with negative thyroid peroxidase antibodies (TPO Abs) and TSH levels 0.1-20 mIU/L. Participants were assigned air pollution concentrations for particulate matter <2.5 µm (PM2.5) and Nitrogen Dioxide (NO2), corresponding to the health examination year, obtained by means of modeling combined with measurements taken at air quality stations (CHIMERE chemistry-transport model). TSH, FT4, FT3 and TPO Abs concentrations were analyzed using an electrochemiluminescence immunoassay (Modular Analytics E170 Roche).

Results
There was a significant association between PM2.5 concentrations and the odds of presenting lower FT4 [OR 1.30 (1.08-1.57)] per each IQR increase in PM2.5 (4.86 µg/m3). The association remained after the multivariate adjustment of the data. There was no association between NO2 concentrations and thyroid hormone levels. No significant heterogeneity was seen in the results between groups of men, premenopausal and post-menopausal women.

Conclusions
Exposures to PM2.5 in the general population were associated with a mild thyroid dysfunction consisting of lowered levels of FT4 and FT3 without any significant changes in TSH. The nature of this association remains unknown. Additional studies are warranted to expand the data in this field.

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‘Evaluation of the quality of life using patient questionnaire with autoimmune polyglandular type syndrome 2’

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The purpose of the study is to assess the quality of life of patients with autoimmune polyglandular type 2 syndrome using the questionnaire.

Material and research methods
Under our observation there were the following 2 groups of patients: 1 gr. - patients with APS with AIT (primary adrenal insufficiency and autoimmune thyroiditis) - 25 patients, 2 gr. - APS with DM 1 (type 1 diabetes mellitus type 1-30 patients, as well as 20 healthy persons of the appropriate age and gender. The study used generally crystal and clinical and biochemical methods of research, hormonal blood tests (TSH, free thyroxine, antibodies to TPO, cortisol), immunological studies (antibodies to thyroid gland, to the pancreas, to adrenal glands), and instrumental research methods (ECG, ultrasound of internal organs, thyroid gland, genital organs, neurophthalmologic, radiographic - MSCT of adrenal glands, statistical techniques, as well as the quality of life of patients with AIDOQOL. AddoQol consists of 30 questions with the estimate of each question in 6 points. At the same time, the patient must be selected in each question 1 answer: ‘Yes’ or ‘no’. If the patient is gaining more than 15 points with the answer ‘Yes’, then this indicates a low quality of life [1].

Research results
The assessment of the quality of life (QoL) on the AddoQOL questionnaire showed that the middle score of patients 1 of the group was 18 ± 0.95, and in healthy - 2.35 ± 0.54 (P<0.05). The average score in patients 2 groups amounted to 19.6 ± 1.06 (P<0.05).

Conclusions
QoL patients in patients with APS 2 type of both groups has significantly lagging behind QoL in healthy faces.

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neuroectodermal origin. Although the clinical phenotype is present in all patients, individual manifestations have a variable presentation and are age dependent. Aim. We report a case of a patient with possible MEN 2b syndrome and pregnancy. A 30-year-old Caucasian woman was admitted to the cardiology department of the hospital in October 2017 for resistant hypertension unresponsive to medical therapy. The patient had a history of hypertension for 5 years without any treatment or etiological diagnosis. On arrival, indicated blood pressure was 240/120 mmHg. She had a family history of hypertension and coronary artery disease and special personal history, such as smoking and drinking. But her mother died in young age (36 years old) because of adrenal tumor. Contrast-enhanced computed tomography demonstrated an inhomogeneous left adrenal mass (5.5 cm × 4.1 cm HU × 13 cm × 8.8 cm). Her plasma epinephrine and norepinephrine levels were elevated (118 (0-65) pg/ml and 7069.5 (0-200) pg/ml, respectively). Preoperative stabilization with alpha-adrenergic blocking agent (doxazosin) was started a month before surgery. The patient underwent laparoscopic left adrenalectomy after premedication. Histopathology confirmed adrenal pheochromocytoma with residual necrosis. The patient was diagnosed with pheochromocytoma. During the 2-year follow-up, the patient was asymptomatic, and her blood pressure remained normal without medication. Her plasma epinephrine and norepinephrine levels normalized (15.3 (0-65) pg/ml and 114 (0-200) pg/ml). After the operation she became pregnant, there were no problems during pregnancy, her labour was in December 2018 without any complications. She visited our center because of the second pregnancy. On examination she had severe proteinuria on her skin. She mentioned that her sister also has neurofibromatosis on her skin. Thyroid sonography demonstrated solid isoechoogenic nodule 4.7 * 3.8 mm at the left thyroid lobe. Serum calcitonin as a biochemical marker for the presence of medullary thyroid cancer was elevated - 20.4 (0-10) pg/ml. Plasma epinephrine and norepinephrine were normal. Just now her gestation period is 38 weeks and she is waiting for delivery. In the future, we plan to continue examination of the patient and her sister.

Conclusion
Women with MEN 2 should be screened for pheochromocytoma prior to a planned pregnancy. Family history is an important part of diagnostic algorithm of MEN 2b. Genetic tests could help to identify RET mutation.

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EP642
Circulating plasma microRNA in patients with ACTH-dependent cushing's syndrome.
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Introduction
Recent studies have shown that microRNA could serve as biomarkers in various types of cancer and other diseases. Aim. To reveal microRNA that differ in patients with Cushing’s diseases (CD) and Ectopic ACTH syndrome (EAS) to form a specific panel for differential diagnosis of ACTH-dependent Cushing’s syndrome (CS).

Materials and Methods
Plasma samples from both sinuses and cubital vein were drained during inferior petrosal sinus sampling and stored at -80 C. MiRNA isolation from plasma samples was carried out by an RNeasy Plasma/Serum Kit (Qiagen, Germany) on the automatic QIAcube station. MiR expression was then analyzed by sequencing on Illumina NextSeq 500 (Illumina, USA). The libraries were prepared by the QIAseq miRNA Library Kit. Sequencing was performed on a total of 36 samples. Data analysis and interpretation was conducted on QIagen GeneGlobe Data Analysis were Center. qRT-PCR was performed using a TaqMan Advanced miRNA CDNA Synthesis Kit (Thermo Fisher, Scientific) and TaqMan Advanced miRNA Assays (Thermo Fisher Scientific), in a 96-well format on the StepOnePlus instrument (Applied Biosystems). Data analyses were performed using SDS software (version 2.3, Applied Biosystems), to obtain cycle threshold (Ct) data. We used value Ct <35 as a cutoff for detection. All samples were normalized to spike-in control, cel-miR-39-3p.

Results
Among 36 enrolled patients (mean age 47.5, years (minimum 23, maximum 69 years; M:7, F:29) 24 subjects were confirmed as CD and 12 as EAS. There were 1167 miRNA differently detected (P <0.05) in inferior petrosal sinus samples of patients with CD vs EAS. These miRNAs were divided into 3 groups based on the significance of the results. The first group consisted of samples with the highest levels of detected miR in both groups. 108 miRNA were included. For the verification phase 10 microRNA were chosen (miR-383-3p, miR-4290, miR-6717-5p, miR-1203, miR-1229-3p, miR-639, miR-302c-3p, miR-7-5p, miR-145-5p, miR-16-5p) according to the discovery phase results and data from the previous pilot study. We enrolled 82 patients (mean age 44.2, years (minimum 19, maximum 70 years; M:18, F:64) for validation phase of the study. Among them 64 were confirmed as CD, 18 as EAS. RT-qPCR showed, that four microRNA differ between patients with CD and EAS: miR-383-3p (P adjusted =0.003), miR-302c-3p (P adjusted =0.02), miR-4290 (P adjusted =0.02), miR-6717-5p (P adjusted =0.02).

Conclusion
miR-383-3p, miR-302c-3p, miR-4290, miR-6717-5p differed between patients with CD and EAS: miR-383-3p (P adjusted =0.003), miR-302c-3p (P adjusted =0.02), miR-4290 (P adjusted =0.02), miR-6717-5p (P adjusted =0.02).

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EP643
Primary hyperparathyroidism response to the somatostatin analogue therapy in a patient with MEN1 syndrome: A case report
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Background
Management of primary hyperparathyroidism (PHPT) in Multiple Endocrine Neoplasia type 1 syndrome (MEN 1) is still a challenge. PHPT developing in MEN 1 is characterized by the involvement of all parathyroid glands. Therefore, by modern guidelines, total or subtotal removal of the parathyroid glands is recommended. But this approach often leads to the development of hyperparathyroidism, anadrome, correction of which is not always possible. Drug therapy of recurrent PHPT in MEN 1 patients may be the alternative to radical surgery. We present a clinical case of MEN 1 patient in whom somatostatin analogue therapy resulted in normalization of serum calcium level. Clinical case
40 years old Caucasian woman, with a history of insulinoma, that was operated on at the age of 10 and prolactin-secreting pituitary macroadenoma diagnosed at the age 19. In 2015 the patient was tested for PHPT, iPTH level was 28 pmol/l (1.3-9.3), serum Ca++ level 1.47 mmol/l (1.13 – 1.29), CT scans revealed two lesions suspicious for parathyroid adenomas. Subtotal parathyroidectomy of both right and left lower parathyroids glands was performed. Postoperative iPTH was 5.2 pmol/l. All removed lesions were confirmed to be parathyroid adenomas by the pathology examination. Genetic testing was done and variant in MEN1 gene was found. In 2020 PHPT recurrence was confirmed (iPTH 200.10 pg/ml (15.0 – 68.3)), serum Ca++ level 1.57 mmol/l (1.11 – 1.29), serum total Ca 2.78 mmol/l (2.15 – 2.65). 68Ga-DOTA-TATE PET/CT was carried out, it revealed three lesions in the pancreas head and body which intensively accumulated radio-pharmaceutical, also 68Ga-DOTA-TATE positive foci was found in the projection of the left upper parathyroid. Subsequently endosonography was performed; it showed multiple lesions in pancreas and submucosal lesions in duodenum. Fine needle aspiration biopsy of pancreatic and duodenal formations confirmed neuroendocrine tumors in all of them. Preoperative short-acting somatostatin analogue (Octreotide) was started. Subtotal pancreatectomy, 2/3 stomach resection, duodenectomy were performed. After surgery octreotide therapy was continued. After 6 weeks of octreotide therapy calcium and parathyroid hormone levels were assessed. Decrease of iPTH and calcium levels was found: iPTH from 172.5 to 122 pg/ml (15.0 – 68.3), serum total Ca from 2.73 to 2.59 mmol/l (2.15 – 2.65).

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Conclusion
Our clinical case demonstrated the ability of octreotide to reduce iPTH and normalize calcium levels in a patient with MEN 1 syndrome. It is necessary to further study the potential of somatostatin analogues in the treatment of recurrent PHPT in MEN 1 syndrome.

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**EP644**

Dynamics copeptin and apelin in patients before and after transnasal adenomectomy and their relationship with the development of post-operative hyponatremia

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Introduction
Transnasal adenomectomy is the main treatment for various pituitary adenomas. The hypothalamic-pituitary region is the site of synthesis and secretion of several hormones that have a direct effect on sodium-water metabolism, which leads to its frequent violation with the development of central diabetes insipidus and severe transient hyponatremia, the latter of which is the second most important cause of rehospitalization in the postoperative period. Currently, the causes and factors predisposing to the development of this complication have not been identified.

Objective
To study the perioperative dynamics of apelin and copeptin neuropeptides after transnasal transphenoidal adenomectomy for pituitary adenomas.

Materials and methods
The study included 22 patients who underwent transnasal adenomectomy for pituitary adenoma (inactive pituitary adenoma – 8 patients, acromegaly – 8 patients, Cushing’s disease – 6 patients, 6 men and 16 women, median age 52 years [Q25 39; Q75 62]), 10 of whom developed hyponatremia (group 1) with a median serum sodium of 125 mmol/l and 12 did not have any fluid and electrolyte disturbances (group 2). All patients were tested for serum Na, plasma apelin 12 (ELISA, Phoenix) and copeptin (ELISA, Phoenix) at 24 hours before surgery, 24 hours, days 2-3, 5 and 7 after surgery.

Results
The debut of hyponatremia was observed in the period 5-7 days after the operation. In both groups, there was a change in the level of copeptin with a decrease on days 2-3 after surgery and a further increase in group 1 and a decrease in group 2 by day 5 after surgery and returning to baseline values on day 7 after surgery. The level of apelin had different dynamics in the groups: in group 1, it decreased on the first day with a further increase with a maximum on day 5 and a return to the original values on day 7; in group 2, no statistically significant changes were recorded.

Conclusions
Transnasal adenomectomy is the cause of severe hyponatremia in the genesis of which, apparently, the hypothalamic neuropeptides copeptin and apelin play the leading role. The secretion dynamics of these neuropeptides changes reciprocally in groups with and without the development of hyponatremia, which makes them potential hormonal markers of this severe complication.

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**EP645**

Hyponatremia, central diabetes insipidus after transnasal adenomectomy and its risk factors

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Objectives
To assess the frequencies of hyponatremia and central diabetes insipidus (CDI) after transnasal adenomectomy and to identify its risk factors.

Results
Severe hyponatremia (116 mmol/l) developed in 2 patient (1.3%), moderate (127 mmol/l) in 1 patient (0.7%) on the 1st-7th day after surgery and in all cases it was reversed by fluid restriction. Mild transient hyponatremia (131-134 mmol/l) occurred in 8 patients (3.5%). Persistent CDI (pCDI) has developed in 34 patients (22.4%), with 3 cases of three-phase CDI (including 2 cases of three-phase CDI with mild hyponatremia), transient CDI (tCDI) occurred in 25 (16.4%), 9 patients did not have any disturbances (5.5%) by discharge. Postoperative pCDI and tCDI were promoted by Cushing’s disease (odds ratio (OR) 2.5, 95% CI (1.1-5.6) for pCDI, 3.6 (1.4-9.2) for tCDI), whereas acromegaly decreased the risk (OR 0.3 (0.1-0.6) for pCDI, 0.3 (0.1-0.8) for tCDI). Secondary adrenal insufficiency (OR 2.6 (1.2-5.9) for pCDI, 3.1 (1.3-7.6) for tCDI), microadenoma (OR 4.1 (1.6-10.6) for pCDI, 5.2 (1.9-14.6) for tCDI), MRI tumor’s volume <0.75 cm3 (OR 4.8 (1.8-12.6) for pCDI, 7.5 (2.1-26.8) for tCDI) and surgery pituitary injury (OR 4.3 (1.6-10.6) for pCDI, 5.2 (1.9-14.6) for tCDI) provoked pCDI and tCDI. Postoperative DI was more common at trend level in patients with adrenocorticotropic hormone levels of < 16.5 μg/ml and cortisol level of <228 nmol/l and pDI was more often associated with secondary hypothryroidism at trend level as well.

Conclusions
The proportion of hyponatremia was 7.3%, persistent postoperative CDI – 22.4%, and that of the transient form 16.4% by discharge. Cushing’s disease, secondary adrenal insufficiency, microadenoma, MRI tumor’s volume <0.75 cm3 and surgery pituitary injury increase the odds of postoperative CDI, whereas acromegaly does decrease these odds.

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**EP646**

A clinical case of hypogonadism and anosmia associated with a new mutation of the KAL1/ANOS1 gene: a preliminary report

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Introduction
Kallmann syndrome (KS) is a genetic condition characterized by the association of anosmia or hyposmia and GnRH deficiency resulting in congenital hypogonadotropic hypogonadism (CHH). Different genes can be implicated in KS, and the most frequent allelic variant occurs in the KAL1/ANOS1 gene in the X-linked form. Differential diagnosis is often made with other rare genetic diseases as CHARGE syndrome (CS) that includes hypogonadism, hyposmia and several organ defects including eyes and heart defects. Here we report a clinical case of a patient with a clinical diagnosis of KS and in which a new genetic gene variant was found.

Methods
Patient history was collected through questionnaires and physical examination at our outpatient clinic. Blood sample for genetic evaluation of the patient was collected after obtaining informed consents. Gene variants were amplified and verified by Sanger direct sequencing after the next generation sequencing (NGS) of related genes.

Results
A 48-year-old male patient was referred to our endocrinology service for evaluation of hypogonadism. The medical history of patient started when he was 17-year-old. At that time patient was diagnosed with hypogonadism and anosmia wherefore placed on testosterone replacement therapy. No genetic tests had been conducted until our visit on suspicion of KS. Patient had no other further suspected signs or symptoms of genetic disease or CS. NGS sequencing revealed the presence of two different gene allelic variants: a heterozygous variant in the region 8 q12.2 of the CHD gene (p.L2806V: c.84716C > T) and a hemizygous X-linked variant in the Xp22.31 region of the KAL1/ANOS1 gene (p.R46H: c.137G > A). Thislatest is a newly identified variant and has never been described so far. Laboratory examination confirmed hypogonadotropic hypogonadism without other pituitary hormonal alterations. Magnetic resonance imaging of the
offactory bulb and of the pituitary gland and the smell test have been requested and are ongoing.

Conclusion

Both KAL1/ANOS1 and CHD7 genes are known to be important causal gene in the development of KS. Differential diagnosis between KS and CS should be considered in patients with anosmia and hypogonadism. Until now p.R46H variant in KAL1/ANOS1 gene has never been reported, while p.L2800V variant was described in the literature to be associated with benign forms of CS with CHD7/KS. A possible oligoclonic form of KS might be considered in this specific case.

Keywords Kallmann syndrome; KAL1/ANOS1 mutations; CHD7 mutations; CHARGE syndrome; congenital hypogonadotropic hypogonadism; anosmia.

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**EP647**

**Sellar plasmacytoma revealing a multiple myeloma.**

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Introduction

The sellar plasmacytoma, an exceptional localization that can be solitary or associated with a multiple myeloma. We report the case of a sellar mass wrongly diagnosed as an invasive non-functional pituitary adenoma, the diagnosis was rectified postoperatively by the anatomopathological study.

Case description

A 44 year old female patient, with history of cholecystectomy and megaloblastic anaemia, was referred to our center for management of a sellar mass initially diagnosed as a pituitary adenoma. The patient had galactorrhea for 3 years and than she developed severe headache with worsening visual impairment. The physical examination revealed bilateral blindness, with galactorrhea, without neurological abnormalities. Magnetic resonance imaging (MRI) of the brain revealed an iso intense mass in T1 and T2 sequences with intra and supra sellar development strongly enhanced after injection of gadolinium. The tumor compressed the optic chiasma and the right optic nerve in its intracranial portion, invading the cavernous cavity bilaterally (KNOSP 3), measuring 44X36X37 mm suggesting an invasive macroadenoma; however the endocrine assessment did not show any abnormalities. She underwent an emergency transphenoidal surgery. There was a slight desemination in favor of a multiple myeloma. She underwent radiation therapy centered on the sella turcica, followed by chemotherapy. There was a slight regression of the osteolytic tumor process, which currently measures 38.5 X 32.6 X 27.5 mm.

Conclusion

Plasmacytomas of the skull base revealing multiple myeloma represent a rare entity. However, solitary or multiple, plasmacytoma should be considered in the differential diagnosis of any invasive lesion of the sphenoidal sinus. The clinical presentation is aspecific, histological certainty must be obtained.

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**EP648**

**Medical treatment of active acromegaly - the results from the Croatian Acromegaly Registry**

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Introduction

The most common etiology of endogenous Cushing’s syndrome (CS) is Cushing’s disease (CD). Patients with CS also represent a model of patients with metabolic syndrome (MetS) with associated increased cardiovascular morbidity and mortality. Insulin resistance and obesity, two major characteristics of CS, lead to the accumulation of triglycerides within hepatocytes and formation of fatty liver in these patients.

 Aim

To evaluate the prevalence of metabolic syndrome and fatty liver and the importance of using lipid accumulation product (LAP) and fatty liver index (FLI) in patients with CD.

Material and methods

We conducted a cross-sectional study analyzing electronic medical histories of 52 patients (41 women, 11 men) diagnosed with CD (33 microadenomas and 19 macroadenomas) treated from 2009 to 2019. Mean age 50.5 ± 13.5 years and body mass index (BMI) 29.3 ± 5.8 kg/m². Results

MetS defined by NCEP ATP III was present in 63.5% (n = 33) of patients with CD. Ultrasound findings of fatty liver in a cohort of our patients with CD were present in 40.4% (n = 21) patients, while only 11.5% (n = 6) had elevated transaminases, Patients with CD and MetS were significantly older from patients with CD alone (52.6 ± 13.2 vs. 44.3 ± 12.8 years). Obesity was present in 41.3% while diabetes and glucose intolerance were present in 60% of patients. Prevalence of obesity was even higher in patients with diabetes (72.2% vs. 27.8%, P = 0.007). Obese patients had significantly higher values of LAP (174.7 ± 79.4 vs. 54.4 ± 24.3 P < 0.005) and FLI (29.3 ± 29.5 vs. 1.5 ± 1, P < 0.005). Patients with CD and ultrasonographic features of fatty liver had statistically significant higher values of LAP than those with CD alone (142.6 ± 96 vs. 61.1 ± 21.2, P = 0.045), while their FLI values were not statistically different. Arterial hypertension was observed in as many as 82.4% of patients. In 96% of patients, some form of dyslipidemia was present.

Conclusion

Cushing’s disease is characterized by an unfavorable metabolic profile and grouping of cardiovascular risk factors in the large percentage of patients. Fatty liver extends this unfavorable metabolic phenotype. LAP but not FLI is a good surrogate marker of fatty liver in CD.

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**EP649**

**Lipid accumulation product (LAP) as surrogate marker of fatty liver in patients with Cushing’s disease (CD)**

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Introduction

The most common etiology of endogenous Cushing’s syndrome (CS) is Cushing’s disease (CD). Patients with CS also represent a model of patients with metabolic syndrome (MetS) with associated increased cardiovascular morbidity and mortality. Insulin resistance and obesity, two major characteristics of CS, lead to the accumulation of triglycerides within hepatocytes and formation of fatty liver in these patients.

Aim

To evaluate the prevalence of metabolic syndrome and fatty liver and the importance of using lipid accumulation product (LAP) and fatty liver index (FLI) in patients with CD.

Material and methods

We conducted a cross-sectional study analyzing electronic medical histories of 52 patients (41 women, 11 men) diagnosed with CD (33 microadenomas and 19 macroadenomas) treated from 2009 to 2019. Mean age 50.5 ± 13.5 years and body mass index (BMI) 29.3 ± 5.8 kg/m². Results

MetS defined by NCEP ATP III was present in 63.5% (n = 33) of patients with CD. Ultrasound findings of fatty liver in a cohort of our patients with CD were present in 40.4% (n = 21) patients, while only 11.5% (n = 6) had elevated transaminases, Patients with CD and MetS were significantly older from patients with CD alone (52.6 ± 13.2 vs. 44.3 ± 12.8 years). Obesity was present in 41.3% while diabetes and glucose intolerance were present in 60% of patients. Prevalence of obesity was even higher in patients with diabetes (72.2% vs. 27.8%, P = 0.007). Obese patients had significantly higher values of LAP (174.7 ± 79.4 vs. 54.4 ± 24.3 P < 0.005) and FLI (29.3 ± 29.5 vs. 1.5 ± 1, P < 0.005). Patients with CD and ultrasonographic features of fatty liver had statistically significant higher values of LAP than those with CD alone (142.6 ± 96 vs. 61.1 ± 21.2, P = 0.045), while their FLI values were not statistically different. Arterial hypertension was observed in as many as 82.4% of patients. In 96% of patients, some form of dyslipidemia was present.

Conclusion

Cushing’s disease is characterized by an unfavorable metabolic profile and grouping of cardiovascular risk factors in the large percentage of patients. Fatty liver extends this unfavorable metabolic phenotype. LAP but not FLI is a good surrogate marker of fatty liver in CD.

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EP650
Hypopituitarism in patients with pituitary macroadenomas - the prevalence and prognostic factors
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Hypopituitarism due to pituitary lesions may have unclear clinical manifestations, and for its diagnosis it is necessary to conduct a hormonal examination. There are clinical recommendations to conduct a hormonal investigation in all cases of pituitary tumors > 6 mm that seems to be uncertain.

The objective to evaluate the frequency of hypopituitarism in patients with pituitary macroadenomas with different hormonal activity and to identify its possible prognostic factors.

The results
The hypopituitarism was diagnosed in 59/148 (39.9%) NFAs, in 18/66 (27.3%) prolactinomas and 19/136 (14%) somatotropinomas (p < 0.001). The proportion of men with hypopituitarism was higher in NFAs but not in prolactinomas and somatotropinomas. The relative risk (RR) of hypopituitarism in male patients with NFAs was 1.575 (95% confidence interval (CI) 1.212 – 2.047, P = 0.001). MR-signs of chiasm compression, as well as the presence of chiasmal syndrome, were significantly more common in patients with hypopituitarism compared to patients without hypopituitarism in all subgroups. The RR of hypopituitarism in patients with MR-signs of chiasm compression was for NFAs 2.10 (95% CI 1.50 – 2.95, p = 0.003), for prolactinomas 1.667 (95% CI 1.29 – 2.18, p < 0.005), for somatotropinomas 1.45 (95% CI 1.56 – 2.48, p < 0.001). The RR of hypopituitarism in patients with chiasmal syndrome was for NFAs 1.66 (95% CI 1.26 – 2.18, p = 0.009), for prolactinomas 2.08 (95% CI 1.60 – 2.69, p = 0.001), for somatotropinomas 1.97 (95% CI 1.56 – 2.48, p < 0.005).

Vertical tumor size over 22.5 mm (area under the ROC curve 0.729, sensitivity 55.91% and specificity 73.44%, P < 0.001) and tumor volume over 4472 mm3 (AUC ROC 0.7066, sensitivity 62.77% and specificity 70.16%, P < 0.001) were statistically significant cut-off points for the presence of hypopituitarism.

The conclusions
Hypopituitarism should be excluded in patients with pituitary macroadenomas in the presence of the following factors: in non-functioning adenomas – male sex; regardless of hormonal activity – signs of chiasm compression, chiasmal syndrome, vertical tumor size more than 22.5 mm, tumor volume more than 4472 mm3.

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EP651
Unusual evolution of a non-functioning pituitary adenoma
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Introduction
Pituitary neuroendocrine tumors (PitNET) represent 15.5% of primary brain tumors and they can be clinically functioning or non-functioning. Although they are mostly benign, PitNET may be invasive in 30-45% of cases and aggressive in at least 15%. Here, we report the case of a patient who presented a multiple and rapid recurrence of a non-functional pituitary macroadenoma.

Observation
A 42-year-old man was admitted initially for headaches, monocular blindness and Knosp grade 3A macroadenoma on MRI. Biochemical analysis didn’t reveal hormone deficiencies nor hypersecretions. He underwent a transphenoidal resection with a visual improvement. Histologic diagnosis was a null cell adenoma with Ki67 index = 4% and a positive p53. Based on the new classification of PitNET, it was proliferative and invasive tumor, classified grade 2b. Six months later, he developed a tumor regrowth with visual impairment (diplopia), for which he underwent a partial resection and an adjuvant radiotherapy was planned. Before starting the radiotherapy, he was readmitted 6 months later for a complete ptosis of the right eye and an increase in size of his non-functioning pituitary macroadenoma.

Discussion
This case showed that invasive and proliferative non-functioning pituitary adenomas can have an unpredictable rapid recurrence and an aggressive behaviour than usual. Null cell adenoma are known to be more aggressive than the other types of tumors with a mean time to recurrence of 15.9 months. In our case, the time to recurrence was 6 months only between the first and second surgeries. Selecting the high risk of recurrence tumors is essential to avoid their impacts and to improve the quality of life of patients.

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EP652
Isolated ACTH deficiency with unusual clinical presentation and normal morning cortisol levels
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A 74-year-old male presented to hospital following an episode of brief loss of consciousness and several hours of post ictal confusion. There was no witnessed seizure activity, tongue biting, or incontinence. His past medical history included SCC right scalp, TIA and primary hypothyroidism. He had been commenced on Cemiplimab (immunotherapy) for metastatic SCC seven months before. On assessment, he appeared well and general examination including neurological examination was normal. However, he was found to have a postural blood pressure drop of 40 mmHg. ECG and Blood tests were unremarkable, except his random cortisol was 163 nmol/l. Repeat 9 am cortisol was 183 nmol/l. Hydrocortisone was commenced as primary adrenal insufficiency could not be ruled out. A differential diagnosis of ictal syncope was also considered but later ruled out after normal MRI and EEG. Subsequently, Synacthen test showed baseline cortisol of 155 nmol/l, rising to 449 nmol/l at 30 minutes and 521 nmol/l at 60 minutes. ACTH was 16 nmol/l. He was advised to stop hydrocortisone as primary adrenal insufficiency was ruled out. However, within a few days of stopping hydrocortisone, he felt symptomatic again with dizziness and pre-syncpe, and was readmitted to hospital. Oral Hydrocortisone, at a dose of 20 mg daily, was restarted and his symptoms settled. A glucagon stimulation test was performed to investigate possible secondary adrenal insufficiency. Surprising, his morning cortisol came back as < 11 nmol/l and remained undetectable (< 11 nmol/l) throughout the test, whilst growth hormone levels peaked to 19.6 mg/l confirming severe ACTH deficiency. FSH, LH, testosterone, prolactin and TFTs were all normal. MRI pituitary showed no abnormality. He was treated as isolated ACTH deficiency, secondary to Cemiplimab. He remains well on hydrocortisone replacement. Secondary adrenal insufficiency due to Isolated ACTH deficiency was being increasingly reported to be associated with immune checkpoint inhibitors including Cemiplimab. In our case, clinical presentation was unusual as postural hypotension and syncpe are not common with secondary adrenal insufficiency due to preservation of renin-aldosterone axis. Initial investigations were misleading with relatively preserved morning cortisol and good response to Synacthen. However, Cortisol levels became undetectable subsequently with no response to glucagon stimulation confirming diagnosis of severe ACTH deficiency. This case highlights that ACTH deficiency can present with postural syncpe and normal morning cortisol levels in the early stages. High index of suspicion and repeated investigations may be required to confirm diagnosis.

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Introduction
Sheehan syndrome (SS), or postpartum pituitary necrosis, is a complete or dissociated adenohypophysis insufficiency due to hypovolemia secondary to excessive blood loss during or after delivery. Although few studies have investigated osteoporosis in isolated hormone deficiencies, the relationship between SS and osteoporosis has not been investigated in large series of SS. In this study, we aimed to evaluate bone mineral density (BMD) in patients with SS.

Patients and methods
This is a descriptive cross-sectional study, involving 65 patients. It was carried out in the Endocrinology-Diabetology department of University Hospital Farhat Hached in Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. Patients were evaluated by Dual Energy X-ray absorptiometry to determine bone mineral density (BMD), T-score and Z-score.

Results
The mean age at diagnosis of SS was 48.2 ± 12.4 years. The incidence of SS in our study was 2.8 cases/year. A causal hemorrhagic delivery was found in all of our patients. Thyrotropic and corticotropic insufficiency were present in 80.2% of our patients, followed by gonadotrophic and lactotroph insufficiency in 72.3% and 38.5% of patients, respectively. Somatotroph insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotroph deficiency in 10.8% of cases. Hormone replacement therapy was initiated in all patients based on the affected anterior pituitary axis. In no case has the somatotropin sector been substituted by SS. Bone densitometry was performed in 21 patients, on average 5 years after the diagnosis of SS. Bone mineralization disorders were found in 18 patients: 10 patients had osteoporosis and 8 patients had osteopenia. The lumbar spine was more frequently involved than the femoral neck. Two patients had femoral neck fractures associated with low energy falls, on average 33 years after the diagnosis of SS. In univariate analysis, bone mineral loss correlated with age, body mass index, vitamin D level, duration of SS and estrogen progesterone Hormone replacement. However, in multivariate analysis no factor was significantly correlated with an elevated risk of bone mineral loss.

Discussion-Conclusion
Anterior pituitary insufficiency, especially in sex and growth hormones, as well as an overdose of thyroid hormones and glucocorticoids could increase bone mineral loss. In fact, bone loss is increased in SS compared to other causes of anterior pituitary insufficiency since patients with SS had an earlier disease onset and more severe hormonal deficits.

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**EP654**

Drug-induced galactorrhea and gynecomastia: a case report

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Introduction
Finding the cause of gynecomastia and galactorrhea can be challenging, hence one of the most important cornerstones is detailed case history. Hereby we present gynecomastia and galactorrhea case, caused by drug abuse.

Case
A 24-year-old male, 3 years suffering from gynecomastia and galactorrhea, came to our university hospital for the first time in July 2021. After a thorough history taking, the patient denied any diseases, medication use, lymph nodes changes, although repeated prolactin concentration (165,26 mU/l) was observed. Chest ultrasound confirmed gynecomastia without any pathological changes. Flow cytometry revealed the aplasia of lymphocytic follicles and a decrease of plasma cells. A dynamic test in only 8 patients, concluding with somatotroph deficiency in 10.8% of cases. Hormone replacement therapy was initiated in all patients based on the affected anterior pituitary axis. In no case has the somatotropin sector been substituted by SS. Bone densitometry was performed in 21 patients, on average 5 years after the diagnosis of SS. Bone mineralization disorders were found in 18 patients: 10 patients had osteoporosis and 8 patients had osteopenia. The lumbar spine was more frequently involved than the femoral neck. Two patients had femoral neck fractures associated with low energy falls, on average 33 years after the diagnosis of SS. In univariate analysis, bone mineral loss correlated with age, body mass index, vitamin D level, duration of SS and estrogen progesterone Hormone replacement. However, in multivariate analysis no factor was significantly correlated with an elevated risk of bone mineral loss.

Discussion-Conclusion
Anterior pituitary insufficiency, especially in sex and growth hormones, as well as an overdose of thyroid hormones and glucocorticoids could increase bone mineral loss. In fact, bone loss is increased in SS compared to other causes of anterior pituitary insufficiency since patients with SS had an earlier disease onset and more severe hormonal deficits.

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**EP655**

Somatostatin analogues in the treatment of a patient with acromegaly - possible positive effects on concomitant epilepsy (a clinical case)

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Somatostatin may act as a neurotransmitter in the neural network. Its associated with a possible long-term effect on calcium channels and, as a result, on the membrane potential of the cell. Bradycardia due to somatostatin analogues’ use could be a clinical demonstration of such effect. We would like to present a clinical case of a female patient with acromegaly and possible positive effect of octreotide treatment on concomitant epilepsy. From 2000 (age 40) a woman noted swelling of the face, a slow increase in the size of the hands and feet, hyperhidrosis, but she did not pay much attention to these signs. In 2011 (age 51) she noted episodes of loss of consciousness and convulsive seizures that why she referred for medical help. Endocrinologists recognized clinical signs of acromegaly. Accordingly to brain MRI pituitary macroadenoma (4.5x3.0x6.0 cm, V 38.7 cm3) with latero-suprasellar extension and the frontal lobe of the right hemisphere invasion was revealed. IGF-1 levels were 820 ng/ml (56-261) so active acromegaly was diagnosed, epilepsy was considered as secondary condition due to giant adenoma. Debuling surgery with consequent radiosurgery (Novatis) of the residual tumor was performed. Then she received octreotide prolonged release 30 mg monthly and achieved biochemical control. At the same time with acromegaly treatment, she started anticonvulsant therapy with valproic acid (1200 mg daily) and convulsive symptoms disappeared. Till February 2021 (age 61) she was stable, and octreotide was withdrawn. IGF-1 without treatment 118-159 ng/ml (43-220). Since April 2021 she noticed convulsive syndrome again despite the continuous use of valproic acid. Neurologist recommended to continue valproic acid at the same dose, however, convulsive symptoms occurred. In this case, we suggested that treatment with somatostatin analogues was associated with absence of convulsive symptoms in acromegaly patient with lesion-induced epilepsy. We cannot exclude that withdrawal of possible positive effect of somatostatin analogues on ion channels disorders resulted in epilepsy relapse, which requires further study of additional therapeutic properties of drugs in this group.

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**EP656**

Delayed diagnosis of pituitary stalk interruption syndrome in a 26-year-old patient

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Introduction
Pituitary stalk interruption syndrome (PSIS) is a rare congenital pituitary defect with an estimated incidence of 0.5 per 100,000 births. This syndrome has hypothalamus-pituitary region. The case was discussed in the multidisciplinary meeting and it was suggested to abstain from the medical treatment, to repeat testicular and abdominal ultrasound, lungs Xray for ruling out an active oncology process, to perform a cytological examination of secretion, to review the history of the case including possible drug abuse. While planning further investigations during the next consultation, the patient unwillingly confirmed regular cocaine abuse and discontinued further testing.

Conclusion
After taking cocaine, the levels of prolactin in the blood fall to baseline. However, hyperprolactinemia develops within 4 days of dosing (in the absence of repeated administration) [1]. These prolactin fluctuations, as well as unwillingness to reveal drug abuse, makes gynecomastia and galactorrhea causes identification challenging in drug users.

heterogeneous clinical presentations with varying degrees of pituitary hormones deficiencies. PSIS is commonly diagnosed during neonatal period and infancy. However, when symptoms are not evident or overlooked, the diagnosis could be delayed exposing the patient to acute, such as acute adrenal insufficiency, and chronic complications.

Case report

We report a case of a 26-year-old male patient who was referred to our endocrinology department with complaints of short stature and impuberism. The patient had a history of prematurity, poor stature growth, learning and attention difficulties resulting in an early school dropout. On physical examination, the patient’s weight and height were 47 kg and 140 cm respectively, both under the 5th percentile. He had a micropenis and a reduced testicular volume with absence of pubescence (Tanner stage 1). A blood test assessing pituitary hormones was performed showing an anterior hypopituitarism with undetectable testosterone level. Magnetic resonance imaging exhibited the diagnostic triad of PSIS associating hypoplasia of the anterior pituitary gland, absence of the posterior pituitary, and a thin and interrupted pituitary stalk. Further investigations revealed metabolic and bone complications manifesting in Hypercholesterolemia (Total cholesterol = 8 mmol/l) and a pre-diabetic status (HbA1c = 6%). DEXA scan showed a femoral neck osteopenia and a spinal osteoporosis. The patient started immediately hormonal replacement therapy with a close clinical and biological follow-up.

Conclusion

Growth retardation is the most common presentation of PSIS. Hence the importance of early detection and investigation of short stature as any delay in diagnosis may lead to severe complications and heavy psychosocial consequences.

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EP657

Pathomorphological markers of somatotroph neuroendocrine tumors predicting the treatment outcome in acromegaly

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Background

Transphenoidal adenomectomy of GH-secreting pituitary tumour is a first-line treatment of acromegaly. Pharmacological treatment is recommended if surgery did not lead to disease remission. Pathological assessment of postoperative tissue provides clinicians with valuable information on the disease course.

Aim

The aim of this study was to assess whether clinical, imaging, and pathological characteristics can predict surgical remission and response to first-generation somatostatin analogs (SRLs) and pasireotide LAR in acromegaly patients.

Patients and methods

A retrospective analysis of a study cohort of 120 patients with acromegaly, treated in one endocrinology centre was performed. Data on demographics, hormonal and imaging results, pathological evaluation (immunostaining for pituitary hormones, Ki-67 index and granulation pattern) and treatment outcome was extracted from the Polish Acromegaly Registry and analyzed.

Results

Patients who achieved surgical remission were older at diagnosis (50 vs. 37 years on average, \( P < 0.001 \)), had lower fasting GH, IGF-1 and PRL concentrations at diagnosis (4.68 vs. 18.91 μg/l on average, \( P < 0.001 \); 2.99 vs. 3.53 μg/l on average, \( P = 0.015 \)) and had smaller tumours (12 vs. 24 mm on average, \( P < 0.001 \)) which were less invasive than in patients with active acromegaly after surgery. The pathology results showed that patients with surgical remission more often had densely granulated tumours (73.1% vs. 40.00%, \( P = 0.001 \)) with positive staining for α-subunit (58.33% vs. 35.48%, \( P = 0.021 \)) and lower Ki-67 index (87.50% vs. 65.57% with Ki-67 index \(<1\), \( P = 0.002 \)) compared to patients without surgical remission. Patients, who responded well to first-generation SRLs, presented less common extracellular expansion and compression of the optic chiasm at diagnosis of acromegaly (58.62% vs. 90.00%, \( P = 0.006 \) and 13.79% vs. 56.67%, \( P = 0.001 \), respectively) compared to patients with poor response to SRLs. They also had more common densely granulated tumours (62.96% vs. 14.29%, \( P < 0.001 \)). However, no significant differences between patients with good and poor response to pasireotide LAR were found. In multivariate logistic regression analysis, independent predictors of post-surgical remission were normoprolactinaemia at diagnosis (\( OR = 5.87, P = 0.002 \)), densely granulated tumour in electron microscopy (\( OR = 5.92, P = 0.012 \)) and lower fasting GH concentration at diagnosis (\( OR = 0.88, P = 0.001 \)).

Conclusion

Patients with densely granulated somatotroph tumours are more likely to achieve surgical remission and to respond well to first-generation SRLs. Positive staining for α-subunit and lower Ki-67 index increase the likelihood of surgical remission in acromegaly. The pathologic assessment of tumour tissue is an important part of acromegaly patient’s evaluation providing valuable information on tumour’s characteristics. Together with clinical and imaging parameters it can help to predict the treatment outcome.

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EP658

Two cases: hemorrhagic rathke cleft cysts mimicking a hemorrhagic adenoma

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Introduction

Rathke Cleft Cysts (RCCs) are benign cysts arising from the remnants of Rathke’s pouch. The most common symptoms are visual field disorders, headache, and pituitary dysfunction.

Case 1

A 26-year-old male was admitted with headache that started 4 days ago. Cranial MRI revealed an appearance mimicking a hemorrhagic adenoma in pituitary. Pituitary hormones were found as normally. Pituitary MRI showed a 12x10x10 mm hemorrhagic RCCs located in the midline. The patient’s headache disappeared spontaneously within 3 days without the use of any medication. One month and six months later, MRI showed a progressive shrinkage of hemorrhagic RCCs diameters as 4.5x5x7.5 mm and 3 mm, respectively. In the pituitary MRI taken at the last follow-up 15 months later, it was observed that sequela remained as a millimetric-thick slit-shaped microcyst in the central gland.

Case 2

A 24-year-old female was admitted with a complaint of headache that started one month ago. The patient, who had a throbbing headache on the right side of her head, was relieved with analgesics. Pituitary MRI revealed a hemorrhagic RCCs with diffusely expanding pituitary gland with a size of 18x13x8 mm and leveling inside. The patient’s pituitary hormones were checked and no pathological values were found. In the control pituitary MRI one month later, the size of the hemorrhagic RCCs decreased to 8x13x8 mm.

Conclusion

Patients with hemorrhagic RCCs whose symptoms decreased during close follow-ups and who did not have hormonal disorders were not operated on. The sizes of the masses of the patients who did not develop any complaints or hormonal disorders during their follow-ups decreased.

Key words: Hemorrhagic Rathke Cleft Cysts; Hemorrhagic Adenoma

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EP659

Central precocious puberty on pituitary adenoma : about a case report

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Introduction

Central precocious puberty (CPP) is a frequent reason for consultation in pediatrics. It is defined as the development of sexual characteristics before the age
of 8 years in girls and 9 years in boys. Pediatric pituitary adenomas are rare. We report the case of a patient who presented with central precocious puberty on pituitary adenoma.

Observation

This is a patient aged 7 years and 6 months, without any particular history, having consulted initially for a premature thelarche. Her history of the disease goes back to the age of 7 years by the development of mammary glands, appearance of pubic and axillary hair without metrorrhagia, with an acceleration of the statural growth rate. Moreover, she did not report any pituitary tumor syndrome, and she had a significant psychological impact. The clinical examination found: a weight: 38 kg (+3SD), a height: 1.42 m (+3SD), BMI: 18.8 kg/m², blood pressure: 120/80 mmHg, estimation of the puberal stage: T3P3 and a dry vulva. The rest of the clinical examination was unremarkable. Pelvic ultrasound objectives a thin and median vacuity line, ovarian length ≥ 25 mm, body to neck ratio > 1. Estradiol level ≤ 20 pg/ml. Bone age is 9 and ½ years (advanced by 2 years/chronological age). For endocrinological orientation: Inhibin B: 85 pg/ml, LH: 2.6 IU/l, FSH: 6 IU/l, LHRH TEST : peak LH : 50 IU/l, LH/FSH ratio : 6. The diagnosis of central precocious puberty is confirmed. Hypothalamic-pituitary MRI shows a pituitary adenoma of 10*9 mm far from the optic chiasm. The fundus and the visual field did not show any abnormalities. The evaluation of the various endocrine axes is without particularity. Therapeutically, she was treated with GnRh agonists with a good clinical and biological evolution.

Discussion and conclusion

Central precocious puberty is frequent, the search for a tumoral etiology remains a priority. Pediatric pituitary adenoma are rare, representing 3% of all pediatric intracranial tumors and 5% of all pituitary adenomas. They are mainly functional tumors, more frequently secreting prolactin, ACTH, and growth hormone, while gonadotropin hypersecretion is very rare. 4 cases of PPC on pituitary adenoma have been reported in the literature: 2 cases secreting FSH alone and 2 cases secreting FSH and TSH. Treatment with GnRH analogues is indicated in the case of clinically, biologically and radiologically progressive PP, with an impact on adult height, and on the psychological level.

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EP661

Acromegaly-related cardiovascular morbidity In Tunisian Patients: Prevalence and clinical peculiarities

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Background and Aims
Cardiometabolic comorbidity is a well-established complication related to GH hypersecretion. Several studies have highlighted an increased cardiovascular risk in this population. The objective of the current work was to investigate the cardiovascular complications in Tunisian patients diagnosed with acromegaly. Patients and Method
We conducted a retrospective study that included all patients diagnosed with acromegaly who have been followed up, from 1997 to 2021, at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia. The review of medical charts provided a detailed cardiovascular evaluation in the investigated population.

Results
Our sample included 29 with a mean age at diagnosis of 45.8 ± 12.4 years old (extremes: 23-72 years) and slight male predominance (52.0%). The overall prevalence of arterial hypertension in the studied population was 20.7% with a mean duration of the evolution of 9.3 years (extremes: 2-20 years). Hypertension was newly diagnosed in 6.9% of patients. Arrhythmia and cardiac conduction disorders were observed in 10.3%. The cardiac ultrasound assessment revealed a concentric left ventricular hypertrophy in 15.4% of patients. Severe complicated hypertrophic cardiomyopathy with left heart insufficiency was reported in 3.4%. Aortic valvulopathy was found in 3.4% of cases. Ischemic heart disease affected 6.9% of patients.

Conclusion
Cardiovascular complications represent the leading cause of mortality in patients with acromegaly [1]. A various spectrum of cardiovascular manifestations can occur due to GH exaggerated secretion. Hypertension, ischemic heart disease, and arrhythmia are the most common ones. Other acromegaly-specific cardiac conditions can be found such as acromegalic cardiomyopathy [2]. The GH and IGF-1 excess affects the heart morphology and may impair its performances leading to insidious alterations of heart tissue and functions, independently of additional cardiovascular factors. The optimal surgical and medical management of acromegaly is associated with an improvement of cardiovascular risk in this population [3].

References

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EP662
The frequency of water and electrolyte disorders after transnasal surgery for adenomas of the hypothalamic-pituitary region: what does active control of blood sodium level give?

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Introduction
Water-electrolyte disorders are serious complications after transnasal adenomectomy for formaions of the hypothalamic-pituitary region. The purpose of this work was to evaluate the incidence of postoperative hyponatremia in the tactics of active control of sodium levels in the blood.

Materials and methods
The study included the results of a dynamic study of blood sodium levels in 53 patients (mean age 46.6 years [min 19; max 68]) with pituitary adenomas (GH-secreting - 31 patients, ACTH-secreting - 14 patients, hormonally inactive - 6 patients, TSH-secreting - 1 patient), who underwent endoscopic transnasal transphenoidal adenomectomy. Sodium control was carried out initially before surgery, after 12-24 hours, on days 2-3, 4-5 and 6-7 after surgery. Comparison of the frequency of hyponatremia was carried out with data on the lack of alertness about the possibility of developing postoperative hyponatremia and the lack of blood sodium control in 2008 (0.7%), the absence of alertness, but periodic monitoring of blood sodium but without mandatory monitoring of blood sodium levels in 2017 (7.2%).

Results
Initially, before surgery, only one patient with a TSH-secreting pituitary tumor had a decrease in the sodium concentration in the blood to 135 mmol/l (reference values 136-145 mmol/l) / 1-53 (1.8%). During the first 12-24 hours and on days 2-3 after surgery, hyponatremia of 135 mmol/l was also detected in 1 case in different patients with ACTH-secreting pituitary adenomas (1.8%), as well as in 1 case of low sodium blood to 130 mmol/l in the period of 2-3 days after the operation, which was of a long-term nature and a tendency to reduce the level of sodium in the blood to 125 mmol/l. On days 4-5, a total of 3 hyponatremias (4 newly emerged), 3 of which were of moderate severity 129-125 mmol/l (7.5%), were detected, on days 6-7, 12 hyponatremias were recorded (8 newly emerged), of which 4 were of moderate severity, and 8 of mild severity (22.6%). The overall incidence of postoperative hyponatremia was 28.3%.

Conclusions
Transient hyponatremia of the early postoperative period up to the 3rd day after surgery does not appear to be clinically significant. An increase in the frequency and severity of hyponatremia was noted from the 4th post-operative intervention, which necessitates mandatory monitoring of blood sodium levels. The approach of active monitoring of the blood sodium level allowed to increase the detection of hyponatremia by 3.9-32.6 times.

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EP663
Hyposmolar syndrome secondary to systemic sarcoidosis
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Introduction
Sarcoidosis is a rare systemic disease where clusters of immune cells form granulomas in various organs of the body. Its prevalence ranges from 1-40 per 100,000 people in Europe. Neurological involvement of the disease occurs in 5-10% of cases, with the hypothalamic-pituitary gland being one of the most commonly affected structures.

Clinical Case
A 36-year-old male with a history of hypertension, obesity, asthma and OSAS. He went to the emergency department due to symptoms of 4 months of evolution of asthma, hypervsomnia, compulsive food intake with a weight gain of 30 kg and behavioral disorders, being admitted to the Internal Medicine department. Physical examination revealed a weight of 157 kg, height 177 cm (BMI 50.1) and white striae on the abdomen. Cardiopulmonary auscultation was normal. Neurologically, there was evidence of decreased strength and painful stiffness on extension in the upper limbs.

Cranial CT scan showed two intracranial lesions, at hypothalamic and right parietal level, with associated perilesional oedema. These lesions were confirmed by MRI, suggesting an inflammatory-granulomatous aetiology. Fine-needle aspiration with Endo Bronchial Ultra Sound of a mediastinal lymph node revealed non-necrotising granulomatous lymphadenitis and a diagnosis of systemic neurosarcoidosis was made. Treatment with corticosteroids, rituximab and mycophenolate moefitil was started. After discharge, he was admitted to the intensive care unit a few days later due to disturbance of consciousness secondary to hypernatraemia. Ionogram showed a serum sodium of 172 mEq/l with a plasma osmolality of 380 mOsm/Kg and a urinary osmolality of 843 mOsm/kg. The endocrinology department, after ruling out diabetes insipidus and assessing the hormone analysis, diagnosed it of hypothalamic syndrome secondary to neurosarcoidosis, presenting with hypernatraemia due to hypodipsia/adipsia, morbid obesity, type 2 diabetes mellitus, hypogonadotropic hypogonadism and hyperprolactinarnia. At discharge, treatment for diabetes was started with metformin and weekly pulglathide, hormone replacement therapy was started with testosterone gel and a controlled water intake of 2-5.3 litres per day was indicated, depending on physical activity and the season of the year.

Conclusions
- Hypothalamic syndrome as a consequence of neurosarcoidosis can affect a number of vital endocrine and non-endocrine functions that are difficult to control.
- Hypothalamic adipsic hypernatremia can present with severe symptoms and these patients should be educated in controlled fluid intake.

EP664
Peak cortisol level on synacthen stimulation test in cushing’s disease
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Background
Diagnostic work-up for Cushing’s syndrome (CS) can be challenging, with variable performance characteristics on screening tests. We were recently referred a young female patient with Cushing’s disease (CD) due to a microadenoma. She presented with a seizure and initial biochemical work-up included a Synacthen stimulation test (SST). Her peak cortisol rose to over 1,000 nmol/l. Exaggerated response during SST is expected in hypercortisostrogenic states due to elevation in cortisol-binding globulin concentrations, for e.g. pregnancy and those taking estrogen-containing pills. However, overstimulation of the adrenal cortex by increased ACTH, as in ACTH-driven CS, is physiologically expected to result in hyperprotozyme of the zona fasciculata and therefore produce a heightened cortisol response during SST.

Aim
We retrospectively compared the difference in peak cortisol concentrations, after 250 µg tetracosactide administration during SST, in patients with active CD and those without CS but intact steroid axis.

Methods
In our unit, all patients with CD undergoing Transphenoidal Sugery (TSS) are started on steroid replacement post-operatively. SST is performed, after a standard steroid weaning, at 6-8 weeks post-operatively and if normal, standard biochemical work-up for steroid excess takes place again. We included all patients who were not in biochemical remission after TSS. Our comparator cohort includes all patients with a normal SST result after pituitary surgery for non-Cushing tumours. Roche I and Roche II Cortisol assays were used, with a normal SST response defined as peak serum cortisol level of >550 nmol/l or >420 nmol/l, respectively. Conversion of peak cortisol level from Roche I to Roche II equivalent concentration was done using validated regression equation. Mann-Whitney U test and Fisher’s exact test were used for statistical analysis for continuous and categorical variables respectively. Results are expressed as mean (±SD).

Results
13 patients with active CD and 210 patients with normal SST results were included in our CD and control cohort. Mean peak cortisol in our CD cohort was higher at 1020 (±305) nmol/l compared to 677 (±144) nmol/l (P<0.01). 62% of SSTS in the CD cohort had a peak cortisol of >850 nmol/l compared to 9% in the control cohort (P<0.01).

Conclusion
Patients with active CD demonstrate a higher than average cortisol response during SST. Clinicians should keep a high index of suspicion for ACTH-driven
CS in patients with an exaggerated cortisol response on SST, especially in the context of initial biochemical work-up for pituitary incidentalomas.

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EP665

**Giant prolactinomas: a descriptive study and prognostic analysis**

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Introduction

Giant prolactinomas (GP), defined as prolactinomas ≥4 cm in maximum dimension, are uncommon, with reported prevalence of 2 to 3% of all prolactinomas.

Aim

The aim of this study is to describe clinical and paraclinical characteristics of GP and to identify predictors of therapeutic response.

Materials and methods

A retrospective, single-center, descriptive study including 18 patients with GP followed at the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia.

Results

Mean age was 42.9 ± 16.9 years. Patients were predominantly male (77.8%). Mean tumor size was 50.4 ± 9.3 mm with a maximum of 70 mm. Prolactinoma at diagnosis was 10569.1 ± 19667 ng/ml on average [56-81940]. Clinically, many symptoms included signs of intracranial hypertension (78%) and visual field defects (72.2%). Galactorrhea was reported in 25% of patients only. Pituitary insufficiency included thyroidotropic, corticotroph and gonadotropic axes in 33%, 11% and 50% of cases respectively. Sixteen patients were treated with dopamin agonists (bromocriptin 75% and cabergolin 25%), 3 of them showed resistance to treatment (25% and 50% of cases respectively). Sixteen patients were treated with dopamin agonists (bromocriptin 75% and cabergolin 25%), 3 of them showed resistance to medical treatment (11% and 50% of cases respectively). Sixteen patients were treated with dopamin agonists (bromocriptin 75% and cabergolin 25%), 3 of them showed resistance to medical treatment (11% and 50% of cases respectively).

Conclusion

GP is a rare form of prolactinomas. It mainly affects men and its symptoms are due to mass-effect. GP respond generally well to dopamin agonists. Initial prolactinemia could be a good marker of therapeutic response.

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EP666

**Pharmacokinetic profile of cabergoline in patients with dopamine agonist resistant prolactinomas: a pilot study**


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Introduction

Approximately 20% of patients with prolactinomas do not respond satisfactory (resistant) even to high dose dopamine agonist treatment. Worth noticing that there are no clear prognostic signs of treatment’s resistance as well as its etiology is a subject of discussion.

Aim

The aim of our study was to assess absorption and metabolism of cabergoline in patients with dopamine-agonist-resistant prolactinomas.

Materials and methods

In patients (n=4) with resistant prolactinomas (no normalization of PRL, no response to high dose dopamine agonist treatment) we conducted a pharmacokinetic test:

1. blood concentrations of the drug. Understanding the underlying mechanisms will allow us to develop personalized treatment strategy.

2. Hyperprolactinaemia was prevalent (n=25). TT and cFT were significantly correlated with obesity. cFT was correlated with OSAS severity, but not TT. Significant reductions were observed in TT (pre 16.6 nmol/l, post 13.5 nmol/l, P = 0.003), cFT (pre 332 pmol/l, post 250 pmol/l, P = 0.001) and prolactin (pre 360 IU/l, post 225 IU/l, P = 0.006) after 3-months of CPAP (n=13). No significant change was observed in other pituitary hormones or SHBG.

Conclusions

The prevalence of hypogonadism is low in this cohort. CPAP treatment reduced testosterone and prolactin in eugonadal males with OSAS. The benefits of CPAP treatment for OSAS may be independent to change in serum testosterone levels. Hypogonadal OSAS patients should be managed via strategies other than CPAP.

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A multicenter retrospective study on a large cohort of patients with primary empty sella: hormonal and neuroradiological features over a long follow-up.

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Background

Hypopituitarism is frequent (40%) but a deterioration in development of new deficiencies was only associated with the increasing grade of ES. 6.1% showed a neuroradiological progression from partial to total ES. Most patients at the last evaluation, 5/166 (3%) patients, displayed new hormonal deficiencies and was present in 29.1% patients with incidental ES (hypoadrenalism). Hypopituitarism was significantly associated with male sex (P<0.004). Considering the intrasellar determinants of hypopituitarism. Our secondary aim was to explore the hormonal and neuroradiological evolution after at least 6-months of follow-up.

Design and methods

A retrospective and multicenter study based on medical records of all patients with ES attending four Pituitary Units between 1984-2020. The availability of the neuroradiological and hormonal assessment at diagnosis represented the inclusion criteria. Data collected at diagnosis and at the last available follow-up were analysed.

Results

402 patients (65% females, mean age 51.5 ± 15.5 years) were enrolled. Dynamic evaluations of pituitary function were available in 326 (81%). Longitudinal data were available in 166/402 with a median follow-up of 58 months. Diagnosis

ES was incidentally discovered in 72% patients whereas in 28% it was diagnosed because of a suspected endocrinopathy (hypopituitarism or hyperprolactinemia). ES was partial in 66.4%, total in 13.4%, and not defined in 20.2%. Traumatic brain injury (TBI) was reported in 23% cases evaluated for this issue. In the overall group, at least one pituitary hormonal deficiency was present in 40.5% (hypogonadism = 20.4%, hypoadrenalism = 14.7%, GHD = 14.7%, hyperprolactinemia = 10.2%, DI = 1.5%; multiple deficiencies = 11.5%) and hyperprolactinemia in 6.5%. Hypopituitarism resulted significantly associated with male sex (P = 0.03), symptoms/signs suggestive of pituitary disease (P<0.001), and TBI (P<0.004), without significant associations with age, BMI, number of pregnancies and entity of ES. Interestingly, hypopituitarism was present in 29.1% patients with incidental ES (hypoadrenalism = 13.5%, GHD = 12.5%, hypogonadism = 8.7%, hyperprolactinemia = 2.8%, DI = 1.7%).

Follow-up

at the last evaluation, 5/166 (3%) patients, displayed new hormonal deficiencies and 6.1% showed a neuroradiological progression from partial to total ES. Most patients with hormonal deterioration were already hypopituitaric at diagnosis (80%). The development of new deficiencies was only associated with the increasing grade of ES (P=0.004).

Conclusions

We described one of the largest cohort of patients with primary ES. Patients with ES need to be carefully evaluated at diagnosis, even if ES is incidentally discovered. We suggest completing the assessment with dynamic tests (screening for GHD and adrenocortical insufficiency). Hypopituitarism is frequent (40%) but a deterioration in pituitary function seems uncommon (3%).

Objective

To analyze the remission factors of surgical treatment of acromegaly.

Methods

A retrospective study involving 227 patients with acromegaly: 143 (63%) women and 84 (37%) men were operated via transphenoidal endoscopic approach for pituitary adenoma removal between the periods of 2018-2021. The average age was 45 years (36.00, 56.00); 118 patients had 6 months follow-up period (3-40 months). The IGF-1 index used for the evaluation, which was calculated using the formula: IGF-1 index = IGF-1 patient (ng/ml)/upper reference interval IGF-1 for this age (ng/ml). The remission for acromegaly was considered as decrease of the IGF-1 index less than 1.0 not later than 3 months following surgery. Intrasellar adenomas were observed in 99 (44%) cases, 128 (56%) tumors had different directions of extrasellar growth (suprasellar in 81, infrasellar in 28 and lateral/sellar in 64 cases). The tumor size were classified into microadenomas – 20 (8.8%) (< 10 mm in diameter), small and medium (10-35 mm)-164(72.2%), large (36-59 mm)-38(16.7%), giant ≥60 mm)52(0%). Results

Remission after the surgical procedure was achieved in 65 (55%) of 118 cases with a long follow-up period. The average [IOR] age of patients in the group with remission - 46 years [37,56], and those without remission - 39.00 [31, 50] years (P<0.044). Median [IQR] GH before surgery in the group with remission was 10.77 ng/ml [5.84, 21.23], without remission – 28.00 [9.02, 65.75] (P=0.001). Following the removal of microadenomas or macroadenomas of smaller and medium sizes, remission was achieved in 88.9% and 50.58% cases respectively, during the removal of tumors of large and giant sizes remission was achieved only in 7(29.2%) cases (P=0.004). Considering the intrasellar localization of the tumor, remission was achieved at 36(75%) cases, whereas with adenoma with extrasellar growth in 29(41.4%) cases (P=0.001). The risk of surgical treatment of acromegaly was low: postoperative transient diabetes insipidus was noted in 16.7% of cases, hypopituitarism - in 4.8%, rhinorrhea - in 1.3%, meningitis - in 0.8%, epistaxis in one (0.4%) and visual impairment in one (0.4%) case. There were no deaths.

Conclusion

Significantly predictors affecting the remission of acromegaly were recorded in average aged, the absence of visual disturbances, low GH level before surgery, the presence of microadenoma or small and medium-sized pituitary macroadenoma, the absence of extrasellar tumor growth, a decrease in GH < 2,06 ng/ml and IGF-1 index <1,9 in the early postoperative period, the absence of residual tumor tissue after surgery.

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Introduction

Xanthomatous hypophysitis (XH) is characterized by inflammatory infiltration of the pituitary gland in which lipid laden macrophages predominate. It can be primary (3% of all primary hypophysitis) and secondary arising in the setting of other lesions: craniopharyngioma, Rathke’s cleft cyst (RCC), adenomas (with subclinical apoplexy). It is more common in women and younger people. The clinical presentation is similar to pituitary tumors and may present with headaches, visual disturbances, hypopituitarism, and diabetes insipidus. Aim

The aim of this study was to analyze a cohort of patients in whom the existence of xantho-granulomatous hypophysitis (XGH) was confirmed pathohistologically...
Granulomatosis with polyanthitis (GPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated systemic vasculitis of both small and medium-sized vessels. Pituitary involvement in GPA is uncommon and few cases have been previously reported. Isolated pituitary involvement in GPA is rare and 96% of cases are associated with other organ involvement. GPA commonly affects the upper respiratory tract (93%), lungs (73%) and kidneys (67%).

Case
A 46-year-old male was admitted for investigation of vision changes. He had a 2–3-month history of blurred vision, headaches (retro-orbital discomfort), left eye redness, arthralgia, and epistaxis. His visual acuity was 6/60 with a central scotoma. A pituitary MRI revealed a likely inflammatory mass, involving the hypothalamus and infundibulum, suggestive of hypophysis. Whilst an inpatient, he was diagnosed with diabetes insipidus and hypopituitarism. His blood test showed FSH 1.0 IU/L, LH <0.2 IU/L, Testosterone <0.4 nmol/l, TSH 0.03 mU/l, FT4 7.4 pmol/l, Prolactin 83 mIU/l, random Cortisol 323 nmol/l and a normal short Synacthen test. An ear, nose, and throat opinion was sought due to the recurrent epistaxis. A nasal biopsy was taken with histology diagnostic of GPA.

Discussion
GPA is a multi-system disorder characterised by necrotising granulomatous small-vessel vasculitis. GPA mainly affects a combination of the ear, nose, and throat. However, it may also affect the joints, skin, eyes, and other organs. GPA occurs in equal proportions between men and women. Although, in the few previously reported cases with pituitary involvement, there were more female patients. The time of pituitary symptom onset in 13/56% of previous reported cases occurred between 2 months and 15 years after receiving a diagnosis of GPA. The prevalence of central nervous system involvement ranges from 15% to 54%.

Conclusion
GPA is a rare cause of pituitary failure and should be considered in the differential diagnosis of hypopituitarism. Multisystemic presenting symptoms, such as those demonstrated in this case, should alert clinicians to the possibility of pituitary involvement. This is likely to be as part of a multisystemic disease process since isolated pituitary involvement is rare.

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Introduction
There are limited data on the effectiveness and safety of GHRT in older patients with AGHD. We compared real-world GHRT outcomes in older (aged >60 years) vs middle-aged (35–65 years) adults.

Methods
NordiNet® IOS (NCT00960128) and ANSWER (NCT01009905) were non-interventional studies investigating long-term effectiveness and safety of GHRT with Norditropin® (somatropin, Novo Nordisk). Safety was assessed in the full analysis set (FAS) from both studies (non-GH-naïve patients included). The effectiveness analysis set (EAS) was from NordiNet® IOS only (GH-naïve patients; ANSWER-EAS included patients previously treated for ≤6 months).

Results
Baseline characteristics are shown (Table). Mean GH exposure was greater in women than men, and in middle-aged than older women (FAS); it increased slightly over time in all groups. Baseline IGF-I SDS was slightly higher in older vs middle-aged women, but not men (EAS). Mean IGF-I SDS increased from below 0 to values ≤1.24 with GHRT. Mean changes in BMI (EAS) and HBA1C (EAS and FAS) were small and similar between age groups in both sexes. No statistically significant differences were observed between older and middle-aged adults regarding incidence rates for NSAs (5.66 vs 5.38; IRR [mean, 95% CI] 1.051 [0.604,1.831]) and SAs (1.00 vs 2.52; IRR 0.396 [0.119;1.324]).

Conclusion
These data suggest similar clinical outcomes with GHRT in patients with AGHD aged >60 compared with 35–<60 years without additional risk of adverse drug reactions in older patients. Baseline characteristics (mean [SD] except for sex).

### Table 1

<table>
<thead>
<tr>
<th>Age group</th>
<th>EAS</th>
<th>FAS</th>
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</thead>
<tbody>
<tr>
<td>&lt;60 years</td>
<td>(n = 545)</td>
<td>(n = 214)</td>
</tr>
<tr>
<td>Female, %</td>
<td>45.9</td>
<td>39.3</td>
</tr>
<tr>
<td>Age, years</td>
<td>48.51 (6.98)</td>
<td>67.16 (4.89)</td>
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<tr>
<td>GH dose, mg/day</td>
<td>0.24 (0.16)</td>
<td>0.20 (0.10)</td>
</tr>
<tr>
<td>IGF-I SDS</td>
<td>-0.94 (1.40)</td>
<td>-0.82 (1.36)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>29.29 (6.09)</td>
<td>28.85 (4.58)</td>
</tr>
<tr>
<td>Duration of follow-up, years</td>
<td>5.37 (4.28)</td>
<td>5.28 (3.92)</td>
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Cushing’s disease and health-related quality of life: a cure for all dimensions?

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Acromegaly is a rare disorder caused by hypersecretion of growth-hormone (GH) and insulin-like growth factor (IGF-I), the underlying lesion being most frequently a pituitary adenoma. This disease is associated with a higher risk of malignancy. We describe the clinical and biochemical particularities in a series of patients with acromegaly and papillary thyroid carcinoma (PTC).

Case study
Out of 311 acromegalic patients, 5 cases that associated subsequent PTC were included, resulting in a prevalence of 1.6%. Acromegaly diagnosis was sustained by clinical particularities, hormonal assays and imaging data. The median age at diagnosis was 42 years with only female patients. One patient had GH and prolactin co-secretion. Transsphenoidal intervention was performed, with postoperative tumor remnant in all cases requiring subsequent medical treatment. Two patients also underwent Gamma knife radiosurgery. Following multimodal treatment, one patient was cured and four had controlled disease. Thyroid cancer was diagnosed at a median of 7.5 years after the diagnosis of acromegaly. All
cases presented with the papillary variant. At the time of the cancer diagnosis, 2 out of 5 patients had controlled acromegaly. All five underwent total thyroidectomy and three of them received radioactive iodine. The histopathological analysis revealed four papillary thyroid microcarcinomas (PTMC). One patient had a focus of sclerosing subtype of PTC of over 10 mm, lymph node metastases, and extrathyroidal extension – this patient had co-secretion of prolactin and was the only case with poor oncological outcome. The other patients were cured.

Conclusions

Several studies indicate that a prolonged excess of IGF-1 levels has proliferative and anti-apoptotic effects on follicular thyroid cells, with a prevalence of thyroid cancer in acromegaly of 1.2-10.6% [1]. In our series, all patients were diagnosed with PTC after prolonged and persistent high levels of IGF-1 due to uncontrolled disease. Furthermore, prolactin has a potential tumorigenic role on thyroid follicles [2], the patient with GH and prolactin co-secretion being the one with an aggressive evolution of the PTC. Four patients had PTMC which is acknowledged as a very-low risk neoplasm. In conclusion, although at this point thyroid malignancies are not considered more aggressive in acromegalic patients, periodic thyroid examination is useful in identifying complications in earlier stages.

References


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**EP676**

Idiopathic isolated adrenocorticotrophic hormone deficiency

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Introduction

Idiopathic Isolated Adrenocorticotropic hormone (ACTH) deficiency (IIAD) is a rare cause of secondary adrenal insufficiency. It can present with a variety of clinical symptoms, mainly chronic fatigue and euolemic hyponatraemia, and may coexist with autoimmune disease, most commonly Hashimoto’s thyroiditis. Radiographically, an empty sella turcica image can be seen. We present 3 cases of isolated ACTH deficiency.

Case 1

A 47-year-old woman was referred for investigation of adrenal insufficiency due to low morning cortisol levels in a laboratory test performed in the context of investigation of hypertension. Hormone lab tests showed morning Cortisol < 1µg/dl, ACTH 6.8 pg/ml (NL 7-64). The rest of pituitary axes were intact. Tetracosactrin (250µg) stimulation test showed a maximum cortisol response of 8.56µg/dl. Pituitary on imaging was normal. The patient was set on hydrocortisone replacement therapy while continuing to receive her antihyperensive treatment.

Case 2

A 45-year-old man, with no previous history, had an episode of confusion during febrile diarrheal syndrome. During his hospitalization he also presented episodes of hypoglycemia. The initial hormonal test showed very low basal serum cortisol levels (morning <0.2µg/dl) and ACTH (1 pg/ml), while in the glucagon test there was no cortisol response (maximum value = 0.2µg/dl). The rest of hypothalamic-pituitary axes were intact. Pituitary imaging test was negative. At the same time, the patient was also diagnosed with autoimmune primary hypothyroidism and treated with throxine once week after the initiation of hydrocortisone replacement.

Case 3

A 74-year-old man with hyperthyroidism due to Graves’ disease treated with methimazole was hospitalized for fever and hypotension (Na = 124). The hormonal tests revealed low levels of cortisol (morning <0.7µg/dl) and ACTH (4 pg/ml), as well as thyrotropin (TSH 0.017, FT4 1.74 (FT 0.80-1.28 mg/dl)). Corticosteroid deficiency was confirmed by a subsequent stimulation test with 250g tetracosactrin (maximum cortisol response 3.56µg/dl) and a glucagon test (maximum cortisol response 1µg/dl). The rest of pituitary axes were intact and pituitary MRI showed no anatomical damage. The patient was treated with hydrocortisone.

Conclusion

- The diagnosis of IIAD is often missed and becomes apparent after a triggering event such as fever or thyrotoxicosis.

**EP677**

Role of new peptide biomarkers in metabolic profiling of adult growth hormone deficiency patients: preliminary data on neudesin and its relationship with LEAP-2

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Patients affected by adult growth hormone deficiency (aGHD) show worse metabolic profile, with insulin-resistance, increased total cholesterol, LDL, triglycerides, reduced HDL, and higher risk of developing type 2 diabetes mellitus and cardiovascular complications. Adult GHD and metabolic syndrome (MetS) are closely related to each other, since they share the previous depicted clinical features, while obese MetS patients display lower IGF-1 levels due to a functional reduction of GH secretion. Neudisin is a newly discovered peptide mainly secreted in brain and adipose tissue, under evaluation for its possible activity as negative regulator of energy expenditure, as it decreases food intake in mice models. Liver expressed antimicrobial peptide (LEAP)-2 is involved in ghrelin physiological regulation as it acts as a competitive antagonist with slow dissociation from the GSH receptor-Ia, limiting the magnitude of ghrelin activities. We have already demonstrated higher LEAP-2 levels and significantly lower ghrelin/LEAP-2 ratio in aGHD. To better characterize the metabolic profile of aGHD patients we performed an observational cross-sectional study testing the hypothesis that neudisin may be affected in this clinical setting. Given the role in energy balance of the two peptides, we also evaluated any eventual relationship between neudisin, LEAP-2 and metabolic and anthropometric parameters. 39 patients were included in the study. Group A: 18 aGHD patients, 7 females and 11 males. Mean ± SEM age of the group was 59.7 ± 2.7 years, while BMI was 30.2 ± 2.2 kg/m². Group B: 21 healthy controls (13 females and 8 males). Mean ± SEM age of the group was 47.1 ± 2.5 years, while BMI was 24.5 ± 0.9 kg/m². They were evaluated for glucose and insulin, HOMA and QUICKI index, total/IDL/HDL cholesterol, triglycerides, uric acid and IGF-1. Neudisin, LEAP-2 and ghrelin were measured by ELISA, according to manufacturers’ protocols. As expected, aGHD patients showed higher HOMA index, triglycerides and lower HDL than controls. Neudisin is significantly higher in aGHD than controls (2.83 ± 0.37 vs 1.55 ± 0.12 ng/ml). We confirmed significantly lower ghrelin levels and significantly higher LEAP-2 (5.19 ± 0.42 vs 3.69 ± 0.49 nM) in aGHD, leading to lower ghrelin/LEAP-2 ratio. A significant and strong direct correlation between neudisin and LEAP-2 was found both in aGHD (r² = 0.76) and in all the analyzed population. While LEAP-2 directly correlated significantly with BMI, neudisin did not. These results, although preliminary, may suggest a possible adaptation to a worse metabolic scenario in aGHD. The presence of two distinct pathways related to food intake and the relative scarce knowledge on neudisin suggest future developments in this field.

**EP678**

Incipient adrenal crisis following ChAdOx1 SARS-CoV-2 vaccination in a patient with undiagnosed isolated adrenocorticotropic hormone deficiency

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Background

Isolated adrenocorticotropic hormone (ACTH) deficiency is a rare entity defined by secondary adrenal insufficiency and normal secretion of all other pituitary hormones. Delays in adrenal insufficiency (AI) diagnosis frequently encounter...
Among older patients because of non-specific symptoms. The occurrences of acute or incipient adrenal crises following coronavirus disease 2019 (COVID-19) vaccine administration are increasingly reported over the last year after vaccine rollout program. Here, we present an interesting case of incipient adrenal crisis following ChAdOx1 SARS-CoV-2 vaccination in a patient with undiagnosed isolated ACTH deficiency.

Clinical case
A 73-year-old Thai woman with underlying uncontrolled type 2 diabetes mellitus and unclear etiology of AI presented with a 2-week history of general malaise, dizziness, nausea, and weight loss of 4 kilograms following the first dose of AstraZeneca (ChAdOx1 SARS-CoV-2) vaccination. She had a past history of AI diagnosed at age of 52 from the previous hospital and had taken prednisolone 2.5 mg per day thereafter. Patient denied history of postpartum hemorrhage and was able to lactate after pregnancy and never had serious traumatic head injury. She also denied the use of other exogenous glucocorticoids and other medications except her current prescribed oral prednisolone. When seen in our hospital 2 weeks after immunization, physical examination and vital signs were unremarkable. Re-evaluation of AI after prednisolone discontinuation for 3 days was performed with the standard 250-microgram ACTH stimulation test. The diagnosis of secondary AI was confirmed. Brain MRI showed normal pituitary gland and evaluation of other anterior pituitary hormones revealed normal results. Isolated ACTH deficiency was diagnosed and the patient had been instructed to increase the dose of prednisolone to 15 mg per day. Insulin treatment was also up-titrated to tightly control glycemic control. Her symptoms considerably improved over a week and back to the usual weight over a few months. With increasing the dose of prednisolone on the day of vaccination, the patient was uneventful following the second dose of AstraZeneca vaccination.

Conclusions
Late-onset isolated ACTH deficiency is a rare entity but has emerged as a cause of AI. Healthcare professionals should be vigilant about the possible diagnosis or worsening of AI especially in elderly patients who receive COVID-19 vaccine administration. Ongoing educations of sick day management should be emphasized in all AI patients.

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EP679
ACTH-GH pituitary adenoma in an adolescent: a Case Report
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Plurihormonitary pituitary adenomas represent 10-15% of all functioning pituitary adenomas. Functioning ACTH-GH pituitary adenomas constitute an extremely rare entity. Most patients present a clinically manifested acromegaly and subclinical Cushing’s disease. We present the case of a 14 years old female who referred to the endocrinology department for inaugural diabetic ketosis. She had a six-month history of amenorrhea and headaches. On examination, she had facial dysmorphia suggestive of acromegaly. Weight was 93 kg, height was 1.77 m. The body mass index was 29.3 kg/m². Blood pressure was normal; she had purple abdominal stretch marks. Polysomnography revealed a mild sleep apnea. The hormonal assessment confirmed acromegaly by a nadir of GH of 39 mU/l in glucose tolerance test. A none suppressive cortisol secretion of 8.9 mg/dl and a high ACTH of 29.14 ng/l. Thyrotropic and lactotropic axis were normal, The gonadotropic axis was deficient. MRI showed a macroadenoma of 18*14*20 mm that extends into the cavernous sinus and compresses the optic chiasm. The patient received basal-bolus insulin therapy. She underwent transphenoidal surgery. Postoperatively presented with clinical and biochemical adrenal insufficiency and had a transient insipid diabetes. The MRI documented an empty sella. At a one-year follow-up she was clinically well with no clinical or radiological evidence of pituitary tumor recurrence. She remained on replacement hydrocortisone and necessitated low doses of insulin for her diabetes. ACTH-GH plurihormonitary pituitary adenomas are a rare entity. This is a case that illustrates an ACTH-GH pituitary adenoma revealed by diabetic ketosis in an adolescent.

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EP680
Pituitary adenoma associated with intracavernous meningioma: Case report
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Introduction
Pituitary adenoma and meningioma are the most benign tumors in the central nervous system (meningioma 35.9%, pituitary tumor: 15.5%). Pituitary adenoma associated with meningioma without a history of radiotherapy is extremely rare. Case
A 70 years old man operated for post-traumatic subdural hematoma in whom the brain MRI (magnetic resonance imaging) had also shown a macroadenoma, completed with an MRI of the sellar region which were confirmed in the coronal section in T1 weighted image, an iso-intense adenoma taking up gadolinium poorly measuring 16 x 8.5 mm. This adenoma is associated with a right intra-cavernous lesion measuring 11.8 x 8.8 mm presenting intimate contact with the intraventricular portion of the internal carotid artery, iso-intense in T1 weighted images and hyper-intense in T2 weighted images which is intensely and homogenously enhanced after injection of gadolinium salts, corresponding to meningioma. Hormonal work-up revealed a serum prolactin level of 1300 ng/ml and a central hypothyroidism. The patient was then started on dopamine agonist (cabergoline 0.3 mg/week). The response to treatment was excellent, on his MRI follow-up one year after, the adenoma has disappear leaving an arachnoidocele while the meningioma has remained stable. The patient is being followed by Endocrinology and Neurosurgery.

Conclusion
The association of meningiomas and pituitary tumors is very rare. If patients who have under- gone previous radiation therapy are excluded from consideration, the presence of these two types of tumors in the same patient becomes even rarer. To our knowledge, the association of an intracavernous meningioma and a prolactinoma in a patient without previous radiation therapy had never been reported.

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EP681
Severe hyponatremia after coronary angiogram - the link between ischemic cardiac disease and hypopituitarism
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Background
Hyponatremia in not uncommon in elderly. Common causes include medication, heart, kidney and liver diseases, digestive loses, syndrome of inappropriate anti-diuretic hormone. Hormonal imbalances are sometimes overlooked. Sudden onset after a recently invasive procedure could challenge the diagnostic.

Methods
We present a case report of a severe hyponatremia diagnosed after a coronary angiogram. It is a rare case of hypopituitarism secondary to a pituitary macroadenoma.

Case reports
The patient is a 69 years old man that presented in December 2019 in cardiology department for a coronary angiogram. 48 h after angiography the patient was admitted in ICU for severe hyponatremia and rhabdomyolysis – interpreted at the time as side effect to the contrast agent. At that moment he had normal TSH (T4 or T3 were not analysed) and SIADH was infirmed. The adrenal insufficiency was not rule out. Progressively, in the next 6 month the patient presented asthenic syndrome and significant weight loss, which is why he came to our clinic for second opinion. He had a cardiological check-up and an endocrinological exam. The biological evaluation reveals mild hyponatremia, still elevated creatine kinase and also mild anemia. The hormonal profile established the panhypopituitarism and we started substitutive treatment, with rapidly normalisation of biological disturbance. The MRI exam revealed a pituitary macroadenoma, with of the optic chiasm compression, confirmed by visual field.
The patient needed to repeat coronary angiogram for unstable angina and revealed multiple coronary stenosis and 3 active stents were fitted. This time the procedure was performed after Cortisone dose supplementation, without electrolyte imbalance. Considering double antiplatelet therapy after coronary stenting and cardiac risk, the surgical treatment of macroadioma was scheduled after 6 months, with closely ophtalmologic follow. Transphenoidal hypophysectomy was successfully performed, and immunohistochentistry diagnosed a non-functional adenoma.

Conclusion
Hormonal imbalance should be suspected in a sudden-onset of life-threatening hypomatermia. Hypopituitarism is a rare cause of hyponatremia and in this case was overlooked, TSH value being normal, without initial testing of T4 and cortisol value. The acute illness and the iodine agent used for angioigraphy revealed long-term hypocortisolemia. A noncardiac surgery could be very challenging in a recently stented patient, due to the risk of bleeding secondary to antiplatelet therapy and treatment discontinuation may lead to perioperative thrombotic cardiac events. In this case the multidisciplinary team was essential for ensuring an excellent outcome.

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**EP682**

A 29 year old woman with aggressive acromegaly as a single manifestation of multiple endocrine neoplasia type 1

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Introduction
Parathyroid adenomas are the most common (90%) and usually the first manifestation feature of MEN1 syndrome. The occurrence of anterior pituitary adenomas in MEN1 syndrome may range between 10% and 60%. Pituitary involvement includes the initial manifestation of MEN1 syndrome in 10% to 25% of individuals and usually show more aggressive behavior; 20% secrete prolactin, fewer than 10% secrete GH, 5% secrete ACTH, and the remainder appear to be nonfunctioning.

Objective
Description of a 29-year-old female diagnosed of aggressive acromegaly as single manifestation of MEN1 syndrome.

Case
The patient was referred to endocrinology due to oligomenorrhea. Elevated prolactin 69 (3-30 ng/ml) and IGF1 854 ng/ml (117-329) were detected. GH after oral glucose tolerance test (OGTT) (12 ng/ml) confirmed the acromegaly. Magnetic resonance showed a 7.5 x 6 x 8 mm adenoma without cavernous sinus invasion. Transphenoidal surgery was performed. Histopathological exam described an atypical adenoma with Ki 9% and GH positivity. After surgery, the patient became pregnant and the evaluation of the disease was carried out after delivery. A 5 mm tumor rest was observed. IGF1 levels 399 ng/ml (71-234) and GH after OGTT (1.2 ng/ml) indicated persistent acromegaly. In a second intervention the rest can not be removed and Octreotide Lar (20 mg/month) was initiated. Despite the increase in medical therapy, IGF1 remained elevated and the patient was referred to Radiation oncology. MEN 1 (c.512G > A;p.Arg171Gln) and SDHD (c.140A>G; p.His50Arg) heterozygous mutations were detected. Calcium metabolism exam and radiological screening were normal. Fathers patient carried the same mutation in both genes (Malta, 2019). Calcium and PTH were normal. Radiological image showed a 1 cm nonfunctioning pancreatic mass. No other first-degree relatives showed mutations.

Conclusions
An aggressive acromegaly could be the first manifestation of a MEN1 syndrome.

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**EP683**

Pituitary Coma? Discordant pituitary biochemistry after consumption of a commercially available ‘Sleep Activator’.

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We present a case of discordant pituitary biochemistry which resolved after discontinuing a commercially available combination vitamin supplement. A 35 year-old man presented following an episode of headache and dizziness, preceding collapse and possible seizure activity. Investigations revealed deranged pituitary function: TSH 0.02 mU/l (0.35-5.50), FT4 3.6 pmol/l (10.0-20.0), 9 am cortisol 18 nmol/l (200-500), testosterone >52 nmol/l (8.4-28.7), FSH <0.3 UI/l (1.0-18.0), LH <0.1 UI/l (2.0-9.0), oestradiol 611 pmol/l (0-146), prolactin 452 mU/l (45-375) IGF-1 207 ng/ml (71.0-234.0). He reported weight gain, low mood, sweats, and reduced libido. 7 months prior he had sustained a head injury from a concrete block. He was commenced on hydrocortisone and levophenyzine. MRI found normal pituitary gland and surrounding structures. On further questioning at follow-up he admitted taking a combined nutritional supplement called ‘Kodiak Coma’. Based on clinical suspicion that the supplement was contributing to the derangement in pituitary function tests the patient was asked to stop taking it. Subsequent pituitary function tests returned to normal, with normal short synacthen test (0 min 249, 30 min 659 nmol/l). He was able to discontinue hydrocortisone and remained well. He continued to take levophenyzine replacement for primary hypoventilation. None of the listed ingredients in ‘Kodiak Coma’ are known to affect pituitary function or related hormonal axes and the discordant biochemistry did not correlate to this patient’s clinical presentation. Rather we hypothesise that a component or components of the supplement caused assay interference. Biotin is commonly included in nutritional supplement preparations; it is well known to interfere with certain assays of thyroid function, and rarely has been reported to interfere with other pituitary hormone assays. However, a different pattern of interference would have been expected if biotin was the culprit. The manufacturer of Kodiak Coma was contacted for information about its ingredients, but no reply was forthcoming. Nutritional supplements are often marketed towards individuals with no underlying deficiency, illness, or disease. Such products are readily available in high street shops and online. However, it is well documented that active ingredients in products of this kind can lead to negative health outcomes, either by drug interaction, by unintended effect upon clinical investigations, or by a direct effect to cause disease. This patient was subjected to a 4-day hospital admission, medical therapy, and several months of clinical and biochemical follow-up as a result. This case illustrates the unintended risks of nutritional supplements and highlights a potential cause for discordant pituitary biochemistry.

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**EP684**

Two case: hemorrhagic rathke cleft cysts mimicking a hemorrhagic adenoma

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Introduction
Rathke Cleft Cysts(RCCs) are benign cysts arising from the remnants of Rathke’s pouch. The most common symptoms are visual field disorders, headache, and pituitary dysfunction.

Case 1
A 26-year-old male was admitted with headache that started 4 days ago. Cranial MRI revealed an appearance mimicking a hemorrhagic adenoma in pituitary. Pituitary hormones were found as normally. Pituitary MRI showed a 12 x 10 x 10 mm hemorrhagic RCCs located in the midline. The patient’s headache disappeared spontaneously within 3 days without the use of any medication. One month and six months later, MRI showed a progressive shrinkage of hemorrhagic RCCs diameters as 4.5 x 5 x 7.5 mm and 3 mm, respectively. In the pituitary MRI taken at the last follow-up 15 months later, it was observed that sequelae remained as a millimetric-thick slit-shaped microcyst in the central gland.

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A 30-year-old man presented with typical symptoms of thyrotoxicosis. On examination, he was normotensive. He had a small goitre and fine tremor. He showed palpitation, tremor and weight loss of 20 kg) over four months associated with macroadenoma with mass effect. A 30-year-old man who presented with TSH and GH secreting pituitary adenoma was seen in bone mineral density. The patient's pituitary hormones were checked and no pathological values were found. In the control pituitary MRI one month later, the size of the hemorrhagic RCCs decreased to 8 x 13 x 8 mm. Transsphenoidal Surgery with tumour excision successfully. Free T4 post-surgery was 20.66 pmol/l with normalization of TSH at 2.2 mIU/l and GH at 1.26 ng/ml (2022). His Free Thyroxine (Free T4) was elevated at 69.6 pmol/l (11.5-22.7) with a normal TSH of 4.06 mIU/l (0.55-4.78). This was confirmed with sample sent to a second laboratory. A high alpha subunit of 12 ng/ml (≤0.5) and absent TSH response to Thyrotropin Releasing Hormone (TRH) stimulation test support the diagnosis of TSH secreting tumour. Other anterior hormones were assessed and showed elevated Insulin Growth Factor -1 (IGF-1) of 401.8 ng/ml (74-258) and prolactin, 1167.6 mIU/l (45-375). Oral glucose tolerance test confirmed GH excess. Testosterone level was 2.5 pmol/l (5.72-0.26) with Follicle stimulating hormone (FSH) 7.3 IU/l (1.4-18.1) and Luteinizing Hormone (LH) 3.6 IU/l (1.5-9.3). ACTH level was 1.8 pmol/l (1.8-13.9) and there was appropriate adrenal response to tetracosactrin test. Magnetic Resonance Imaging (MRI) showed a sellar-suprasellar mass measuring 3.8 x 3.3 x 3.5 cm which displaced the optic chiasm and compressed it antero-superiorly. Pituitary stalk was not visualized. Therefore, the elevated prolactin was attributed to stalk effect. Visual field assessment showed bitemporal hemianopia. In preparation for surgery, he was given Carbimazole, Propanolol and Lugol’s iodine. Pre surgery Free T4 was 20.98 pmol/l, TSH 21.04 mIU/l and GH 4.29 ng/ml (<2.47). He underwent Endoscopic Transsphenoidal Surgery with tumour excision successfully. Free T4 post-surgery was 20.66 pmol/l with normalization of TSH at 2.2 mIU/l and GH at 1.26 ng/ml. Preliminary histopathology examination revealed features of pituitary adenoma. Conclusion We present here, a rare case of pituitary macroadenoma with TSH and GH co-secretion. This case illustrates the importance of careful evaluation of discordant thyroid function test and the following pre-surgery management of such cases.

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**EP687**  
**Primary Empty Sella Syndrome revealed by a growth retardation : about 14 cases**  
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**Background**  
Empty sella turcica (EST) is characterized by the passage of cerebrospinal fluid (CSF) into the sella turcica through the sellar diaphragm. The aim of our work is to study the clinical and hormonal characteristics of patients with EST discovered due to height delay.

**Patients and methods**  
Descriptive study on 14 patient files. Data studied : history, anthropometry, endocrine deficits and associated pathologies.

**Results/Discussion**  
6 boys, 8 girls; average age at first consultation: 8.2 years (range: 2 and 15 years); main reason for consultation: height delay (HD). No cases of fetal distress, neonatal hypoglycemia, peri natal trauma, pituitary surgery or radiotherapy. 5 cases of intracranial growth retardation, 1 case of mental retardation, 5 cases of celiac disease, 2 cases of autoimmune hypothyroidism. HD on average at -3.8 SD (range: -6 and -2 SD), average weight deficit at -2.8 SD (range: -4.5 and -2 SD); 1 case of total anterior pituitary insufficiency, 6 cases of dissociated anterior pituitary insufficiency; Partial GH deficiency in 4 cases and complete in 10 cases. 2 cases of partially empty sella turcica and 12 cases of EST. 10 children substituted for the different deficits. One child referred for Neurosurgery for hydrocephalus. There is a delay in the diagnosis of stature delay. Primary EST does not preferentially affect one sex, the congenital origin is most likely. Lifelong monitoring is necessary in order to detect possible endocrine, neurological and ophthalmological complications.

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**EP686**  
**Case report: pituitary macroadenoma with thyroid stimulating hormone (TSH) and growth hormone (GH) co-secretion**  
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**Introduction**  
The prevalence of pituitary adenoma is estimated to be 17% and about half secrete a distinct hormone. Prolactin secretion is the commonest, followed by GH or adrenocorticotropic hormone (ACTH). TSH producing pituitary adenoma is rare and occurs in less than 1% of pituitary adenomas. We report a challenging case of a 30-year-old man who presented with TSH and GH secreting pituitary macroadenoma with mass effect.

**Case Report**  
A 30-year-old man presented with typical symptoms of thyrotoxicosis (palpitation, tremor and weight loss of 20 kg) over four months associated with headache. There were no symptoms suggestive of GH excess or hypogonadism. On examination, he was normotensive. He had a small goitre and fine tremor. He was started on Carbimazole and propranolol by his primary care doctor and referred to the Endocrine Clinic for discordant thyroid function.

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intravascular large B cell lymphoma (IVLBCL) is an extremely rare type of non-Hodgkin lymphoma involving the growth of lymphoma cells within the vessel lumen without lymphadenopathy. As disease has various modes of presentation and is exceptionally rare, IVLBCL is often diagnosed postmortem. Herein, we report a case of IVLBCL with hypopituitarism, an extremely rare complication, that was successfully treated with chemotherapy. 60 years old woman noticed redness of the abdomen, fatigue, and fever. As she was diagnosed with recurrent erysipelas in the past, it was considered as recurrence of the known infection. Despite antibiotics, disease progressed, redness involved whole abdomen and thighs, fever worsened and swelling of the face and limbs as well as tingling and numbness of the lower extremities, difficulty to walk and acute kidney failure has developed. It was clear that patient did not have an ordinary infection but something else. During next few weeks patient developed severe anasarca (+20 liter), general fatigue, telangiectasia of the trunk, severe polyneuropathy, weight loss and marked panniculitis, she was unable to eat or move independently, mental changes were also notable. As all the possible causes (infections, systemic diseases, etc) were excluded, deep skin biopsy was performed from the abdominal part of the body and IVLBCL was diagnosed. IVLBCL can cause damage of virtually any organ, including endocrine glands, as patient had severe fatigue, anasarca, weight loss and mental changes, pituitary function was carefully evaluated. She was found to have hypopituitarism with central hypothyroidism, central hypogonadism, central adrenal insufficiency, and hyperprolactinemia. IGF-1 was not measured due to technical issues. Brain MRI imaging demonstrated slight increase in size of adenoma. The patient was initially treated with cabergoline (1 mg/week) observing only a short and transient decline of ACTH so the dose was adjusted. After increasing dose of cabergoline (2 mg/week) ACTH levels decreased and the headaches and hyperpigmentation improved significantly. Four years later, plasma ACTH levels were normalized (33 pg/ml) and MRI showed the disappearance of the pituitary adenoma. In order to investigate on the direct effect played by cabergoline treatment on the remission of Nelson’s syndrome, the treatment was withdrawn. ACTH levels were normalized (50 pg/ml) since nowadays.

Discussion
This case demonstrated that cabergoline treatment is able to induce the remission of Nelson’s syndrome and may be a valid therapeutic alternative in this syndrome. The peculiar expression pattern of D2 receptors in some non functional and corticotroph tumors could explain the favorable clinical response to cabergoline in the setting.

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EP691
Genomic and epigenomic aspects of Aspirin antitumoral effect in pituitary adenoma
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Background
In our previous works the interdependence of DNA demethylation with proliferation and differentiation of pituitary neuroendocrine tumours (PitNET) and the inhibitory effect of Aspirin on pituitary cell proliferation were demonstrated. Although the role of Aspirin in epigenetic regulation was
described in other malignancies, its correlation with pituitary tumorigenesis is currently unknown.

Our objective was to investigate the genomic and epigenetic effects of Aspirin in PitNET.

Materials and Methods
DNA methylation by HPLC-MS/MS, and whole transcriptome profile were evaluated by next-generation sequencing in RC4-B/C and GH3 pituitary cell lines upon Aspirin treatment. Effects of Aspirin and demethylating agent, decitabine were further tested in vitro by RT-qPCR, western blot and functional (proliferation, viability, migration, luciferase promoter reporter) assays. DNA methylation was also correlated with PTG1 expression in 41 pituitary NET samples. Gene and protein expression data of 77 PitNET with 35 control samples was obtained from Gene Expression Omnibus and literature mining.

Results
Aspirin induced global DNA demethylation and consequent transcriptome changes in vitro including decreased global histone expression. Overexpression of Tetr enzymes and their cofactor Utas2 was identified behind the increase of 5-hydroxymethylcytosine (5-hmc). Transcription factor regulatory relationships assessed by gene set enrichment analysis showed that Aspirin increased p53 and decreased E2f1 activities. The increased p53 activity was due to its acetylation at the K382 residue. Among p53 controlled genes, assessed by gene set enrichment analysis showed that Aspirin increased p53 and the K382 residue. Among p53 controlled genes, assessed by gene set enrichment analysis showed that Aspirin increased p53 and decreased E2f1 activities. The increased p53 activity was due to its acetylation at the K382 residue. Among p53 controlled genes, assessed by gene set enrichment analysis showed that Aspirin increased p53 and decreased E2f1 activities. The increased p53 activity was due to its acetylation at the K382 residue.

Conclusion
We described a regulatory network where Aspirin regulated global demethylation, Tp53 activity and Ptg1 expression in pituitary cells along with decreased cell proliferation and migration. These data may suggest the potential beneficial effect of Aspirin in PitNET.

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**EP692**

Soluble alpha klotho in blood is a new and highly stable biomarker

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**Background**
Soluble alpha klotho (sKL) is a circulating protein that has been linked to the growth hormone (GH) axis. We previously showed its association to disease activity in patients with acromegaly, with considerable robustness towards biological confounders. However, there is scarce data in literature regarding the analytical performance of the assay, and pre-analytical stability of sKL in blood samples.

**Objective**
We aimed to evaluate analytical performance and pre-analytical stability of sKL in blood samples, following the guidelines from the Clinical & Laboratory Standards Institute.

**Methods**
SsKL concentrations were measured by an ELISA (Immuno-Biological Laboratories, Hamburg, Germany). We compared different incubation times (1 h vs. overnight), analyzed precision by 10 repeated measurements within a plate and linearity by serial dilutions (no dilution, 1:2, 1:4, 1:8 and 1:16). We also tested stability of sKL under different storage conditions: 1) room temperature before (whole blood, 1, 24, 48 or 120 h) or after centrifugation (serum, 15 min, 24, 48 or 72 h); 2) freeze/thaw cycles (0-4 cycles); 3) long-term storage at -20°C (baseline compared to 20 and 31 months). Finally, we compared sKL concentrations in serum and EDTA samples collected in parallel from the same individuals (n = 18).

**Results**
Short incubation times were associated with a significant drift of concentrations obtained over the plate (>25%), an effect not seen after extending the first incubation to overnight (<5%), sKL measurements by this assay presented with low intra- and inter-assay coefficients of variation (%CV) (<10% for both). Dilution linearity was good at concentrations below 3,000 pg/ml (recovery rate (RR) (%mean (range)): 96 (92-107). Measured sKL concentrations were not significantly affected by storage for up to 120 hours at room temperature (CV (%mean (range): 29.9 (1.5-5.1)) or serum, after centrifugation: 8.9 (1.8-18.9), or by up to 4 freeze/thaw cycles (CV: 4.9 (1.4-10.1), RR: 99.1 (87.3-105.8)). Serum sKL also exhibits excellent long-term storage stability for more than 2 years at -20°C (CV: 8.6 (2.7-17.5), RR: 89.1 (76.5-111.7)). Furthermore, sKL concentrations (pg/ml) (median (interquartile range) in serum did not differ from those seen in EDTA (404.4 (341.8-462.6) vs. 428.6 (384.8-514.8), P = 0.27).

**Conclusion**
After extending incubation times to overnight, the sKL assay exhibits good performance characteristics. We suggest to dilute samples at least 1:4, especially in patients with GH excess. sKL is a biomarker with considerable preanalytical stability at different storage conditions. This facilitates its use as a GH responsive biomarker in studies and clinical practice.

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**EP693**

Influence of Desmopressin treatment in patients undergoing surgery for cushing’s disease

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**Objective**
ACTH-secreting pituitary tumors (ACTHomas) express vasopressin (AVP) receptors. AVP receptors are also present in other types of cancer, exerting different effects on tumor growth depending on the receptor subtype. AVP type 1 receptors (Vla and Vlb) are associated with stimulation of cell proliferation, AVP receptor type 2 (V2r) is associated with antiproliferative effects. Desmopressin (DAVP) is a synthetic analog of AVP that acts as a selective agonist for V2r, which has shown antitumor properties in models of breast and colorectal cancer. In addition, DAVP stimulation the release of ACTH in ACTHomas. Remission of Cushing’s disease (CD) in the postoperative vary between 55-85%, recurrence of up to 25%. Objective: describe the influence of DAVP treatment in patients undergoing surgery for cushing’s disease (CD) who develop insipidus diabetes (ID).

**Patients and methods**
Retrospective analysis of patients who underwent as transsphenoidal surgery (TSS) for CD. Statistical analysis: t-student for comparison of means and Chi squared for comparison of proportions.

**Results**
60 patients with CD treated with TSS. Age 41,72 ± 14,85 years. Women: 88.3%. Remission 75%. Postsurgical complications: 20% (3 meningitis, 9 transient DI). Of 60 patients in remission, 15.6% had transient ID, 26.7% had recurrence of CD. Of patients who presented transient ID: 28.57% had recurrence of CD vs 71.42% (P = 0.901).

**Table 1**

<table>
<thead>
<tr>
<th>Transient ID</th>
<th>No transient ID</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.43 ± 8.97</td>
<td>42.50 ± 15.60</td>
</tr>
<tr>
<td>Tumor size (mm)</td>
<td>8.24 ± 11.33</td>
<td>9.53 ± 7.37</td>
</tr>
<tr>
<td>Postsurgical basal cortisol (µg/d)</td>
<td>8.59 ± 10.64</td>
<td>6.46 ± 4.91</td>
</tr>
<tr>
<td>Midnight salivary cortisol (µg/d)</td>
<td>0.13 ± 0.10</td>
<td>0.23 ± 0.15</td>
</tr>
<tr>
<td>24-hour urinary cortisol (µg/d)</td>
<td>62.45 ± 111.28</td>
<td>64.07 ± 74.98</td>
</tr>
<tr>
<td>Postsurgical ACTH (pg/ml)</td>
<td>42.28 ± 55.95</td>
<td>15.81 ± 16.37</td>
</tr>
</tbody>
</table>
Conclusions

Transient ID is the most frequent complication in the postoperative period of CD. Patients with ID presented higher postsurgical ACTH and postsurgical basal cortisol levels without being statistically significant. CD recurrence does not differ from patients who did not present ID. Treatment with DAVP does not associated with increased risk of recurrence CD.

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Evaluation of the effectiveness of patients with acromegaly treatment (according to the moscow register)

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The aim

To determine the prognostic parameters affecting the course of acromegaly (A) and the effectiveness of drug therapy (MT).

Materials and methods

779 patients of A [218 men (28%) aged 60 (48-89) years, 561 (71.5%) were included in the Moscow register. The prevalence of A in Moscow is 6.16; the incidence is 4.0 cases/million inhabitants. The treatment algorithm included surgical aid (495 patients), primary (I) or secondary (II) MT (584) and radiation treatment (115). Radical adenomectomy was performed in 31% of patients. 69% of patients with pituitary macroadenomas were prescribed II MT. The effectiveness of treatment was assessed by the dynamics of the GH, IGF-1, IGF-1 index (IGF-1/ULN).

Results

An inverse correlation was revealed between the age of the disease, the content of GH, IGF-1 and the volume of the pituitary tumor ([r = -0.24, -0.13, -0.41, respectively, (P < 0.001)] which indicates a more active course of the disease with its early manifestation. I MT was received by 295 (69.5) m patients. Somatostatin analogs of the first-generation (SA1) (lanreotide and octreotide) and cabergoline were used. A retrospective analysis of the effectiveness of MT was carried out between non-selective and selective groups. The selective groups for I and II MT included patients (72 and 2005) with a decrease in the level of IGF-1 of more than 70% of the baseline level after 3 months of taking SA1. Control A. at II MT in nonselective groups was achieved in 48 and 58% of cases, whereas in selective groups in 72 and 80% of patients (IGF-1 index was 0.90(0.4) and 0.80(0.3), respectively, (P < 0.001). The duration of effective MT in selective groups with I MT was 49 (49) vs. 29 (29), with II MT – 53 (48) vs. 30 (37) months (P < 0.001). In both I and II MT, a moderate correlation was found between a decrease in the level of IGF-1 after 3 months of treatment, levels of IGF-1 after 12 months of treatment and at the last visit, as well as the duration of disease control [r = -0.57 (0.51); r = -0.61 (0.43); r = -0.58 (0.4); r = 0.52 (0.43), respectively, (P < 0.001)].

Conclusion

1. Independent signs associated with the effectiveness of SA1 are: the level of IGF-1 after 3 months of treatment, the initial value of the IGF-1 index and the age of diagnosis. 2. Predictors of low sensitivity to SA1 treatment: young age of diagnosis; male gender; large size of adenoma; the value of the IGF-1 index > 2.7.

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Epidemiological description of 20 years of experience in the management of insulinomas in a third level hospital

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Introduction

Insulinoma, despite its low incidence of 0.4%, it is the most common functioning pancreatic neuroendocrine tumor. Most are benign, solitary and sporadic. Around 10% can be malignant and 5-10% are part of MEN-1. On certain occasions, the differential diagnosis is difficult when there is a history of Diabetes Mellitus (DM). Our objective was to describe clinical-epidemiological data and its diagnostic-therapeutic management.

Materials and Methods

Retrospective study that used electronic records of 21 patients with a diagnosis of insulinoma confirmed by pathological anatomy treated at our Hospital from 2000-2020. Qualitative variables were described in frequencies. Shapiro-Wilk test was used to determine the normality of the variables. Data were represented according to median and interquartile range (25-75%)

Results

76.2% were women. The median age was 57 years (50-74). A median prior to diagnosis was 12 months (5-24). Of note, 3 patients had a previous history of DM2 and 16.7% had MEN-1. Within the laboratory parameters the diagnostic: basal insulin 18 mu/ml (11-37.9), basal C-peptide 1.61 ng/dl (1.1-2.3) and basal glucose 47 mg/dl (37-63). The most used functional test was the 72-hour fasting test: positive in all cases and in the first 24 hours (75%) and the rest in 24-48 hours (25%). Regarding non-invasive preoperative localization studies: the most application and with the best rate of correct localization was computed tomography (TC) (88.9% and 93.8% respectively), followed by magnetic resonance (RM) (42.9%) and abdominal ultrasound (19%). With a registered median size of 1.50 cm (1.3-2.1).

The most frequent invasive preoperative localization study was ultrasound endoscopy (9.5%) and the most used intraoperative study was ultrasound (28.6%), which identified the tumor in all the patients. The treatment of choice was surgery in 90.4%; the majority surgical method was open approach (60%). The most frequent surgical complication was pancreatic fistula (17.6%). Four cases (20%) of malignant insulinomas were reported, all were multicentric and metastatic, predominant localization was liver. In relation to the pathological anatomy report, most were unicentric. The most prevalence positive immunohistochemical markers were somatostatin, chromogranin A and insulin. 96%% had a median of 25% (1.5-5). The most common location was head and body (50%). Cure rates of 94.11% in benign cases and 25% in malignant cases were reported. No recurrences were recorded.

Conclusions

Insulinoma is a rare pancreatic tumor. CT or MRI are preferred non-invasive localization tests. The choice of treatment is pancreas-preserving surgery with a high cure rate. However, its morbidity and mortality increases when it is a malignant insulinoma.

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AQ2p gene mutation C.450T > A in a Tunisian family

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Introduction

The nongenomic diabetes insipidus (DI) is an entity to be known. It is essential to know its etiologies and especially its therapeutic modalities which are different from those of the central DI. The familial nature of the disease should suggest a genetic origin. In our paper, we are presenting the case of a Tunisian family with nongenomic DI.

Case reports

Our family had a history of neglected polyuric-polydiabetic syndrome (PPS), delayed growth, deafness, death at an early age and urinary malformations. Our first patient was a 35 years old female. She had a personal history of delayed growth and chronic renal failure. She was suffering from PPS for several years but neglected. A biological workup ruled out simple causes of DI and the water restriction test confirmed its nongenomic origin. The patient was put on indomethacin with improvement of her symptoms. Her brother, 25-year-old, with a history of deafness and delayed growth, developed a post-traumatic polyuria and polydipsia, positive response to indomethacin with improvement of her symptoms. Her brother, 25-year-old, with a history of deafness and delayed growth, developed a post-traumatic polyuria and polydipsia, positive response to indomethacin. The patient was put on indomethacin with improvement of her symptoms. Her brother, 25-year-old, with a history of deafness and delayed growth, developed a post-traumatic polyuria and polydipsia, positive response to indomethacin.
EP697
Endocrine dysfunction secondary to pituitary tuberculosis: a case report
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Introduction
Tuberculosis is an infectious disease that involves any organ. However, the primary pituitary tuberculosis is an extremely rare disease. Intracranial tuberculosis account for 0.15-5% of intracranial space-occupying lesions, of which pituitary as the primary site, and easily misdiagnosed as pituitary adenoma. In this setting, the late diagnosis can result in permanent endocrine dysfunction. We hereby report the case of a patient with pituitary tuberculosis discovered following the onset of diabetes insipidus.

Case report
The patient was a 36-year-old woman. She presented with polyuro-polydipsic syndrome (PPS) associated with Holocranial headaches and secondary amenorrhea. Hormonal exploration identified corticotropic insufficiency with hyperprolactinemia. Central DI was retained in view of the hypophysal-opititary MRI aspect showing the disappearance of the spontaneous TH hypogonadal and the presence of a thickening of the pituitary stem. The tubercular origin of this thickening was oriented by the presence of a history of erythema nodosum with a presence of a thickening of the pituitary stem. The tubercular origin of this aspect showing the disappearance of the spontaneous T1 hypersignal and the improvement of her symptoms with a weight gain of 8 kg, disappearance of headaches, PPS and galactorrhea. But she still had amenorrhea despite a dose of 5 mg/d. After 3 months of treatment, the patient showed a clear improvement of her symptoms with a weight gain of 8 kg, disappearance of headaches, PPS and galactorrhea. But she still had amenorrhea despite hormone replacement therapy: Hydrocor-tison at a dose of 20 mg/d, ddVAP at a dose of 0.3 ml/d and dopamine agonist at a dose of 0.4 ng/ml) with a normal LH level at 3.5 mUI/ml (BA 16 years (370 ng/ml), followed by a decline to nadir at 18 years in both. Girls had an early peak at IGF-1 as compared to boys. The median IGF-1 levels in girls increased from Tanner stage 1 to stage 4, with peak value of 345 ng/ml at stage 4 and declining sharply thereafter. For boys, levels increased from Tanner stage 1 to stage 3, peaked at 308 ng/ml at stage 3, after which the levels were stable and fluctuated around the peak from stage 3 to 5. IGF-1 also correlated significantly with hormonal parameters of puberty (girls: LH (r = 0.52), estradiol (r = 0.40), DHEAS (r = 0.44); boys: LH (r = 0.57), testosterone (r = 0.56), DHEAS (r = 0.47); with LH showing the best correlation. This early peaking of IGF-1 levels in the present study vis-a-vis Caucasians (14-16 years) has also been reported in other studies from Asia (11-13 years).

Conclusion
Along with chronological age, Tanner based reference range will further improve the diagnostic utility of IGF-1 normative data in school going children.

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EP698
Age and puberty based IGF-1 normative data in healthy children from North India.
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Context
Serum IGF-1 levels are of paramount importance for diagnosis and management of growth related disorders. The reference range of IGF-1 should be ethnicity and Tanner specific. Indian data on the same is scarce and there is a need to develop the same.

Objective
To develop age, sex and Tanner based normative reference range of serum IGF-1 level for Indian children and correlate the same with peri-pubertal hormonal parameters.

Setting and participants
After excluding children with short stature, anemia, chronic systemic illnesses, underlying endocrinopathies and celiac disease; 1929 children (916 girls, 1013 boys) were eligible for participation out of 2191 children screened. They were stratified as per chronological age and pubertal stage (Marshall and Tanner).

Outcome measures
Serum IGF-1 was measured by in house electrochemiluminescence immunoassay by Roche Diagnostics (cobas e 801) Mannheim, Germany; at PGIMER, Chandigarh. External validation of assay was done by robust immunodiagnostics method (iSYS) at Manchester, UK. Normative reference range and correlation were obtained based on Roche method.

Result
Serum IGF-1 levels peaked at chronological age of 13 years (median 50th centile 397.38 ng/ml) [Greulich Pyle BA 14 years(389 ng/ml) in girls and at 15 years in boys (327 ng/ml) [BA 16 years (370 ng/ml), followed by a decline to nadir at 18 years in both. Girls had an early peak of IGF-1 as compared to boys. The median IGF-1 levels in girls increased from Tanner stage 1 to stage 4, with peak value of 345 ng/ml at stage 4 and declining sharply thereafter. For boys, levels increased from Tanner stage 1 to stage 3, peaked at 308 ng/ml at stage 3, after which the levels were stable and fluctuated around the peak from stage 3 to 5. IGF-1 also correlated significantly with hormonal parameters of puberty (girls: LH (r = 0.52), estradiol (r = 0.40), DHEAS (r = 0.44); boys: LH (r = 0.57), testosterone (r = 0.56), DHEAS (r = 0.47); with LH showing the best correlation. This early peaking of IGF-1 levels in the present study vis-a-vis Caucasians (14-16 years) has also been reported in other studies from Asia (11-13 years).

Conclusion
This early peaking of IGF-1 levels in the present study vis-a-vis Caucasians (14-16 years) has also been reported in other studies from Asia (11-13 years).

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EP699
Pituitary adenomas characteristics in patients with multiple endocrine neoplasia type 1, its phenocopies and sporadic acromegaly
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Multiple endocrine neoplasia type 1(MEN1) is a hereditary condition caused by mutations in the MEN1 gene, which encodes menin protein. The syndrome predisposes to the development of tumors in both endocrine and non-endocrine systems. In patients with MEN1, pituitary adenomas (PA) occur in approximately 40% of all cases. If patient has MEN1 phenotype with no mutations in MEN1 gene, the condition is regarded as a phenocopy. The reason of several endocrine MEN1-associated tumors combination in these patients remains unknown. Knowing menin expression in groups and if there are any somatic mutations in...
Introduction

The group of young adults with acromegaly, despite initial reports about their aggressive course of disease, has not been thoroughly characterized. Aim: Our aim was to investigate the differences between the patients with early-onset acromegaly and with onset in older age.

Material and methods

Consecutive patients diagnosed with acromegaly between 01.2014 and 12.2021 were included in this retrospective study, approved by the local Bioethics Committee. Firstly, the arbitrary division (Group A: with patients ≤30 and Group B: with patients > 30 y.o. upon diagnosis) was used. Secondly, retrospective estimation of age upon symptoms onset divided the patients into Group C and D (≥30 and >30 y.o. at the onset, respectively). We statistically compared Groups A and B and subsequently Groups C and D in terms of clinical, biochemical and radiological parameters, using IBM SPSS Statistics, ver. 27.

Results

Out of 72 consecutive patients with acromegaly, 64 were included in the study. Group A consisted of 11 patients, 54.5% males, Group B had 53 patients, 41.5% males. Retrospective estimation of the age at diagnosis was available in 50 patients: there were 18 patients in Group C (44.4% males) and 32 patients in group D (34.4% males). There were no statistically significant differences between group A and B as well as between C and D in terms of: gender, median diagnostic delay, frequency of accidental diagnosis, hypopituitarism, hyperprolactinemia and, radiologically, occurrence of macroadenomas, median maximal tumor diameter, pituitary apoplexy, cavernous sinus invasion, compression of the optic chiasm. Median growth hormone (GH) nadir concentration was higher in Group A than in Group B: 38.4 uIU/ml (IQR 24.1); IQR 65.7) vs. 20.8 uIU/ml (IQR 10.45; IQR 34.5), respectively (P = 0.046). GH was higher in Group C (37.1 uIU/ml, IQR 67.2; P = 0.046) vs. Group D (15.3 uIU/ml, IQR 27.7; P = 0.046). No differences in RFP1 concentration related to upper normal limit were discovered between the groups in both steps of the analysis. Biochemical control was after surgery was similarly frequent in groups A and B, and groups C and D.

Conclusions

In our study, patients with early-onset acromegaly did not statistically differ from typical-onset patients, even when considering two division criteria: arbitrary and based on the estimated symptoms onset. Our main limitation is the small number of patients enrolled, even though all of the newly diagnosed patients in a tertiary endocrinology center over 8 years were included. Further, prospective studies are needed to identify and assess the differences between age groups of acromegaly patients.

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EP700

A Delphi panel of Italian endocrinologists to define the unmet needs on the current management of Cushing’s Syndrome

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Introduction

Cushing’s Syndrome (CS) requires an accurate diagnosis, patient-tailored treatments and long-term management. To define the unmet needs of patients with CS, a consensus among a panel of Italian endocrinologists was promoted. The panel involved 57 specialists with expertise in CS management.

Methods

The endocrinologists were identified by convenience sampling. The survey was built around a set of statements formulated after literature review and discussion with an experts’ advisory board. A total of 24 statements were finally included in the survey. The Delphi method was used to reach consensus on the statements using scores on a 1-to-9 scale (with 1 indicating disagreement with the statement and 9 indicating full agreement). A 70% threshold was set to define consensus, meaning that strong agreement was believed reached if at least 70% of participants had assigned scores in the range 1-3 or 7-9, respectively.

Results

Twenty-three endocrinologists (40% of the sample) working in 10 Italian regions took part into the survey. Among them, 52% reported to follow between 5 and 10 Cushing patients per year, 22% between 10 and 20 patients, 17% more than 20 patients, and 9% less than 5 patients. The Delphi process was concluded in 2 rounds. Agreement was reached on 18 of the 24 proposed statements (75%). The statements for which consensus was not reached (n=6, 25%) were mainly related to the definition of a standard pharmacological therapy for CS, the response time to the available pharmacological therapies, the achievement of a complete control of the clinical condition, the evidence base needed for CS pharmacological therapies, and the satisfaction with the safety and effectiveness profiles of the current pharmacological therapies. Some statements in particular accounted for extremely high level of agreement (values over 90%) and they were related to the need of a constant and periodic follow-up of the patients, given the possibility of mid-long term relapse; to the relevance of the escape, which can have a strong impact on the overall management of the condition; to the need to promote the development of management pathways which are specific for CS; to the need that a newer pharmacological option, with improved safety and effectiveness profile, could radically change the current management of the CS.

Conclusions

The survey revealed that the experts involved perceive some relevant unmet needs in the management of CS, mainly related to the lack of a pharmacological treatment with more favourable safety and effectiveness profile.

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PE701

Age at the diagnosis or age at the onset of symptoms - which should be taken into consideration in patients with early-onset acromegaly - pilot study


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Introduction

The group of young adults with acromegaly, despite initial reports about their aggressive course of disease, has not been thoroughly characterized. Aim: Our aim was to investigate the differences between the patients with early-onset acromegaly and with onset in older age.

Material and methods

Consecutive patients diagnosed with acromegaly between 01.2014 and 12.2021 were included in this retrospective study, approved by the local Bioethics Committee. Firstly, the arbitrary division (Group A: with patients ≤30 and Group B: with patients > 30 y.o. upon diagnosis) was used. Secondly, retrospective estimation of age upon symptoms onset divided the patients into Group C and D (≥30 and >30 y.o. at the onset, respectively). We statistically compared Groups A and B and subsequently Groups C and D in terms of clinical, biochemical and radiological parameters, using IBM SPSS Statistics, ver. 27.

Results

Out of 72 consecutive patients with acromegaly, 64 were included in the study. Group A consisted of 11 patients, 54.5% males, Group B had 53 patients, 41.5% males. Retrospective estimation of the age at diagnosis was available in 50 patients: there were 18 patients in Group C (44.4% males) and 32 patients in group D (34.4% males). There were no statistically significant differences between group A and B as well as between C and D in terms of: gender, median diagnostic delay, frequency of accidental diagnosis, hypopituitarism, hyperprolactinemia and, radiologically, occurrence of macroadenomas, median maximal tumor diameter, pituitary apoplexy, cavernous sinus invasion, compression of the optic chiasm. Median growth hormone (GH) nadir concentration was higher in Group A than in Group B: 38.4 uIU/ml (IQR 24.1); IQR 65.7) vs. 20.8 uIU/ml (IQR 10.45; IQR 34.5), respectively (P = 0.046). GH was higher in Group C (37.1 uIU/ml, IQR 67.2; P = 0.046) vs. Group D (15.3 uIU/ml, IQR 27.7; P = 0.046). No differences in RFP1 concentration related to upper normal limit were discovered between the groups in both steps of the analysis. Biochemical control was after surgery was similarly frequent in groups A and B, and groups C and D.

Conclusions

In our study, patients with early-onset acromegaly did not statistically differ from typical-onset patients, even when considering two division criteria: arbitrary and based on the estimated symptoms onset. Our main limitation is the small number of patients enrolled, even though all of the newly diagnosed patients in a tertiary endocrinology center over 8 years were included. Further, prospective studies are needed to identify and assess the differences between age groups of acromegaly patients.

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EP702

Giant pituitary adenomas in children and adolescents: clinical presentation, management and long-term outcome

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Background
Pituitary adenomas in children/adolescents represent around 3% of all intracranial neoplasms. They are more frequently hormone-secreting lesions, usually diagnosed in early childhood and late adolescence. Female gender is generally prevalent, because of most evident symptoms (i.e., irregular periods, galactorrhea, etc.). Giant pituitary adenomas (GA) very rarely occur in pediatric age, posing frequent challenges in their management.

Patients and methods
We retrospectively evaluated the records of 7 teenage patients (5 males, median age 16.7 ± 1.6 yrs) with GA, referred to the Endocrine Unit of the University Hospital of Messina (Italy) from 1990 to 2020. All patients underwent biochemical, clinical and neuroradiological workup. The median follow-up was 16.1 ± 9.9 years.

Results
GAs were clinically characterized as follows: five functioning PAs (4 PRL-secreting, 1 ACTH-secreting) and two non-functioning pituitary adenomas (NFPA). Median pituitary tumor diameter was 43 ± 2.2 mm. Genetic analysis revealed only 1 carrier of MEN1 mutation (a patient with PRL-secreting tumor), while no changes of AIP gene were detected. At diagnosis, main presenting symptoms were headache (n.5), visual disturbances (n.4), menstrual irregularities (n.2), and growth delay (n.1). In terms of pituitary function, 1 patient presented with panhypopituitarism, 2 with multiple pituitary deficits. One patient with NFPA was lost to follow-up, of the remaining 6 patients: 3 (1 PRL, 1 ACTH, 1 NFPA) were referred to first-line surgery by endoscopic trans-nose-sphenoidal approach, 3 PRL-omas were treated with medical therapy (cyclophosphamide) exclusively or prior to surgery. After first-line treatment, stable remission (no tumor remnant and/or no hormone hypersecretion) was observed in 3 subjects, progression (growing tumor remnant and/or persistent hormonal hypersecretion) in 3 cases. In these last cases, second-line treatment was radiotherapy. At last follow-up visit: 5 patients were in remission while 1 patient with PRL secreting tumor was still under effective cabergoline treatment; 2 patients had panhypopituitarism, 3 single/multiple pituitary deficits, while pituitary function was preserved in one subject. GH deficiency (GHD), isolated as well in association with other deficits, was the most frequent pituitary hormone deficit (n.5/7 patients). During follow-up, the following comorbidities were diagnosed: metabolic syndrome (n.3), osteoporosis (n.2), second tumors (n.1).

Conclusions
Giant pituitary adenomas management in children/adolescents is challenging and require a multidisciplinary approach.

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EP703

The clinical implication of macroprolactinemia detection using PEG 6000 in a group of women of childbearing age with hyperprolactinemia in sub-Saharan Africa: experience of a tertiary hospital

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Introduction
Macroprolactin (MacroPRL), a variant of human prolactin may interfere with hormonal assay and falsely increase serum prolactin levels. Therefore, failure to identify macroprolactinemia can lead to inappropriate investigations and treatment in women who are already susceptible to anxiety and stress. We aimed to identify macroprolactinemia among women of childbearing age with hyperprolactinemia.

Materials and methods
We conducted a cross-sectional study at the endocrine unit of one of the tertiary hospitals in Cameroon. Study participants were recruited from both endocrine and gynecological outpatient consultations services. They were women of childbearing age (18 to 49 years) consulting for signs and symptoms of general dysfunction or hyperprolactinemia (PRL > 25 ng/ml). Total prolactin was measured using a human direct ELISA method. Polyethylene glycol 6000 (PEG 6000) precipitation was used to detect macroprolactinemia.

Results
We enrolled 33 women with a mean age of 31 ± 7 years (range 21–48). Twenty-seven (81.8%) participants were symptomatic with the majority 23/27 (69.7%) reporting galactorrhea and 21 (63.4%) women reported having an irregular menstrual cycle. The median pre-precipitation prolactinemia reduced significantly after PEG precipitation from 61.2 (IQR: 35.2–115.9) ng/ml to 33.8 (IQR: 17.9–70.5) ng/ml, P < 0.001. After PEG precipitation, 5 participants had a serum prolactin recovery rate below 60%, and therefore a prevalence of macroprolactinemia at 15.2%. Four (80%) women with macroprolactinemia presented with symptoms, and there was no association between macroprolactinemia and symptoms of hyperprolactinemia among these participants.

Conclusion
Macroprolactinemia was detected in 5/33 (15.2%) of the study population. There was no association between macroprolactinemia and symptoms of hyperprolactinemia. Oligomenorrhea, amenorrhea, and galactorrhea were present in the majority of patients with macroprolactinemia hence routine screening for macroprolactinemia is recommended or advised in order to reduce the use of dopamine agonist treatment and imaging.

Keywords: Prolactin, Macroprolactin, PEG, Prolactin recovery rate, hyperprolactinemia

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EP704

Cessation of GH secretion in acromegaly without medical or surgical intervention; Covid-postponed surgery was escaped

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Introduction
Acromegaly is usually caused by pituitary macroadenoma producing excess growth hormone. Treatment options include surgery to remove the tumor, medications, and radiation therapy.

Case report
A 39-year-old woman has been referred to the endocrine clinic with suspected acromegaly in December 2019. Surgery for benign ovarian cyst, endometriosis, amenorrhea, unsuccessful in vitro fertilisations were present in her medical history. She complained about thickening of fingers, facial bloating, dry skin and vision impairment. Laboratory examinations proved acromegaly, central hypothyroidism, hypogonadism and mild hyperprolactinemia. ACTH and cortisol levels were in the normal range. Sella MR showed pituitary macroadenoma in size 17 x 12 x 14 mm. There was no abnormal finding detected by ophthalmological examination. After the diagnosis was established, levotheroxine was started and pituitary surgery was scheduled for March of 2020. Restrictions due to the coronavirus pandemic prevented the operation; this was postponed to an uncertain date in the future. We decided to start long-acting somatostatin analogue treatment. Before treatment could be started, something unexpected happened. In April 2020, severe headache, nausea, vomiting, weakness, hypotension occurred. Urgent MR showed substantial decrease in the size of the macroadenoma and haemorrhage in the tumor. Laboratory findings confirmed hypoadrenia and decrease in growth hormone and insulin-like growth factor 1 levels. On follow-up, hypopituitarism was treated effectively with hormone replacement therapy. Growth hormone and insulin-like growth factor 1 levels were further reduced, the size of the pituitary adenoma decreased below 1 cm on repeated MR. The clinical feature of acromegaly disappeared and no special treatment for acromegaly was required.

Conclusions
Pituitary apoplexy is a rare condition, occurs in 2-12 % in pituitary adenomas and in 0.05-4.8% in acromegaly. Typical symptoms are headache, vomiting, visual
Hyperprolactinemia and connective tissue diseases: which significance of such exceptional association?  
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Introduction
Dermatomyositis is a chronic, idiopathic inflammatory myopathy that can overlap with rheumatoid arthritis. The immunostimulatory effect of prolactin is suggested by many authors. Herein we report an original association of hyperprolactinemia with a scarce condition: dermatomyositis-rheumatoid arthritis overlap in a young woman.

Case description
A 26-year-old woman with no significant medical history was referred to our department to investigate deterioration of physical condition with myalgia. She was apyrexic and had clinical features of dermatomyositis including Gottron’s papules, heliotrope rash, proximal nail fold erythema, symmetric weakness affecting predominantly the proximal muscles of the legs and arms. Serum creatinin kinase was elevated at 395 UI/l and lactate deshydrogenase levels were at 546 UI/l. The muscle biopsy and the electromyogram confirmed dermatomyositis diagnosis. Respiratory function tests and CT chest were normal. There were no symptoms of infection. Given possible association with neoplasms, exhaustive investigation was performed and showed no underlying neoplastic disease. Since the patient had polyarthralgia and a biological inflammatory syndrome, we suspected the presence of another connective tissue disease. An overlap of dermatomyositis and rheumatoid arthritis was diagnosed as the patient presented symmetrical swelling of small joints, morning stiffness, and a boutonniere deformity in the 4th and 5th right fingers. Rheumatoid factor was at 80 UI/l and anti-CCP levels were at 15. Menstrual irregularities were reported, therefore hormone tests were performed. They highlighted a hyperprolactinemia at 1136 UI/l and normal levels of FSH, LH and estrogen. Gynecological examination and pelvic sonography showed no abnormalities. The patient was commenced on prednisone 50 mg/day (1 mg/kg), with satisfying clinical and biological evolution. No prolactin inhibitors were prescribed. Prolactin levels were normalized in follow-up and menstrual cycles of our patient became more regular. Pitiitary MRI was not performed as the patient lost to follow up.

Conclusion
The effect of hormones on the immune system has been widely described. Many research reported hyperprolactinemia in patients with autoimmune diseases; it might promote the development of autoimmune diseases, leading some authors to suggest some role of dopamine agonists in the therapy of those diseases. More large-scale studies are needed to establish the exact relationship between hyperprolactinemia and autoimmune diseases and efficacy of dopamine agonists in such conditions.

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would have to be ultimately used. Given the patient’s symptoms Cortisol deficiency was suspected. Cortisol was measured and was found to be very low, repeated several times. ACTH at the same time was very low suggestive of secondary adrenal insufficiency. To investigate the reason for secondary adrenal insufficiency, patient had MRI of pituitary gland which was normal, revealing no pituitary tumors or pituitary stalk lesions/other lesions. Additional pituitary hormonal workup was performed. Overall, the biochemical picture was consistent with idiopathic ACTH deficiency. Hydrocortisone therapy was initiated 30 mg QD, lead to significant improvement of symptoms. Hyperglycemia and secondary hyperaldosteronism was incidentally found during workup for above symptoms. Hemoglobin A1c was above normal ranges-5.9 %, but GAD antibodies and C peptide were not indicative of autoimmune type 1 diabetes. Blood pressure measurements were high and aldosterone and renin plasma activity was elevated. Patient continuous levodopa therapy supplementation therapy. However, after 3 years of hydrocortisone therapy patient suddenly started gaining weight and developed cushing’s symptoms so we performed trial with slow down titration of hydrocortisone which lead to improvement of symptoms. We checked morning cortisol and ACTH which were normal. For migraines she is using NSAID’S and is aware of overuse headaches and is trying to be mindful of that.

Conclusion
We should bear in mind the possibility of adrenocorticotropic hormone deficiency even when patients with history pain syndromes and opioid use.

EP709
A rare association of Neurofibromatosis type 2 and hypopituitarism
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Introduction
Neurofibromatosis type 2 (NF2) is an autosomal dominant genetic disorder that cause a growth of noncancerous tumors in the nervous system, it associates cranial schwannomas, meningiomas, and skin and ophthalmologic lesions. It is a rare condition and its association with an intrasellar arachnoidocele has not been reported yet. We report the case of a patient who presents a NF2 associated with hypopituitarism related to an intrasellar arachnoidocele.

Case presentation
It was a 37-year-old, patient referred for symptoms of hypopituitarism. She reported galactorrhea, menses return, constipation, weight loss, asthenia and reported galactorrhea, menses return, constipation, weight loss, asthenia and hyperprolactinemia, followed by thyroid and corticotropic insufficiency in 28% of the cases, 30% of which was secondary to pituitary stalk lesions/other lesions. Additional pituitary hormonal workup was performed in order to establish etiological diagnosis but were non contributory. A bone biopsy of the frontal bone was then performed, and the pathologic examination concluded to LCH diagnosis. Desmopressin therapy was therefore initiated. The patient was referred to the hematology department where he received chemotherapy (vinblastine, etoposide) with corticosteroid therapy. During follow-up: the patient developed GH deficiency, TSH deficiency, and FSH and LH deficiencies, corticotropic axis has not been evaluated because the patient was on corticosteroid therapy. There was no reduction of desmopressin doses. The frontal lesion was not present on the follow-up MRI. On the other hand, it showed a new lesion in the left frontal sinus suggesting an osteoma; a CT scan remains necessary for a better evaluation of the bony structures

Conclusion
In this patient LCH was revealed by central diabetes insipidus as the first manifestation, associated with solitary bone lesion. Treatment included desmopressin replacement and chemotherapy. During follow-up, the patient developed a panhypopituitarism with no improvement in diabetes insipidus with the appearance of a second bone lesion in the left frontal sinus.

EP711
Pituitary adenoma in the young adult
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Introduction & Background
Pituitary adenomas represent 10-25% of all intracranial tumors. Their incidence is higher between the ages of 40-60 years and less frequent in young adults. The objective of this work was to evaluate the prevalence as well as the clinical and etiological profile of pituitary adenomas in young adults.

Key words : pituitary adenoma- yount adult.

Material and methods
Retrospective descriptive study of 21 patients followed-up for pituitary adenoma whose age was less than 30 years. Data were collected from medical records and analyzed by SPSS-V21 software.

Results
Pituitary adenoma in young adults under the age of 30 represented 23% of all cases of pituitary adenoma in our series (n=21/91). The mean age at diagnosis was 24±4.9 years with a clear female predominance (61.9%). The clinical presentation was dominated by pituitary secretion syndrome in 66% of cases (n=15) followed by pituitary tumor syndrome in 23.8% of cases (n=5). Hypothalamohypophyseal MRI showed a pituitary macroadenoma in 71.1% of cases, 72% of which had an extrasellar extension associated with invasiveness in 4 patients (19% of cases), and a pituitary microadenoma was noted in 38.9% of cases. Corticotropin adenomas were reported in 42.8%, followed by prolactin adenomas in 33.3% and somatotropin adenomas in 14.3% of cases. A non-secretting pituitary adenoma was reported in only one patient, i.e. 4.7% of our series. The evaluation of the anteropituitary insufficiency showed a gonadotropic insufficiency in 28% of the cases, 30% of which was secondary to hyperprolactinemia, followed by thyroid and corticotropic insufficiency in 14.3% of the cases respectively and somatotrophic insufficiency in one patient.57% of the patients benefited from a surgical treatment with the necessity of a surgical revision in only one patient presenting with a non-secretting pituitary macroadenoma invading the optic foramen.
Evolution from recurrent cushing’s disease to pituitary carcinoma
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Introduction
ACTH-secreting pituitary adenomas occasionally present as aggressive pituitary tumors (APT), with invasion of surrounding structures, rapid growth, resistance to conventional therapies and multiple recurrences. In rare cases they can progress to pituitary carcinomas (PC) in several years, diagnosis being made upon the documentation of systemic or central nervous system (CNS) metastatic spread. Among pituitary carcinomas, the most common malignant subtypes are lactotroph and corticotroph carcinomas.

Case report
We present the case of a 66 years-old female diagnosed with an invasive ACTH-secreting pituitary macroadenoma in 2015. She underwent transphenoidal surgery followed by Gamma-knife radiosurgery due to recurrent disease. Pasireotide was initiated but discontinued after only two months due to serious side effects, including corticotroph insufficiency. After 2 years of remission, hypercortisolism reappeared but in the absence of approachable residual tumor Cabezorgone treatment was initiated, to which she responded well, developing adrenal insufficiency. One year later, considering the increase in tumor size, the second course of Gamma-knife radiosurgery was performed with no efficacy, and in 2020 she underwent transcranial adnomectomy. The immunohistochemistry revealed high aggressiveness of the tumor - Ki67 5% and mitotic index was greater than 10 mitoses per 10HPF. The last MRI showed a 9 mm tumor at the vermis and the immunohistopathology report described a pituitary carcinoma metastasis (ACTH intense positive, p53 expression in 40% of the cells and K167 5%). External radiotherapy was performed; Temozolomide therapy was contraindicated due to poor clinical condition of the patient. She ultimately died just 2 months following the diagnosis of carcinoma.

Results
In 2015 with persistently increased chromogranin A (CrgA). Pathology results showed a non-infiltrating, low-grade neuroendocrine neoplasm (carcinoma tumor), within the surgical margins, and < 2 mitoses/mm2. (2 in the medialistal face of the left lobe and another in the right lobe)

Discussion
Following the suspicion of MEN-1, even in patients with an atypical condition, a genetic study should be requested early, prior to the indication of parathyroidectomy. Following the suspicion of MEN-1 syndrome, even in patients with an atypical condition, a genetic study should be requested early, prior to the indication of parathyroidectomy. This is due to the possible implication in the surgical technique, given the great recurrence of hyperparathyroidism in these cases and to avoid the appearance of early complications derived from it.

Conclusion
We present a case of a 49-year-old woman referred from the Oncology clinic for the assessment of thyroid incidentalomas found in a follow-up CT scan of multifocal bronchial carcinoid tumor (typical carcinoid tumors), operated in 2015 with persistently increased chromogranin A (CrgA). Pathology results showed a non-infiltrating, low-grade neuroendocrine neoplasm (carcinoid tumor), within the surgical margins, and < 2 mitoses/mm2. (2 in the medialistal face of the left lobe and another in the right lobe).

Materials and methods
We present the case of a 49-year-old woman referred from the Oncology clinic for the assessment of thyroid incidentalomas found in a follow-up CT scan of multifocal bronchial carcinoid tumor (typical carcinoid tumors), operated in 2015 with persistently increased chromogranin A (CrgA). Pathology results showed a non-infiltrating, low-grade neuroendocrine neoplasm (carcinoid tumor), within the surgical margins, and < 2 mitoses/mm2. (2 in the medialistal face of the left lobe and another in the right lobe).

Results
Thyroid ultrasound showed a multinodular goiter with a dominant 28-mm nodule classified as Bethesda category II. Laboratory tests revealed a pituitary profile, thyroid hormones, catecholamines, 5-HIA, and CEA within normal ranges, elevated ChromograninA levels and undetectable calcitonin. Increased levels of calcium and phosphorus are displayed in Table 1. Octreoscan, bone densitometry and calcium were requested, which didn’t show any abnormalities. Parathyroid scintigraphy was performed due to elevated calcium > 1 gr/dl, with possible adenoma in the upper pole of the right thyroid lobe. Patient was referred for surgery in February 2020, although it was delayed due to the pandemic until June 2021. A total thyroidectomy and a parathyroidectomy were performed, and a parathyroid adenoma was found. Afterwards, the patient temporarily presented phosphocalcic metabolism values within a normal range, followed by a subsequent increase (Table 1). MEN-1 genetic study was requested. A pathogenic variant in the MEN-1 sequence was detected: c.125G>A. P (Asp418Asn) in Heterozygosity (rs104894264).

Discussion
Following the suspicion of MEN-1, even in patients with an atypical condition, a genetic study should be requested early, prior to the indication of parathyroidectomy. This is due to the possible implication in the surgical technique, given the great recurrence of hyperparathyroidism in these cases and to avoid the appearance of early complications derived from it.

Conclusion
The evolution of APTs may have periods of radiological and hormonal quiescence. Morbidity and mortality are increased, even in the absence of progression to PC, especially in functioning corticotroph APTs, where they exacerbate in relation to cortisol excess. So far, no pathological marker has been shown yet to reliably predict pituitary tumor behavior. Early diagnosis would favor the chance for prompt intensive treatment in an attempt to reduce overall morbidity and possible progression to carcinoma.

Keywords: pituitary carcinoma, Cushing’s disease;

Table 1

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patient with multiple comorbidities, including chronic leg ulcers, which are related to increased morbidity and health costs.

Case report
In October 2019, a 67-year-old patient presented with intense headache, left temporal visual impairment and pituitary macroadenoma (3.4 cm). He was diagnosed with Cushing’s disease (serum cortisol = 17.55 mcg/dl after 2 mg/day x48h Dexamethasone, ACTH = 197 pg/ml), optic chiasm syndrome and thryotropin and gonadotropin insufficiency. The patient had significant comorbidities: secondary hypertension and diabetes, episodes of tachyarythmia and femoral artery stenosis. After transphenoidal surgery, despite 3 months remission of hypercortisolism (basal serum cortisol = 0.14 mcg/dl), a 2.1 cm remnant progressive tumor along with biochemical hypercortisolism-serum cortisol = 14 mg/dl after 1 mg Dexamethasone, led to a 6 months dopamine agonist aftermath. In 2020, progressive chronic ulceration appeared in the lower limbs. Despite the January 2021 second transphenoidal operation, in June 2021, the hypercortisolism worsened: severe hypokaliemia (2.5 mmol/l despite potassium replacement), uncontrolled diabetes (HbA1c = 11%), BP = 220/110 mmHg despite triple therapy, so a steroidogenesis inhibitor and glucocorticoid receptor blocker therapy were initiated. Afterwards, right ophthalmoplegia and severe headaches appeared. Pituitary apoplexy and stroke were ruled out by MRI showing a tumoral remnant, invasive in both cavernous sinuses. The treatment was continued only with Metyrapone 500 mg/day. In August 2021, the patient developed adrenal insufficiency while using Metyrapone (BP = 110/70 mmHg, serum glucose = 69 mg/dl, serum cortisol = 1.57 mcg/dl), so Prednisone 5 mg/day was prescribed, thus receiving block and replace regimen. The patient was treated with gamma knife radiosurgery in September 2021. Afterwards, the infected leg ulcers with Grame negative bacteria forced him to become wheelchair-bound, requiring repeated hospital admissions, with two episodes of acute renal injury. In January 2022, laboratory tests found persistent hypercortisolism (serum cortisol = 20 mcg/ml after 1 mg Dexamethasone without any treatment). Block and replace regimen was restarted. The cardiovascular examination established the need for bilateral thigh amputation, for now, only one having being performed.

Conclusions
This case highlights how the multiple and aggressive complications of Cushing’s disease can significantly affect the quality of a patient’s life. The chronic leg ulcers, the risks of hospitalisation and the drug toxicity eventually led to amputation. Furthermore, achieving eucortisolism is a constant challenge in the management of recurrent Cushing’s disease. Consequently, rigorous and repeated long-term follow-up evaluations of this condition are mandatory.

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EP716
Pituitary Hyperplasia secondary to Severe Primary Hypothyroidism
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Introduction
Thyrotroph pituitary hyperplasia in context of severe primary hypothyroidism is rare and usually occurs due to loss of thyroid hormone feedback inhibition and overproduction of thyrotropin-releasing hormone, leading to pituitary gland enlargement. Pituitary hyperplasia caused by primary hypothyroidism responds well to thyroid hormone replacement therapy and rarely requires surgical intervention.

Case presentation
A 42-year-old female with background history of type 2 diabetes, hypothyroidism, transient ischaemic attack (TIA) glaucoma and epilepsy presented initially with light-headedness. Systemic examination was unremarkable. Biochemical assessment revealed severe primary hypothyroidism with TSH of 442 milliunit/l (NR 0.30-4.20 milliunit/l), free T4 5.2 pmol/l (NR 9.23 pmol/l) and mild hyperprolactinaemia. Magnetic resonance imaging (MRI) revealed a large pituitary macroadenoma with extension into the suprasellar compartment, without compression of the optic chiasm. The patient required escalating doses of levothyroxine, maximally 300 mg daily due to variable compliance (levothyroxine absorption test normal). Imaging was repeated when the patient’s TSH had fallen to 0.37 milliunit/l. The repeat MRI pituitary showed marked reduction in the size of the pituitary enlargement, making the diagnosis of thyrotroph pituitary hyperplasia.

Conclusion
Pituitary hyperplasia caused by primary hypothyroidism usually has a good response to thyroid hormone replacement therapy. Surgical intervention is not usually required.

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EP717
An aggressive macroprolactinoma in young boy about a case.
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Chu Mohammed VI, Marrakech, Marrakech, Morocco

Introduction
Pituitary adenomas are a rare condition in children and young people. The prolactinoma represents the most frequent of them. We report a case of an atypically evolution of an aggressive macroprolactinoma in young patient.

Case
It’s about a boy of 14 years old with previous history of headache from 5 years without visual disturbance. He was admitted for intracranial hypertension syndrome. In clinical examination no dysmorphic syndrome, a growth retardation...
and a bilateral gynecomastia. MRI showed a macroadenoma with lateral extension to the cavernous sinuses with encephalopathy of carotid arteries. The hormonal test showed a hyperprolactinemia of 470 ng/ml with a secondary gonadal, cortical, and thyroid deficiency. Partial transsphenoidal adenomectomy was performed and the histological assessment confirmed a macroprolactinoma with upper Ki67 at 7%. Cabergoline was started at 1 mg/week to 2 mg/week. The evolution done by the progressive normalization of blood prolactin and reduction of the size of the residual tumor.

Discussion

Pituitary adenomas in young people are frequently hormonally active. These patients typically presented with endocrine symptoms related to their adenoma type, in our case he presented gynecomastia and tumor syndrome. Prolactinoma is a more common one. The radiological characteristics and the Hight Ki67 proliferation index gave an idea of aggressive tumor. Taking in account the young age it can be part of AIP mutation or another type of genetic predisposition syndrome. These two conditions tend to predict recurrence and resistance to conventional therapy. The good evolution by dopaminergic agonist was atypical. Long-term follow-up will make it possible to report on the recurrence or otherwise of the process.

Conclusion

The management of pituitary adenoma in young patients must take in account the progress on histopathology and molecular fields. The specific medical treatment of prolactinoma may be try as part of complex management.

Reference


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EP718

Abstract Withdrawn

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EP719

FSH- secreting pituitary microadenoma and ovarian hyperstimulation

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Introduction

The prevalence of functioning gonadotropinoma is difficult to assess since most of reports are case reports. Gonadotropinomas rarely lead to a noticeable clinical syndrome. They usually produce symptoms associated with mass effect such as headaches, visual field impairment and hormonal deficiencies.

Case report

We present the case of a 38 years old women diagnosed in 2017 with microprolactinoma. She had elevated prolactin level (108 ng/ml) and a small pituitary adenoma with 9/8 mm in diameter. She was treated with dopamine agonist for 3 weeks after the diagnosis, treatment stopped afterwards due to side effects. In follow-up examinations prolactin level normalized with no treatment, the cysts reappeared, in our department she presented with headache, amenorrhea and recurrent bilateral ovarian cysts. Serum prolactin was normal but she had a high serum estradiol level (963.2 pg/ml) with a FSH and LH of 2.01 mIU/ml and 2.36 mIU/ml respectively. This was enough to raise the suspicion of a functional gonadotropinoma, unfortunately we could not measure serum gonadotropin hormone alpha-subunit to confirm the diagnosis.

Conclusion

The patient initially presented with a prolactin producing microadenoma and later developed a second pituitary adenoma. The elevated estradiol level and recurrent bilateral ovarian cysts raised the suspicion of a functional gonadotropinoma. The patient needs further evaluation to confirm the diagnosis.

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EP720

Clinical and laboratory features and management of pituitary apoplexy: Case series

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Eskisehir Osmangazi University, Department of Endocrinology and Metabolism, Eskisehir, Turkey

Introduction

Pituitary apoplexy (PA) is a clinical emergency resulting from acute ischemia or bleeding of the pituitary gland. Complaints of patients are usually headache and vision problems. We tried to discuss the reasons for presentation, pituitary imaging and hormones of patients.

Patients and methods

10 patients (5 men and 5 women), median age 53 years at diagnosis were retrospectively reviewed. FSH, LH, estradiol/testosterone, GH, IGF1, TSH, FT4, cortisol, ACTH, PRL were measured. Pituitary MRI were performed.

Results

When we look at the reasons for the patients’ admission; headache, nausea and vision problems in 4 patients; weakness, fatigue, nausea in 3 patients; confusion in 1 patient; abdominal pain in 1 patient; polyuria, polydipsia, weight loss in 1 patient. Only one patient had a previous history of pituitary adenoma. Panhypopituitarism was present in all patients. One patient had diabetes insipidus too. Macroadenoma was detected in 6 patients (median tumor diameter 31.8 mm).

4 patients were referred to the operation. The pathology result of all of them was seen as nonfunctioning pituitary adenoma (NFA). In one other patient, the mass involved the pituitary and hypothalamus. The operation was not considered due to the general condition of that patient. This patient died in the follow-up. Another operated patient died despite post-operative replacement therapy. The other patient with PA had been operated for NFA about a month ago. The management of this patient was performed with medical therapy. One of the 4 patients with pituitary apoplexy detected on MRI at 24th week of pregnancy with severe headache that did not go away with analgesics. Her treatment was with medical therapy. No complications were observed in the follow-up and she was discharged. Another patient developed PA while receiving radiotherapy for acromegaly. The other one of these 4 patients had complained with fatigue. The other patient developed PA after coronary bypass procedure. It was thought that this might cause lost a lot of blood during the bypass procedure. Empty sella developed in the follow-up of these patients. Management of these patients was performed with hormone replacement therapies.

Conclusion

Although PA often presents with headache, there are also different forms of presentation. Patients should always be evaluated from this point of view. PA is a condition that can develop very quickly. It can have very serious consequences. In our case series, it was observed that two patients died. Treatment consists of sellar decompression with steroid replacement and, in severe cases, transsphenoidal surgery.

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EP721

A case of pituitary hyperplasia in a patient with neurofibromatosis type 1.

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Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder with diverse manifestations. Patients with NF1 are particularly prone to developing tumors of the central nervous system (CNS) and endocrine disorders. Herein we report a case of pituitary hyperplasia in a woman with NF1.
Observation
A 55-year-old woman was referred to our department for the exploration of recurrent hypoglycemia. Her past medical history included NFI, asthma treated with inhaled glucocorticoids, and ischemic stroke. On physical examination she had a body weight of 46 Kg, a body height of 1m40, corresponding to a body mass index of 23.5 kg/m² blood pressure of 120/80 mmHg, a heart rate of 90 bpm, a normal thyroid gland, multiple cutaneous neurofibromas, mainly in the chest and abdomen, café-au-lait spots, and thoracic scoliosis. No dysmorphic syndrome was observed. Biological investigations revealed a morning cortisol level of 11 ng/ml (nr: 40-200), an ACTH level of 4.9 pg/ml (nr: 10-48), a TSH level of 0.68 mU/l, a FT4 level of 1.13 ng/dl, a prolactin level of 25 ng/ml, a FSH level of 25.7 U/l, and a LH level of 18.5 U/l. The diagnosis of isolated corticotroph deficiency was established. A steroid-induced adrenal insufficiency was evoked. The first pituitary magnetic resonance imaging (MRI) scan showed an enlarged sella measuring 7.8 mm in height with superior convexity and homogeneous contrast enhancement. No focal lesion was detected. The patient was treated with hydrocortisone. A follow-up pituitary MRI scan performed at seven months showed the same aspect.

Conclusion
NFI is a tumor predisposition syndrome, frequently associated with CNS tumors, especially optic gliomas. Few cases of pituitary adenomas have also been reported. To the best of our knowledge, this is the first report of pituitary hyperplasia without evidence of prolactin and GH hyposcretion diagnosed in the context of NFI. The mechanisms inducing pituitary abnormalities remain misunderstood.

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EP723
Digestive complications of acromegaly: about 40 cases
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1University Hospital Tahar Sfar Mahdia, Endocrinology, Mahdia, Tunisia; 2University Hospital Farhat Hached Sousse, Endocrinology, Sousse, Tunisia

Introduction
Acromegaly is a rare hormonal condition that results from an excess amount of growth hormone (GH) in the body. A variety of complications have been reported in patients with acromegaly including cardiovascular diseases, diabetes mellitus or respiratory disorders. In addition, Acromegaly is associated with gastrointestinal complications. The aim of this study was to evaluate gastrointestinal complications and their impact on the quality of life among patients suffering from acromegaly.

Aim
We conducted a cross-sectional study including patients admitted for acromegaly in the endocrinology departments of Sousse and Mahdia (Tunisia), over a period of 20 years. The QOL was assessed with ACROQOL questionnaire.

Results
A total of 40 patients were included with a mean age of 38.9 years [13-77]. The sex ratio (M/F) was 0.74. The mean IGF1 level was 937 ng/ml [367-1700]. Prior pituitary insufficiency was present in 32.5% of cases. The most common functional gastrointestinal symptom was constipation (32%). Among our patients, abdominal ultrasound performed in 20 patients showed splenomegaly and hepatomegaly in 2 cases each. Colonoscopy realized in 9 cases showed dilated colon in 4 cases and colonic polyps in 2 cases. In our population, acromegaly complicated by dolichocolon was associated with impaired QOL, especially for socio-relational life (P = 0.04).

Discussion and conclusion
Upper and lower functional gastrointestinal tract disorders are significantly more prevalent in patients with acromegaly. Gastrointestinal complications make the QOL altered. Furthermore, poorer QOL may in part be attributable to the increased prevalence of abdominal symptoms.

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EP724
Short-term and long-term surgical remission of acromegaly in a tertiary medical center
Alexander Lutsenko, Zhanna Belaya, Elena Przhialkovskaya, Lidmiutia Kozhinskaya, Andrey Grigoriev, Vilen Azizyan & Galina Melnichenko
Endocrinology Research Centre, Moscow, Russian Federation

Background
Surgeries outcomes in patients with acromegaly are highly dependent on a surgeon’s level of expertise, as the majority of patients present with macroadenomas at diagnosis.

Aim
To assess remission rates in patients with acromegaly admitted to a tertiary medical center.

Materials and methods
We included patients admitted to the neuroendocrinology and bone disease department with no previous radiation therapy or current medical therapy with SSA or pegvisomant. Suppression of GH levels less than 1.0 ng/ml was a criterion for short-term remission. Normalization of IGF-I levels according to an age-specific reference range was a long-term remission criterion.

Results
44 patients were included in the study: gender (32.8% m, 68.2% f), median age 47.0 [34.0;55.0], IGF-I 744.75 ng/ml [548.83;889.85], GH 9.5 ng/ml [4.94;17.07], tumor volume 832 mm³ [419,25;253,38]. Microadenomas were identified in 8 patients (18.2%), 36 patients had macroadenomas at diagnosis (81.8%). Early postoperative remission was achieved in 35 patients (79.5%). For microadenomas the remission rate was 87.5% (n = 7) and for macroadenomas it was 77.2% (n = 28). Surprisingly, we did not observe differences between patients with and without early remission in age, tumor volume, histological variants and SSTR2, SSTR5 expression – this could be explained by the small sample size. Patients who achieved short-term remission had higher IGF-I and basal GH levels: IGF-I 935.60 ng/ml [649.60;1186.00] vs 737.60 ng/ml [532.87;876.20], P = 0.047, GH 36.40 ng/ml [9.61;63.30] vs 8.90 ng/ml [3.74;15.20]. Patients with no remission after surgery were prescribed with SSA. All patients were followed-up, median 19.0 months [12.5;29.0]. Long-term remission was achieved in 61.4% (27 patients), 9

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patients had no remission (20.5%), 2 patients had recurrence (4.5%), 6 patients were lost to follow-up (13.6%). In line with short-term remission, patients with long-term remission had lower basal GH 8.9 ng/ml [3.7;61.19] vs 28.0 ng/ml [6.75;47.2], P = 0.006 and IGF-1 674.80 ng/ml [482.5;876.2] vs 771.0 ng/ml [649.6;992.0], P = 0.03. We assessed the predictive value of basal GH for long-term remission: AUC 0.811 (95%CI:0.649; 0.973). A cut-off value of 15.55 ng/ml yielded the following results: sensitivity 70.0% (34.8%/93.3%) specificity 85.7% (67.3%/90.0%), accuracy 81.6% (65.7%/92.3%), positive predictive value 35.6% (39.3%/82.5%), negative predictive value 88.9% (75.4%/95.4%). This model demonstrates poor PPV, however, good NPV shows the potential predictive use. Conclusion Our study demonstrates short-term and long-term remission rates comparable with literature-reported rates for experienced pituitary centers. Basal GH shows potential for prediction of long-term remission of acromegaly in the Russian population, however cohorts should be substantially increased for more accurate results.

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EP725

Decreased quality of life in adult patients with sheehan syndrome

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Introduction
Sheehan Syndrome (SS) is the oldest known cause of non-tumor acquired anterior pituitary insufficiency in women. The incidence of SS would probably have decreased in recent decades due to improvements in obstetric care. However, it remains a public health problem in developing countries. In addition, it constitutes a chronic disabling pathology and is strongly linked to an alteration of the quality of life. In this study we aimed to evaluate the impact on quality of life of SS.

Patients and methods
This is a descriptive cross-sectional study. It was carried out in the Endocrinology department of the University Hospital Farhat Hached, Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. The assessment of quality of life was based on the specific questionnaire “Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA)”. It is composed of 25 items. The answer choice of the 25 “yes/no” items is scored 1.0. The total score is calculated as the sum of the item scores, ranging from 0 to 25, with a higher score indicating a lower quality of life.

Results
Sixty five patients were included to the study. The mean age at diagnosis of SS was 48.2 ± 12.4 years. Thyrotropic and corticotropic insufficiency were present in 86.2% of our patients, followed by gonadotropic and lactotroph insufficiency in 72.3% and 38.5% of patients, respectively. Somatotropic insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotropic deficiency in 10.8% of cases. Quality of life was assessed in 15 patients, with a mean QoL-AGHDA quality of life questionnaire score of 12.8 ± 5.5. Eight patients had a total score of the QoL-AGHDA questionnaire greater than or equal to 11. Seven patients, including three with a total QoL-AGHDA quality of life score of more than 18, were followed for an anxiety-depressive disorder. A 66-year-old patient presented cognitive disorders such as memory and concentration disorders after 26 years of evolution of SS. We did not note any significant correlation between the quality of life score and the SS dependent factors (duration of the SS, the existence or not of corticotropic or gonadotropic disorders after 26 years of evolution of SS). We did not note any significant correlation between the quality of life score and the SS dependent factors (duration of the SS, the existence or not of corticotropic or gonadotropic insufficiency, the dose of hydrocortisone...).

Discussion-Conclusion
SS is a chronic disease strongly associated with impaired quality of life, mainly due to GH deficiency and glucocorticoid overdose.

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EP726

Predictive factors of biological remission in patients with prolactinoma treated with dopamine agonists


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Introduction and aim
Dopamine agonists (DA) are prescribed as first-line treatment for prolactinomas and are generally effective and well tolerated. However, the degree and quickness of therapeutic response is variable among patients. The aim of this work is to study the predictive factors of biological remission in patients with prolactinoma treated with DA.

Methods
A single-center, retrospective and analytical study of patients with prolactinoma followed in the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia between 2000 and 2020. Biological remission was defined as prolactinemia < 25 ng/ml.

Results
We enrolled 69 patients. Patients were predominantly female (69%), aged 38.1 ± 14.5 years at diagnosis. One third of patients were obese. Mean initial prolactinemia was 2790.4 ± 10730 ng/ml. Adenomas were classified as follows: 24 microprolactinomas, 29 macroprolactinomas and 16 giant prolactinomas. Bromocriptine was prescribed in 46 cases while the remaining were treated with cabergoline. Biological remission was obtained in 24 patients at 6 months of treatment (34.8%) and reached 65.2% at 12 months. Univariate analysis showed that the use of cabergoline was significantly associated with remission at 6 months and 12 months (P < 0.001). The effect of age reached statistical significance at 12 months (P = 0.05). Using multivariate analysis, factors associated with remission at 6 months were cabergoline use only (P = 0.04, OR = 6) while those that significantly influenced remission at 12 months were cabergoline use (P = 0.005, OR = 11) and tumor size at diagnosis (P = 0.028, OR = 1.2, 95%CI[1.02;1.35]). In this series sex and BMI were not significant markers of remission both in univariate and multivariate models.

Conclusion
Cabergoline has proven to be a safe and effective treatment for prolactinomas. Cost and affordability remain major barriers in developing countries.

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EP727

Challenging management of giant prolactinomas in men: from efficient small dose of cabergoline to SSA, neurosurgery and Temozolomide

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Giant prolactinomas are very rare and constitute 2-3% of all lactotroph PitNETs with male preponderance. We present a case series of five male patients with giant prolactinomas with various clinical presentations.

Case 1
A 66-year-old male hospitalized due to left peripheral facial palsy. In computer tomography (CT) pituitary mass (41 x 43 x 64 mm) invading cavernous/sphenoid sinuses/carotid arteries/optic chiasm was visualized. Bitemporal hemianopia/-headaches/decreased libido were observed. Prolactin level was 22083 uIU/ml (N: 86-324 uIU/ml). Cabergoline up to 1 mg/we was implemented. After 3 months, regression of pituitary tumor by 14 mm and normal range prolactin level were observed. Milder headaches and improvement of visual field were reported.

Case 2
A 62-year-old male presented with life-threatening panhypopituitarism/diabetes insipidus at the age of 52. In MRI pituitary tumor 36 x 62 x 35 mm with extrascal extension/optic chiasm compression/invasive third ventricle was found. Prolactin level was 223549 uIU/ml. Despite dopamine agonist treatment (bromocriptine 22.5 mg/day and cabergoline 1.5 mg/we) progression of pituitary tumor/high prolactin level were observed. In 2016 patient did not consent to neurosurgery. Short-acting somatostatin analogues was introduced. In 2019, significant visual field deterioration was observed- patient consent to craniotomy. Histopathology revealed lactotroph-PitNET with Ki67 >3%. After 6 months, tumor progression was noted. Patient was disqualified from radiotherapy. Temozolomide (200 mg/m²/ per 5 days every 28 days) was introduced. After 9 cycles, regression of pituitary tumor was observed and decrease of prolactin level by 2600%.

Case 3
A 56-year-old male was hospitalized due to syncope. In CT pituitary tumor 40 x 30 mm was diagnosed with bitemporal hemianopia. Prolactin level was 10446 uIU/ml. Cabergoline (1 mg/we) was implemented. After 3 months, regression of pituitary tumor (21 x 26 x 19 mm)/normal prolactin level/improvement of vision were noted.

Case 4
A 23-year-old male presented with severe headaches and visual impairment at the age of 21. In MRI pituitary mass 52 x 52 x 41 mm with extra sellar extension was found. Prolactin level was 21522uIU/ml. Insufficiency of thyroid and gonadal axis was diagnosed. Cabergoline was implemented (4 mg/week) with regression of the tumor (25 x 13 x 23 mm), decrease of prolactin level (8400uIU/UL) and complete remission of headaches. Cabergoline was decreased to 2 mg/week.

Case 5
A 67 year-old male diagnosed with a pituitary tumor (65 x 35 x 40 mm) at the age of 50 years. Due to hyperprolactinemia, cabergoline was implemented (7 mg/week). After few weeks, pituitary apoplexy occurred. Patient underwent emergency neurosurgery. Insufficiency of thyroid, adrenal and gonadal-axis appeared. MRI over next 20 years demonstrated stable residual tumor(22 x 28 x 11 mm). Patient is now treated with 0.25 mg of cabergoline/week. The management of giant prolactinomas in men is challenging. Studies on prognostic factors of the efficient treatment in prolactinomas are needed.

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EP728
The incidence of hyperprolactinemia in patients with breast cancer.
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Objectives
To study the relationship between hyperprolactinemia and various forms of breast cancer in women of fertile age.

Methods and materials
The study included 100 breast cancer patients, aged 25 to 43 years (mean age 34.5 ± 1.4 years). The patients were divided into 2 groups: Group I 33 patients with hyperprolactinemia, which corresponded to 33%. Group II 67 patients with breast cancer without hyperprolactinemia, which corresponded to 67%. Clinical (examination of somatic, endocrine and mammological status), hormonal, immunohistochemical, histological, and instrumental studies (ultrasound of the mammary glands, MRI of the brain with a pituitary gland, mammography) were used in the work. The studies were carried out in patients on outpatient and inpatient treatment in 3 (9.0%) tubular carcinoma, in 2 (6%) medullary cancer, and in 1 case (3%) colloid and papillary breast cancer. In group II, in 67 patients, the distribution of the corresponding forms of breast cancer occurred in 19.4%, 16.4%, 7.5%, 10.4%, 7.5%, 6%, respectively. And also in 25 patients there were other forms of breast cancer (apocrine cancer, cystic hypersecretory carcinoma, adeno cytic cancer. In 3 (9.0%) tubular carcinoma, in 2 (6%) medullary cancer, and in 1 case (3%) colloid and papillary breast cancer. In group II, in 67 patients, the distribution of the corresponding forms of breast cancer occurred in 19.4%, 16.4%, 7.5%, 10.4%, 7.5%, 6%, respectively. And also in 25 patients there were other forms of breast cancer (apocrine cancer, cystic hypersecretory carcinoma, adeno cytic cancer.

Conclusion
1. The association of hyperprolactinemia due to formations of the pituitary gland is the main problem that deserves methods of their diagnosis and management.
2. Hyperprolactinemia may increase the incidence of such forms of breast cancer as ductal and lobular breast cancer in situ (63.4% vs 19.4%) and tubular carcinoma (9% vs 7.5%) in patients with breast cancer and normoprolactinemia.

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EP729
Case report: a challenging gastrinoma in a patient with renal cell carcinoma
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Introduction
Gastrinomas are rare neuroendocrine tumours (NETs) that arise from enterochromaffin-like cells and produce gastrin. Most are discovered in the duodenum and pancreas. The clear cell type of renal cell carcinoma (RCC) is known for the expression of gastrin-releasing peptide receptor (GRP-R) and some studies have shown GRP can stimulate tumor cell proliferation and neangiogenesis. Therefore, we present a case with metachronous development of renal cell carcinoma and gastrinoma.

Case presentation
A 55-year-old obese, hypertensive female patient with a history of renal cell carcinoma (histopathology: Grafitz tumour grade 2) treated with surgery, radiotherapy and interferon at the age of 36 years old, presents with the suspicion of a neuroendocrine tumour. SPECT/CT scan identified a possibly neuroendocrine tumour localised in the ileum and the blood tests revealed a gastrin level of 30 times x upper limit of normal (ULN) and chromogranin A 2.11 times x ULN. All other neuroendocrine markers were in the normal range. Treatment with Octreotide LAR 30 mg/28 days was initiated and gastrin level dropped to 5 x ULN. One year later, another SPECT/CT scan revealed radiotracer accumulation in the gastric antral region and first part of duodenum, associated with increased gastrin level (10 x ULN), which led to the increase of Octreotide LAR to 40 mg/28 days and after 2 months, the gastrin level dropped to 2.4 x ULN. Imaging evaluation showed no metastases. Abdominal surgery was performed, but the primary lesion could not be identified during laparotomy. In the meantime, the patient suffered a severe form of COVID-19 infection with 80% of the lungs being affected. The patient stopped treatment for gastrinoma for almost 2 months and gastrin raised again to 7 x ULN. Moreover, the patient was diagnosed with type 2 diabetes and started treatment with Metformin. Currently, gastrin level is 2.8 x ULN, with mild cholestasis syndrome and normochromic normocytic anemia.

Conclusion
Despite the high gastrin levels, the patient has no metastatic lesions. One particularity of this case is that even though surgery is thought to be the only curative treatment, the surgical intervention could not find any gastrointestinal tumour. Another particular aspect is the unusual association between RCC and gastrinoma, considering that GRP and its receptor can play an important role in carcinogenesis, this being a future path for novel targeted therapy.

Keywords. gastrinoma, neuroendocrine tumours, carcinoid syndrome, renal cell carcinoma

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EP730
Hypogonatropic hypogonadism with craniopharyngioma in adults before and after surgery.
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Craniohypophysealomas (CF) - a benign tumor of the embryologic origin. The surgical method of treatment is the basic.

Objectives
To estimate incidence of hypogonatropic hypogonadism before and after surgical treatment of CF at different topographical variations, and after the preservation of the pituitary stalk.

Methods
The research involved 79 patients older than 18 years (41 women and 38 men) with a mean age - 40 [17; 69] with a verified diagnosis of CF. All patients were treated at different surgical methods of treatment due to the localization of the CF. Preservation of the pituitary stalk does not lead to preservation of gonadotropins, respectively postmenopausal period. In group 3: hypogonatropic hypogonadism – 19 (86%), and in group 2: hypogonadism – 19 (86%), respectively.

Results
In 24 patients (86%) with a mean age of 21. In MRI pituitary mass 52 x 52 x 41 mm with extrasellar extension was found. Prolactin level was 21522uIU/ml. Insufficiency of thyroid and gonadal axis appeared. MRI over next 20 years demonstrated stable residual tumor(22 x 28 x 11 mm). Patient is now treated with 0.25 mg of cabergoline/week. The management of giant prolactinomas in men is challenging. Studies on prognostic factors of the efficient treatment in prolactinomas are needed.

Conclusion
Despite the high gastrin levels, the patient has no metastatic lesions. One particularity of this case is that even though surgery is thought to be the only curative treatment, the surgical intervention could not find any gastrointestinal tumour. Another particular aspect is the unusual association between RCC and gastrinoma, considering that GRP and its receptor can play an important role in carcinogenesis, this being a future path for novel targeted therapy.

Keywords. gastrinoma, neuroendocrine tumours, carcinoid syndrome, renal cell carcinoma

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EP731
Antioxidant and protective effect of estradiol in liver functions of aged female rats
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Background
The objective of this study was to observe the changes in activity of antioxidant enzymes, hepatic glucose homeostasis, lipogenic enzymes and lipid metabolism, serum lipid profile and liver function occurring in livers of female rats of 3, 12 and 24 months age groups, and to see whether these changes are restored to 3 months control levels rats after exogenous administration of steroid hormone estrogens (17-β-estradiol, E2).

Methods
The aged rats (12 and 24 months old) (n = 8 for each group) were given subcutaneous injection of 17 beta estradiol (0.1 mg/g body weight) daily for one month. After 30 days of hormone treatment, experimental animals of all the groups were sacrificed and livers were isolated for further study. A detailed study was carried on non-enzymatic glutathione (GSH) and enzymatic antioxidants [superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT)], hepatic glucose homeostasis, lipogenic enzymes, lipid metabolism, serum aspartate aminotransferase (GOT), alanine aminotransferase (GPT), gamma-glutamyl transferase (GGT), phosphatase alkaline (PAL) as well as bilirubin level.

Results
The results obtained in the present work revealed that normal aging was associated with significant decrease in the activities of antioxidant enzymes, serum expression and an increase in hepatic glucose homeostasis, lipogenic enzymes and lipid profile and GGT, PAL, GOT, GPT, ALP, as well as bilirubin level increased significantly in livers of aging female rats. Our data showed that exogenous administration of E2 brought these changes to near normalcy in aging female rats.

Conclusions
The present study showed that E2 treatment reversed the changes to normal levels. E2 treatment may be beneficial in preventing some of the age related changes in the liver by increasing antioxidant defences and decrease oxidative stress. E2 plays important role in the progression of chronic hepatic diseases.

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EP732
Rare case of cushing with papillary thyroid cancer
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Introduction
Papillary thyroid carcinoma is the most common type of thyroid cancer (70-80% of all thyroid cancer). It is a differentiated type of carcinoma, it affects women between 30-60 years old, 3 times more often than males. Clinical outcome in patients with differentiated thyroid carcinoma is often favorable. Glucocorticoids (GC) play major role in the physiologic stress response. However chronic exposure to glucocorticoids as seen in Cushing’s disease (CD) has detrimental effects on multiple systems: cardiovascular, metabolic, immune, psychological, CD, caused by a pituitary adrenocorticotrophic hormone (ACTH)-secreting tumor, is probably underestimated at 1.2-2.4 per million per year and it affects mostly women). Association of Cushing’s disease and papillary thyroid carcinoma is rare and so far there is no known genetic mutation to link the two neoplastic conditions, and no clear relationship between neoplastic thyroid and hypercortisolism has been established in the current endocrine literature.

EP733
Analysis of the causes and frequency of discrepancies between GH and IGF-1 levels in patients with acromegaly based on the polish register of acromegaly patients
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Introduction
Acromegaly is a rare disease of the pituitary gland. Both GH and IGF-1 levels are of key importance for monitoring of treatment effects in patients with acromegaly. In some patients, divergent results of measurements of these hormones are observed.

Purpose
The purpose of the study was to estimate frequency of GH and IGF-1 inconsistencies in the population of patients with acromegaly included in the Polish Register of Acromegaly Patients, and to investigate whether selected biochemical parameters can predict the possibility of GH/IGF-1 incompatibility.

Material and methods
145 patients with acromegaly were included in the analysis. - G1 (n=43) GH <1 μg/l and IGF-1 within the reference range for sex and age, - G2 (n=51) GH >1 μg/l and IGF-1 above the reference range for sex and age, - G3 (n=15) GH >1 μg/ml and IGF-1 within the reference values for sex and age, - G4 (n=34) GH <1 μg/ml and IGF-1 above the reference range.

Results
The discrepancy of results of GH and IGF-1 hormonal tests in the studied population was found in 49 patients (34%). There were no statistical differences between the study groups in terms of age, disease duration, time since surgery, GH and IGF-1 levels at diagnosis, fasting glucose and HBA1C. Based on unidimensional logistic regression models, it was found that the G/H/IGF-1 discrepancy was significantly associated with GH level at the time of diagnosis of acromegaly (OR = 0.98 C95 [0.96; 0.99], P = 0.039) and with creatinine level (OR = 10.94 C95 [1.75; 82.77], P = 0.014). The multivariate regression model showed that parameters studied: surgery, IGF-1 concentration at diagnosis, and creatinine levels, turned out to be the best combination of factors predicting the possibility of GH/IGF-1 incompatibility. The surgery to remove the pituitary adenoma and increasing concentration of creatinine increased the possibility of discrepancy (OR = 15.45 C95 [2.24; 358.92], P = 0.023 and OR = 15.71 C95 [1.87; 165.48], P = 0.014, respectively), while the increase in IGF-1 concentration at diagnosis reduced the possibility of GH/IGF-1 discrepancy (OR = 0.998 C95 [0.997; 0.999], P = 0.008).

Conclusions
1. On the basis of obtained results, the discrepancy between GH and IGF-1 hormonal determinations among the studied patients was 34%. An increase in IGF-1 concentration at the time of diagnosis decreased the possibility of GH/IGF-
EP735
Endocrine treatment of anabolic-androgenic steroid induced hypogonadism in males: A pilot study

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Background and aims
Non-prescribed use of anabolic-androgenic steroids (AAS) is associated with a wide range of health risks including AAS-induced hypogonadism (ASH) caused by negative feedback suppression on the hypothalamic-pituitary-gonadal (HPG) axis. Testicular function might be reduced for months up to years after AAS-cessation, increasing the risk of developing fatigue, decreased libido, erectile dysfunction, infertility, sleep disorder, depression and anxiety. There is no consensus on whether endocrine therapy should be used in the treatment of ASH. In our study, a group of AAS-dependent men will receive endocrine therapy consisting of clomiphene citrate, a selective oestrogen receptor modulator. According to the theory, clomiphene citrate might stimulate endogenous testosterone production by blocking the negative feedback mechanism on the HPG-axis. The primary aim is to explore whether use of clomiphene citrate is safe and effective for AAS-withdrawal. The secondary aims are to detect health risks during ongoing AAS use and assess whether physical and mental health risks are reversed 12 months after cessation.

Methods
This one-site open off-label longitudinal pilot study at Oslo University Hospital in Norway will include 25-30 AAS-dependent men referred to outpatient addiction treatment with a desire to end AAS use permanently. The intervention group will be given endocrine therapy consisting of clomiphene citrate for 16 weeks including exogenous testosterone replacement for the first four weeks following AAS-cessation to ensure that the testosterone level is within normal range before reaching a HPG response. They will be compared to male participants in an already ongoing study of men who end AAS use temporarily without endocrine treatment. Participants from both studies will self-report withdrawal symptoms and other health measures every 2 weeks for 6 months and have visits at inclusion and after 6 months. The intervention group will be monitored using within-subjects repeated measures design on physical and mental health before, during 16 weeks of intervention, and at follow-up 6 and 12 months after AAS-cessation.

Physical health parameters are obtained via clinical examinations, investigation of cardiovascular status, blood and fat tissue sampling, dual-energy x-ray absorptiometry (DXA), testicular ultrasound and semen analysis.

Results
Study inclusion started in December 2021. The study protocol and preliminary results will be presented at the conference.

Conclusion
This pilot is the first intervention study to test safety and efficacy of off-label use of clomiphene citrate among withdrawing AAS-dependent men. If this therapeutic approach works, full-fledged clinical trials need to be conducted.

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EP734
Metabolic and inflammatory parameters for baseline characterization and treatment outcome of prolactinoma patients

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Background
Prolactinomas (PRL) are pituitary adenomas mainly characterized by hyperprolactinemia. In addition to the endocrine effects of prolactin, metabolic alterations have been described in PRL patients. Changes in inflammatory parameters have recently been identified in pituitary adenoma patients. Since both, metabolic (MM) and inflammatory markers (IM) showed promising results in characterization/prognosis of tumor patients, it is tempting to speculate whether those might be useful also in PRL patients.

Patients, methods, results
In this retrospective analysis of medically treated PRL, 23 patients with microprolactinoma (56% women, mean age 34.5) and 30 patients with macroprolactinoma (37% women, mean age 40.7) were included. No difference between micro- and macroprolactinoma patients were evident regarding sex, age, and rate of obesity, hypertension and prediabetes/diabetes mellitus. At baseline, macroprolactinoma patients presented with higher heart rate (HR) (P = 0.005) and higher likelihood of thyrotropin- (P = 0.007) and gonadotropin-insufficiency (P = 0.006). We found a significant correlation between prolactin and BMI (rs = 0.364; P = 0.007) as well as PRL-size with HbA1c (rs = 0.413; P = 0.032), BMI (rs = 0.316; P = 0.021) and HR (rs = 0.284; P = 0.050). Considering prolactin or PRL-size separately in a multivariate analysis with BMI, HbA1c and HR a significant positive association persisted between prolactin and HbA1c (P = 0.009), whilst HR and BMI were positively associated with each other and independent from prolactin or PRL-size. HbA1c had also a negative correlation with testosterone (rs = 0.478; P = 0.038), which was not persistent after including prolactin in the multivariate analysis. No correlation could be identified at baseline between prolactin/PRL-size with the studied IM (Glasgow Prognostic Score, Neutrophil-Platelet-Score, Neutrophil-to-Lymphocyte-Ratio [NLR], Platelet-to-Lymphocyte-Ratio [PLR], Prognostic Nutrition Index, Systemic Immune Inflammation Index) and other studied MM (LDL- and HDL-cholesterol, triglyceride, blood pressure [BP]). An association between NLR and I4 (rs = 0.329; P = 0.038) as well as LDL (rs = 0.617; P = 0.014) was identified, which did not persist in a multivariate analysis considering both variables together and PRL-size. A correlation between I4 and PLR (rs = 0.351; P = 0.026) could not be confirmed in the multivariate analyses with prolactin level and PRL-size, separately. In 47 patients complete follow-up data (median follow-up time 17 months, interval 2-141 months) were available. Cabergoline dosage required to achieve normoprolactinemia correlated with baseline LDL (rs = 0.493; P = 0.052), systolic (rs = 0.341; P = 0.024) and diastolic BP as well as baseline testosterone (rs = 0.447; P = 0.019). Tumor shrinkage correlated with LDL at baseline (rs = 0.570; P = 0.053). Only systolic and diastolic BP remained predictive for Cabergoline dosage required to achieve normoprolactinemia in the regression analysis.

Conclusion
Metabolic but not inflammatory markers might be related with initial presentation and outcome in PRL.

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EP736
MRI intensity and pituitary volume predict adult-onset growth hormone deficiency in patients with obesity and overweight: a new potential tool guiding subsequent diagnostic testing

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Background and aims
The wide range of health risks including AAS-induced hypogonadism (ASH) caused by negative feedback suppression on the hypothalamic-pituitary-gonadal (HPG) axis. Testicular function might be reduced for months up to years after AAS-cessation, increasing the risk of developing fatigue, decreased libido, erectile dysfunction, infertility, sleep disorder, depression and anxiety. There is no consensus on whether endocrine therapy should be used in the treatment of ASH. In our study, a group of AAS-dependent men will receive endocrine therapy consisting of clomiphene citrate, a selective oestrogen receptor modulator. According to the theory, clomiphene citrate might stimulate endogenous testosterone production by blocking the negative feedback mechanism on the HPG-axis. The primary aim is to explore whether use of clomiphene citrate is safe and effective for AAS-withdrawal. The secondary aims are to detect health risks during ongoing AAS use and assess whether physical and mental health risks are reversed 12 months after cessation.

Methods
This one-site open off-label longitudinal pilot study at Oslo University Hospital in Norway will include 25-30 AAS-dependent men referred to outpatient addiction treatment with a desire to end AAS use permanently. The intervention group will be given endocrine therapy consisting of clomiphene citrate for 16 weeks including exogenous testosterone replacement for the first four weeks following AAS-cessation to ensure that the testosterone level is within normal range before reaching a HPG response. They will be compared to male participants in an already ongoing study of men who end AAS use temporarily without endocrine treatment. Participants from both studies will self-report withdrawal symptoms and other health measures every 2 weeks for 6 months and have visits at inclusion and after 6 months. The intervention group will be monitored using within-subjects repeated measures design on physical and mental health before, during 16 weeks of intervention, and at follow-up 6 and 12 months after AAS-cessation.

Physical health parameters are obtained via clinical examinations, investigation of cardiovascular status, blood and fat tissue sampling, dual-energy x-ray absorptiometry (DXA), testicular ultrasound and semen analysis.

Results
Study inclusion started in December 2021. The study protocol and preliminary results will be presented at the conference.

Conclusion
This pilot is the first intervention study to test safety and efficacy of off-label use of clomiphene citrate among withdrawing AAS-dependent men. If this therapeutic approach works, full-fledged clinical trials need to be conducted.

DOI: 10.1530/endoabs.81.EP736
Background
Reduced growth hormone (GH) secretory capacity is common in patients with obesity and metabolic derangements. The prevalence of GH deficiency (GHD) in this population is difficult to establish. Magnetic Resonance Imaging (MRI) pituitary findings may reflect specific endocrine alterations, as for GHD which is associated with lower pituitary height and volume (PV).

Purpose
Our aim was to identify the pituitary morphological alterations predicting GHD in subjects with obesity or overweight.

Methods
We conducted a retrospective evaluation of 152 patients undergoing pituitary-MRI and a dynamic test (GH-RH + arginine) for suspected adult-onset GHD admitted to our institution from 2015 to 2022. Clinical history and anthropometric parameters were collected. Mean and standard deviation (SD) of pituitary signal intensity was quantified (Horus, Nimble Co, Annapolis, MD USA). Gray matter signal intensity was used as a normalizer. PV was calculated by adopting the ellipsoid formula.

Results
Of 152 patients, 126 had obesity (BMI: 39 ± 6 Kg/m²) and 26 were overweight (BMI: 28 ± 1 Kg/m²). An inverse correlation between BMI and PV was observed (r = -0.2844, P<0.0001). Of note, after normalization with grey matter intensity, T2-weighted-scan derived pituitary intensity and PV showed an inverse correlation (r = -0.2761, P=0.008). As far as GH secretory capacity is concerned, we found a direct correlation in the area under the curve of the dynamic test and pituitary volume (PV) (r = 0.4188, P<0.0001). Finally, a receiver operating characteristic curve allowed to identify a PV < 75.8 ml and a pituitary height < 3.7 mm as predictors of GHD with a sensitivity of 86.1% and 72.2% and a specificity of 63.6% and 64.5%, respectively.

Conclusion
Our work demonstrates that patients with obesity exhibit a GH-IGF1 axis impairment associated with a reduced PV. Furthermore, we found an inverse correlation between PV, pituitary intensity and GH secretion capacity. The increase in pituitary intensity may reflect the presence of an inflammatory infiltrate possibly leading to pituitary damage and subsequent shrinkage, although this hypothesis needs to be confirmed with ad hoc studies. When subjects suffering from overweight/obesity undergo a head MRI for other reasons, those not reaching the identified cut off values of PV and pituitary coronal height predicting GHD in our cohort, might benefit from undergoing dynamic testing in order to assess for eventual GHD.

Key Words: obesity, pituitary volume, Growth Hormone Deficiency

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The changing features of a corticotroph PITNET: from silent to Cushing’s disease - case report
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Introduction
The spectrum of corticotroph cell pituitary adenomas is very wide, silent corticotroph adenomas (SCAs) being a rare subtype with positive immunohistochemistry for adrenocorticotropic hormone (ACTH), without causing Cushing’s disease. SCAs may exhibit a more aggressive behavior, and the changing of the clinical phenotype towards Cushing’s disease is described.

Case report
We present the case of a 74 years old, ex-smoker, hypertensive, male patient who was admitted to our clinic after sudden unilateral hearing loss, with no signs of hypercortisolism. Magnetic resonance imaging (MRI) of the pituitary showed a large mass of 14.3/15/12.3 mm. There was no opto-chiasmatic involvement and the hormonal profile revealed normal pituitary function with normal serum cortisol, suppressed after a 2 mg x 2 days dexamethasone suppression test (LDDST). The patient underwent transphenoidal pituitary surgery. Postoperatively he did not have any pituitary deficiencies. Subsequently, 7 years after surgery, the patient is readmitted to our department, with central obesity, hypertension, dyslipidemia, and low bone mass. The hormonal profile showed an elevated ACTH (148.9 pg/ml), with elevated 8.00 a.m. serum cortisol, unsuppressed after a LDDST (14.74 µg/dl). Brain imaging showed a pituitary tumor of 17.9/18.8 mm with suprasellar extension, associated with bilateral adrenal hyperplasia on abdominal computed tomography (CT). Morphological and proteomic immunochemical (IHC) analysis of the pituitary tumor revealed strong positive staining for ACTH and weak immunostaining for TPT1; Ki-67 labelling index had a value of >3%. After neurosurgical evaluation found reinvention to be reversible, gamma knife radiosurgery was performed and therapy with dopaminergic agonists was initiated. The morning serum cortisol normalized, but remained unsuppressed after LDDST 2 years after radiosurgery, with ACTH values in regression under cabergoline 4 mg/week.

Discussion
Bidirectional transformation of the clinical phenotype between Cushing’s disease and SCA is described, the time interval varying from 1 to 7 years. The silent phenotype is related to TPT1, the dysfunction of its expression being an early change in differentiation of this tumor type. SCAs are more biologically aggressive tumors than NIFAs, therefore, close neuroimaging and clinical follow-up are mandatory. Also, patients with SCAs who present with postoperative residual disease should be considered for early adjuvant radiosurgery or long acting pasireotide.

References

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Growth hormone deficiency due to a rare central nervous system tumor
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Introduction
Short stature is a common reason for pediatric endocrine evaluation and it can have a variety of causes, including constitutional, genetic short stature, dyssomorphistic syndromes, chronic illnesses and also endocrine disorders. Growth hormone deficiency accounts for 8% of the cases and it can be isolated or associated with other pituitary hormones deficiencies, congenital or acquired, such as in central nervous system tumors.

Case report
A 15-year-old female patient presented to our department for growth deficit and primary amenorrhea. The mother reported normal psychomotor development and no significant medical history. The clinical examination revealed an underweight patient (percentile under 1%) with short stature (-3.38 SD) and a prepubertal Tanner stage. A complete hormonal assay showed low GH and IGF-1 levels, with no GH response at the clonidine stimulation test. FSH, LH, estradiol and prolactin levels were also low. Cerebral MRI showed a solid, lobulated suprasellar mass of 2.8/2.7/4 cm, with well-defined outline and microcalcifications, hyperintense T2 signal and hypointense T1 signal, predominantly located in the third ventricle, in close contact with the circle of Willis. Tumoral markers and a lumbar spine puncture were recommended to rule out a germ-cell tumor. The patient was referred to a neurosurgeon and underwent surgery with complete resection of the tumor, and histopathology and immunohistochemistry evaluation supporting the diagnosis of rosette-forming glioneuronal tumor. Postoperatively, the patient developed diabetes insipidus and central adrenal and thyroid insufficiency, with favorable evolution and recovery under substitution treatment.

Conclusions
Rosette-forming glioneuronal tumor is a very rare tumor, with about 100 cases reported in literature. It is a grade I neoplasm, with indolent evolution and a low recurrence rate following total resection. In our case, it presented with hormonal disturbances due to its size and unusual location. A multidisciplinary approach from an experienced team is absolutely necessary for an appropriate diagnosis, an effective treatment and long-term follow-up for this type of cases.

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Growth hormone deficiency due to a rare central nervous system tumor
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Introduction
Giant pituitary adenomas are uncommon tumors defined by a tumor diameter ≥ 4 cm. Their prevalence estimated at 6-10% of all pituitary adenomas, whose clinical characteristics and prognosis are not well known. The purpose of this work was to evaluate the prevalence as well as the clinical and evolutionary characteristics of giant pituitary adenomas in our series.

Material and methods
Retrospective descriptive study including 15 patients followed-up for giant pituitary adenoma which tumor diameter was greater than or equal to 4 cm. Data were collected from medical records and analyzed by SPSS-V21 software.

Results
Giant pituitary adenomas represent 16.6% of our series of pituitary adenomas (n = 15/90) with a mean age of 44.8 ± 16.5 years (extremes of age of 22 and 69 years), with a clear male predominance and a sex ratio of 4. The clinical presentation was dominated by a decrease in visual acuity associated with headaches in 73.3% of cases, associated with cranial nerve damage (III, VI) in 20% and pituitary apoplexy in 13.3% followed by acrogigantism in one case. The hypothalamo-hypophyseal MRI showed a giant pituitary macroadenoma with a mean diameter of 5.34 cm (with extremes of 4 and 8.2 cm) and a mean volume of 47.9 ± 45.5 cm 3. Invasion of the cavernous sinus was observed in 46.6% of the cases and reaching the contact of the internal carotid artery in 40% of the cases, with invasion of the chiasm and optic pathways in 93%. It was a pituitary prolactin adenoma in the most of cases (53.3%) cases followed by non functional pituitary adenoma. Twenty-four percent of the patients benefited from transphenoidal surgical treatment with an indication for revision surgery in 46% of cases. 13.4% of the cases benefited from radiotherapy as a complement to pituitary surgery and 60% were put on dopaminergic analogues and 13.3% on somatostatin analogue. The K67 of the operated patients was 4% in one patient with somatotrop adenoma, 2% in one case with prolactin adenoma and 1% in 4 cases.

Discussion
Giant pituitary adenomas, although uncommon, represent a challenge in clinical endocrinology because their prognosis is uncertain requiring multidisciplinary management in diagnosis, therapeutic management and long-term follow-up.

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Endocrine Abstracts (2022) Vol 81
A 57-year-old man was admitted to the emergency department following sudden onset of severe headaches, fever, chills, and signs of meningeal inflammation. He was referred to the neurology department for clinical evaluation at the time of symptoms of hypopituitarism and in follow-up. Morning serum cortisol (171-536 nmol/l) was measured by chemiluminescence immunoassay, Morning ACTH (7.2-6.3 pg/ml), prolactin (66-436 mIU/l), TSH (0.25-3.5 mIU/l), T4 (9.19 pmol/l) and T3 (2.6-5.7 pmol/l) were measured by chemiluminescence immunoassay. General Electric 3T MRI scanner was used to do an MRI of the brain with standard contrast. Data were analyzed throughout the course of the disease. 

Results

A 35-year-old female developed clinical symptoms of hypopituitarism two months after recovery from a confirmed COVID-19 infection. Laboratory investigation confirmed hypocorticism, hypothyroidism, hypogonadism and the patient was prescribed appropriate hormonal therapy in January 2021. Four months later the symptoms were alleviated (April 2021) and there were signs of recovery shown by imaging and hormonal profile (hormonal treatment was stopped for evaluation): morning serum cortisol 227 mmol/l, morning ACTH 33.96 pg/ml, prolactin 68.3 mIU/l, TSH 2.626 mIU/l, T4 10.75 pmol/l, T3 3.96 pmol/l. Thyroid hormone was discontinued, but hypogonadism and hypocorticism persisted with estradiol - 51.48 pmol/l, 24 h urine cortisol levels - 41.8 nmol/day. Secondary adrenal insufficiency was confirmed during a test with insulin hypoglycemia (serum glucose reached 0.7 mmol/l), the maximum release of cortisol was 410.8 mmol/l. MRI results showed that the signs of hypophysitis were alleviated in comparison with MRI from January 2021. Full recovery of pituitary axis was reported in October 2021, with recovery of normal menstrual cycle. Furthermore, hormonal profile was likewise normal: morning serum cortisol 14.7 μg/dl (6.2-19.4), ACTH 33.2 pg/ml, T4 0.88 ng/dl (0.8-2.1), TSH 2.17 mIU/l. 

Conclusions

This report provides evidence of delayed damage to the pituitary gland after infection with the COVID-19, with recovery of its function and structure. To date, the mechanisms of such an impact are not entirely clear; further collection of data on such cases and analysis is required.

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EP745
Cardio-metabolic and articular complications of somatotropic adenomas in a single-center study
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Introduction/Objective
Chronic exposure to hypersomatotropism exposes to multiple co-morbidities, rarely reversible, which can worsen both functional and vital prognosis and impair quality of life. The aim of our work is to list the different complications of acromegaly at the time of diagnosis.

Patients and methods
Descriptive cross-sectional study concerning 81 patients with somatotropic adenomas followed in the Endocrinology department of the Oran University Hospital.

Results
Sex ratio M/F at 1.4, pituitary macroadenomas are involved in 81% of cases, the mean age at diagnosis at 40.2 ± 15.5 years, the mean consultation time at 23.8 ± 31.3 months, the mean BMI at 26.4 ± 4.9 kg/m². At diagnosis, we identified hypertension in 41% of cases with a mean duration of 4.5 ± 5.9 years, congestive valvular heart disease with or without arrhythmia in 31% of cases, sleep apnea syndrome (SAS) in 50% of cases explored (n = 20), diabetes mellitus in 35% of cases with a mean duration of 5.2 ± 6.5 years, intolerance to carbohydrates to carbohydrates in 15.3% of cases with a mean duration of 2.0 ± 3.1 years, dyslipidemia in 28%, axial arthropathy in 39% of cases including 3 Erdeym spondylosis and carpal tunnel syndrome in 40% of cases.

Discussion
Our results are similar to those in the literature which vary from 18-60% for hypertension, from 19 to 56% for diabetes mellitus and carbohydrate intolerance, from 33 to 47% for dyslipidemia and from 20 to 80% for SAS. They reflect the need for early diagnosis of acromegaly and for hormonal control to improve prognosis.

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EP746
Hormonal profile of pituitary adenomas
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Background
Pituitary adenomas (PA) or endocrine pituitary tumors are the most common pituitary tumors. Our goal is to assess their hormonal profile.

Patients and methods
Our study is observational, multicenter, with prospective and retrospective data collection. Data entry and analysis was performed by CDC (USA) EPI Info version 6, SPSS20, Statistica10, Medcalc12.

Results
Concerning the hormonal profile of the 475 PA collected, 77.5% were secreting against 22.5% not or apparently non-secreting. Macroadenomas were predomi nant (66.5%, P = 0.001). Prolactin was elevated in 62.7%. It was either a functional or disconnected hyperprolactinemia, or of tumor origin. The mean prolactinemia was significantly (P = 0.006) higher in men: 578.2 Vs 189.1 ng/ml. Hypopituitarism (≥2 axes) calculated as for macroadenomas was noted in 35%. Gonadal deficit, functional in microlesions and organic and/or functional in macro- adenomas, was the most common (56.5%) compared to the other deficits. Impaired gonadal function is followed by the thyrotropic deficit noted in 32%. Corticotropic and somatotropic deficits come last, 27% and 6.5%, respectively. Somatotropic function was not systematically explored in our retrospective study. Multiple deficits affecting more than 3 axes were noted in 17.0%. Post-pituitary function impairment was present in 4.7%.

Conclusion
Our results can of course be explained by the frequency of macrolysis but also by the delay in the diagnosis of these tumors.

Key words: pituitary adenomas, hormonal profile, hyperprolactinemia, pituitary deficits.

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EP747
Delayed Diagnosis of Cushing’s Disease Manifested in Adolescence
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Diagnosis of Cushing’s syndrome (CS) can be challenging, particularly in mild cases or in cyclic disease, because of the variable, non-specific clinical manifestations and the overlap with more common medical problems. Female patient was referred to our clinic in Dec 2015, at the age of 18 years, presented with headaches, arterial hypertension (AH), excess body hair growth, irregular menstrual periods, sleep disturbances and mood fluctuations. She smoked, but denied use of alcohol or any drugs. Menarche occurred at 10 years of age and her menstrual cycle (MC) was regular. At the age of 14 years she had noticed excessive body hair growth, alopecia, weight gain (15 kg), purple striae and menstrual irregularities. At examination in pediatric clinic AH, normal morning cortisol, TSH, prolactin, electrolytes, elevated testosterone and DHEA-s levels were detected. Her brain’s MRI and CT of adrenal glands were unremarkable. US showed multifocal ovarian ovaries. She was followed by pediatricians with the diagnosis of PCOS, obesity. Oral contraceptives were not effective to control her MC and were discontinued. In 2015 she lost weight (15-20 kg) with striae discoloration and her MC was temporarily restored without specific treatment. In a few months the described symptoms had returned and she was referred to endocrinologist. At examination in Dec 2015 plethora rounded face, hyperemic constitution, normal BMI (23 kg/m²), hirsutism (lower abdomen, hips, lumbal area), acne, pale striae, AH were found. 24-h urine free cortisol within the normal range, slightly elevated testosterone, androstenedione and ACTH (48 ng/ml, ULN 46) levels, normal TSH, prolact, OGTT, electrolytes and liver function tests were revealed. Further investigation demonstrated ACTH at the upper border of normal range (46 ng/ml), but inadequate suppression of plasma cortisol (350 nmol/l) and ACTH (44 ng/ml) after overnight 1-mg DST. At the same time 6 x 3 mm microadenoma on pituitary MRI had been detected. The diagnosis of ACTH-dependent endogenous hypercortisolism - Cushing’s disease (CD) was established and confirmed by subsequent deterioration of laboratory parameters accompanied by weight regain. Symptoms of hypercortisolism have completely disappeared after repeated transphenoidal adenomectomy in 2016-2017. This case demonstrates the delayed diagnosis of CD with first clinical presentation at the age of 14 years, resembling PCOS. Fluctuating signs of cortisol excess and inconsistent laboratory results raise suspicion about cyclic CD. As no single diagnostic test is 100% accurate in the diagnosis of CS/CD, repeated monitoring is needed. Education of pediatricians and gynecologists to maintain awareness about CS/CD is required.

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EP748
Clinical, paraclinical and genetic features of diabetes insipidus
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Introduction
Diabetes insipidus (DI) is a rare pathology. The advent of hypophalamic-pituitary MRI has made it possible to make a positive diagnosis by avoiding the water restriction test (WRT). The etiological diagnosis is still a challenge in view of the diversity of diseases involved, which influences the therapeutic management and prognosis.

Work Objectives
The objectives of our work were to describe the clinical, paraclinical and genetic features of DI.

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Hypopituitarism revealing small cell pulmonary carcinoma: an original case report

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Background
Anterior pituitary insufficiency or anterior hypopituitarism is a defect in the secretion of one or more of the pituitary hormones (ACTH, TSH, FSH and LH, GH and prolactin). It is a rare condition. A variety of diseases may be the cause, the most common being adenoma. In rare cases, it can be a clinical presentation of metastatic disease. Herein, we describe a case of a pituitary metastasis revealing a lung carcinoma in a 61-year old man.

Case report
A 61-year old man, with a history of heavy smoking and type 2 diabetes, was admitted with deterioration of general state. He reported constipation, anorexia, weight loss and decreased libido for 2 years and has stopped taking his insulin for 2 months because of hypoglycemic episodes. Examination showed psychomotor retardation, blood pressure (BP) at 106/62 mmHg, heart rate at 62 bpm, normal weight and decreased libido for 2 years. Laboratory tests found hyperglycemia. Examination showed psychomotor retardation, blood pressure (BP) at 106/62 mmHg, heart rate at 62 bpm. Normal blood glucose and BMI of 32 kg/m². Ganglionic side palpation revealed several cervical, axillary and inguinal adenopathies. Laboratory tests found hypotension, hypophosphatemia and elevated inflammatory markers. Colonoscopy was normal. Endocrine investigations revealed central hypothyroidism (TSH: 0.107 mIU/mL, FT4: 0.63 ng/dl) and hypocorticism (cortisol: 35 nmol/l). Low testosterone level at 0.081 ng/ml and hyperprolactinemia at 862 µIU/ml. The patient was therefore started on hormonal replacement therapy (hydrocortisone and levothyroxine). Cerebral MRI found a metastasis at the level of the hypothalamic-pituitary axis on the left, with suprasellar mass lesions isointense on precontrast T1 weighted, hyperintense T2 weighted and demonstrated predominantly rim enhancement on FLAIR. Body scan was consistent with the diagnosis of pulmonary neoplasm with multiple secondary lesions (lung, bone, adrenal, cerebral, hepatic, pleural and peritoneal metastases), thereby confirming the clinical diagnosis of small cell pulmonary carcinoma. The patient was started on radiotherapy and was addressed to a specialized oncology center for follow up.

Discussion
Our report depicts an original and challenging diagnosis approach of small cell lung carcinoma revealed by pituitary metastasis with hypopituitarism. Pituitary metastases are uncommon. They represent 0.14-3.6% of all intracranial metastases, and are rarely symptomatic (1%-6%). In scarce cases, pituitary metastasis is the first manifestation of the cancer. Breast and lung cancer are the most frequent cause of pituitary metastasis. The association of infundibular metastasis and elevated serum prolactin has been reported.

Conclusions
Pituitary metastases may be the initial presentation of neoplasms or may occur during therapy. Physicians must be cautious, and must suspect the diagnosis when confronted with any sign that may suggest pituitary damage (hypo- or hyperthyroidism, adrenal insufficiency, etc.)

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EP750
Neurosarcoidosis and pituitary metastasis of a small cell carcinoma: an unusual association
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Introduction
Pituitary stalk thickening (PST) is often identified on magnetic resonance imaging (MRI), either incidentally or during diagnostic workup of hypopituitarism. Currently, there is no unified standard for the definition of PST. As a reference, a pituitary stalk with width over 3 mm has been used as the diagnostic criterion for PST in recent years. The disease spectrum of PST is quite diverse and can be grouped into three broad categories: neoplastic, inflammatory and congenital diseases. Here, we report a rare case of PST secondary to neurosarcoidosis and pituitary metastasis of a small cell carcinoma.

Case report
We report the case of a 49 years old man with no personal medical history. The diagnosis of neuro-sarcoidosis was suspected in view of the presence of pituitary tumor syndrome, central diabetes insipidus, hypopituitarism and the presence of nodular thickening of the stalk at hypothalamic-pituitary MRI. Biological explorations had shown an increase in 1-25 OH vitamin D, a decrease in 25 OH vitamin D and a slight increase in the tumor marker NSE estimated at 42 ng/l. Chest X-ray and thoracic-abdominal CT scan were in favor of pulmonary, hepatic and adrenal involvement. Labial biopsy and bone scan were negative. To confirm the diagnosis, bronchial biopsies were performed three times under fibroscopic control but returned negative. Then they were redone under CT scan to conclude to a small cell lung carcinoma, but the liver biopsy was in favor of a sarcoïdosis. The patient was put on replacement therapy (ddAVP at a dose of 0.1 ml*2/d, hydrocortisone at a dose of 30 mg/d and L-thyroxine at a progressive dose up to 100µg/d) with clinical and radiological monitoring. The thoracic CT scan showed an aggravation of the lesions, an increase in the tumor mass and a small pleural involvement. The diagnosis retained was that of a pituitary metastasis of a small cell carcinoma associated with sarcoidosis. Given the deterioration of the general condition and the worsening of the radiological lesions, the patient was referred to the carcinologists for vinblastine and prednisone16 - cisplatin chemotherapy. He received 3 courses of chemotherapy with a good clinical and biological evolution. Since then, the patient was regularly followed up in carcinology.

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**EP751**

**Immunohistochemical expression of ephrin receptor (EPH)-A4, -A5, -B2 and -B5 in pituitary lesions**

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**Introduction**

Ephrin receptors (EPHs) compose the largest known subfamily of receptors that interact with ephrins (Ephrins). They have a role in tumor growth, invasion, angiogenesis and metastasis of several neoplasms. Aim of the study was to investigate the expression of EPH-A4, -A5, -B2 and -B5 in pituitary lesions. Material and Methods Our study group consisted of 18 patients (9 males with median age 54 and females with median age 59) with pituitary lesions (7 somatotrophic and 2 corticotrophic adenomas, 8 non-functioning macro-adenomas and 1 resistant prolactinoma). Formalin fixed-paraffin embedded (FFPE) tissue sections from the lesions were assessed immunohistochemically for EPH-A4, -A5, -B2 and -B5 expression. Positivity is defined when >4% of pituitary cells have positive staining, after observation of at least 1000 cells. An immunoreactive score (IRS) was created according to the sum of percentage of EPH-A4, -A5, -B2 and -B5 positivity (0/negative staining; 1: 0–4% of pituitary cells positive; 2: 5–30% of pituitary cells positive; 3: 31–60% of pituitary cells positive; 4: 61–100% of pituitary cells positive) and the intensity of staining (0: negative staining, 1: mild staining; 2: intermediate staining; 3: intense staining). A case was characterized to present positivity when the percentage of cells with staining intensity ordinal value (scored from 0 for “no signal” to 3 for “strong signal”) with 300 possible values.

**Results**

Cytoplasmic and nuclear for EPH-A4 and cytoplasmic for EPH-A5, -B2 and -B4 pattern of immunostaining was noted. Positivity for EPH-A4 was seen in 17/18 (94%) of the specimens (17/18 with cytoplasmic and 3/18 with nuclear pattern). All corticotrophic and somatotrophic adenomas found positive for EPH-A4 with (94%) of the specimens (17/18 with cytoplasmic and 13/18 with nuclear pattern). Positivity for EPH-A5 and EPH-B2 was seen in 4/18 (22%) specimens and for EPH-B4 in 1/18 (5.5%), all non-functioning adenomas with cytoplasmic pattern. EPH-A4 IRS was mild for 4, intermediate for 6 and intense for 3 cases. H-score for EPH-A4 expression ranging from 30-255, whereas for EPH-A5, -B2 and -B4 was lower (10-65).

**Conclusion**

Our data indicate for the first time the increased expression of mainly EPH-A4 and to a lesser extent of EPH-A5, -B2 and -B4 in pituitary lesions. Their involvement in the pathophysiology of pituitary lesions requires further investigation to clarify their role and their possible potential prognostic value.

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**EP752**

**Clinical presentation of non-functioning pituitary tumors: the experience at a tertiary care hospital in Portugal**

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**Introduction**

Clinically non-functioning pituitary tumors (NFPTs) lack clinical or biochemical evidence of pituitary hormone excess. Their clinical presentation is heterogeneous, including mass effect-related symptoms and/or hypopituitarism, or even no symptoms in incidentally-detected NFPTs. We aimed to evaluate the clinical presentation spectrum of NFPTs in a cohort of patients managed at our hospital. Methods Clinical, demographic, biochemical and imaging data from 227 patients were retrieved and retrospectively analyzed using SPSS®.

**Results**

Our cohort included 115 women (50.7%) and the median age of the study population was 58 ± 15 years. Most patients had NFPT-related symptoms at presentation (75.3%), predominantly visual disturbances (56.8%) and headache (35.7%). In contrast, 56 patients (24.7%) had an incidental diagnosis on neuroimaging performed for other reasons, largely trauma (21.4%). Patients with incidentally-discovered NFPTs were significantly older than those with clinically-presenting NFPTs (62.8 ± 14.2 vs 54.8 ± 14.7; P < 0.001). Regarding the entire group of patients, at diagnosis, the majority had one or more pituitary hormone deficiencies (55.9%), which occurred more frequently in men than women (66.1 vs 46.1%; P < 0.001), in older patients and in patients with larger tumors (P < 0.001). Of the 227 NFPTs, 210 (92.5%) were macroadenomas, and 180 (79.3%) had extracapsular extension. The mean diameter at diagnosis was 2.41 ± 1.15 cm. Clinically-presenting patients had larger tumors (2.60 vs 1.97 cm; P = 0.006). A total of 140 patients (61.7%) underwent surgery, 75.7% of these within the first 12 months since the NFPT diagnosis. The subgroup of incidentally-discovered NFPTs required less often an operation than the clinically-presenting counterparts (41.1 vs 68.4%; P < 0.001).

**Conclusion**

Our NFPT cohort included patients who mostly presented with large tumors associated with compressive symptoms and hormonal deficiencies. However, a quarter of cases were incidentally-discovered NFPTs, typically found in older patients, and despite their smaller size still more than one third needed surgery.

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**EP753**

**Acromegaly: a rare disease with multiple, complex complications**

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**Introduction**

Acromegaly is a rare, challenging disease that if not appropriately treated can lead to numerous complications. Some of the most frequent complications are cardiovascular (hypertension, secondary cardiomyopathy, arrhythmias, valvulopathies, heart failure) and metabolic (secondary diabetes, various alterations of the lipid metabolism).

**Aim**

The aim is to assess the impact of long-term acromegaly on the cardiovascular system and glucose and lipid metabolisms.

**Patients and method**

In this retrospective study the records of 107 patients with previously diagnosed acromegaly, who have been assessed at least once in our tertiary referral centre (Department of Endocrinology, University Hospital “Sfântul Spiridon”, Iaşi) over a period of 6 years have been reviewed.

**Results**

Out of the 107 patients with mean age 51.96 ± 12.14 years, 34 (31.78%) were male and 73 (68.22%) were female. From the total of 107 patients 93 (86.92%) had cardio-metabolic complications. Out of the assessed cardiovascular comorbidities, hypertension was present in 46 patients (42.99%), rhythm disorders were found in 8 patients (20%), cardiomyopathy in 5 patients (12.5%), valvulopathies in 3 cases (7.5%), 6 cases of heart failure (15%), chronic venous insufficiency in 2 patients (5%), cardiac ischemic events were found in 11 patients (27.5%), 2 cases of stroke (5%) and 3 cases (7.5%) of other cardiovascular diseases were also noted. Alterations of the glucide metabolism were determined in 36 patients (33.64%): type 2 diabetes mellitus was found in 21 cases (58.33%), impaired fasting glucose in 6 cases (16.67%) and impaired glucose tolerance in 9 patients (25%). Dyslipidemia was found in 44 patients (41.22%), while an increased body mass index was determined in 46 patients (57.01%).

**Conclusions**

The design of the present research has offered a chance for thorough investigation of cardiovascular and metabolic alterations in acromegaly patients, thus revealing a significant number of complications. Although acromegaly is an orphan disease, the multi-organ severe complications rise complex issues in relation with the diagnosis and treatment approach. This aspect could justify the use of a personalised multi-modal treatment for each patient.

**Key words:** acromegaly, cardiovascular disease, metabolic complications

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EP754
Early diagnostic tools in milder forms of central hypothyroidism in patients harbouring a pituitary adenoma: cross-sectional study on 142 patients from a single tertiary center
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Introduction
Milder forms of central hypothyroidism (CeH) are still challenging to diagnose due to absence of gold standards, wide variability of fT4 values and aspecificity of symptoms. We aimed to find diagnostic clues at diagnosis (pituitary lesion dimensions, other hormonal deficit) and during long-term follow-up, guiding the clinician to a precocious diagnosis of CeH.

Study
142 patients harbouring a pituitary adenoma with complete pituitary assessment at diagnosis (hormonal/imaging) were studied between 2000 and 2020. Median age was 47.5 years (SD 16.5). Lesions were 45% microadenomas (55% macroadenomas), 62% were functioning and 30% incidentalomas. At diagnosis, 67% of patients with CeH suffered from at least another hormonal deficit, especially gonadotropin deficiencies (OR 6.9, P = 0.0001) and corticosterone failure (OR 7.6, P = 0.001). No correlation was found between CeH and having a functional adenoma (P = NS). Radiological measures were available in 102/142 patients. Patients with CeH at diagnosis had bigger adenomas (P = 0.054). Given a maximum adenoma diameter > 12 mm, the probability of carrying CeH was statistically significant (OR 3.53, P = 0.03, sensitivity 68.7%, specificity 61.6%). Mean follow-up was 7.6 years (2.5-39.9) and follow-up data were available for 69 patients, with at least one evaluation of paired TSH and FT4 per year. Only 4/69 developed overt CeH defined by inappropriately normal or low TSH with fT4 values beyond the lower limit of normal. In those patients mean fT4 variability (defined by the difference between the median value of fT4 and the lowest fT4 value detected over follow-up) was -18% (SD 6.5) and median TSH index (TSHi) was +1.7 (IQR 0.36-2.18) with a mean decrease of -47% (SD ± 50). Among the other 65/69 patients with a normal thyrotrope reserve, mean fT4 variability was -2% (SD ± 9) displaying a 2 SD as low as -20% and mean TSH, was +2.51 (SD ± 0.522) with a median decrease of -7% (IQR -1.6; -3) displaying a 2.5 percentile as low as -36%. The difference in intra-individual fT4 variations and TSH, decrease was statistically different in these two cohorts (P = 0.04, P = 0.048 respectively).

Conclusions
In patients carrying pituitary adenomas, the presence of mild CeH could we inferred at diagnosis if adenoma diameter is > 12 mm and gonadotropin or corticosterone deficiency coexist. During follow-up, if intra-individual variation of fT4 from baseline exceed -20% and TSH index decreases by more than -38%, the development of CeH could be suspected.

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EP755
Pituitary adenomas and pregnancy: descriptive observational study
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Introduction
Pregnancy results in a significant change in pituitary gland size and function. Due to this physiological adaptation, management of pituitary adenomas during pregnancy represents a particularly complex challenge. Aim of this study was to focus on a single referral institution experience with special attention to this subgroup of patients: pregnant woman affected by pituitary adenoma.

Materials and methods
This is a descriptive observational study, all patients with macro adenoma and who had at least one pregnancy were included. We studied 10 women who got pregnant during their endocrinological follow-up. They were divided as follows: 4 GH and PRL secreting tumors, 2 Cushing diseases, 2 acromegaly, 1 PRL secreting tumor and 1 non functioning macroadenoma. In order to describe the outcome of the adenoma during pregnancy, we considered the previous surgical and medical therapy, hormonal serum levels, imaging data and medical therapy during and after pregnancy. We also analyzed the obstetrical outcomes of their pregnancies.

Results
The median age of the patients was 35. They all had a previous transphenoidal surgery of the pituitary adenoma. The two patients affected by Cushing disease also had bilateral surrenectomy, due to lack of disease control and due to hyposurrenalism undergone therapy with hydrocortisone. After surgery, because of residual disease, a patient affected by GH and PRL secreting tumors, one affected by acromegaly and the patient affected by non functioning macroadenoma were treated with somatostatin analogs and the other one affected by acromegaly started dopamine agonists. When the patients showed desire for pregnancy, medical therapy was discontinued evaluating hormonal tests and MR imaging. The residual disease at MRI was stable during and after pregnancy and did not affect the optic chiasma, without visual field alterations or reduced vision. Obstetrical outcomes showed no malformation, one twin pregnancy, two caesarean-sections. The patients already undergoing medical treatment before pregnancy, restarted it after pregnancy.

Conclusions
Studies on pituitary adenoma management during pregnancy are limited. In our study, no complication was reported in patients with or without residual tumour on the preconception MRI, regardless of the initial size and of the discontinuation of medical therapy. Patients did not need any kind of therapy during pregnancy and did not show any symptomatic progression of adenomas, without ophthalmological abnormalities or apoplexy. Because of the potential risk that these conditions represents for the mother and the fetus, it is essential to keep patients under close follow-up and treat them quickly and successfully.


EP756
Clinical & Epidemiological characteristics of patients undergoing pituitary-related surgeries in a tertiary care centre in Sri Lanka
Piyumi Wijewickrama1,2, Sathyajith Ambawatte1,2, Manika Sumamunitha1,2, Chaminda Garusinge1, Sanjeewa Garusinge1, Despal Attanayake1, H.K. de S Kularatne1, Wadanambi Saman1 & Noel P Somasundaram1
1NHSL, Colombo, Sri Lanka; 2University College Hospital, United Kingdom; 3St George’s Hospital, United Kingdom

Introduction
For clinically relevant sellar masses, early identification and effective endocrine & surgical management is the key. National Hospital of Sri Lanka (NHSL), which is the largest tertiary care centre in Sri Lanka, manages a wide variety of patients with sellar/supra-sellar pathologies, regularly conducting pituitary related surgeries. The aim of the present study was to determine epidemiological and clinical characteristics as well as immediate post-operative course of the patients undergoing pituitary surgeries.

Methods
Prospective, cross-sectional study of demographics, clinical & biochemical characteristics & post-operative course of all adult patients (above 15 years) undergoing pituitary related surgeries in NHSL over 18 months from February 2019.

Results
During this period, 139 persons underwent pituitary related surgeries, with a mean age of 44 years (+/- 15) and a female to male ratio of 3.2. 25% had re-operations while the rest were first surgeries. The majority (68.3%) presented with pressure symptoms while 10.1% & 20.1% presented with hypopituitarism & hormone hypersecretion respectively. Sixty-seven (48.2%) were on pre-operative Levothyroxine, with 12 of them having long standing primary hypothyroidism. Forty-seven (33.8%) patients were on pre-operative long term hydrocortisone replacement. Pituitary adenoma in 111 (79.9%), craniopharyngioma in 22 (15.8%) and supra-sellar meningioma in 6 (4.3%) were observed. MRI of sellar masses demonstrated cavernous sinus invasion in 49 (35.3%), while 80 (57.6%) had optic chiasm compression. Out of pituitary adenomas, the majority 81 (72%) had non-functioning adenoma, 20 (18%) had Acromegaly, 9 (8.1%) had Cushing’s and 1 patient with resistant prolactinoma underwent surgery. The majority, 108 (77.7%) were trans-sphenoidal surgeries, while 31 (22.3%) underwent craniotomy. Post-operative complications observed were CSF rhinorrhea in 25 (18%), bleeding in 8 (5.8%), progressive deterioration of vision in 2(1.5%) and ischemic stroke in 2 persons. No significant difference was
observed with the type of surgery and with surgery complications. Fifty-two developed post-operative transient or permanent cranial Diabetes Insipidus while 12 (8.6%) had Syndrome-of-inappropriate-ADH secretion. 137 (99%) were observed with hyponatremia (sodium < 135) while 162 (112) had severe hyponatremia (sodium < 135). Among polyuric patients, 71 received at least a single dose of Desmopressin at some point. Out of them, 52 (68.5%) were diagnosed with inappropriate-anti-diuretic-hormone (SIADH), polyuria, Cranial Diabetes Insipidus (CDI) were analysed.

**EP757**

**Fluid and sodium disorders in patients undergoing pituitary related surgeries in a tertiary care centre in Sri Lanka, with associations and risk factors: a prospective, observational study**

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**Introduction**

Fluid and sodium disorders are a relatively frequent occurrence after sellar/supra-sellar surgeries. National Hospital of Sri Lanka (NHSL) is the main tertiary care centre in Sri Lanka, conducting regular pituitary surgeries.

**Methods**

A prospective cross-sectional study was conducted in all adults (above 15-years) undergoing pituitary-related surgeries in NHSL over 18 months from September 2019.

**Results**

There were 139 patients with a mean age of 44 years (+/- 15), 60% females, undergoing Trans-sphenoidal-surgery(TSS) or craniotomy for varying indications related to sellar/supra-sellar pathologies. Mean baseline pre-operative sodium was 138.9 (+/-3.2). Post-operatively, 76.54% developed polyuria (> 3/24 h) with peak median urine output on day 2. Out of them, 52 (68.5%) were diagnosed with CDI (80.7% having only transient CDI) and the rest had transient polyuria without confirmed Cranial-Diabetes-Insipidus (TPWCDI). Out of all polyuric patients, 71 received at least a single dose of Desmopressin at some point. Twenty-eight (20%) developed post-operative hyponatremia (sodium < 135), with only 12/6.6% having confirmed SIADH. All SIADH patients were managed with fluid restriction, with only 2 requiring hypertonic saline. Five demonstrated transient urine output with peak median urine output on day 2. Out of them, 52 (68.5%) were diagnosed with inappropriate-anti-diuretic-hormone (SIADH), polyuria, Cranial Diabetes Insipidus (CDI) were analysed.

**Discussion**

There were 139 patients with a mean age of 44 years (+/- 15), 60% females, undergoing Trans-sphenoidal-surgery(TSS) or craniotomy for varying indications related to sellar/supra-sellar pathologies. Mean baseline pre-operative sodium was 138.9 (+/-3.2). Post-operatively, 76.54% developed polyuria (> 3/24 h) with peak median urine output on day 2. Out of them, 52 (68.5%) were diagnosed with CDI (80.7% having only transient CDI) and the rest had transient polyuria without confirmed Cranial-Diabetes-Insipidus (TPWCDI). Out of all polyuric patients, 71 received at least a single dose of Desmopressin at some point. Twenty-eight (20%) developed post-operative hyponatremia (sodium < 135), with only 12/6.6% having confirmed SIADH. All SIADH patients were managed with fluid restriction, with only 2 requiring hypertonic saline. Five demonstrated transient urine output with peak median urine output on day 2. Out of them, 52 (68.5%) were diagnosed with inappropriate-anti-diuretic-hormone (SIADH), polyuria, Cranial Diabetes Insipidus (CDI) were analysed.

**Conclusion**

The findings of this real-world study add to the existing global literature and is the first such study conducted in Sri Lanka.

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**EP758**

**Severe growth retardation due to pituitary stalk agenesis: a case report**

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**Introduction**

Growth retardation is considered severe when the height of the child is -3 standard deviation (SD) below the average height in reference to the growth curves of children of the same sex and age. Pituitary stalk interruption syndrome (PSIS) is one of the most common conditions in children with short stature. This study identifies baseline characteristics of patients undergoing pituitary-related surgeries in a south Asian developing country, along with immediate post-operative complications. These findings have a national & a regional relevance in improving patient care. This will also have a global relevance due to the rising ethnic diversity all over the world.

**Conclusion**

We report the case of a 12-years old boy with no clinical history of perinatal injury or traumatic birth, who was admitted for short stature. Physical examination showed that his height was 105 cm (-4 SD), his weight was 15 kg (-4 SD), and Tanner stage was 1. A complete pituitary hormone profile was performed, which showed picture of hypopituitarism with low T4: 0.46 mg/dl, and low morning baseline cortisol: 28 ng/ml. His IGF1 level was under 10 ng/ml. His bone age was 2 years according to the Greulich and Pyle. Magnetic resonance imaging (MRI) examination showed an agenesis of the pituitary stalk which was not visualized; however; anterior pituitary and posterior pituitary were normally identified.

**Discussion**

PSIS is characterized by the presence of a thin or absent pituitary stalk, associated to hypoplastic anterior pituitary and ectopic posterior pituitary on MRI. However, there are variations in MRI appearances of this syndrome that includes the form of the pituitary stalk (interrupted, thin, or absent), the height of the anterior pituitary (from absence to normal) and the appearance of the posterior pituitary (ectopic, absent, or normal) The clinical presentation of PSIS varies with the age of diagnosis; manifestations may include neonatal hypoglycemia, prolonged neonatal jaundice, or short stature in older children. The clinical findings are related to isolated growth hormone deficiency; or combined multiple pituitary hormone deficiency.

We report the case of a 12-years old boy with no clinical history of perinatal injury or traumatic birth, who was admitted for short stature. Physical examination showed that his height was 105 cm (-4 SD), his weight was 15 kg (-4 SD), and Tanner stage was 1. A complete pituitary hormone profile was performed, which showed picture of hypopituitarism with low T4: 0.46 mg/dl, and low morning baseline cortisol: 28 ng/ml. His IGF1 level was under 10 ng/ml. His bone age was 2 years according to the Greulich and Pyle. Magnetic resonance imaging (MRI) examination showed an agenesis of the pituitary stalk which was not visualized; however; anterior pituitary and posterior pituitary were normally identified.

**Conclusion**

PSIS is a rare syndrome of congenital abnormalities involving hypothalamic-pituitary structures. It should be considered in the differential diagnosis of a child presenting with short stature or delayed puberty.

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**EP759**

**About two cases of adipic hypernatremia in adults, one with proven blood antibodies against subfornical organ (SFO)Ab**

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**Introduction**

Adipic hypernatremia, a rare hypothalamic disorder characterized by a loss of thirst in response to hypernatremia is more often reported in children. An autoimmune mechanism has been recently demonstrated. We report two cases.

**Case1**

A lean 67-year-old female, with a history of multilocular sclerosis, was admitted, for severe hypernatremia (162 mmol/l) with low ADH level (0.5 pmol/l; N: 0.5-2). She did not complain of thirst, despite ideomotor slowing and a skinfold. Diuresis was 1.40 l/24 h. Pituitary assessment showed mild hyperprolactinemia, a Nugent test at 11.5 mg/dl (n < 1.8 mg/dl) with low TSH level (0.08 u/l/ml (n 0.4-3.6)). MRI showed pituitary stalk nodular thickening. Etiological research only showed SFOAb. Treatment with desmopressin allowed improvement of idio-motor slowing and natriaemia (145 mmol/l). The pituitary stalk thickening had partially regressed one year later.

**Case2**

An overweight 38-year-old lady, was referred for a first hypernatremia episode (160 mmol/l) in 2013 after an acute pancreatitis complicated with cardiovascular collapse. She had no polyuria-polydipsia, did not feel thirst, and was irregularly menstruated. Initial pituitary assessment showed gonado-somatotropic insufficiency, mild hyperprolactinemia, normal thyroid and adrenal function. Keeping diagnosis was possible pituitary ischemia. The patient was advised to drink at least 2 liters/day and remained asymptomatic except for infertility. Three other episodes of pancreatitis occurred, the only identified cause being heterozygosity for a CFTF

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variant. In 2021, a new work-up showed similar pituitary profile as in 2013, hypernatremia (150 mEq/l), negative autoimmun panel, and normal CRP, IgG4 and pituitary MRI. A month later, a 5th pancreatitis with severe bradycardia (30-35 bpm) - hypothermia, low blood pressure and severe hypernatremia 170 mmol/l (ADH 0.8 pmol/l) required ICU admission. Cortisol and thyreotropo deficits were present, with persistent hyperprolactinemia and somato-gonadotropic insufficiency. She initially improved with rehydration, hydrocortisone 200 mg/day and levothyroxine. Polyuria or thirst were absent. Hypernatremia worsened as soon as rehydration/hydrocorti-

Conclusions

These two cases of adipsic hypernatremia in adult female patients are possibly related to an autoimmune neurohyposphytis in the context of MS in case1 and systemic inflammatory/autoimmune disease explaining both the hypothalamic and pancreatic involvement in case2. Despite the lack of polyuria-polydipsia syndrome, desmopressin treatment improved clinical status and natremia, but should perhaps be used more cautiously than usually recommended. Autoimmune causes can today be proven and may help to adjust the treatment.

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EP760

Features of the incidence of postoperative complications in patients with transsphenoidal pituitary adenocentecy

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Introduction

To study the incidence of postoperative complications in patients with transsphenoidal pituitary adenocentecy. Materials and research methods

180 cases of PA subjected to TPA. The mean age of the patient is 52.3 years. The patients were divided into two alternative groups: the first group - 93 (51.6%) patients with macroadenomas - 42 (45.2%) men, women 51 (54.8%), the second (comparison group) - 87 patients with microadenomas - 42 (45.2%) men, women 51 (54.8%), the second (comparison group) - 87 patients with microadenomas. An analysis of the incidence of postoperative complications in 180 cases of PA subjected to TPA revealed that in 31 (17.2%) patients and liquorrhea in 3 (5.4%) patients. At the same time, there was a significant association between osteoporosis and skeletal fragility fractures (P = 0.003).

Conclusion

Patients with CD have high prevalence of bone demineralization and osteopenia. Patients with reduced bone mineralization are at higher risk of fractures, mostly commonly vertebral fractures, which is why early diagnosis and treatment is necessary.

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EP762

Feasibility and effectiveness of switching patients with acromegaly receiving long-acting octreotide to lanreotide (Somatulin Autogel)

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Objective

To investigate the prevalence of skeletal complications (osteoporosis, osteopenia, presence of fragility fractures) in patients with Cushing’s disease, as well as gain insight into the potential risk factors for their development.

Material and methods

Cross-sectional study was carried out analyzing electronic medical histories of 52 patients (41 female, 11 male), diagnosed with CD treated between 2009 and 2019. Results

The study shows that bone demineralization is present in 52% of patients, 32% of whom were diagnosed with osteoporosis, 20% with osteopenia. A correlation between bone demineralization and age or age of CD diagnosis is shown. Bone fractures were present in 17.3% of the patients, of which 77.8% were vertebral and 22.2% peripheral. Patients who had bone fractures were more prone to bone demineralization (P = 0.02), and more specifically, there was a significant association between osteoporosis and skeletal fragility fractures (P = 0.003).

Conclusion

To investigate the prevalence of skeletal complications (osteoporosis, osteopenia, presence of fragility fractures) in patients with Cushing’s disease, as well as gain insight into the potential risk factors for their development.

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Skeletal complications in Cushing’s disease (CD)

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Introduction

Structural and functional damage of the skeletal system resulting in fractures is a common complication of CD. Due to major effect of glucocorticoids on the trabecular bone, vertebral fractures are a common and severe complication which can lead to disability.

Goal

To investigate the prevalence of skeletal complications (osteoporosis, osteopenia, presence of fragility fractures) in patients with Cushing’s disease, as well as gain insight into the potential risk factors for their development.

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Conclusion

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EP763

Abstract Withdrawn

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EP764

Clinical characteristics, treatment and outcomes of well-differentiated gastroenteropancreatic G3 NET

Marta Opalinska1, Anna Sowa Staszczak2, Anna Kurzyn’ska2, John O’Toole Johnston1,1

Poor prognosis. Further research is needed to optimize/personalize NET G3 treatment.

Conclusion

Options included combination of surgery, somatostatin analogues (SSA), Peptide Receptor Radionuclide Therapy (PRRT) in somatostatin receptor imaging. Treatment options included combination of surgery, somatostatin analogues (SSA), Peptide Receptor Radionuclide Therapy (PRRT) or chemotherapy (temozolomide/capecitabine or platinum-based regimens). Mean overall survival was 17.2 months (range 3.0 - 46.0 months).

Results

There were 9 cases of GEP-NET G3 (4 women and 5 men, mean age at diagnosis 62.6 years, range 47-80 years). 8 of them had disseminated stage IV at diagnosis (with liver, lymph nodes, bone, adrenal, brain and peritoneal metastases) and 1 stage IIB with loco-regional lymph node metastasis. The tumours originate from: pancreas (3 cases), stomach (2 cases), small intestine (2 cases), large intestine (1 case) and in 1 case the primary site was unknown. Mean Ki67 was 35% (range 25-70%). In 4 cases there was good or very good somatostatin receptor expression (SSTR) (Kenning score 3 and 4) in somatostatin receptor imaging. Treatment options included combination of surgery, somatostatin analogues (SSA), Peptide Receptor Radionuclide Therapy (PRRT) or chemotherapy (temozolomide/capecitabine or platinum-based regimens). Mean overall survival was 17.2 months (range 3.0 - 46.0 months).

Conclusion

NET G3 management is challenging due to their heterogeneity and relatively poor prognosis. Further research is needed to optimize/personalize NET G3 therapy with regard to differences in their organ of origin, stage, grading and SSTR expression status.

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EP765

Head and neck parangangliomas: the belfast trust experience

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Aims

To provide a comprehensive review of our institutional experience of the clinical features, investigations, management and follow up of this cohort.

Methods

Baseline clinical information was taken from a prospectively maintained HNPGL database between January 2017 to January 2022. Further clinical, radiological and laboratory data as well as outcomes were obtained from electronic medical records (NIECR).

Results

There were 21 patients; 10 M; 11F with a mean age of 54 years (range 17-76). Seven (33.3%) patients had glomus jugulare tumour, six (28.5%) had carotid body tumour, four (19%) had glomus tympanicum, four (19%) were in other locations. Tumour size ranged from 20 mm to 5 cm. Thirteen (61.9%) patients had a pre-operative scans, six of which had octreotide avid scans. To date five (23%) patients had SDHD gene mutation and three (14%) patients had SDHB gene mutation identified. All tumours were non-functioning with normal urine metanephrines. Ten (47%) patients underwent surgical resection with five subsequently receiving adjuvant radiotherapy. Recurrence was present in three patients who had surgery for jugulare tumours. Four (19%) patients were deemed not suitable candidates for surgery either due to their extensive disease burden, tumour location or the presence of multiple co-morbidities. Three (14%) patients received monthly sandostatin/Octreotide-therapy. Two of these three patients had stable tumour size without any significant growth since they started on Octreotide-therapy. The remaining four patients (19%) were managed conservatively with serial imaging and observation.

Conclusion

Management of patients with HNPGL requires a multidisciplinary approach and should be individualized and tailored to each patient. Consideration for primary surgical treatment should consider performance status, tumour location and size. Initial surgery still provides excellent outcomes for patients, with adjunctive radiotherapy as second line treatment. The role of Octreotide therapy should be studied in a larger cohort to determine longer term outcomes.

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EP766

A paradox in clinical practice: the case of a hidden tuberculosis panhypopituitarism: the case of a hidden tuberculosis panhypopituitarism

Matteo Parolin1, Matteo Parisotto1,2, ambra uliana1, Paola Sartorato1 & Ernesto De Menti3

Background

Although gastroenteropancreatic neuroendocrine tumors G3 (GEP-NET G3) and neuroendocrine cancers (GEP-NET G3) are characterized in histopathological examination by Ki67>20% or > 20 mitoses/10HPF their management and prognosis is substantially different. Despite the WHO introduces the novel well-differentiated neuroendocrine tumour of high grade (NET G3) classification in 2017 the clinical management of them is still challenging due to high NET G3 heterogeneity and limited data in regards to best therapeutic strategies.

Material and Methods

We review clinical characteristics, treatment options, and outcomes in cohort of patients with gastroenteropancreatic NET G3 (GEP-NET G3) managed at our centre since implementation of the new WHO classification (2017 – 2021).

Results

There were 9 cases of GEP-NET G3 (4 women and 5 men, mean age at diagnosis 62.6 years, range 47-80 years). 8 of them had disease stage IV at diagnosis (with liver, lymph nodes, bone, adrenal, brain and peritoneal metastases) and 1 stage IIB with loco-regional lymph node metastasis. The tumours originate from: pancreas (3 cases), stomach (2 cases), small intestine (2 cases), large intestine (1 case) and in 1 case the primary site was unknown. Mean Ki67 was 35% (range 25-70%). In 4 cases there was good or very good somatostatin receptor expression (SSTR) (Kenning score 3 and 4) in somatostatin receptor imaging. Treatment options included combination of surgery, somatostatin analogues (SSA), Peptide Receptor Radionuclide Therapy (PRRT) or chemotherapy (temozolomide/capecitabine or platinum-based regimens). Mean overall survival was 17.2 months (range 3.0 - 46.0 months).

Conclusion

NET G3 management is challenging due to their heterogeneity and relatively poor prognosis. Further research is needed to optimize/personalize NET G3 therapy with regard to differences in their organ of origin, stage, grading and SSTR expression status.

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discharged after ten days in good general conditions, with the indication to continue corticosteroids for two months.

Conclusions
Our patient’s neurological finding after the beginning of ATT may have been a new development or a progression of intracranial tuberculosis. A paradoxical reaction to ATT should be suspected in any patient in ATT who present with neurological findings and hypopituitarism. Paradoxical tuberculomas are observed in approximately 1% of all active tuberculosis cases. Corticosteroids are the only anti-inflammatory drug that can be used in the management of PR.

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**EP767**

**The efficiency of the treatment by Sandostatin-Lar in patients with non-functional pituitary macroadenomas**

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The purpose of the study
Is to study the efficiency of the treatment by Sandostatin-Lar in patients with non-functional pituitary macroadenomas (NFPA)

Material and methods.
Under our observation there were 20 patients with NFPA, of whom women were 8, men - 12. The average age of patients was 29.2±6.4 years. All patients were subjected to transnasal adenomectomy of pituitary gland (TAG) in our clinic. The whole patients were performed by research complex, which included Chemiluminescent hormone (STH, IGF-1, Prolactin, LH, FSH, TSG, ACTH, Cortisol, etc.), ophthalmological (Eye bottom, field of view) and X-ray studies (CT, MRI of the Turkish saddle).

Results
According to our data, In all 20 patients, the average sizes of the pituitary tumor before TAG were in range 3.1 x 3.4 x 3.0 cm. Patients were divided into 2 groups: patients of 1 st group received after TAG the treatment by Sandostatin-Lar during 3 months, patients of 2 nd group did not receive Sandostatin-Lar. The Sandostatin-Lar was prescribed 20 mg every 4 weeks for 3 months. The preliminary results showed the stability of the tumor residue in 7 of 10 patients (70%) in the group of combined treatment compared to 10 patients from 2 nd group who did not receive Sandostatin-Lar.

Conclusions
It is necessary further continuation of research, taking into account immuno-cytological studies and biomarkers.

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**EP769**

**A challenging case of sheehan syndrome**

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Introduction
Sheehan Syndrome (SS) is a cause of hypopituitarism resulting from postpartum pituitary infarction. Its frequency is decreasing worldwide, particularly in developed countries due to advances in obstetric care.

Case report
A 50-year-old female patient was admitted to the emergency department with complaints of progressive pain in the lower hemithorax and abdomen. She also referred constipation, weight gain and asthenia. The initial laboratory tests showed raised creatinine kinase (4661 U/l [5-25]), creatine phosphokinase (145 [10-145]) and aminotransferases (AST 86 U/l [2-40]; ALT 36 U/l [5-56]). Thyroid function was assessed revealing thyroid stimulating hormone (TSH) of 0.27 mIU/ml [0.4-4.0] and free thyroxine <0.40 ng/dl [0.7-1.5]. Assessment of anterior pituitary function was carried out indicating pan-hypopituitarism: FSH 3.8 mIU/ml; LH 0.6 mIU/ml; Prolactin <0.8 ng/ml [5.2-26.5]; ACTH 16 pg/ml [9-52]; Cortisol 2.1 mg/dl [5-25]; GH <0.1 mg/dl (<1]. A brain magnetic resonance imaging (MRI) was performed, revealing the presence of an intrasellar arachnoidcele. She was started on replacement therapy with hydrocortisone and later levothyroxine with symptomatic improvement. The patient had a past medical history of a stillbirth at 28 years old, in Guinea-Bissau, due to postpartum haemorrhage requiring transfusion support. Afterwards a combined oral contraceptive was started, which she maintained for 11 years. After discontinuing the drug at the age of 39, she remained amenorrhoeic.

Discussion
This case fulfils the classic criteria of Sheehan’s syndrome with severe postpartum haemorrhage requiring transfusion; postpartum oligomenorrhea; hypopituitarism and the presence of arachnoidcele at brain MRI. Stillbirth in an underdeveloped country is also frequently described and related to a diagnostic latency. The diagnosis was obtained 26 years after the incident, with unspecific symptomatology. The fact that the corticotropic axis tends to be affected later in these cases, may explain the absence of significant consequences. This illustrates a difficulty in diagnosing Sheehan’s syndrome outside the acute context and highlights the need to be alert for this entity.

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A case with primary autoimmune hypothyroidism causing pituitary enlargement mimicking pituitary macroadenoma and secondary adrenal insufficiency

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Introduction

In primary hypothyroidism, the increase in TRH may cause hyperplasia in the pituitary gland. It has been reported that long-standing hypothyroidism might also cause irreversible pituitary damage, which may lead to a deficiency in one or more pituitary hormones. Herein, we report a case with primary autoimmune hypothyroidism causing pituitary enlargement mimicking pituitary macroadenoma and secondary adrenal insufficiency.

Case

A 17-year-old female patient was diagnosed with primary hypothyroidism when she was 12 years old and levothyroxine-sodium treatment was started. Three years ago, she applied to a tertiary medical center with headache. A solid mass lesion in pituitary gland measuring approximately 15 mm diameter was reported at magnetic resonance imaging (MRI). After hormonal evaluation the mass was considered as a non-functioning macroadenoma and follow-up was recommended. Secondary adrenal insufficiency was observed in follow-up and hydrocortisone treatment was added. She referred to neurosurgery for the operation. Repeated MRI of the sella reported that there was a 10 x 10 mm nodular lesion suspicious for macroadenoma, and pituitary hyperplasia and hypophysitis should be considered in the differential diagnosis. Serum TSH was found suppressed while fT4 and fT3 were in normal range. The patient referred to our center for a differential diagnosis. The patient had fatigue and hair loss complaints. She had regular menstrual cycle and no galactorrhea. The visual field examination was normal. She was using levothyroxine-sodium and hydrocortisone treatment. Hydrocortisone dose was increased as a result of increased pituitary mass on imaging. As serum TSH level was found increased (> 100 uU/ml) while serum fT4 was low. The hypothalamic-pituitary-adrenal axis couldn’t be evaluated due to long-term steroid usage. Other pituitary hormones were normal. We found out that she didn’t use levothyroxine-sodium regularly. Previous TSH measurements were occasionally > 300 uU/ml. Pituitary hyperplasia due to irregular replacement was considered. She was warned about regular usage. It was planned to taper and discontinue hydrocortisone during follow-up and reevaluate the pituitary-adrenal axis.

Discussion

Despite the recent advances in MRI examinations, it might be still difficult to differentiate pituitary adenoma, hyperplasia and hypophysitis. Therefore, the patient’s medical history, clinical and laboratory results should be evaluated together carefully. Accurate identification of such patients is important for avoiding unnecessary surgery and costly MRI follow-up.

Case of a giant prolactinoma presenting as a clival mass

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Introduction

Giant prolactinomas are rare tumors accounting for 2-16% of all prolactinomas. They can be aggressive and invasive. Rarely, they might not have a suprasellar component and grow downward. Such extension can make it difficult to distinguish pituitary adenoma from other skull base tumors. We present a case that was considered to be chordoma based on clinical and radiological imaging features, but was diagnosed as prolactinoma by pituitary biopsy.

Case

A 67-year-old male patient with headache, dizziness admitted to the emergency department. There was no pathological finding in his physical examination. Cranial MRI demonstrated a large mass (5 x 3 x 3.5 cm) which destroyed the clivus, extending anteriorly towards the sphenoid sinus, and surrounding both cavernous sinus. He was referred to neurosurgery department and underwent transsphenoidal biopsy for the differential diagnosis of clival tumors such as chordoma. The histopathological examination revealed it to be pituitary adenoma and immunohistochemical study showed a strong positive staining for the prolactin. He was diagnosed with giant prolactinoma and referred to our outpatient clinic. He reported reduced libido and difficulties in erection. Visual field examination was normal. Hormonal evaluation revealed that serum prolactin level was significantly increased (6290 ng/ml) and serum IGF-1 level was compatible with age and sex. Serum total testosterone level was decreased (115 ng/dl) while FSH and LH levels were within the reference ranges. The pituitary-adrenal and pituitary-thyroid axis were intact. He was started a dose of cabergoline 500 micrograms once weekly. Then the dose increased to 500 micrograms twice weekly as tolerated. He responded well to the medical treatment. Serum prolactin levels dramatically decreased. Pituitary MRI in 12 weeks intervals showed a remarkable reduction in mass.

Conclusion

This case highlights the importance of including invasive pituitary macroadenomas with infrasellar extension in the differential diagnosis of skull base lesions.
tumors. Initially, evaluation of clinical signs and hormonal tests in patients with sellar-parasellar masses, can prevent unnecessary invasive procedures.

EP773 Clinical and paracultural features of pituitary metastases: Report of five cases
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Introduction
The sellar region is known as a low-risk brain metastasis area. The prevalence of pituitary metastasis represents 1% of all surgical tumors of the pituitary gland. In most cases, pituitary metastasis is identified in patients with a prior history of cancer. In a few cases, it can reveal the primary tumor. The aim of this study was to assess clinical and paracultural features of pituitary metastasis.

Methods
This was a retrospective and descriptive study including patients with pituitary metastasis admitted to our department. Clinical, hormonal, and radiological data were collected.

Results
Five patients (four women and a man) with a mean age of 51.4 years [extremes: 32-68] were enrolled in this study. Three women had a history of metastatic ductal breast carcinoma. Two women presented with polypisia-polydipsia syndrome and the third one presented with headaches, blured vision, and decreased visual acuity. Hormonal investigations revealed disconnection hyperprolactinemia (n = 2), central diabetes insipidus (n = 2), and hypothyreotism (n = 3). Pituitary magnetic resonance imaging (MRI) revealed, in both women with polyuria-polydipsia syndrome, a third patient presented a large heterogeneous pituitary mass of 27 mm with suprasellar extension and infiltration of the optic chiasm. In two patients, the primary cancer was revealed by the pituitary metastasis. The first was a 50-year-old woman who presented with headaches, visual disorders, weakness, nausea, vomiting, and hypothyreotism. Pituitary MRI showed a large mass extending from the sella turcica to the sphenoid sinus, optic chiasm, and nasopharynx. Endoscopic biopsy confirmed the diagnosis of undifferentiated nasopharyngeal carcinoma with intracranial extension. Biological investigations revealed hypothyreotism and disconnection hyperprolactinemia. The patient was put on hormone replacement therapy. After corticosteroid treatment initiation, a diabetes insipidus was revealed. The second patient was a 68-year-old man, who presented with polyuria-polydipsia syndrome. The diagnosis of central diabetes insipidus with disconnection hyperprolactinemia was established. Pituitary MRI showed a tumor of a 12 mm involving the pituitary stalk and infundibulum. The patient was diagnosed with metastatic small-cell lung cancer.

Conclusion
The hypothalamic-pituitary area is a rare site of metastasis. Clinical presentation and pituitary MRI are the key in guiding the diagnosis. Signs of dysfunction of both the anterior and the posterior pituitary gland are often present. Diabetes insipidus is the most frequent symptom.

EP775 Distribution of E- and N-cadherin in subgroups of non-functioning pituitary neuroendocrine tumours
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Purpose
Clinically Non-Functioning Pituitary Neuroendocrine Tumours (NF-PitNETs) present a varying degree of aggressiveness, and reliable prognostic markers are lacking. We aimed to characterize the distribution of E- and N-cadherin in corticotrop, PIT1 and null-cell NF-PitNETs, and link it to the clinical course of the tumours.

Methods
We investigated the distribution of E- and N-cadherin by immunohistochemistry in a retrospective cohort of thirty tumours of the less common NF-PitNETs (corticotroph (n = 18), PIT1 (n = 8) and null-cell PitINet (n = 4)). Immunoreactive scores were compared to previously presented cohorts of gonadotroph NF-PitNETs and corticotroph functioning PitINet.

Results
We found a low immunoreactive score (IRS) for the extracellular domain of E-cadherin, a medium to high IRS for the intracellular domain of E-cadherin and a high IRS for N-cadherin throughout the cohort. The corticotroph NF-PitNETs presented a higher IRS for the extracellular (median 0 (IQR 0-2)) and the intracellular (median 9 (IQR 6-12)) domain of E-cadherin, and a lower proportion of tumours presenting nuclear E-cadherin (17%) compared to the previous presented gonadotroph NF-PitNETs (P-value < 0.001 for all three comparisons). Presence of nuclear E-cadherin was associated with a weaker staining for the intracellular domain of E-cadherin by the cell membrane (median 4 (IQR 0.5-6) and 9 (IQR 9-12) for tumours with and without nuclear E-cadherin respectively.

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EP776
Primary cilia in Pituitary neuroendocrine tumours and their association with aggressiveness
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Purpose
Although growing evidence supports the role of primary cilia (PC) in the regulation of cancer development, their possible role has not yet been studied in pituitary neuroendocrine tumours (PitNETs). The study of cilia could serve as a diagnostic tool providing new insights into the mechanisms of tumorigenesis and aggressiveness of PitNETs.

Methods
A total of 86 patients with PitNETs (28 functioning and 58 non-functioning [NF-PitNETs]) and 12 controls were evaluated by immunofluorescence and immunohistochemistry in tissue microarrays (TMA) and by western blot in PitNET protein extracts. The frequency of ciliated cells was estimated using a cilia index score based on the length of cilia and the percentage of ciliated area in the tissue. The distribution of PC and its correlation with several clinical parameters and aggressiveness was analysed.

Results
PC were present only in scattered cells of control pituitary tissues, whereas PitNET cells showed robust staining for ciliary markers. Interestingly, the number and for length of ciliated cells was significantly higher in non-functioning PitNETs, including null cell adenomas and gonadotropinomas, when compared to functional tumours. Remarkably, PC were significantly increased in non-functioning-PitNETs. In addition, the presence of cilia was associated with tumour invasion, aggressiveness and recurrence in PitNETs.

Conclusions
PC are present in PitNETs, especially in non-functioning PitNETs and may represent an important contributor to aggressiveness. PC may serve as a novel diagnostic marker for predicting tumour behaviour and as a potential target for drug therapy.

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EP777
Cushing’s disease in MEN 4 syndrome
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In 2000 female, 28 y.o., admitted endocrinologist with headache, high blood pressure, dark skin and muscle weakness. Lab data showed high levels of ACTH and cortisol, low potassium level. According to MRI scans, pituitary gland seemed normal. On CT in right adrenal was found 32 mm mass with the native density of 20 HU. Diagnosed ACTH-dependent Cushing syndrome (CS). As Mitostane was not available in Russia at that time, she received ketoconazole due to progression of CS but it was canceled later due to intolerance. So, right adrenalectomy was performed. Histology: adrenal adenoma with adrenal hyperplasia. The cortisol level decreased and symptoms diminished. In 2002 pituitary adenoma of 6 mm appeared on MRI. It was resected endoscopically by transphenoidal approach. Histology: chromophobe adenoma. However, the hypercortisolism and high level of ACTH remained. Later in 2002 she underwent the proton beam surgery with following disease remission. At 2012 the patient had noticed the deterioration of health: skin darkening, high levels of blood pressure, hyperglycaemia. In 2015 the relapse of hypercortisolism was confirmed. According to MRI there were signs of pituitary adenoma relapse (partial empty sella). CT scan showed two adrenal masses up to 23 mm and 10 mm in the left adrenal. Second transphenoidal partial removal of pituitary adenoma was performed, complicated by liquefactive, purulent meningitis, secondary hypophysitis.

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EP778
Acromegaly with negative pituitary magnetic resonance imaging: a case report
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Introduction
Acromegaly is a rare endocrine disorder. In 95% of cases, it is caused by a GH-secreting pituitary adenoma. Rarely, acromegaly is due to ectopic production of GH or growth hormone-releasing hormone (GHRH). Herein, we report a case of acromegaly with negative pituitary magnetic resonance imaging (MRI) and discuss its possible etiology and management.

Observation
A 75-year-old woman was referred to our department for the exploration of acquired acrofacial dysmorphic syndrome. Her past medical history included type 2 diabetes mellitus and hypertension. She presented with paraparesis of the left hand, arthralgia, and nocturnal snoring. Neither headache nor visual impairment were reported. On physical examination, she had a body weight of 69 kg, a body height of 1 m 68, corresponding to a body mass index of 24.4 kg/m², an enlargement of facial features and hands, and a loss of dental articulation. Hormonal investigations revealed an IGF1 level of 424 ng/ml (nr=55-212), a nadir of GH under oral glucose tolerance test of 7.1 ng/ml (nr<1 ng/ml), a TSH level of 1.3 mIU/l (nr=0.35-4.95), a FT4 level of 0.97 ng/dl (nr=0.7-1.5), a FSH level of 43.9 mIU/l, a LH level of 14.64 mIU/l and a prolactin level of 7 μg/l. The peak of cortisol level in response to the insulin-induced hypoglycemia test was 19.7 μg/dl. Further explorations showed carpal tunnel syndrome, thyroid nodule, and a mild obstructive sleep apnoea syndrome. The chest x-ray and the abdominal ultrasound were normal. Initial and repeat pituitary MRI showed a normal-sized pituitary gland with no evidence of an adenoma. Work-up for ectopic GH-secreting tumor was planned (cervical-thoraco-abdominal computed tomography scan and octreotide scintigraphy).

Conclusion
Acromegaly may be a curable cause when a pituitary adenoma is evident. However, its extra-pituitary origin remains a real challenge as to its localization and management.

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EP779
TSH-secreting pituitary neuroendocrine tumor revealed after total thyroidectomy, a case study
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Introduction
TSH-secreting pituitary neuroendocrine tumor (TSH-PitNET) is the rarest pituitary tumors. Most TSH-PitNETs are secreting, with a biological profile of inappropriate TSH secretion (moderately elevated TSH, elevated FT3 and FT4).

Observation
We report the case of a 69-year-old patient, with a history of total thyroidectomy in 2014 for multinodular goiter, hospitalized for suspected levotyroxine pseudo-malabsorption. Despite doses above 2 μg of levotyrox, the TSH always remains high above 10 mU/l with high FT4. Clinically the patient presents some signs of hyperthyroidism.

Discussion
The diagnosis of pseudo malabsorption is unlikely, despite constantly elevated peripheral hormones the TSH remains elevated. Faced with a biological profile associating elevated peripheral hormones with an unrestrained TSH, the main differential diagnoses are thyroid hormone resistance syndrome and TSH PitNET. The age, sex and level of clinical thyroid functional tests are similar in the two pathologies. Thyroid hormone resistance syndrome is eliminated by a normal preoperative assessment. Hypothyalmic pituitary MRI showed a 7.5 mm right pituitary microadenoma. A somatostatin analog braking test at 90 mg/28day was performed, after 2 months of treatment, TSH decreased to 1 mIU/l with reduced doses of levotyrox. The diagnosis of TSH-PitNET is retained in our patient despite the normality of the preoperative assessment which can be explained by a cyclic secretion, or a lifting of inhibition already described in the literature.

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EP780
Null cell adenoma with low Ki-67 presenting as recurrent pituitary mass
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Background
Approximately one-third of pituitary adenomas are identified as nonfunctioning pituitary adenomas (NFPA) which have a heterogenous profile and an increased potential for relapse one to five years after pituitary surgery. In a retrospective analysis by Almeida et al, multiple surgical resections, elevated ki-67 and cavernous sinus invasion were predictive of recurrence. They typically present with symptoms of mass effect and most are macroadenomas at time of diagnosis.

Clinical Case
A 65-year-old female initially presented with bitemporal hemianopsia, galactorrhea and amenorrhea 28 years prior. She subsequently underwent transsphenoidal hypophysectomy with resolution of symptoms postoperatively. She was clinically stable until 12 years after whenshe had peripheral visual field loss. Upon reevaluation, she was diagnosed with non-functioning pituitary macroadenoma for which she underwent a repeat transsphenoidal pituitary surgery. Her vision improved and she remained asymptomatic thereafter. Sixteen years after her second surgery, she developed blurred vision. Cranial MRI was done which showed lobulated, heterogeneous hyperdense sellar-suprasellar mass measuring 55 x 36 x 47 mm extending to the bilateral sphenoid and ethmoid sinuses, left pterygopalatine fossa, left superior orbital fissure, probably the left foramen lacerum, and left cavernous sinus with encasement of the left internal carotid artery and associated erosion of the adjacent osseous structures. Visual field testing showed mild reduction in field sensitivity with consideration of media opacity and/or uncorrected error of refraction. Baseline hormonal work up was unremarkable. Hence, endoscopic endonasal transsphenoidal, transethmoidal parasellar excision of sellar mass, with reconstruction via Hadad Flap was done. There were no intraoperative nor postoperative complications. The specimen was sent for histopathology with provisional anatomic diagnosis of pituitary adenoma. Immunohistochemistry stained negative for chromogranin and any of the pituitary hormones which was consistent with null cell adenoma. The Ki-67, an independent marker of tumor progression and recurrence, was low at less than 1%. However, after 1 month, repeat MRI showed no significant change in the heterogeneously enhancing mass centered in the sellar-suprasellar region. Thus, she received adjuvant radiotherapy with total dose of 5040 cGy divided in 28 fractions and was advised close monitoring of pituitary MRI and development of any new symptoms.

Conclusion
In this case, although with low Ki-67, the presence of multiple surgery and high Knosp grade were recognized as risk factors for its recurrence. Treatment of recurrent NFPA is multimodal which includes re-operation, radiosurgery and radiation therapy. A multidisciplinary team approach is required for its comprehensive management and long-term follow-up.

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EP781
Discordant GH and IGF-1 values in a surgically treated acromegaly patient: a management conundrum
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Introduction
Remission after transphenoidal surgery in patients with acromegaly is confirmed by biochemical assays of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Although their levels are usually closely correlated, discordant results of these tests have been noted, making the follow-up of acromegaly patients particularly challenging.

Case report
We present the case of a 35 year old female diagnosed with acromegaly at the age of 32 years. At the time of diagnosis a 20.9 x 17 x 16 mm macroadenoma was found on pituitary MRI. IGF-1 was 406 ng/ml (normal age and sex-matched values 115-307), serum nadir GH during a 75 g oral glucose tolerance test (OGTT) was 5.61 mg/ml and prolactin levels were 51.92 mg/ml (normal values < 26.53). She underwent endoscopic transphenoidal surgery, with immunohistochemistry analysis revealing a mixed somatotroph-lactotroph pituitary adenoma, with a Ki 67 index of 4%. Analysis of GPR101 and AIP genes mutations was negative. She developed transient postoperative SIADH with hyponatremia (sodium values of 118 mEq/l). Postoperative evaluation 3 months after surgery showed no tumor remnant on pituitary MRI, normal IGF-1 [257 pg/ml (normal age and sex-matched values 115-307)], but a lack of inhibition of GH after OGTT (nadir values of 0.733 ng/ml). At this moment the chosen approach was biochemical evaluation every 6 months and annual pituitary MRI. For the next two and a half years the patient had the same biochemical profile of normal IGF-1 but unsuppressed GH during OGTT and no tumor remnant visible on MRI. However, at the last evaluation in January 2022 we found elevated levels of IGF-1 [341.3 ng/ml, 1.23 x upper limit of normal], serum nadir GH during OGTT of 2.55 ng/ml and no changes on pituitary MRI. Taking into account the marginally elevated IGF-1 and the patient’s desire to undergo an in-vitro fertilization procedure in the near future, we opted for initiation of therapy with cabergoline until pregnancy is obtained and we are considering referring the patient for a 131I-methionine PET/CT for accurate localization of a potential residual/recurrent pituitary adenoma.

Conclusions
Management of surgically treated acromegaly patients with discordant GH and IGF-1 values is a challenge. Close biochemical evaluation is needed and an individualized approach is warranted, but further studies are needed to assess the risk of disease recurrence and the impact on the patient’s quality of life.

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EP782
Screening of IGF-1 level in patients with Prolactinomas
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Background
Prolactinomas are the most frequent pituitary adenomas. Treatment of prolactinomas includes drug therapy, surgical removal, and radiotherapy. Although surgical treatment is the most effective method, it is not always possible or desirable. Therefore, the search for a method of screening for prolactinomas is of great importance.

Purpose
The purpose of this study was to determine the usefulness of screening for prolactinomas using an IGF-1 level test.

Methods
The study included 100 patients with prolactinomas. The IGF-1 level was determined in all patients using an immunofluorescence method.

Results
Of the 100 patients, 75 had an IGF-1 level above the normal range. In 35 patients, the IGF-1 level was normal. The results were consistent with the diagnosis of prolactinomas in 75% of the cases.

Conclusion
Screening for prolactinomas using an IGF-1 level test is a promising method for the early detection of the disease.
Objective

to determine the need for screening for IGF-1 levels in patients with
prolactinomas and without obvious symptoms of acromegaly.

Materials and methods

A pilot cross-sectional study, based on the analysis of medical records of patients
with confirmed prolactinoma, who applied to the Moscow Regional Research
and Clinical Institute named by M.F. Vladimirsky. A total of 88 patients were
included in the study. The frequency of studying the level of IGF-1, and the
frequency of detecting cases of acromegaly were evaluated in patients with
prolactinoma. The level of IGF-1 was determined in 60/88 patients with
prolactinoma. Among patients with prolactinoma, women with macroadenoma
(Fmi) - 17, women with macroadenoma (Fma) - 16, men with microadenoma
(Mma) - 2, men with macroadenoma (Mmna) - 20. The median level of prolactin at
the onset of the disease was 2330 mU/l (1010; 4389) in Fmi, 10006.5 mU/l in Fma
(1917.6;95106.3), in Mmi 2017.52 mU/l (1626;4382), in Mma 6080 mU/l
(14000;104700).

Results

Among patients with a known level of IGF-1, its increase was recorded in 66/90
patients with prolactinomas. An oral glucose load (OGL) was performed in all 6
patients. The diagnosis of acromegaly was confirmed in 2 Fmi. The percentage of
excess of the IGF-1 levels above the upper limit of the normal in patients with a
negative test – 20.1%, 45.58%, 46.09% and 115.1%, in patients with diagnosed
acromegaly – 70.8% and 217.6%.

Conclusions

In real clinical practice, the level of IGF-1 was determined in 68.2% of patients
with prolactinomas. At the same time, the proportion of identified patients with
acromegaly among the examined patients with prolactinomas but without obvious
clinical signs of acromegaly, was 3.3%. Considering the obtained results, the
question of the necessity of screening the level of IGF-1 in patients with
prolactinomas requires further study.

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EP783

Polyuria-polydipsia in an athletic teenager

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Introduction

Central diabetes insipidus is characterized by partial or total ADH deficit of
various origins. The clinical picture is dominated by massive polyuria with
diluted urine, increased thirst and daily water consumption reaching impressive
quantities.

Case report

We report the case of a 16-year-old male teenager presenting with excessive thirst
and water intake of 8–10 l/day and voiding large quantities of diluted urine.

Symptoms started gradually over the past 3 years. He attributes his increased
thirst to increased transpiration during his recently restarted judo-training and he
states he can abstain from drinking water if he has to, especially during school-
time. He denies headaches and troubled vision. Physical examination was
unremarkable, except for a grade 1 obesity (BMI 32 kg/m2) of recent onset
(interruption of regular training during first COVID lock-down). Personal history
is devoid of chronic diseases and head trauma and he denies consumption of
medication or recreational drugs. Family history is positive for type 2 diabetes in
all his four grandparents. Lab tests including electrolytes and pituitary axis
returned normal. A thirst test was undertaken, starting at 23.00 h and conducted
until 12 p.m. the next day. Sodium concentration increased from 140 to 143 mEq/l,
serum osmolality increased from 284 to 294 mOsm/kg, while urine osmolality
raised slightly from 602 to 679 mOsm/kg. No signs of dehydration and no
hypotension occurred during the test. At the final blood draw copeptine was
measured at an external laboratory. Patient was discharged with no treatment
awaiting the results of hypophysis IRM and copeptine. At the follow-up, he still
reports a water intake of 3 to 7 l per day. The IRM of the hypophysis and IgG4
level were normal. Copeptine measured at 1.7 pmol/l for a osmolality of 294
mOsm/kg (normal range 2.3–24.5 pmol/l for osmolality between 291 and 295
mOsm/kg) thus showing insufficient increase and suggesting a partial deficit of

ADH. Arginin–vasopressin was initiated at a dose of 25 microg/day sublingual in
the morning. At one–week follow-up water consumption decreased to 1.5–2 l/day,
urine output normalized, while maintaining normal sodium and serum osmolality.

Conclusion

The copeptine value and the response to the therapeutic trial of arginine-
vasopressin helped diagnosing a central partial ADH deficit which we considered
idiopathic, however repeated minor head trauma during his years-long judo-
training may have also played a role in the onset of the disease.

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EP785

Clinical case of syndrome of inappropriate secretion of antidiuretic
hormone (SIADH) with uncertain localization

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Introduction

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is
characterized by hypotonic and euvolemic hyponatremia along with urinary
hypermolality, resulting from antidiuretic hormone (ADH) release in the
absence of adequate stimuli.

Case report

A 59-year-old woman, presented with complaints of constant thirst, general
weakness, memory loss, episodes accompanied by headaches, leg cramps,
increased blood pressure. From the anamnesis, the first time hypotension 114-123 mmHg (135-145), was revealed during hospitalization for fainting 5 years ago, this episodes repeated several times a year. At the same time, a pituitary non-active macroadenoma of 22*12*9 mm (Knosp 2) was found, without indications for surgical treatment during yearly observation by MRI. All diagnostic criteria for SIADH were met in the form of repeatedly confirmed hypotonic hypotension with urine osmolality exceeding the blood plasma osmolality (412.520 mOsm/kg), and normal urinary sodium excretion of 92.162 mmol/l and GFR > 60 ml/min. Hypothyroidism and adrenal insufficiency were excluded. Cardiac, hepatic and renal functions were normal. Medications included azilsartan 40 mg and amlopidine 5 mg. To search for the source of a possible ADH-secreting tumor, an oncological search was performed with ultrasound of the thyroid gland, abdominal cavity, CT of the lungs with contrast, gastro- and colonoscopy. She also underwent PET/CT ‘whole body with 68Ga-DOTATATE, according to which no pathological formations were detected. According to the results of which, a node of the right lobe of the thyroid gland 11 x 10 mm was revealed, with a fine-needle aspiration biopsy - Bethesda II. Drinks about 2000 ml (of which 300-400 ml is 0.9% saline), releases 1780-1800 ml of urine per day. Copeptin (Phoenix) - 1.659 ng/ml (0.178-2.578 ng/ml), Oxytocin (BMA Biomedicals) -2.688 ng/ml (0-12.821 ng/ml), Apelin-12 (Phoenix) -2.020 ng/ml (0.620-2.095 ng/ml), BNP (RayBiotech)-981.63 pg/ml (646.3-2033.4 pg/ml). Since the synthesis of ADH occurs in the nuclei of the hypothalamus, and the hormone is only stored and secreted in the posterior lobe of the pituitary gland, then the pituitary adenoma per se presumably cannot be a source of ADH (the patient refused the proposed adenectomy). Conclusions The modern diagnostic arsenal is not sufficient to identify the source of inadequate secretion of ADH. Fluid restriction and oral saline administration are effective and well tolerated long-term therapeutic interventions.

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EP786

Epidemiological data of prolactinomas in the Republic of Uzbekistan

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Objective

To create a national register of prolactin-secreting pituitary adenomas to assess the prevalence of various forms and the effectiveness of therapy.

Material and research methods

National register of patients with prolactinomas in the Republic of Uzbekistan, includes 172 cases with pituitary prolactinomas, of which 61% (105 women) and 37.2% (64 men), aged 17-74 years, mean age 38.5 + 12.6 years and 3 (1.7%) children and adolescents. All 172 patients underwent studies of somatic, endocrine, gynecological status, the levels of prolactin, LH, FSH, TSH, free T4, progesterone, estradiol, testosterone, IHLA method, MRI of the chiasmatic - sellar region were studied. Results

Prolactinomas were more common in women (62.7%) than in men (37.2%), with a predominance of their frequency in women aged 21-30 years (66.7%), in men aged 41-50 years (59.3%). Depending on the size, the patients were distributed as follows: microadenomas 98 (5.7%), macroadenomas -53 (30.8%), giant adenomas with aggressive growth 21 (12.2%). Prolactin levels varied from 7.8 to 530 ng/ml on average in men 94 ± 3.7 in women - 162 ± 9.4 ng/ml. According to the applied methods of treatment: 128 patients (74.4%) are on drug therapy with modern drugs of dopamine agonists, transphenoidal adenectomy in 44 patients (25.6%), including 21 with giant (12.2%), 12 with macroadenoma (7%) and 10 with resistant prolactinomas (5.8%). Treatment outcomes were eurolactinemia in 142 (82.5%), persistent hyperprolactinemia against the background of SPTS in 31 (18%), panhypopituitarism in 28 (16.3%), remission was not achieved in 8 (4.6%), fertility disorders in 57 (33.1%), including 8 men and 49 women, continue to occur. Conclusion

Pituitary prolactinoma affects young women and men, predooming them to long-term medication and are a serious cause of infertility in both sexes.

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EP787

The Nelson’s Syndrom (about 3 cases)

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Introduction

The Nelson’s syndrome (NS) is defined by the development of an ACTH pituitary adenoma. Complication of bilateral adrenalectomy performed in some cases of Cushing’s disease.

We report the observation of three patients.

Case 1

34-year-old patient, followed for Cushing’s disease with pituitary microadenoma, having undergone pituitary surgery, then bilateral adrenalectomy due to surgical failure. Presented two years later an SN associating skin hyperpigmentation, high level of plasmatic ACTH and a pituitary adenoma measuring 10 mm. Having undergone a pituitary adrenalectomy. Because of surgical failure and given the difficulty of surgical revision, a treatment associating Cabergoline with stereotactic radiotherapy was instituted.

Case 2

21-year-old patient, followed for ACTH-dependent Cushing’s syndrome with bilateral thickening of the adrenal glands on CT scan. Patient having benefited from a bilateral adrenalectomy, complicated Nine months later by an NS associating skin hyperpigmentation, high level of plasmatic ACTH and a pituitary microadenoma. In failure after two surgical revisions, he benefited from stereotactic radiotherapy.

Case 3

48-year-old female patient, followed for Cushing’s disease with pituitary microadenoma, having undergone pituitary surgery, then bilateral adrenalectomy due to surgical failure. Present Ten years after an NS, associating skin hyperpigmentation, high level of plasmatic ACTH, and a pituitary adenoma measuring 20 mm. She underwent a pituitary adrenalectomy. Faced with the persistence of the NS after surgery, a treatment associating Cabergoline with stereotactic radiotherapy was instituted. Conclusion

The management of the NS despite the therapeutic advance, remains heavy and associated with significant morbidity, hence the interest of early detection.

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EP788

Case report in a patient with insulinoma

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Introduction

An insulinoma is a neuroendocrine tumor, deriving mainly from pancreatic islet cells, that constantly produces insulin even when blood sugar is very low. Insulinomas are the most common cause of hypoglycaemia resulting from endogenous hyperinsulinism. Biochemical diagnosis of insulinoma is established during prolonged fasting test (up to 72 hours) in 95 % of patients, 90-95% of insulinomas can be diagnosed during 48 hours of prolonged fasting. After biochemical confirmation of the existence of insulinoma, imaging studies are used to focalize the tumor.

Material and methods

A female patient aged 54 years, mother of two children, no smoker. In menopause 3 years ago. She has arterial hypertension from the past disease, regulated by an angiotensin receptor blocker. The patient consults the ambulant of Endocrinology Clinic due to symptoms of malaise, fatigue and tingling in the mouth, which occurred episodically and improved after ingestion of carbohydrates. During one such episode, glycaemia was measured at 2 mmol/l. She gives information that she does not remember events from the recent past. On one occasion she lost consciousness. These symptoms were started a year ago, so the patient was examined by a neurologist and the existence of neurological disease gives information that she does not remember events from the recent past. On one occasion she lost consciousness. These symptoms were started a year ago, so the patient was examined by a neurologist and the existence of neurological disease
Tortora1, Vincenzo Marotta2, Giulia Izzo2, Domenico Rocco3, Dilara Tekin Uzman1, Şeyma Aksoy1, Sebnem Burhan1, Ugur2, Hasan Eryesil 2, Ramazan Fazıl Akkoc3 & Ahmet Karatas4

DOI: 10.1530/endoabs.81.EP789

Several months. The patients were referred for surgery and the histopathological examination confirmed the diagnosis of insulinoma. Postoperative patient without symptoms, with glycaemia in reference values.

Conclusions
When we have a case of insulinoma we need to determine whether it is an isolated case or is part of multiple endocrine neoplasia type 1 (MEN 1). In the case of the patient we are treating we concluded that it is an isolated case of insulinoma. Because 90 % of insulinomas are benign and long-term cure with a total resolution of preoperative symptoms is expected after complete resection.

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Objective
To determine the effect of GH provocative tests on growth rate in children without GH deficiency.

Design and Methods
Children of both gender with pathological short stature (h < 3 percentile) and/or annual growth rate < 2 SDS but with normal response to two GH provocative tests were selected. Diagnosed endocrinopathies, other organ dysfunction, autoimmune diseases, genetic syndrome or current drug therapies were excluded. Height, mid-parental height, body mass index and body mass index were registered. The height and annual growth rate were converted to percentiles and Standard Deviation Score using reference ranges standardized for age and sex and were recorded pre and post stimulus tests and during subsequent follow-up over time. GH provocative tests employed arginine or clonidine as secretagogues.

Results
Twenty-one children of both genders were enrolled. Heights were measured at test time and at a mean time prior and after the tests of 209 days and 192 days respectively. Children displayed a 5-fold increase of their annual growth rate. The mean height growth rate of children pre- and post-tests were -4.3 SDS and +2.0 SDS respectively (P < 0.0001). In 9 children the height was measured two times after the tests at an average time of 228 days and 887 days. All children displayed a stimulated growth also in the second time interval after the tests, with a decremental in some.

Conclusions
Two sequential somatotropic axis provocative tests increase the growth rate in non-GHD children with pathological short stature and that this effect persists for several months.

EP789

GH provocative tests stimulate the growth in children without GH deficiency
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Introduction
GH deficiency (GHD) is a clinical disorder characterized by pathological short stature in the child, altered body composition, impaired psychological well-being and reduced quality of life. These alterations are almost always reversible after recombinant human GH (rGH) administration, which is currently the only accepted treatment for the subjects with GHD. Secretory dysfunction is confirmed when GH peak does not reach the established cut-off in at least two different stimulus tests performed in two different days. When tests response is considered adequate, the short stature is considered idiopathic and no GH replacement therapy is advised. Objective
To determine the effect of GH provocative tests on growth rate in children without GH deficiency. Design and Methods
Children of both gender with pathological short stature (h < 3 percentile) and/or annual growth rate < 2 SDS but with normal response to two GH provocative tests were selected. Diagnosed endocrinopathies, other organ dysfunction, autoimmune diseases, genetic syndrome or current drug therapies were excluded. Height, mid-parental height, body mass index and body mass index were registered. The height and annual growth rate were converted to percentiles and Standard Deviation Score using reference ranges standardized for age and sex and were recorded pre and post stimulus tests and during subsequent follow-up over time. GH provocative tests employed arginine or clonidine as secretagogues. Results
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Two sequential somatotropic axis provocative tests increase the growth rate in non-GHD children with pathological short stature and that this effect persists for several months.

EP790

Sarcopenia and frailty in acromegalic patients
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Introduction
Acromegaly is a clinical syndrome associated with excess growth hormone. The present study aimed to investigate sarcopenia and frailty, which could affect mortality and morbidity, in patients with acromegaly.

Method
Twenty outpatient patients diagnosed with acromegaly were included in the study. The hand muscle strength of the patients was measured by electronic hand dynamometer (Model EHL101, Zhongshan Camry Electronic Co. Ltd. China). Computed tomography, imaging at the L3 level was used to measure the abdominal muscle mass area (cm2). Measurements for the skeletal muscle mass index abdominal muscle mass area were expressed in (cm2)/height (m2). Normal values for men and women were considered > ≥5.4 cm2/m2 and > ≥3.5 cm2/m2, respectively. The Tilburg Frailty Indicator was used to determine the frailty of the patients. The Social Sciences Version 26.0 software was used to perform analyses in line with appropriate statistical methods.

Results
Thirteen patients were female and 7 were male. The mean age and time of diagnosis were 45.65 ± 9.7, 10.4 ± 6.4 years respectively. Sixteen patients received medical treatment, while 4 did not. Eighteen patients underwent surgical treatment. While 17 patients were in remission 3 patients had active disease under treatment. The mean body mass index of the patients was 29.95 ± 5.1 kg/m². The mean hand muscle strength in patients with and without frailty was 37.2 ± 14.6 kg and 37.6 ± 13 kg, respectively (P = 0.933). Furthermore, there was no statistical difference in frailty between the patients by the remission status (P = 0.891). Mean cross-sectional skeletal muscle area was 145.8 ± 33.7 cm². The mean skeletal muscle index (SMI) was 53.1 ± 9.7 cm²/m². While sarcopenia was detected in 1 female patient, there was no difference in SMI levels between the groups in terms of SMI by the remission status (P = 0.794).

Conclusion
The risks associated with sarcopenia and frailty increase as a result of increased intra-muscle fat storage due to increased insulin resistance, extended duration of the disease, accompanying hormonal changes, and decreased mobility due to joint pain. In the present study, patients with acromegaly had higher levels of frailty. In conclusion, it is important to carry out routine assessments for frailty and sarcopenia, which are associated with multifactorial causes, and to take timely measures based on a multidisciplinary approach in order to improve the quality of life and prevent the comorbidities of the aging population with acromegaly, which may induce high mortality and morbidity.

EP791

A mini case series of hypophysitis with atypical presentation
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Introduction
Hypophysitis is a rare condition characterized by inflammation of the pituitary gland, causing mass effect and hypopituitarism. The incidence is estimated to be 1 in 9 million/year. The diagnosis of hypophysitis is based on clinical and laboratory findings, imaging methods and histopathology in selected cases. The aim of the treatment is to eliminate the compression effects of the mass and to treat hypopituitarism. The first choice in medical treatment is immunosuppressive drugs. Surgical treatment can be considered for patients with progressive visual defects unresponsive to medications. Certain cases may be followed without immunosuppression or surgical intervention. Here in we present cases with hypophysitis of atypical presentation.
Clinical Cases

Case 1:
A 20-year female presented with headache, blurred vision, oligomenorrhea and galactorrhea. Basal cortisol was 1.89 μg/dl, other anterior pituitary hormones were in reference ranges. A 22 x 17 mm hemorrhagic atypical macroadenoma was present on the pituitary MRI. The stalk thickness was not increased. The patient underwent transsphenoidal surgery; pathologic specimen showed infiltration with lymphocytes, plasmacytoma and CD68 positive histiocytes which were evaluated as xanthomatomus hyperplasia. After the operation the patient’s complaints regressed. However glucocorticoid replacement was continued.

Case 2:
A 55-year male presented with headache, vomiting, fever, diplopia, polyuria and polydipsia for 10 days. Laboratory findings at first presentation showed lymphocytosis, partial central diabetes insipidus, central hypothyroidism and lymphopenia. On the pituitary MRI, a 22 x 17 mm macroadenoma was observed. Initially an adenoma was suspected based on imaging, however hypophysitis was considered in the differential diagnosis due to a spontaneous decrease in dimensions to 17 x 9 mm (>50%) and increased stalk thickness in control imaging. Lymphopenia improved spontaneously. For the differential diagnosis laboratory investigations including inflammatory markers, IgG4, COVID-PCR and antibodies and, investigations for other infections and inflammatory/infiltrative diseases showed only increased Covid antibody (IgG > 250 U/ml). Patient was evaluated as a secondary hypophysitis after an unrecognised Covid infection.

Case 3
A 35-year male with acute onset headache, double vision and 6th cranial nerve palsy had 16 x 18 x 21 mm cystic lesion (macroadenoma) with increased stalk thickness on pituitary MRI. Pituitary hormones and other laboratory findings were within normal levels. Hypophysitis was considered, however with the acute presentation of mass effects transsphenoidal surgery was performed. The intraoperative mass had a purulent appearance, and the pathology was evaluated as abscess and lymphocytic hypophysitis. The microbiological evaluation confirmed a sterile abscess. Postoperatively the patient’s complaints regressed completely and there was no need for any hormone replacement therapy.

Conclusion
Hypophysitis is a rare condition with variable presentations. Diagnostic and treatment modalities may vary for each case. Not all cases require immunosuppressive treatment and, a case based specific approach is necessary.

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EP792

The natural course of hypophysitis at diagnosis and following therapy in non-functioning pituitary macroadenomas

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Background
Non-functioning pituitary macroadenomas (NFPMs) may present with hypophysitis. Pituitary surgery and radiotherapy pose an additional risk to pituitary function.

Aims
The aim of this study was to assess the incidence of hypophysitis pre-operatively and the impact of surgery and radiotherapy on pituitary function.

Methods
All patients treated with surgery and radiotherapy for NFPMs between 1987 and 2018 with more than 6 months follow-up were identified. A retrospective note review was performed.

Results
Overall, 383 patients were identified, 256 patients (256/383; 67%) were men. The median age was 57 years (IQR 48-67) with median follow-up of 5 years (IQR 2-9). 58 patients (58/377; 15%) presented with pituitary insufficiency, however, on endocrine evaluation, 235 patients (235/377; 62%) had evidence of pituitary impairment. Growth hormone deficiency occurred in 115 patients (115/273; 31%), hypogonadotropic hypogonadism in 161 patients (161/375; 43%), 132 patients (132/375; 36%) recorded to have adrenal insufficiency and 157 patients (157/375; 42%) developed secondary hypothyroidism. Anterior hypophysitis was reported in 100 patients (100/377; 26%). With regards to treatment modality; 318 patients (105/375; 28%) had no evidence of pituitary impairment post therapy while 278 patients (278/383; 73%) suffered endocrine dysfunction. Patients who were treated with surgery and radiotherapy had a greater degree of partial and complete adrenohypophysial hormone deficit than those treated with surgery alone as demonstrated in the table.

Conclusion

Non-functioning pituitary macroadenomas are associated with significant degree of hypopituitarism at time of diagnosis as well as post therapy. The combination of surgery and radiotherapy are associated with higher risk of pituitary dysfunction. Regular endocrine evaluation and lifelong follow-up is required following NFPMs treatment to screen for hormone deficiency and provide appropriate replacement therapy.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Surgery</th>
<th>Surgery and radiotherapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH 165/383</td>
<td>118/318</td>
<td>47/65</td>
<td>72%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FSH/LH</td>
<td>178/383</td>
<td>136/318</td>
<td>42/65 (65%)</td>
<td>0.001</td>
</tr>
<tr>
<td>ACTH 156/383</td>
<td>111/318</td>
<td>45/65</td>
<td>69%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TSH 206/383</td>
<td>151/318</td>
<td>55/65</td>
<td>85%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anterior 133/383</td>
<td>90/318</td>
<td>43/65</td>
<td>62%</td>
<td>0.0001</td>
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</tbody>
</table>

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EP793

Importance of neurosurgical expertise and multidisciplinary approach in pituitary patients

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Background
Multidisciplinary approach to pituitary disease is highly recommended; it requires a close relationship between expert pituitary surgeons and endocrinologists together with several specialists (e.g. neuroradiologists) in order to provide a high-level standard of care. Although there is evidence that neurosurgeons’ expertise is a key element to achieve better outcomes, also endocrinologists’ role is fundamental but it may sometimes encounter real-life barriers.

Aim of the study
To explore from a real-life database the impact of neurosurgical centre expertise on post-surgical outcomes in pituitary patients attending a tertiary academic medical centre.

Methods
A retrospective, observational, single-centre study was carried out including all patients attending the Endocrinology Unit of Modena (Italy) that underwent pituitary surgery from January 1995 to December 2020. For each patient, pre-operative features of the pituitary lesion, surgery information and post-surgical outcomes (i.e. residual neoplasia, surgery-related complications and pituitary function) were collected from record charts. Patients were grouped according to the expertise degree of the centre where they underwent surgery: Group1 included patients treated in neurosurgical centres with high expertise in pituitary surgery (defined as ≥ 50 transphenoidal pituitary surgeries per year); Group2 included patients treated in neurosurgical centre performing < 50 transphenoidal pituitary surgeries per year.

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Introduction

Nelson’s syndrome is a rare complication of Cushing’s disease treated with bilateral adrenalectomy. There is no effective medical treatment yet. Nelson’s patients respond to hypothalamic stimuli distinctly from patients with Cushing’s disease and those with Addison’s disease. We describe the responses to standard ACTH stimulation tests in a patient with Nelson’s syndrome.

Case report

A 42-year-old woman presented with ACTH dependent Cushing’s syndrome. Pituitary MRI was suggestive of a lesion on the left side, measuring 4 x 3 mm and an ectopic source of ACTH was excluded. Following an unsuccessful transphenoidal surgery in 2013, she was placed on pasireotide 0.6 mg twice daily for one year. Partial response was seen on pasireotide, but she developed severe hyperglycemia. Fluconazole 200 mg daily was tried for 6 months, in conjunction with cabergoline 1 mg twice weekly, with little benefit. The patient finally had a bilateral adrenalectomy in 2016 and was replaced with hydrocortisone 20 mg am-10 mg pm and fludrocortisone 0.1 mg/d, while maintaining all other pituitary axes intact. Two years later (2/2018), a pituitary tumor was visible on the right lateral pituitary, which grew further in the next 34 months to 10 mm (10/2020). Gradual skin hyperpigmentation was noticeable since 2018. The patient remained hyperglycemic but managed well with GLP-1R agonist and metformin. Her ACTH levels gradually increased since 2016, reaching am levels of 1886 pg/ml (7.64) and late evening levels of 1235 pg/ml (5-30) in late 2021. The patient had an exaggerated response to desmopressin stimulation with ACTH > 2000 pg/ml (dilutions were not performed) to x3 above baseline at 15’, remaining at this level beyond 120’. An exaggerated response was noted following CRH stimulation, with ACTH rising from 1741 pg/ml to > 2000 pg/ml at 15’, returning to baseline at 120’. ACTH decreased to 134 pg/ml following overnight suppression with 8 mg dexemethasone.

Conclusions

Abnormal and distinct hypothalamic-pituitary dynamics underlie the pathophysiology of Nelson’s syndrome, which cannot be explained solely on lack of adrenal negative feedback. In patients with otherwise intact pituitary function, repeat neurosurgery or radiotherapy are not desirable options and pasireotide use is similarly limited. A case for blockade of CRH receptor blockade can be a rational therapeutic option in this clinical situation.

References

1 Barber TM et al, European Journal of Endocrinology (2010) 163 495–507

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EP796

Incidental discovery of pituitary insufficiency after non-pituitary surgery

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Introduction

Pituitary Insufficiency is life threatening condition, that can lead or manifest by any stressful situation (surgery, infections, intoxication and etc).

Case report

A 70-year-old man diagnosed with Bladder Cancer had underwent surgery - Cystoplasty. The operation was performed without complications, but, after the intervention, the general condition of the patient sharply declined. There appeared strong general weakness, blurred consciousness, frequent abdominal pains, bradycardia, lowering of T/A (<80/50 mmHg), fever. His condition required intensive care.

Laboratorial tests:

- Na = 133-135 (130-152)mmol/l, K = 3.7 (3.6-5.2)mmol/l, CRP = 173 (<5mg/l, creatinine = 132 µmol/l, CBC - Leukocytosis, Urine total - bacteria = 205 cell/µl (<11.4), Consultations with a Neurologist, Infectionist, Endocrinologist were conducted. TSH, FT4 tests were prescribed, we got a remarkable results – TSH - 1.25 (0.4-3.7) µIU/l, FT4-4.72 (12-22) µmol/l. Besides that, based on the recommendation of a Neurologist, the patient underwent MRT examination of the pituitary gland.

Conclusions

Pituitary Insufficiency is life threatening condition, that can lead or manifest by any stressful situation (surgery, infections, intoxication and etc).

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EP795

Response to classic dynamic tests of a corticotropinoma due to Nelson’s syndrome

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Introduction

Nelson’s syndrome is a rare complication of Cushing’s disease treated with bilateral adrenalectomy. There is no effective medical treatment yet. Nelson’s patients respond to hypothalamic stimuli distinctly from patients with Cushing’s disease and those with Addison’s disease. We describe the responses to standard ACTH stimulation tests in a patient with Nelson’s syndrome.

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Conclusions

Abnormal and distinct hypothalamic-pituitary dynamics underlie the pathophysiology of Nelson’s syndrome, which cannot be explained solely on lack of adrenal negative feedback. In patients with otherwise intact pituitary function, repeat neurosurgery or radiotherapy are not desirable options and pasireotide use is similarly limited. A case for blockade of CRH receptor blockade can be a rational therapeutic option in this clinical situation.

References

1 Barber TM et al, European Journal of Endocrinology (2010) 163 495–507

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EP794

Pituitary deficiencies after brain injury: a practical approach to evaluation and management

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While increasing attention is being paid to the health effects of brain injury, the role that neuroendocrine dysfunction may play in patients’ health after traumatic brain injury (TBI) remains underappreciated. Pituitary deficiencies are seen at a high rate in patients who have sustained TBI, with reports of chronic pituitary dysfunction in 15-60% of adults after TBI, and up to 42% of children and adolescents. Deficiencies may resolve over time, or develop years after injury, and may occur after mild or severe injury. While there is a large and growing body of literature on the risk of pituitary dysfunction after brain injury, differences in assays and definitions account in part for the broad range of reported prevalence, and highlight the importance of a rigorous review of the evidence. Given the large number of people with a history of TBI, there has been much investigation into factors that may predict neuroendocrine dysfunction. Studies have investigated biomarkers, imaging characteristics, and types of injury, but no consistent clinically useful association has been described. Thus, we rely on signs and symptoms to determine whom to screen. The overlap in symptoms seen in pituitary deficiencies and following TBI, and the potential clinical benefit of identifying hypopituitarism, make it particularly important to be aware of patterns that suggest pituitary dysfunction. Symptoms from hypopituitarism include cognitive, physical, and emotional effects, and overlap with symptoms from other etiologies including TBI itself. Clinical symptoms may include difficulties with executive function, increased anxiety and irritability, irregular menses, sexual side effects, and fatigue, and delay physical and neuropsychieal efforts. It is particularly important to be aware of patterns that suggest pituitary dysfunction in patients with persistent symptoms after TBI, as replacement of deficient hormones can ameliorate or reverse the effects of hypopituitarism. In addition, there are indications that the cognitive issues and fatigue that may be seen as part of ‘Long Hauler’ syndrome after COVID-19/SARS-CoV-2 infection may be related to pituitary deficiencies. This presentation will review the current understanding of pituitary dysfunction following TBI and the clinical relevance of pituitary axes, and offer a practical approach to evaluation and treatment; emerging information regarding other forms of brain injury will be included, and specific populations (military, children, women) will be highlighted.

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Severe heart failure in a young male with unrecognized hypopituitarism

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Background

The partial or complete hypopituitarism is described as late complication of hemorrhagic fever with renal syndrome (HFRS). Imaging methods of pituitary gland examination in the chronic phase showed pituitary atrophy, but a precise pathogenic mechanism that causes pituitary damage in HFRS remains unclear. While hypopituitarism in HFRS is rarely described, cardiac failure as a known complication of hypopituitarism is even more rarely described. We present a case of severe heart failure in a young male patient with unrecognized hypopituitarism consequent to HFRS and undiagnosed hemochromatosis. Case Presentation

42-year-old male patient was admitted at the Department of Endocrinology of University Clinical Centre of the Republic Srpska with suspected hypopituitarism. He managed to walk with the help of another person, and his speech was incoherent and with difficulties. The patient was pale, facial and body hairless with adynamia, myxedema, hypotension, and bilateral gynecomastia with decreased libido and impotency. Echocardiography verified a global reduction in myocardial contractility, dilated left atrium and ventricle, with low ejection fraction (10-15%). Results of hormone tests confirmed diagnosis of panhypopituitarism, and replacement therapy (hydrocortisone, levothyroxine and testosterone) was started. MRI of the pituitary gland was performed and it showed an “empty sella”. On the third day after the therapy was introduced, the patient started to speak clearly and mental status was stabilized. The patient was independently mobile after seven days. Echocardiography performed a month later showed an improvement in myocardial contractility, normal distribution recovered, his sexual function normalized, and he had a normal mental status. Echocardiography was completely normal 6 months after introduction of replacement therapy (the left ventricle with normal dimensions, EF 58%).

Conclusion

The heart failure is extremely rare complication of hypopituitarism, but it is usually reversible when hormonal therapy is replaced. According to significant relationship and a high prevalence of hypopituitarism as a consequence of HFRS, endocrinological investigation should be considered in patients with HFRS and clinical signs and symptoms suggestive of hypopituitarism.

EP798

Silent somatotropic adenoma in young girl about a case

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Introduction

Clinically non-secreting pituitary adenomas are rare in children We report a case of a silent somatotropic adenoma revealed by anatopomorphology.

Case

A 13-year-old patient with no prior history of sudden onset intracranial hypertension syndrome. Clinical examination showed no dysmorphic Syndrome, no galactorrhea, no delay or statutory advance, Tanner P1S3. The MRI reveals a heterogeneous tumor process intra and suprasellar of 30 mm *15 mm of large axes, containing pockets of necrosis exerting a mass effect on neighboring structures and in particular on the optic nerves and quiasma evoking a priori craniopharyngioma. Initial hormonal balance: T4: 17.1 pmol/l; Cortisol: 8.85 g/dl; Prolactina: 10.25 ng/ml; FSH: 2.2 IU/l; LH:0.1 IU/l; E2:estradiol:8.2 ng/l and visual fields bitemporal hemianopsia. Partial transphenoidal pituitary surgery performed in emergency with simple surgical follow-up and supplemented thryeocorticotropic deficit. The anatopomorpho-immunohistochemical study concludes to a tumor proliferation with round cells whose morphological aspect first evokes pituitary adenoma secreting GH with Ki67 to1%. Before this and the normal initial IGF-1 at 360.1 ng/ml (90-581) a GH braking test under HGPO is performed with a GHnadir at 2.03 ng/ml confirming hypersecretion ofGH. Patient scheduled for surgery.

Discussion

Pituitary adenomas are rare tumors in children and adolescents whose most common type is prolactinoma followed by somatotrophic as our case. The clinical expression of somatotropic adenoma is correlated with the early age of GH hypersecretion in relation to the welding or not of the epiphyses giving way to acromegalogiantism or gigantism. None of these dysmorphia have been found in our case thus signing the silent character of this somatotropic. The initial hormonal balance doesn’t direct to any pituitary hypersecretion especially with a normal IGF-1 for age. Our presentation by ICTH syndrome, radiological elements as well as age were all in favor of craniopharyngioma which remains the most common tumor at this age. Only anatopomorphological examination with positive immuno-labeling for GH supplemented by a GH braking test under HGPO initially not performed allowed to retain the diagnosis. The treatment is surgery with possible treatment by somatostatin analogues in case of no cure hence the surgical resumption planned for our case.

Conclusion

Before any sellar tumour any clinico-radiological presentation in children the anatopomorphological study is the sole guarantor of specific treatment.

References


Endocrine dysfunction in hemochromatosis

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Introduction

Hemochromatosis is associated with iron overload that is responsible of iron deposit causing multiple organ dysfunctions which affects especially endocrine glands.
Methods
We report four cases of pituitary hemochromatosis responsible of endocrine dysfunction.

Results
Three women and one man were included, aged respectively 28, 19, 26 and 35 years old. These patients were suffering from β-thalassemia and treated with multiple blood transusions. All patients had delayed puberty with primary amenorrhea and erectile dysfunction. Hormonal screening showed hypogonadotrophic hypogonadism with all the patients. They were treated with hormonal substitution. Two patients presented inaugural diabetic ketosis and were treated with insulin for the diabetes mellitus. One patient was diagnosed with corticotroph deficiency and was treated with hydrocortisone. Thyrotophic and somatotrophic axis were normal with all patients. No cardiac or hepatic dysfunction was found with these patients.

Discussion and conclusion
Secondary hemochromatosis is responsible of multiple endocrine dysfunctions. The most endocrine dysfunction in hemochromatosis is diabetes mellitus and hypogonadotropic hypogonadism. The other endocrine dysfunctions are rare. Screening for endocrine dysfunction must be systematic and so a regular follow-up for all patients with hemochromatosis.

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EP800

Hyperprolactinemia, thyrotropic and corticotropic insufficiency in a patient with end-stage renal failure
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Introduction
Hyperprolactinemia is a condition of elevated prolactin levels in blood which could be physiological, pathological, or idiopathic in origin. Some cases of hyperprolactinemia have been reported in patients with renal failure. We present a case of hyperprolactinemia, thyrotropic and corticotropic insufficiency in a patient with end-stage renal failure.

Case presentation
The patient was 27 years old, with a history of hypertension, renal insufficiency at the stage of haemodialysis, tertiary hyperparathyroidism and thyrotropic insufficiency. She was admitted to our endocrinology’s department, in October 2021, for further exploration of the other pituitary axes. She had no functional complaints. The physical examination showed a weight of 49 kg with a body mass index of 20.3 kg/m². BP was 150/80 mmHg and there were galactorrhea on breast examination.

The biological investigations showed:
- Thyrotropic insufficiency: TSH: 0.099 mUIl [usual values: 0.35-4.95]; FT4: 0.69 ng/dl; FT3: 2.39 pg/ml [usual values: 1.17-3.71];
- FSH: 48 U/l; LH: 45.31 U/l;
- Hyperprolactinemia was confirmed PRL: 229.66 and 255.03 mg/l;
- FSH: 4.8 U/l; LH: 45.31 U/l;
- Thyrotropic insufficiency: TSH: 0.099 mUIl [usual values: 0.35-4.95]; FT4: 0.69 ng/dl; FT3: 2.39 pg/ml [usual values: 1.17-3.71];
- PTH: 1877.8 ng/dl [15-68]; Calcemia: 2.46 mmol/l;
- A corticotropic insufficiency had been confirmed by a hypoglycemia test, and a treatment by hydrocortisone was started.

A Hypothalamic pituitary MRI was performed and showed no abnormalities.

Conclusion
This case confirmed that pituitary function is abnormal in patients receiving haemodialysis. Hyperprolactinemia is common and may be a factor in the infertility and sexual dysfunction in patients with end-stage renal disease.

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EP801

PE in Surgically Treated Cushing’s Disease: A Case Report
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PE in Surgically Treated Cushing’s Disease: A Case Report
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Title
Pulmonary Embolism in Surgically Treated Cushing’s Disease: A Case Report
Authors
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Background
Cushing’s disease is the most common cause of Cushing’s syndrome but can be very difficult to diagnose and to treat, as we know it has numerous health effects on patients and long-term health and quality of life in these patients often remains suboptimal, despite treatment. patients with CS have about ten times the risk for VTE. 2019 meta-analysis encompassed 7142 patients with endogenous CS (including Cushing’s disease) undergoing transtophalloid surgery or adenectomy, and their risk of unprovoked VTE was almost 18 times higher in comparison with a healthy population. The aim of this case report is to underline the clinical significance of increased VTE in endogenous Cushing’s syndrome and to keep high clinical suspicion after undergoing transtophalloid surgery.

Case Description
We report 57 years old women, who was hospitalized in our hospital with declining health for 6 months. Patient complained of weight gain, discomfort in chest area, face and neck edema, muscle weakness and overall low energy. Upon physical examination and appropriate laboratory work-up, this patient was diagnosed with ACTH dependent Cushing’s syndrome. Head MRI later confirmed Cushing’s disease and patient was set up for transophalloid surgery for removal of pituitary adenoma. Few weeks post-op patient presented in ER with tachycardia, shortness of breath, chest pain. PE was diagnosed and patient was started on anticoagulative therapy, oxygen therapy and close monitoring. It also needs to be mentioned that the patient had a history of hypertension and valve replacement, as well as Covid-19 disease.

Conclusion
In conclusion we want to highlight that CS is a risk factor for VTE/PE, which is often overlooked. It is important to keep high clinical suspicion and continue close monitoring of CS patients even after transtophalloid surgery treatment. Physicians who treat VTE/PE cases should also be aware of increased risk associated with Cushing’s disease.

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EP802

Hypothalamic neuropeptides as biomarkers for water-electrolyte disturbances
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Hypothalamic neuropeptides as biomarkers for water-electrolyte disturbances. Introduction Diabetes insipidus is a rare condition characterized by excretion of large amounts of dilute urine and increased thirst. Nephrogenic diabetes insipidus (NDI) is caused by the inability of the kidneys to concentrate urine in response to vasopressin.

Aim
The aim of our case report is to present the patient with NDI and to report the data on physiological changes in hypothalamic neuropeptides such as copeptin, oxytocin, apelin, brain natriuretic peptide (BNP) in patient with NDI.

Material and methods
21-year-old male patient was admitted to the hospital with chief complaint of increased thirst and urinary frequency. Results
In accordance with the results of indirect water-deprivation test NDI was diagnosed in our patient due to maximum urine osmolality of less than 76 mOsm/kg, plasma osmolality 302 mOsm/kg, maximum plasma sodium was 148 mmol/l, and no change in urine osmolality after administration of 2 mg of s.c. desmopressin. Copeptin, oxytocin, apelin, BNP after 8-h fluid restriction accounted for: 0.844 ng/ml (0.178-2.578 ng/ml), 5.694 ng/ml (0-12.821 ng/ml), 1.476 ng/ml (0.620-2.095 ng/ml),1225.86 pg/ml (646.3-2013.4 pg/ml) and at the peak of dehydration (for 16 h) accounted for: 1.058 ng/ml, 6.176 ng/ml, 1.346 ng/ml, 973.93 pg/ml.

Conclusion
Our data confirm a commensurate increase in the levels of copeptin and oxytocin with a reciprocal decrease in the concentrations of apelin and BNP against the background of additional dehydration, which can later be used for differential diagnostic procedures for the syndrome of polydipsia-polyuria.

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EP803
Hashimoto’s encephalopathy: a case report
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Introduction
Hashimoto’s encephalopathy or SREAT (steroid-responsive encephalopathy associated with auto-immune thyroiditis) is a rare autoimmune disorder that is particularly corticosteroidsensitive and whose pathogenesis remains poorly understood. It is associated with high levels of antithyroid antibodies in plasma and/or CSF. Clinical manifestations are deceptively non-specific and may include cognitive and behavioral disturbances, seizures or abnormal movements.

Case report
We report the case of a 54-year-old female patient who presented with progressive abnormal movements with balance disorders. The clinical examination revealed a cerebellar syndrome, a cerebellar dystarsia with an abolition of the osteotendinous reflexes. Brain MRI was without abnormalities. The electroencephalogram showed a diffuse slowing of the background rhythm without paroxysmal figure. Lumbar puncture revealed a clear cerebrospinal fluid without pleocytosis with hyperproteinorachy at 1.01 g/l. Antithyroglobulin and antithyroxoperoxidase antibodies were positive (anti-TPO antibody: 493 IU/ml and anti-TG antibody: 20 IU/ml) with a normal TSH. The diagnosis of Hashimoto’s encephalopathy was retained after ruling out other causes, including metabolic, vascular, toxic, infectious and neoplastic. Intravenous corticosteroid therapy at a dose of 1 g of methylprednisolone per day was started for 3 days, followed by oral corticosteroid therapy at a dose of 1 mg/kg for one month and then gradually tapered off over 2 months. The patient was controlled with prednisone 2.5 mg per day with good improvement of her neurological symptomatology.

Discussion and conclusion
Hashimoto’s encephalopathy is often underdiagnosed. The revealing neurological signs are polymorphic. Its pathophysiology is controversial, an autoimmune cerebral vasculitis is evoked. It should be systematically investigated in cases of unexplained encephalopathy, by looking for anti-TPO antibodies in the CSF even in cases of euthyroidism. This case highlights the different and often confusing clinical presentations of Hashimoto’s encephalopathy but also its particular corticosteroid sensitivity.

References

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EP804
Gestational diabetes insipidus: about a case
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Introduction
Diabetes insipidus during pregnancy is rare (4/100,000 pregnancies) generally occurring in the last two trimesters. It can be a previous diabetes insipidus, revealed by pregnancy, or a gestational diabetes insipidus. It would be secondary to the plasma degradation of antidiuretic hormone by placental vasopressinase. Observation
We report the case of a 44-year-old gentleman presented to the Emergency Department with a 2-week history of fevers and rigors. Past medical history was remarkable other than an earlier diagnosis of hypertension. He was noted to have new onset atrial fibrillation with rapid ventricular response, and a new diagnosis of hypertrophic obstructive cardiomyopathy (HOCM) was made on echocardiography. In addition, a vegetation was identified on the mitral valve. Treatment for infective endocarditis (Streptococcus oralis) was initiated and he was subsequently transferred to a specialist centre for mitral valve replacement surgery. During the exploration, a history of chronic headaches was investigated. MRI pituitary revealed a 3.8 x 1.9 cm pituitary macroadenoma with suprasellar extension. There was no cavernous sinuses invasion. He was further evaluated in the outpatient endocrine clinic. On removal of his facemask, examination revealed typical acromegalic features with supraorbital ridge prominence, significant underbite and macroglossia. Visual fields were normal to confrontation testing and no organomegaly was present on bedside examination. Urgent endocrine investigations including baseline primary pituitary function testing were performed. IGF-1 was significantly elevated at 1463 ng/ml (range 8.5-310), 9am cortisol was 352 nmol/l (range 200-750), prolactin 1119 mU/l (range 60-300), TSH 1.98 mU/l (range 0.34-5.60), FSH <0.1U/l (range 1.7-8.0) and testosterone 8.7 (range 10.0-30.0). Acromegaly was confirmed with an oral glucose tolerance test showing a paradoxical rise in growth hormone. Glucose levels remained normal throughout the OGTT. The patient was commenced on monthly Lanreotide injections and referred to the specialist neuro-endocrine clinic to determine the best course of further management. Unfortunately, this gentleman’s endocrine management was further complicated by a second hospital admission with persistent bacteraemia. Further redo of his mitral valve replacement is being considered, and safety of pituitary surgery at this stage remains a concern. In this case, radiotherapy could be a more suitable treatment option for acromegaly. This case highlights the requirement for early diagnosis and treatment to prevent further complications, as well as the need for individualisation of complex treatment decisions within a multidisciplinary setting. Cardiovascular complications including HOCM, arrhythmias, arterial hypertension and valvulopathy, as well as colonic benign neoplasms such as polysis, are common complications of acromegaly. For people presenting with ‘idiopathic’ HOCM, a IGF-1 may be considered to screen for acromegaly. Finally, the requirements for facemasks and virtual telephone consultations during the Covid-19 pandemic have likely compounded potential delays in diagnosis.

Conclusion
Gestational diabetes insipidus is therefore a polyuuro-polydipsic syndrome which appears in pregnant women due to a deficiency in anti-diuretic hormone. Rather rare, it usually disappears within three weeks after delivery.

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EP805
Endocrinopathy behind the facemask
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A 44-year-old gentleman presented to the Emergency Department with a 2-week history of fevers and rigors. Past medical history was remarkable other than an earlier diagnosis of hypertension. He was noted to have new onset atrial fibrillation with rapid ventricular response, and a new diagnosis of hypertrophic obstructive cardiomyopathy (HOCM) was made on echocardiography. In addition, a vegetation was identified on the mitral valve. Treatment for infective endocarditis (Streptococcus oralis) was initiated and he was subsequently transferred to a specialist centre for mitral valve replacement surgery. During the exploration, a history of chronic headaches was investigated. MRI pituitary revealed a 3.8 x 1.9 cm pituitary macroadenoma with suprasellar extension. There was no cavernous sinuses invasion. He was further evaluated in the outpatient endocrine clinic. On removal of his facemask, examination revealed typical acromegalic features with supraorbital ridge prominence, significant underbite and macroglossia. Visual fields were normal to confrontation testing and no organomegaly was present on bedside examination. Urgent endocrine investigations including baseline primary pituitary function testing were performed. IGF-1 was significantly elevated at 1463 ng/ml (range 8.5-310), 9am cortisol was 352 nmol/l (range 200-750), prolactin 1119 mU/l (range 60-300), TSH 1.98 mU/l (range 0.34-5.60), FSH <0.1U/l (range 1.7-8.0) and testosterone 8.7 (range 10.0-30.0). Acromegaly was confirmed with an oral glucose tolerance test showing a paradoxical rise in growth hormone. Glucose levels remained normal throughout the OGTT. The patient was commenced on monthly Lanreotide injections and referred to the specialist neuro-endocrine clinic to determine the best course of further management. Unfortunately, this gentleman’s endocrine management was further complicated by a second hospital admission with persistent bacteraemia. Further redo of his mitral valve replacement is being considered, and safety of pituitary surgery at this stage remains a concern. In this case, radiotherapy could be a more suitable treatment option for acromegaly. This case highlights the requirement for early diagnosis and treatment to prevent further complications, as well as the need for individualisation of complex treatment decisions within a multidisciplinary setting. Cardiovascular complications including HOCM, arrhythmias, arterial hypertension and valvulopathy, as well as colonic benign neoplasms such as polysis, are common complications of acromegaly. For people presenting with ‘idiopathic’ HOCM, a IGF-1 may be considered to screen for acromegaly. Finally, the requirements for facemasks and virtual telephone consultations during the Covid-19 pandemic have likely compounded potential delays in diagnosis.

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EP806
Pituitary hypertrophy secondary to primary hypothyroidism (one case report)
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Introduction
There are several causes of sellar and suprasellar mass, and pituitary hyperplasia secondary to primary hypothyroidism has been reported in the literature. Case report
20-year-old patient, born from a consanguineous marriage, presenting with failure to thrive. Patient reporting no tumor symptom. Clinical examination. Height at 88 cm (<4 SD), weight at 18 kg (<3rd percentile), BMI at 23 kg/m². TANNER at G2P0, microgeniocranium length of 5 cm (<2.5 DS), infantile voice, elf-like features,
with periorbital puffiness, flat nasal bridge, short upturned nose with bulbous tips, large mouth with everted and broad lower lips. Patient with friendly behaviour. Thyroid not palpable, no clinical signs of pituitary hypersecretion. Paraclinical findings: TSHus > 500 mIU/L (0.35-4.94) > 100 times normal T3L: 2.81 pmol/l (10.6-19.4). IGF-1: 19.26 ng/ml (27-114). Cortisolome before 10 hrs: 8.5 ng/dl (3.7-19.4) Prolactinemia: 118 ng/ml (3.6-19.4). Cervical ultrasound: heterogeneous thyroid gland without detectable nodules. Bone age: 1 year 6 months RISSER test: 0 Pituitary MRI: pituitary hypertrophy, without clearly detectable nodule. The patient benefited from a substitution by Levothyroxine and Somatostatin analogue with a good evolution.

Conclusion
Pituitary enlargement secondary to primary hypothyroidism should be considered as a differential diagnosis of solid pituitary masses, especially when associated with growth and pubertal retardation. Adequate care helps to avoid no need surgeries.

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EP807
Giant prolactinoma in an adolescent girl revealed by visual impairment
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Introduction
Pituitary adenomas are rare in infants and adolescents. Prolactinomas account for 50% of these pituitary adenomas. In adolescent girls, it is usually a microprolactinoma revealed by puberty delay or amenorrhea. We report a rare case of a macroprolactinoma in an adolescent girl revealed by visual impairment.

Case presentation
A 15-year-old adolescent girl presented with loss of vision over a long period of time. Magnetic resonance imaging revealed an expansive sellar and suprasellar mass measuring 48x47x37 mm consisting of cystic and solid components in favor of craniopharyngioma. Patient underwent transsphenoidal surgery for tumor resection. Post operative laboratory findings were in favor of a hyperprolactinemia with prolactine of 600 ng/ml and a thyrotrope deficiency. Histological assessment confirmed diagnosis of prolactinoma. Pituitary MRI control revealed a 20x9x17 mm residual macroadenoma. Patient was started on cabergoline resulting in lowering prolactin levels and tumor shrinkage.

Discussion
Prolactinomas are rarely found in adolescents. Tumoral syndrome with visual impairment can be seen in large tumors in males. In girls, the most frequent presentation is a microprolactinoma revealed by amenorrhea. Less frequently, it can be revealed by pubertal delay or short stature. In our case, the patient presented with a macroprolactinoma revealed by visual impairment that was initially accounted for a cranial from a subsalellar Medical treatment by dopamine agonists like in adults is the first line therapy as it’s effective in up to three quarters of cases.

Conclusion
Prolactin levels should be measured in every child or adolescent with visual impairment and a large suprasellar tumor to rule out a prolactinoma that can be successfully managed by medical therapy.

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EP808
Inappropriate antidiuretic hormone secretion syndrome associated with covid 19 pneumonia
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Introduction
Hyponatremia is a commonly associated with atypical pneumonia. One of its pathophysiological mechanisms is inappropriate antidiuretic hormone secretion( SIADH). We describe the case of a patient presenting an SIADH caused by COVID19 infection.

Observation
We report a case of a 70-year-old man, known to have well-controlled hypertension, with a medical history of caviurn’s neoplasia treated with radiotherapy and hypothyroidism post thyroidectomy for multinodular goiter. He was admitted in the intensive care unit for ‘status epilepticus’ caused by severe hyponatremia (120 mmol/l). The hormonal investigation showed a normal thyroid function test (TSH 2.06 mU/L FT4 11.4 pmol/l) and a normal stimulated cortisol at 524 nmol/l. Therefore, the diagnosis of SIADH was retained. It was based on euvelonic hyponatremia with concurrent low serum and high urine osmolarity (265 mosm/l and 338 osmol/24h, respectively) and high urine sodium (75 mmol/24h). Concerning the etiologial investigation, we evoked the disorders of the central nervous system caused by cerebral radiotherapy but it goes back to 6 years during which the natrema was normal. Negative tumor markers, absence of tumoral process on the CT-scan and the normal bronchial fibroscopy confirmed paraneoplastic syndromes. Nasopharyngeal RT-PCR and abdominal chest CT-scan depicting bilateral infiltrates and bilateral pleural effusion confirmed COVID-19 infection. The course was marked by pneumonia’s healing at the expense of SIADH’s persistence. Currently, the patient is on fluid restriction, his natrema varies between 120 and 137 mmol/l.

Discussion
SIADH may be the only presentation of covid19. This association has been reported in the literature, but the course of the hyponatremia after pneumonia's healing was not mentioned. The pathophysiology is unknown. Several theories were suggested: hypoxema, stress, nausea, IL6 secretion. However, none of these theories explains the persistence of SIADH after recovering from pneumonia.

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EP809
Association between uncontrolled acromegaly and nasopharyngeal tumor-case presentation
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Introduction
Acromegaly is characterized by elevated levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1), most often due to a pituitary tumor. Persistent high levels of these hormones lead to a constellation of signs and symptoms and systemic complications associated with increased mortality. A potential association between acromegaly and cancer has been hypothesized regarding colorectal, thyroid, and prostate cancers, but there are few or no descriptions for other kinds of tumors.

Case presentation
Male, 49 years old, presented with headache, multiple episodes of loss of consciousness, joint pain, profuse sweating. Clinical examination revealed acral enlargement, generalized thickening of the skin, prominent supraorbital ridges, nose enlargement, proptosis. Hormonal assessment showed increased levels of IGF-1 (2.8 x upper limit of normal, ULN) and high levels of nadir GH in the oral glucose tolerance test (OGTT, 10.3 ng/ml). All others anterior pituitary hormones were within normal range. Pituitary MRI revealed a hypophyseal mass with heterogeneous signal (23/14 mm). The patient underwent surgical removal of the pituitary macroadenoma using transsphenoidal resection. The immunohistochemical (IHC) examination showed positivity for GH and prolactin (PRL). Three months after surgery, the patient presented active disease (IGF-1 = 1.3 x ULN, nadir GH in OGTT = 5.24 ng/ml), with a small pituitary remnant (9/7 mm). The disease persisted uncontrolled after two years of treatment with Octreotide LAR up to 40 mg/28 days, Cabergoline up to 3 mg/week and Pegvisomant up to 40 mg/week (associated in the last three months, with good control of GH secretion). The patient developed severe obstructive sleep apnoea documented using polysomnography. Fibroscopy reported a glossy, smooth tumor occupying completely the choanal quadrant and pegvisomant was withdrawn. Surgical intervention was performed, and the histopathological examination described a sessile polyp on the background of a chronic erosive rhinopharyngitis. IHC intervention was performed, and the histopathological examination described a sessile polyp on the background of a chronic erosive rhinopharyngitis. IHC analysis revealed a positive cytoplasmatic reaction for GH in tumoral cells. Two months after the nasopharyngeal tumor resection, IGF-1 was within normal range on somatostatin analogue and dopamine agonist.

Conclusion
Active acromegaly defined by GH excess and increased levels of IGF-1 contributes to mitogenesis, delayed apoptosis and malignant proliferation. In the current case, uncontrolled acromegaly was associated with a nasopharyngeal...
Hypopituitarism in adults - the importance of clinical suspicion

EP810

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Introduction

Hypopituitarism is a rare entity that can have different aetiologies. Symptoms are usually progressive and non-specific; therefore, many patients are under-diagnosed and untreated. We present a clinical case of a patient presenting septic shock, hypotension and central hypothyroidism.

Case report

A 46-year-old man was admitted in ICU for septic shock of unknown origin and multiorgan failure. Hormonal profile showed central hypothyroidism, prolactin and gonadotropins deficiency. The integrity of corticotropic axis could not be assessed due to the introduction of glucocorticoids, with a significant decrease in ACTH levels. He was medicated with hydrocortisone 15 mg daily, levothyroxine 75 mcg/day and leuprolide acetate 3.75 mg monthly.

Discussion

Discovering the cause of hypopituitarism can be a challenging. TBI can caused hypopituitarism several years after the event, and can even occur after minor trauma. The onset of symptoms of hypopituitarism after the episode of severe headache and vomiting also raises the possibility of another concomitant event, namely pituitary ischemia/haemorrhage. The hospitalization with septic shock, the detailed clinical evaluation and follow-up of the patient were crucial to detect the occurrence of this condition, associated with high morbidity and whose hormone replacement significantly improved the prognosis and quality of life.

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Hypopituitarism induced Radiotherapy for nasopharyngeal carcinoma: a case report

EP812

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Introduction

Since the hypothalamic-pituitary axis (HPA) is a radiosensitive region, cranial radiotherapy for head and neck malignancies represents a major risk factor for the development of endocrine complications particularly hypopituitarism. 

Case report

A 22 years old girl with a history of a undifferentiated carcinoma of nasopharyngeal type UCNT at the age of 09 years old treated with radiotherapy and chemotherapy was referred to the endocrinology department for investigation of short stature and primary amenorrhea. The patient presented with short stature, height of 146 cm (–3 standard deviations), with normal weight (body mass index 24 kg/m2), Breast Development Scale stage 4 and Pubic Hair Scale stage 4. Endocrinological evaluation showed unstimulated TSH, free T4 and 24 hour cortisol levels were normal. Pituitary MRI showed hypopituitary gland with field was found in 24 (60%) cases, a pathological fundus in 7 cases (17.5%), papilloduema in 4 cases and optic atrophy for the rest. A decrease in visual acuity was observed in half of the subjects (50%). Hormonal deficiencies were corticotrophic, thyrotropic, gonadotropic insufficiency, disconnection hyperprolactinemia and central diabetes insipidus in 80%, 32.5%, 42.5% and 15% respectively.

Conclusion

NFPAs in addition to their incidental discovery, are usually diagnosed lately as macroadenoma which commonly present with symptoms related to the mass effect on surrounding structures. They put at risk the vital and visual prognosis.

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have improved across all measures, survivors are still at risk of developing endocrine disorders, even years removed from therapy. This accentuates the importance of lifelong surveillance.

Conclusion
RIH worsens the quality of life and reduces the life span of patients. Thus, successful management depends greatly on early detection and hormone replacement therapy.

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EP813
Cushing Disease with COVID-19: Protective or Dangerous?
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Introduction
Coronavirus disease-19 (COVID-19) pandemic renders high morbidity and mortality. Glucocorticoid excess is characterized by increased susceptibility to infections due to impairment of the innate and adaptive immune system. Manifestations of Cushing disease (CD) including diabetes mellitus (DM), hypertension, and obesity are risk factors for severe COVID-19 disease. We present three CD patients with different clinical courses of COVID-19. The patients’ general characteristics are summarized in table 1.

Case-1
The patient was a 27-year-old woman with recurrent CD after transsphenoidal surgery. She had DM, hypertension, and obesity. She tested positive for SARS-CoV-2 with dyspnea, cough, chest pain, and fever. She hospitalized at intensive care unit (ICU). A CT scan showed bilateral diffuse ground-glass opacities of both lungs. Significant clinical improvement was achieved on the 13th day of ICU. She discharged from the hospital on 17th day.

Case-2
A 23-year-old woman was diagnosed with CD recently. She had obesity. The COVID-19 nasopharyngeal PCR was positive during preoperative evaluation. Lung involvement wasn’t observed. She survived the COVID-19 disease without symptoms.

Case-3
A 55-year-old woman with CD had a transsphenoidal surgery 2 months ago. She had DM and obesity. She was admitted to our clinic with adrenal insufficiency. She tested positive for SARS-CoV-2 with cough and shortness of the breath. A CT scan showed bilateral pleural effusion and bilateral diffuse ground-glass opacities. She died on the 18th day while treated in ICU.

Conclusions
Cushing disease-associated glucocorticoid excess, immunosuppression and co-morbidities may alter the severity and the course of COVID-19. In contrast, glucocorticoids have shown improve COVID-19 associated mortality in randomized controlled trials. It was also reported that COVID-19 disease infection can be worsened by concomitant hypocortisolism. Herein we report three cases with different prognosis. Thus, patients with CD should be followed more carefully during COVID-19 disease.

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EP814
Exploring a new entity of monotherapy pembrolizumab-associated hypophysitis
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Background
There are increasing number of reports on immune checkpoint inhibitors induced adverse events including hypophysitis. Hypophysitis tends to occur more with Cytotoxic T-lymphocyte-associated protein 4 inhibitors (12.15% of cases) which is a different entity compared to those associated to anti-program death 1 (anti-PD1) inhibitors.

Aim
We describe a case of pembrolizumab-associated hypophysitis and conduct a discussion based on a systematic review of the literature.

Case presentation
A 55-year-old woman presented with headache, nausea and fatigue 3.5 months (5 cycles) after initiation of adjuvant pembrolizumab for a stage 3b (TNM) melanoma. Endocrine profile was consistent with secondary adrenal failure, thyrotropic insufficiency and defective gonadotrophin secretion. Progressive decline of thyroid stimulating hormone and free tetraiodothyronine occurred three months prior to diagnosis. Imaging study showed an enlarged pituitary gland with homogeneous enhancement of the gland and pituitary stalk. After interruption of anti-PD1 therapy and administration of adrenal and thyroid hormonal substitutions improvement was observed. Magnetic resonance study showed declining pituitary mass three months later.

Discussion
Systematic search of literature identified 16 studies reporting 19 patients with single use pembrolizumab-associated hypophysitis. Most patients were treated for melanoma (n=7, 35%) and urogenital or breast neoplasia (n=7, 35%). Time to onset of pituitary insufficiency was most frequently 6 months (range 1.5 to 39.0 months) after treatment initiation. The most prevalent hormonal defect was isolated adrenocorticotropic hormone deficiency. Two studies reported multiple central hormonal defects. In those patients and in our case, increased pituitary mass was observed.

Conclusion
In contrast with the majority of other cases of pembrolizumab monotherapy associated hypophysitis, our case has distinct features. These include early disease onset, after pembrolizumab initiation, panhypopituitarism and increased pituitary mass. Whether or not this is a new clinical entity warrants further investigation. Until then, clinicians should be aware that pembrolizumab monotherapy associated hypophysitis might cover a heterogeneous clinical spectrum.

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EP815
The impact of adenoma size on the clinical course of acromegaly : a comparative study
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Introduction
Acromegaly is a chronic, slowly progressing disease caused in most cases by growth hormone (GH)-producing pituitary adenoma. This rare disorder is associated with a spectrum of various clinical manifestations and treatment outcomes differ between patients. The aim of this study was to evaluate the impact of adenoma size on comorbidities and biochemical status at the diagnosis of disease.

Methods
This is a one-centre cohort study conducted among adult patients with confirmed acromegaly. Baseline data regarding biochemical and radiological status were collected retrospectively. We performed a comparative analytical analysis between two subgroups:
- G1: patients with pituitary adenoma larger than 20 mm (n = 17)
- G2: patients with pituitary adenoma smaller than 20 mm (n = 12)

Results
29 adult patients were included with a mean age at diagnosis of 45.8 ± 12.4 years. Both genders and age did not differ between the two subgroups. Adenoma size greater than 20 mm (G2) was significantly associated with a higher GH level. Furthermore, there was a positive and significant (P < 0.05) correlation between baseline GH level and adenoma size. All patients in G2 had an intact gonadotropic axis, whereas more than half of those in G1 had gonadotropic insufficiency (P < 0.05). The differences in the occurrence of hyperprolactinemia, of corticotropic and thyrotropic insufficiencies were not statistically significant between the two subgroups.

Conclusion
According to our results, the clinical course of acromegaly is influenced by adenoma size at the onset of symptoms. This difference should be considered when treating patients with acromegaly.

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EP816
Clinical and demographic features of acromegaly in tunisian patients: a monocentric retrospective study
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Background and Aims
Acromegaly is a rare condition caused by an excessive secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1), which are responsible for exaggerated somatic growth and distorted proportions. The objective of the current work was to investigate the clinical and demographic features of acromegaly in Mediterranean patients.

Patients and Method
From 1997 to 2021, 29 patients with acromegaly were diagnosed and followed up at the Endocrinology Department of Hedi Chaker University Center, Sfax, Tunisia. We retrospectively reviewed the medical charts of all patients to assess their clinical and demographic characteristics.

Results
We noted a slight male predominance with a sex-ratio of 1.07. The mean age at diagnosis was 45.8 ± 12.4 years old. The diagnosis of acromegaly was more delayed in females (male: 44.1 ± 11.2 vs female: 47.7 ± 13.7 years old).

Symptoms related to tumoral mass effects such as headache and visual impairment were the leading causes of consultation in 31.0%. Changes in appearance brought only 17.2% of patients who had acromegaly to seek medical care. In 27.6% of cases, patients with dysmorphic features were referred by their physicians to the Endocrinology department for further hormonal assessment. The worsening of some nonspecific symptoms such as snoring (10.3%), glycemic imbalance (6.9%), and secondary amenorrhea (6.9%) led to the diagnosis of acromegaly. The mean weight was 82.5 ± 13.0 kg. The average height was 167.3 ± 11.2 cm (extremes: 146-191). The mean BMI was 28.0 ± 7.2 kg/m². Obesity was found in 40.7%. Dysmorphic features were observed in all patients with variable degrees. The dermatologic examination noticed frequently thickening skin (69.0%) and hyperhidrosis (65.5%). A hoarse voice was found in 48.3%. Patients with acromegaly reported asthma, lower back pain, and arthromyalgies in 41.4%, 20.7%, and 10.3%, respectively. The principal general comorbidities associated with this condition were diabetes (34.4%), hypertension (13.7%), and dyslipidemia (10.3%).

Conclusion
Acromegaly is an insidious disease that impacts equally both genders with a prevalence ranging between 2.8 and 13.7 cases per 100,000 people. Clinical manifestations include skeletal and soft tissue deformities, along with cardiorespiratory, neuromuscular, and metabolic disturbances. Most patients are diagnosed at an advanced stage after the onset of tumoral mass effect signs. Better recognition of the clinical landscape of acromegaly by first-line physicians may help in its precocious diagnosis and thus improve its therapeutic outcomes.

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EP817
Pituitary Stalk Interruption Syndrome in a 22-year old Filipino Male : A case report
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Background
Pituitary Stalk Interruption Syndrome (PSIS) is a rare congenital anomaly affecting the pituitary gland with characteristic MRI findings of small or absent anterior pituitary gland, misplaced or absent posterior pituitary gland and very thin or interrupted pituitary stalk (1). Patients with PSIS often presents with signs and symptoms of either isolated growth hormone deficiency or multiple anterior pituitary hormone deficiency and symptoms differ according to age at diagnosis (2).

Case
A 22-year old Filipino male was referred to endocrinology service for evaluation of micropenis. His birth history was unremarkable. Developmental milestones were at par with age. Both parents and 3 siblings were healthy. On examination, his BP was 90/60 mmHg with a height of 139.7 cm, weight of 32 kg, with a eunuchoid proportion. Facial, axillary and pubic hair were absent. His testes were 1 ml in size, with a 1.5 cm-stretch penis. Laboratory findings showed: Total testosterone 0.11 ng/ml (NV: 280.8-8 ng/ml), FSH 0.18 mIU/ml (NV: 1.5-12.40 mIU/ml), LH < 0.100 mIU/ml (NV: 1.70-8.60 mIU/ml), FT4 8.63 pmol/l (12-22 pmol/l), TSH 6.17 uIU/ml (NV: 0.27-4.20 uIU/ml), IGF 1 13.23 ng/ml (120-388 ng/ml), Prolactin 191.40 mIU/l (NV: 86-324 mIU/l), Estradiol < 5 pg/ml (NV: 25.80-60.70 pg/ml), DHEAS 0.07 umol/l (NV: 6.50-14.60 umol/l). ACTH stimulation test was done, baseline cortisol was 78, 27 nmol/l (NV: 172-497 nmol/l), 30 minutes and 60 minutes post ACTH cortisol levels were 290 nmol/l and 60 minutes cortisol: 343. 20 nmol/l respectively indicating intact adrenal gland. His bone age was 14 years. Pituitary MRI results were consistent with pituitary stalk interruption syndrome.

Conclusion
Despite being a rare syndrome, pituitary stalk interruption syndrome should be one of the differential diagnosis in patients presenting with micropenis and short stature. Importance of early recognition of the disease is important because it associated with permanent hormonal deficiencies leading to significant morbidity and mortality.

References

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EP818
Hypopituitarism in tropical countries
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Background
Etiology of hypopituitarism differs in tropical countries compared to the West and includes pituitary abscess, snake bite, HIV infection, Sheehan syndrome, road traffic accidents, iron overload states etc.

Aims and Objectives
The present case series highlights the spectrum of hypopituitarism in tropical countries.
EP819
Demonstration of the effects of asprosin on the sense of smell in female rats with hidden cookie test

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Purpose
Asprosin is a novel glucogenic adipokine produced by the fibrillin 1 (FBN1) gene that is generated and released by white adipose tissue during fasting. Asprosin hormone has been shown to improve the sense of smell in wild-type mice by activating the OlfTR734 receptor and decreasing the time it takes for them to discover hidden food. The purpose of this study was to determine the effects of asprosin on the sense of smell in female rats through the use of a hidden cookie test.

Materials and methods
Twenty-four female Sprague-Dawley rats were randomly divided into 2 groups (n=12) as control and asprosin. Asprosin and saline were intraperitoneally given at a dose of 500 ng/kg and 1 ml/kg to asprosin and control groups, respectively at 14.00 every day for eight weeks. The hidden cookie test was performed four times a day during ad libitum feeding, and the final experiment was repeated 24 h after fasting when all animals were in the estrous phase. Cookies (Chocapic, Nestle) were buried at a depth of 3 cm. They were recorded from 4 angles for 10 minutes. The finding time of the cookie was scored in seconds. T-test was used for the evaluation of the data. In all analyses, P<0.05 was considered statistically significant.

Results
In the hidden cookie test, the meantime of the control group was 445.29±64.58 seconds while it was 450.45±63.46 seconds in the asprosin group (P>0.05). Twenty-four hours after fasting, the average time in the asprosin group was 379.88±55.04 while it was 208.83±58.28 seconds in the control group (P<0.05).

Conclusion
It was found that there was no significant difference in the hidden cookie test performed when female rats were fed. However, asprosin hormone significantly increased the sense of smell due to the test performed after 24 h after fasting. Key words: Asprosin, adipokine, smell, hidden cookie test

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EP821
Preference of acromegaly patients for treatment attributes in Spain

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Background
Acromegaly is a slowly progressive rare disease caused by an increase in growth hormone secretion that causes a subsequent rise in insulin-like growth factor (IGF-1), both contributing to the excessive growth of the extremities, soft tissues and organs, in addition to other comorbidities directly interfering with patient’s quality of life. Acromegaly patients are concerned about their disease and their treatments, however, publications about patient’s opinion towards their disease and treatments are scarce.

Objective
The aim of this study was to gain further insight into the Spanish acromegaly patients’ perspective on their disease, unmet needs and treatment preferences.

Methods
A qualitative study was carried out to determine the attributes and levels of the qualitative. Two-hour-group interviews, comprising 4 and 5 adult patients each, took place in Madrid and Barcelona (September 2019). The group dynamics were conducted by an experienced moderator. The quantitative study was designed as a discrete choice experiment. 142 patients were initially invited to complete the online survey; however, only 67 patients completed the questionnaire. Choice-based conjoint analyses were used to estimate the utilities and values for treatment attributes. Subject preferences were estimated at aggregated levels. Using a Bayesian hierarchical modelling, the percentage of levels and attributes were transformed in utilities.

Results
QoL stood out as the most important attribute for respondents (37%), and IGF-1 together with glucose blood level and tumour size control (Table. 1), were the most important attributes according to participants. The pain associated to the treatment administration method was a secondary attribute. Diarrhoea, administration methods and storage conditions were the less important attributes according to participants and were only relevant for the treatment choice.

Conclusion
Despite acromegaly patients showing a high degree of awareness about the importance of IGF1 levels and tumour size control, our results point out the great relevance that patients award to Health-Related Quality of Life. Notably, patients showed great concern about glycemic level alteration, as well as the
levels of IGF-1 and the tumor size. Patients’ opinion should be taken in consideration when prescribing a treatment, as these patients show high knowledge and awareness about the management of their condition. 

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EP822
Sheehan Syndrome effects on cardiovascular risk
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Introduction
Sheehan syndrome has been for a long time the most frequent cause of hypopituitarism among women in developing countries, including Tunisia. Apart from hormonal deficits caused by SS, young women with SS are exposed to an increased risk of cardiovascular mortality. In this study, we aimed to evaluate the cardiovascular risk in patients with SS.

Patients and methods
This is a descriptive cross-sectional study. It was carried out in the Endocrinology department of the University Hospital Farhat Hached in Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. The estimation of the cardiovascular risk was made in patients who had no proven cardiovascular disease at the time of the diagnosis of SS, based on the Framingham score.

Results
Sixty five patients were included to the study. The mean age at diagnosis of SS was 48.2 ± 12.4 years. Thyrotropic and corticotrophic insufficiency were present in 86.2% of our patients, followed by gonadotrophic and lactotrophic insufficiency in 72.3% and 38.5% of patients, respectively. Somatotropic insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotropic deficiency in 10.8% of cases. A cardiovascular accident among first-degree relatives was noted in 10.7% of cases (5 cases of cerebrovascular accidents and 2 cases of myocardial infarction). Four patients had already proven cardiovascular disease at the time of SS diagnosis. The estimation of cardiovascular risk, using the Framingham equation, involved 39 patients. A very low, low or moderate cardiovascular risk was noted in 26.2%, 16.9% and 10.8% of patients, respectively. However a high cardiovascular risk was noted in 26.2% of patients, aged between 20 and 64 years, 9 men (28.12 %) and 23 women (71.87 %). The mean age at Acromegaly diagnosis was 50+/-5.41 years old and mean age when the first tumor was diagnosed: 46+/-10 years old. GH and IGF-1 mean levels at diagnosis were 21,31 ng/ml and 639 ng/ml respectively. Acromegaly was controlled in 50 % of the patients after therapy.

Results
Twenty-three (75 %) acromegalic patients were diagnosed with different forms of tumors and 15% of these were malignant. Four (44 %) men were diagnosed with tumors and all were benign. The most frequent tumors were multinodular goiter and benign prostatic hyperplasia. Eighteen (75 %) women were diagnosed with tumors, from which 20% (5 cases) were malignant. The most common benign tumor was multinodular goiter and the most frequent malignant tumor was papillary thyroid carcinoma. Acromegaly and diagnosis of tumors coincided in 52 % of the patients, most likely because screening for thyroid pathology was implemented. Among women diagnosed with cancer, one patient died as a result of this pathology.

Conclusions
Both women and men diagnosed with Acromegaly suffered more frequently form benign nodular goiter and only among women there were cases of malignant tumors.

Keywords: Acromegaly, Pituitary, Thyroid

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EP824
What factors predict a favorable response to hormonal therapy in congenital growth hormone deficiency?
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Introduction
Growth hormone (GH) treatment in congenital growth hormone deficiency (CGHD) is indicated to improve the prognosis of the statural prognosis. The aim of this study is to identify the predictive factors of a favorable response to GH therapy.

Patients & Methods
This is a retrospective study, conducted over a period of 27 years, including 30 patients with CGHD treated with hormonal therapy.

Results
The CGHD was diagnosed at a mean age of 8.8 ± 3.6 years with a male predominance. Only 2/2 patients reached the target height. The mean stature gain in standard derivations (SD) was 1.8 ± 1.07 SD. Severe growth retardation (56.7%) was positively correlated with stature response (2 vs 0.75 SD; P = 0.049). The gain under hormonal treatment did not depend on the GH peak during stimulation tests, nor on the combined (33.3%) or total (73.3%) character of CGHD. The radiological assessment showed a significant association between pituitary stem abnormalities and a better response to GH (2.6 vs. 1.6 SD; P = 0.019). The dose and duration of treatment as well as the target size did not influence the evolution under treatment. Only chronological age and delayed bone age at treatment initiation were positively correlated with a good response (P = 0.022 and 0.042 respectively).
Conclusion
The results of GH treatment were more satisfactory on final height than on target height. Large-scale prospective studies are needed to validate the factors that seem to be involved in the statural response.

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**EP825**

Binasal hemianopsia with pituitary adenoma in a 15-year-old girl

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Introduction
Pituitary adenomas represent 10 to 20% of intracranial tumors. In children, craniopharyngioma are the most common tumor of the sellar region. The symptoms can include headache, vomiting, pituitary deficiency and in pituitary adenomas, hormonal excess. The visual examination can find a visual field defect such as a bitemporal hemianopsia. We present a rare case of a pituitary adenoma in a 15-year-old girl with binasal hemianopsia.

Observation
A 15-year-old girl presented frontal headaches and vomiting occurring for a year before her referral to our department. At physical examination, she had a normal blood pressure, and clinical visual field assessment suggested an inferior and right nasal quadrantanopsia. Firstline imaging investigations with cerebral tomography discovered a pituitary adenoma. A biopsy with immunohistochemistry was performed confirming the diagnosis of a plurihormonal LH and prolactin sparsely granulated pituitary adenoma. The magnetic resonance imaging confirmed intra and suprasellar adenoma measuring 26.4*20*21mm abutting optic chiasma and the third ventricle. On hormonal investigations, she had a corticotropin deficiency with a peak cortisol after insulin tolerance test at 300 nmol/l and ACTH levels at 26 pg/ml. She didn’t have thyrotropin deficiency nor diabetes insipidus. Her menses were irregular, with a secondary amenorrhea of one year at three years after menarche. There wasn’t any sign of hormonal excess, the prolactin levels were at 33µg/l probably secondary to the pituitary stalk compression. A type 1 multiple endocrine neoplasia was excluded as there were no family history of endocrine disease and parathormone levels were normal. The visual field assessment concluded to bilateral defects with a pattern of an incomplete binasal hemianopsia. She was put on 15 mg of hydrocortisone and was referred to surgery.

Conclusion
The suprasellar extension of pituitary adenoma abutting the optic chiasma is responsible of a bitemporal hemianopsia as the optic nerves in the chiasma are responsible for the vision in those fields. A binasal defect can be seen in ophthalmologic pathology, but is extremely rare in pituitary adenoma. Pituitary adenoma prevalence in children and adolescents is less than 5%. This case represents an unusual clinical presentation of a pituitary tumor confirmed to be a pituitary adenoma prevalence in children and adolescents is less than 5%. This case represents an unusual clinical presentation of a pituitary tumor confirmed to be a pituitary adenoma.

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**EP826**

Looking for a safe and effective drug: the troubled journey of a Cushings’s Disease patient

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Cushing’s Disease (CD) is severe clinical condition due to an ACTH-secreting pituitary tumor. Here we present the case of a 25-year-old male who came to our attention for hypertension, moon face, acanthosis nigricans, abdominal purple striae and central obesity. The diagnosis of CD was based on the presence of high plasma cortisol after dexamethasone suppression test and elevated urinary free cortisol levels (UFC, 6-fold higher the upper limit of normality (ULN)). The pituitary MRI revealed a small lesion (5.5 mm), which was removed by transsphenoidal surgery, and a prolactinoma was excluded by pathology report. Surgery led to a slight improvement of symptoms. However, two months after the intervention, the patient experienced a worsening of the clinical picture, and the following biochemical assessment was suggestive of an early disease relapse. First, pasireotide was administered, although with low efficacy in reducing cortisol secretion. Then, a novel steroidogenesis-inhibitor, available only for investigational use in the context of a clinical trial, was started, but the patient withdrawn due to safety concerns. Therefore, low dose metyrapone was prescribed. However, severe gastrointestinal side effects occurred, and the drug was discontinued after few months. Furthermore, during imaging follow-up, the suspicion for a recurrent pituitary lesion was raised. Following a multidisciplinary discussion, inferior petrosal sinus sampling was performed, confirming the disease recurrence. Based on the expected low success rate, the team avoided a second surgery. Ketoconazole (600 mg/day) was then administered, leading for the first time to UFC normalization. Unfortunately, the patient developed severe nausea, headache and fatigue, and the dosage was reduced (400 mg/day). As expected, cortisol levels raised and cabergoline (1 mg/week) was then added. Combination therapy led to partial disease control, but a further disease relapse was observed. Therefore, radiosurgery was performed, and the newly available steroidogenesis-inhibitor, osilodrostat, was started as bridge therapy due to persistent hypercortisolism. Osilodrostat was titrated up to 5 mg/day, leading to biochemical control (UFC 5 nmol/l) but, with no side effects. At 7-months follow-up, the patient is currently proceeding with this latter treatment schedule, with no safety issues. Our case report highlights the difficulties encountered during the management of CD. The patient underwent surgery, radiotherapy and six different types of drugs before achieving disease control without adverse events. Therefore, clinical predictors of drug safety and efficacy are strongly needed in a challenging disease such as CD.

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**EP827**

Management of SIADH in patients with acute admissions to hospital: a single centre experience

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Background
Hyponatraemia is a common electrolyte abnormality that is associated with significant morbidity and mortality in patients admitted to hospital. Fluid restriction is the recommended treatment option for the syndrome of inappropriate antidiuretic hormone secretion (SIADH), a common cause of hyponatraemia with significant morbidity and mortality in patients admitted to hospital.

Methods
We collected data for patients with severe hyponatraemia (Serum Na+ <125 mmol/l) identified by our biochemistry lab from all samples they received. Suitable patients were identified over a two-week period. We included all those patients who were admitted to our hospital for any diagnosis and excluded those who were discharged from the emergency department or for tests completed as out-patients. Relevant data was collected from medical paper notes and drug charts with laboratory data available from patients’ electronic patient records. The treatment protocol for SIADH is set out by the hospital guidelines with fluid restriction as first line followed by addition of oral sodium chloride and/or urea salts as second line treatment options. Successful treatment is defined as improvement in serum sodium to >125 mmol/l.

Results
Thirty-eight patients with a mean age of 77 years were identified. The most common reason for admission was confusion and falls (24% and 18% respectively). Approximately one-third of the cases of hyponatraemia was due to SIADH (n=14). For patients with SIADH, successful treatment with fluid restriction alone was required in 43% of cases, combined with oral sodium chloride in another 43% of cases and only 7% required triple treatment combination of fluid restriction, oral sodium chloride and urea salts.

Conclusion
SIADH is a common cause of hyponatraemia in patients with acute hospital admissions. Fluid restriction alone is an effective treatment strategy in many of these patients. Additional solute intake is thought to increase renal free water reabsorption.
clearance and increase electrolyte diuresis. The study demonstrates that additional solute intake in the form of oral sodium chloride or urea salts are potential additional treatment options in those resistant to fluid restriction alone to correct hyponatraemia and their potential role in management of complex cases where strict fluid restriction is contraindicated.

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**EP828**

The third case report of pituitary apoplexy complicated by a subarachnoid hemorrhage and ventricular extension

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Introduction

Pituitary apoplexy is a rare endocrine emergency due to hemorrhage of the pituitary gland. The clinical presentation depends on the extent of bleeding and can deteriorate into a life-threatening condition if complicated by a subarachnoid hemorrhage, as previously described in 2 cases.

Case Description

A 60-year-old woman presented herself at the emergency department because of confusion for several hours. Clinical examination revealed anisocoria with mydriasis of the right pupil in an agitated woman able to move her four limbs but unable to execute commands. Seven months earlier, a macroadenoma with a craniocaudal diameter of 28 mm and compression of the optic chiasma was diagnosed, resistant to treatment with cabergoline and complicated by panhypopituitarism. CT scan of the brain was urgently performed and revealed an extensive suprasellar-hemorrhagic mass and a subarachnoid bleeding with extension to the lateral, third and fourth ventricles. The patient was sedated to enable placement of an external ventricular drain. CT angiography excluded an arterial aneurysm. The day after admission the patient awakened and executed commands. Visual field examination revealed bitemporal hemianopsia. MRI of the pituitary one month after admission showed a heterogenous suprasellar mass with a craniocaudal diameter of 28 mm. Endoscopic transsphenoidal resection of the pituitary mass was performed and anatomopathological examination showed necrotic tissue. Pituitary MRI 3 months postoperative revealed an important resorption of the hemorrhagic zone with a residual collection at the bottom of the sella turcica. Whether this collection is residual hematoma or adenoma could not be differentiated. Visual field examination 3 months postoperatively showed improvement, but was not normal with a bitemporal quadrantanopia. Panhypopituitarism persisted.

Conclusion

This case report described a woman with a pre-existing macroadenoma and a life-threatening presentation of pituitary apoplexy complicated by a subarachnoid bleeding with ventricular extension. Besides having a macroadenoma, this patient had no predisposing factors for apoplexy since it has shown that dopamine agonists are not associated with an increased incidence of apoplexy. Pituitary apoplexy has to be considered in an angiographically negative subarachnoid hemorrhage. However in every patient presenting with a subarachnoid bleeding, even if a medical history of a pituitary adenoma, a cerebral aneurysm was performed and an anatomopathological examination showed necrotic tissue. Pituitary MRI 3 months postoperative showed an important resorption of the hemorrhagic zone with a residual collection at the bottom of the sella turcica. Whether this collection is residual hematoma or adenoma could not be differentiated. Visual field examination 3 months postoperatively showed improvement, but was not normal with a bitemporal quadrantanopia. Panhypopituitarism persisted.

**EP830**

‘Features of cardiovascular complications in patients with cushing syndrome in the republic of uzbekistan (register data)’

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The purpose of the study

Is to study features of cardiovascular complications in patients with Cushing syndrome in the Republic of Uzbekistan (RUz).

Material and research methods

In the period of 2002 to 2021, 317 patients were installed with the following clinical forms of Cushing syndrome (CS): 1) ACTH-dependent CS (ACTH-DCS) - 258 (81.3%) patients, of which women - 174 (54.8%), men - 84 (26.4%), 2) ACTH independent CS (ACTH-iCS) -51 patients (16.08%) of women - 41 (53.5%), and among women - 80 (45.9%), only 125 cases out of 258 (48.4%). In the 2 group of patients with ACTH-iCS among men the CVC frequency was 2 (12.9%), and among women - 80 (45.9%), only 125 cases out of 258 (48.4%). In the 2 group of patients with ACTH-iCS among men the CVC frequency was 45 (12.9%), men - 10 (3.15%). 3) Ectopic CS (ACTH-ECS) -8 patients (2.5%) of women - 8 (100%). The age range is from 4 months to 25 years. 10 patients amounted to a control group. The study used clinical and biochemical, hormonal studies (serum, urine), functional tests, as well as instrumental (neuroophthalmological, radiological - MRI pituitary gland, MSCT of adrenal glands, X-ray absorption densitometry and statistical techniques.

Results

The most frequent complications of the CS were cardiovascular complications (CVC), which developed in 113 (48.9%) patients with a predominance of female 74 (61.3%). Among them, malignant arterial hypertension, acute vascular disasters in the form of myocardial infarction took place more often. In the 1st group of patients with ACTH- DCS total in men, the CVC frequency was 45 (53.5%), and among women - 80 (45.9%), only 125 cases out of 258 (48.4%). In the 2 group of patients with ACTH-iCS among men the CVC frequency was 2 (20.0%), and among women - 13 (31.7%), only 15 cases out of 51 (29.4%). And, finally, in a 3 group of patients with ACTH- ECS in men, the CVC frequency was 1 (33.3%), and among women - 1 (31.7%), only 2 cases of 8 (20%).

Conclusions

Of 317 patients with CS in 142 (44.8%) cardio-vascular complications were recorded and more often in the 1 st group of patients.

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**EP829**

Hormonal and regional complications of craniopharyngiomas

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Background

The craniopharyngioma is a non-endocrine tumor, developed along the infundibulo-pituitary axis, from the 3rd ventricle to sphenoid, histologically benign but locally invasive. It is a tumor with serious complications because of its location, its considerable potential for extension, its tendency to recur, and its adhesions to neighbouring structures. Our aim is to assess hormonal, neuro-ophthalmological and metabolic complications at the diagnosis of craniopharyngiomas.

Patients and methods

It is a multicentre Cross-sectional descriptive study in the town of Oran, with prospective and retrospective data collection. MRI, hormonal, biochemical and ocular tests, made the diagnosis. Data entry and analysis were performed with CDC Epi Info version 6 (USA), SPSS 20, Statistica10.

Results

In our study, we collected 86 non-adenomatous tumours, among them 26 craniopharyngiomas (35%), sex ratio men/women at 1.3. Average age at 17.3 ± 13.5 years (2-56). Mean consultation time 20.5 ± 25.3 (1-96) months (range). Circumstances of discovery: headaches - visual disturbances (79.8%), growth retardation (15.4%) and hypogonadism in adults (20.4%). Average dimensions (mm ± SD): average height 39.1 ± 17.4, transverse diameter 32.2 ± 14.9, antero-posterior diameter 36.0 ± 17.5, extremes 15-95 mm. Extensions (percentage): Supra sellar (88.5), Infra sellar (46.2), posterior (23.1), Multidirectional extensions (38.5). Anterior pituitary insufficiency 96.1%, multiple anterior pituitary deficiencies 77.5%, hypothalamic syndrome 30.8%, epilepsy 11.5%, diabetes insipidus 23%. Neuropsychiatric complications (55.1%), ophthalmological (79.8%), blindness 23%, hydrocephalus 68.7%.

Discussion

Craniopharyngiomas are accompanied by significant pituitary, hypothalamic and neuro-visual morbidity. The consequences of a delay in diagnosis increases the frequency and severity of complications, hence the need for early diagnosis in order to control this morbidity, the burden of which is considerable on the health system.

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**EP892**

Hormonal and regional complications of craniopharyngiomas

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Background

The craniopharyngioma is a non-endocrine tumor, developed along the infundibulo-pituitary axis, from the 3rd ventricle to sphenoid, histologically benign but locally invasive. It is a tumor with serious complications because of its location, its considerable potential for extension, its tendency to recur, and its adhesions to neighbouring structures. Our aim is to assess hormonal, neuro-ophthalmological and metabolic complications at the diagnosis of craniopharyngiomas.

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Results

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Discussion

Craniopharyngiomas are accompanied by significant pituitary, hypothalamic and neuro-visual morbidity. The consequences of a delay in diagnosis increases the frequency and severity of complications, hence the need for early diagnosis in order to control this morbidity, the burden of which is considerable on the health system.

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Acromegaly in the elderly patients
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Introduction
Pituitary adenomas in people over 65 represent less than 10% of all pituitary adenomas, 80% of which are non-functional. Somatotropic adenomas remain very rare. The interest of our study is to describe the clinical, paraclinical and therapeutic profile of cases of senile acromegaly.

Patients and Methods
This is a retrospective study of four senile acromegaly patients followed in our endocrinology’s department.

Results
We report four cases of acromegalic patients, one woman and three men, respectively aged 75, 68, 65 and 69 at the time of diagnosis. Two had been diabetic and hypertensive for 05 years. The circumstances of discovery were a tumor syndrome in two patients, a dysmorphic syndrome in one patient and digestive symptoms secondary to a tumor process in another patient. The diagnosis was confirmed by elevated IGF1, a paradoxical GH response on OGTT and a disturbed GH cycle (two diabetics). Radiological exploration by pituitary MRI showed that it was a macroadenoma in 100% of cases with invasion of the cavernous sinuses and compression of the optic chiasm in two cases. The impact assessment revealed: corticotrophic insufficiency (2 cases), bilateral visual field impairment (2 cases), moderate to severe sleep apnea syndrome (4 cases), hypertrophic heart disease (2 cases), arthropathy peripheral (2 cases), hypertriglyceridemia (1 case), a stenotic tumoral process inaugurating the disease in one patient and polypysosis colon in two other patients, a multinodular goiter (1 case) and a TIRADS 2 nodule (2 cases). Therapeutically, the patient was treated surgically via the transphenoidal approach with simple post-operative follow-up. Given the operative risk and the non-motivation of the two other patients for surgery, they were put on a somatostatin analogue with a favorable outcome. The fourth patient was lost to sight.

Conclusion
Somatotropic adenomas in the elderly patients are rare, characterized by a diagnostic delay. Surgery, if possible, remains the treatment of choice for acromegaly in the elderly, but somatostatin analogues have also shown their effectiveness in the treatment of these patients.

Materials and Research Methods

Target
To study the incidence of postoperative complications in patients with transphenoidal pituitary adenectomy

Materials and research methods
180 cases of PA subjected to TPA for the period from 2018 to 2020 were analyzed. Of these, 102 (56.6) women, 78 (43.3) men, patients were divided into two alternative groups: the first group - 93 (51.6%) patients with macroadenomas - 42 (45.2%) men, women 51 (54.8%), the second (comparison group) - 87 (48.4%) with microadenomas of men - 35 (40%), women - 52 (60%) of the pituitary gland. The age of the patients ranged from 30 to 59 years. The levels of hormones STH, IGF-1, ACTH, cortisol, prolactin, TSH, fT4, LH, FSH, estradiol, progesterone according to indications, MRT/CT of the chiasm-sellar area and the state of the organ of vision were studied. Patients were distributed as follows: depending on the hormonal activity of patients with adrenocorticotrophic hormone secreting Cushing’s syndrome-60, acromegaly-60, inactive pituitary adenoma-60; depending on the size of the formation: 93 (51.6%) were with macroadenomas, 87 (48.3%) with pituitary microadenomas. An analysis of the incidence of postoperative complications in the short term (1 month) revealed that in 81 (45%) patients with hypophysectomy; hypothyroidism in (70.39%); hypogonadism in 50.28%; diabetes insipidus in 7.64%; transient diabetes insipidus in 11.6%; visual acuity deterioration in 2 (1.2%) patients and liquorhea in 3 (5.4%) patients. At the same time, there was a normalization of elevated hormone levels in 133 (74%) patients; 30% improvement in vision; lack of disease dynamics in 47 (26%). Despite the persistent phenomenon of hypopituitarism 47 (26%) and diabetes insipidus 11 (6%), which were mainly observed in 165 (92%) patients with macroadenomas and did not depend on the organ activity of the formation (against 54.30%) cases with microadenomas. In the long-term follow-up of patients after TPA (t 3 months to 1 year), an improvement in pituitary function was noted in the form of restoration of gonadotropic insufficiency, phenomena of transient diabetes insipidus and improvement in hypertensive cephalgia.

Conclusion
The frequency of immediate and long-term complications in most cases is observed in pituitary macroadenomas and does not depend on the hormonal activity of the adenoma.

EP833
'The frequency of postoperative hypopituitarism in patients with non-functional pituitary adenomas (NFPA) after transnasal hypophysectomy'
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The purpose of the study is to study the frequency of postoperative hypopituitarism after transnasal hypophysectomy (THE) in patients with pituitary adenomas.

Methods and Materials
Under our observation there were 24 patients with NFPA, of whom women were 14, men - 10. The average age of patients was 36.4 years. Total of 24 patients were performed for the period from 2016 to 2021 33 surgery in the neurosurgery department., of which THE - 32, 1 - bifrontal craniotomy. At the same time, 3 patients were 2 THE, in 3 - 3 THE, 4 patients with TGE also received radiation therapy. The whole patients were performed by research complex, which included radioimmune hormonal (STH, IGF-1, Prolactin, LH, FSH, TSH, ACTH, Cortisol, etc.), ophthalmological (Eye bottom, field of view) and X-ray studies (CT, MRI of the Turkish saddle).

Results
According to our data, postoperative panhibitionituitarism (deficiency of STH, LH, FSH, ACTH + Diabetes insulin) developed in 6 patients (25%), postoperative partial hypopituitarism (deficiency of STH, LH, FSH) developed in 11 (45.8%) and 7 - STH deficiency (29.1%) developed. Thus, the most pronounced neuroendocrine disorders after THE were detected in 6 (25%) patients.

Conclusions
1) In patients with adenomas of pituitary gland subjected to THE, it is recommended to monitor the levels of all tropic and peripheral hormones of pituitary glands both in the early and later postoperative periods. 2) patients with pituitary adenomas after THE need substitution hormone therapy with appropriate drugs depending on the level of hormones (desmopressin, sex and thyroid hormones, corticosteroid preparations, growth hormone).

EP834
'Case of re-growth of aggressive giant non-functional pituitary adenoma with panhypopituitaryism in 28-years old woman'
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The purpose of the study is to research case of re-growth of non-functional giant pituitary adenoma

Material and research methods
Patient Karimova N, was born in 1994 in Namangan region. Clinical diagnosis: Non-functional giant pituitary adenoma with total variant of growth. The age of the patient ranged from 30 to 59 years.

Materials and methods

Conclusion
1) In patients with adenomas of pituitary gland subjected to THE, it is recommended to monitor the levels of all tropic and peripheral hormones of pituitary glands both in the early and later postoperative periods. 2) patients with pituitary adenomas after THE need substitution hormone therapy with appropriate drugs depending on the level of hormones (desmopressin, sex and thyroid hormones, corticosteroid preparations, growth hormone).
hyperprolactinemia. Primary infertility. Secondary amenorrhoea. The patient considers himself to be ill from 2013 year after marriage. She was operated on the occasion of pituitary adenoma with supra-infra-lateral-sellar growth. Microcellular chromophobe adenoma was histologically determined. In early postoperative period the improvement of vision was marked. In late postoperative period neuroendocrine disorders were left without dynamics. As the patient wasn’t observed regularly, she received Kaverbogin 5 mg twice in week during 6 months. The patient refused from radiotherapy. The worsening of state was marked for the last 6 months, when the above mentioned complaints increased. Results of the study Height is 156 sm, weight is 55 kg. BMI = 24, 4 kg/m2. The skin coverings are pale, dry, clean. A/P=110/70 mm.mer e. Puls rate = 72 beats pm. In blood plasma GH = 0.13 ng/ml (norma 2.5-25 ng/ml), IGF 1 - 88 nmol/l (norma 300 nmol/l), FSH-0.94 Me/ul, LH = 0, 46 Me/ul (norma 3-8 nM/E0), cortisol in the morning = 55.1 nmol/l (norma 260-720 nMOL/l), prolactin = 307 ng/ml (norma 7.8-8 ng/ml), estradiol = 17, 4 pg/ml. Ophthalmological examination. Bitemporal hemianopsia on white color, absence of visual fields on green and red colors from both eyes. MRI: Pituitary macroadenoma with the size 5.6 x 4.3 cm x 5.4 cm. The patient was operated again in our clinic. In the early postoperative period the patient was marked improving of visual fields.

Conclusions

1. For NFPA with small cellular chromophone cells in patients of reproductive age the typical aggressive re-growth of tumor. 2. For prevention of re-growth of pituitary tumor after surgery it is necessary to conduct for patient radiotherapy.

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EP835

Cushing syndrome and disease: A doctor of philosophy study conducted by a patient

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Introduction

Prior to and since the onset of my Doctorate study in 2019, a plethora of on-going research including my own has been conducted into the diagnosis, treatment, and management of Cushing syndrome (CS), and disease (CD). These conditions continue to challenge physicians not only in the diagnosis but how to treat their patients. The wide clinical spectrum of CS and CD produces a medical dilemma as patients’ symptoms, can vary. The typical Cushingoid features which are referred to as the classic symptoms are not always obvious when a patient presents. There are population groups which have increased incidence of CS which includes obesity, diabetes, and osteoporosis. The diagnostic approach is a 3-step investigative process and includes a) a physician’s knowledge of the signs and symptoms, which is crucial to make b) a definitive diagnosis of CS. The third step of this process is c) to identify the reason for excess cortisol. Learning Process

The learning process during this study has been exponential and led to a clearer understanding as to why it took so long for my physicians to make a definitive diagnosis of initially CS and then CD. This personal Cushing’s journey of study revealed the reasons for the twists and turns on the ‘bumpy,’ road to diagnosis, treatment and then remission. Comparing other patients experiences during my study with my own, provided an understanding why we experience pain, changes in our personality, fatigue, a reduction in quality of life (QoL), and in most cases, irreversible comorbidities, my own being osteoporosis. During the process of study, I endeavoured to use my knowledge and skills as a Health Professional, promoting awareness through conference presentations and publications. On the long road to remission, I discovered the importance for Health Professionals, particularly General Practitioners and the public, to recognise patients’ unmet needs.

Study Conclusions

By taking a more patient-centred approach including time to listen to their patients, in parallel with the well-established biochemical and imaging tests would increase early diagnosis and treatment.

Recommendations

Recommendations included identifying target audiences, examples women’s clinics, and methods of screening obese and diabetic patients. Increase in using advanced technologies such as artificial intelligence in identifying early signs, example osteoporosis. Virtual learning platforms for educating Health Professionals, extensive use of thematic analysis in QoL questionnaires and media coverage to raise awareness.

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EP836

Metabolic abnormalities profile of non-functioning pituitary adenomas

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Introduction

Metabolic abnormalities are common in pituitary adenomas and metabolic targeting is becoming a new therapeutic approach to the management of most tumor pathologies, especially pituitary tumors. The objective of this work was to assess the metabolic profile of non-functioning pituitary adenomas.

Material and methods

A retrospective and descriptive study, over a period of 6 years, conducted in the Endocrinology-Diabetology and Nutrition department of Ouja in the eastern of Morocco. The study included 24 patients with histologically confirmed non-functional pituitary adenomas.

Results

The mean age was 50 ± 11.2 years, with a female predominance (58.3% of cases). The average duration of the disease was 1.9 ± 3.6 years. The clinical examination found 50% of the patients to be overweight and 20.8% were obese. The metabolic work-up showed type 2 diabetes in 20.8% of cases and pre-diabetes in 33.3%. Hypertension was found in 16.6% of patients. On the lipid panel, mixed dyslipidemia was revealed in 20.8% of the patients, hypertriglyceridemia and hypoHDLemia < 0.35 g/l were confirmed respectively in 25% of cases and hypercholesterolemia in 12.5% of patients.

Conclusion

Metabolic abnormalities associated with non-functioning pituitary adenomas are correlated with disease progression and prognosis. The evaluation of metabolic status should be emphasized during treatment of pituitary adenoma and control of metabolic abnormalities should be added to their current therapies.

Bibliography

Metabolic abnormalities in pituitary adenoma patients: a novel therapeutic target and prognostic factor; YangDiabetes MetabSyndr Obes. 2015; 8: 357361

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EP837

Kallmann’s Syndrome: case report

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Introduction

Kallmann syndrome, a rare genetic disorder, refers to the association between hypogonadotropic hypogonadism and anosmia or hyposmia due to abnormal migration of olfactory axons and gonadotropin-releasing hormone producing neurons It can be autosomal dominant, autosomal recessive, or X-linked inheritance.

Case report

A 16-year-old male student, presented to endocrinology unit with delayed puberty. He was born to consanguineous parents and had normal delivery. He had normal developmental mile stones. Bilateral cryptorchidism was discovered at age six, associated with hyposmia but no hearing defect or oral cavity abnormalities. He was diagnosed with anosmia. Skull magnetic resonance imaging (MRI) revealed hypo plastic olfactory bulbs and shallow olfactory grooves, along with a normal pituitary gland and a normal pituitary stalk. No history of deepening of voice or morning erection Physical examination: Height : 164 cm, arm span was 169 cm, BMI: 17, no gynecomastia Genital examination showed Tanner stage 1 (penis 3 cm, empty scrotum at time of examination with no corrugation & absent axillary & pubic hair) Neurologic examination was otherwise unremarkable except for decreased sense of smell.

Investigations

ACTH:12 pg/ml (10-60), TSH:3 mU/ml(0.4-5), PRL was 13 ng/dL(N: <20 ng/dl), FSH : 0.71 IU/ml (1.4-18), LH :0.1 IU/ml (Adult:1.7-8.6, prepubertal up to 6), Total Testosterone:1.79 ng/ml (> 2.5 g/ml) Scrotal ultrasound revealed: both testes are ectopic in location rt at the RT inguinal canal, LF seen in left scrotal neck, both tests are small in size for patient age RT 13x5.8x13.6 mm3/IF 10x5x11.3 mm Chromosome analysis showed 46, XY He was prescribed human chorionic gonadotropin 5000 IU weekly for 6 weeks and testosterone cream daily, with a 25 mg of intramuscular testosterone injection and were then increased by
EP838
‘The functional status of pituitary-gonads-cortex axis in women on fertile age with ACTH-dependent Cushing syndrome’
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Aim – to study the functional status of pituitary-gonads-cortex (PGC) axis in women with Cushing syndrome (CS)

Materials and methods
We evaluated 25 women with ACTH-dependent CS without other associated pathology. Mean age of patients was 28.3 years-old. All patients have complaints to amenorrhea and primary infertility. Control group constituted by 20 healthy women with same age All patients underwent clinical and biochemical evaluations including endocrine check, lipids profile, hormonal profile in 14 day of menstrual cycle (LH, FSH, prolactin, free testosterone, estradiol, progesterone, etc), genitalia ultrasonography, electroencephalography (EEG), height, weight, BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio, questioning and other studies.

Results
The investigation of hormonal profile showed anovulation in 19 patients (76%) (mean LH ranged 3.7 ± 1.2 mIU/l, FSH 4.4 ± 1.5 mIU/l) in 14 day of the menstrual cycle and high range of free testosterone levels (mean 3.6 ± 0.3 ng/ml). Besides that, all patients have hypercortisolism. (P < 0.05). The investigation of levels of estradiol and progesterone in 7.14, 21 days of menstrual cycle showed their partial decrease. Most of the patients had central obesity with BMI > 35 kg/m². WC was in normal range 104.3 ± 7.4 cm, HC = 85 ± 5.3 cm, whereas waist-hip ratio > 1.22. Blood tests showed dyslipidemia in all patients (100%).

Conclusions
Most fertile women with ACTH-DCS (76%) have anovulation with high range of free testosterone in all patients with partial decrease of estradiol, progesterone (secondary hypogonadism).

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EP839
Diagnosis of Kallmann syndrome in adulthood
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Introduction
Kallmann syndrome is a rare genetic condition characterized by the association of a hypogonadotropic hypogonadism and anosmia. It results from the failure of GnRH cells to migrate to the hypothalamus and lack of development of the olfactory bulb. The main symptom of Kallmann syndrome is delayed or incomplete puberty usually associated with an impaired sense of smell. We herein describe a case of Kallmann syndrome discovered at the age of 57 years old.

Observation
We report the case of a 57 years old man, with a history of a pathologic fracture, referred to our department for exploration of gynecomastia. The patient didn’t reveal any symptoms such as erectile dysfunction or reduced sex drive, only an anosmia lasting since his youth. Physical examination revealed a grade 2 bilateral gynecomastia, a blood pressure of 150mmHg over 90mmHg. Examination of the external genital organs showed normal pubic hair, a micropenis measuring 5 cm and hypotrophic testis. On hormonal investigations, his testosterone levels were at 0.442 ng/ml, his LH levels were at 0.051 mIU/ml and his oestradiol levels were at 20.55pg/ml (<62pg/ml in male). His prolactin levels were normal at 2.696g/l. Corticotropin and thyrotropin deficiency were excluded. On imaging investigations, he had an osteoporosis with a T-score at -5.2 and hypotrophic non nodular tests. The magnetic resonance imaging of the brain couldn’t be performed as the patient has metallic orthopedic devices. He was put under calcium, vitamin D, bisphosphonates and testosterone therapy after eliminating contraindication.

Conclusion
This case highlights a non-classical presentation of a Kallmann Syndrome discovered during the investigations of gynecomastia. The delay of diagnosis was due to the reluctance of the patient, explaining with the spontaneous onset of puberty, the late diagnosis at this age. The psychological impact of this disease could have been prevented with an early treatment.

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EP840
Evaluation of neuroendocrine dysfunction in the diagnosis of depressive and non-depressive alcohol-dependent persons
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Aims
This study aimed to assess a possible hypothalano-pituitary-adrenal (HPA) axis dysfunction in a population of alcoholics, using a dexamethasone suppression test (DST).

Methods
For this study, 90 participants had been selected, among whom 65% of participants were depressive and 35% of are non-depressive alcoholics. The study included 35 participants were depressive and 35% of are non-depressive alcohol-dependent persons

Discussion
The serum and urinary cortisol were compared between the groups of 89 male patients (65% depressive and 36% non-depressive alcoholics) (Hamilton test), before and after DST. In non-depressive patients, 49% was non-suppressive in DST. In depressive patients, 47% was suppressive in the DST test (serum cortisol).

Conclusions
Discussion
Acute and chronic alcohol intake and alcohol withdrawal induce dysfunction of neuroendocrine and other regulatory systems. The expression ‘neuroendocrine dysfunction’ alludes to an assortment of conditions brought about by imbalances in the body’s chemical creation straightforwardly connected with the pituitary, nerve center, and their tomahawks following TBI.

Introduction
The serum and urinary cortisol were compared between the groups of 89 male patients (65% depressive and 36% non-depressive alcoholics) (Hamilton test), before and after DST. In non-depressive patients, 49% was non-suppressive in DST. In depressive patients, 47% was suppressive in the DST test (serum cortisol). Twenty-four hours urinary excretion in a group of non-depressive patients was suppressed in 79% of cases; depressive patients showed 50.9% non-suppressors. Basal serum cortisol secretion was significantly lower in a group of non-depressive than depressive patients. Also, serum concentrations at 16 h were significantly higher in a group of depressive non-suppressive patients. Basal urinary cortisol excretion was in the normal range in all patients, but after dividing the patients into suppressable and non-suppressable groups, significantly higher (P < 0.002) basal urinary cortisol concentrations were found in the latter.

Conclusions
Based on the DST test and the basal cortisol measurement, the findings reveal that the neuroendocrine dysfunction of alcoholic patients could be present even if the depression is pronounced.

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EP841
Descriptive study of the acromegaly disease activity according to ACRODAT® in a tertiary Hospital in Spain
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Aims
This study aims to evaluate the performance of the acromegaly disease activity according to ACRODAT® in an academic hospital in Spain.

Methods
The study included patients with a diagnosis of acromegaly according to the American Association of Clinical Endocrinologists and the Endocrine Society guidelines. The ACRODAT® score was used to assess the disease activity.

Results
A total of 100 patients with acromegaly were included in the study. The mean age was 56 years, and 60% of patients were women. The median serum IGF-I level was 252 ng/mL, and 75% of patients had levels above the normal range. The median ACRODAT® score was 3.5, indicating active disease.

Discussion
The results of this study highlight the importance of monitoring disease activity in acromegaly to ensure adequate management and prevent complications.

Conclusions
This study demonstrates the effectiveness of the ACRODAT® score in assessing disease activity in patients with acromegaly.

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Central precocious puberty in a young boy associated with bilateral optic pathway glioma in neurofibromatosis Type 1: a case report

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Background and Importance
Precocious puberty refers to sexual characteristics development before the normal age for its development. Neurofibromatosis Type 1 is an autosomal dominant condition with wide spectrum of clinical phenotype of which precocious puberty is common. This case report highlights the importance of recognizing this disease in patient presenting with precocious puberty and screening for optic pathway gliomas should be done and treat it to prevent the future chances of permanent blindness, neurological disability and gonadotropin deficiency.

Clinical Presentation
9 years old male came with chief complaints of decreased/blurring of vision from the age of 3 to 4 years, increased pubic hair growth and multiple regions of skin lesions noticeable for the last 1 year. Clinical examination of the patient revealed classic features of precocious puberty. Hormonal workup showed significantly raised testosterone levels and mildly raised FSH levels. MRI brain was done which showed abnormally thickened bilateral optic nerves and optic chiasma, suggestive of optic nerve glioma. Final diagnosis of Neurofibromatosis Type 1 manifesting as Central Precocious Puberty in association with bilateral optic pathway Glioma was made.

Conclusion
By this case report, physician’s attention is directed towards the importance of recognizing this disease with precocious puberty and screening for optic pathway glioma should be done, even when patient don’t have any visual symptoms and treat it early which will help in preventing the complications of optic pathway glioma in long term and ultimately shall benefit patients in part of their increased survival, satisfaction and decreasing morbidity.

EP843
Acrornagl-related dysmorphic syndrome In Mediterranean Patients: A monocentric retrospective Survey

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Background and Aims
Acrornagl is an insidious disease related to hypersecrection of growth hormone (GH) that leads to several cardiovascular, respiratory, and metabolic comorbidities. The onset of dysmorphic body changes is one of the earliest signs of this condition. The objective of the current work was to describe the clinical manifestations of dysmorphic modifications characterizing Mediterranean patients diagnosed with acromegaly.

Patients and Method
We conducted a retrospective study that included all patients diagnosed with acromegaly who have been followed up from 1997 to 2021, at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia. The review of medical charts provided a detailed description of dysmorphic features in the investigated population.

Results
Our sample included 29 with a mean age at diagnosis of 45.8 ± 12.4 years old (extremes: 23-72). No significant gender differences was reported (sex-ratio = 1.07). Dysmorphic features were observed in all patients with variable degrees. Patients diagnosed with acromegaly presented with facial changes in 96.5% of cases. Cranial ridges (41.1%), frontal skull bossing (48.3%), and enlarged nose (75.9%) were frequently recorded. Similarly, jaw and oral deformities were very common among the studies population such as prognathism (72.4%), enlarged lips (55.2%), and mandibular overgrowth with maxillary widening and teeth separation (37.9%). Macroglossia was found in 48.3% of cases. Acrmal modifications occurred in more than 80% with swelling thin-skinned hands in 51.7% and enlarged shoe size in 82.8% of cases. Skeletal axial involvement was present in 24.1% including kyphoscoliosis and diffuse skeletal hyperostosis.

Conclusion
Comorbidity and mortality rates in acromegaly are significantly higher compared with healthy subjects due to its delayed diagnosis and therapeutic difficulties [1]. Unlike North America and Northern Europe, acromegaly remains largely underdiagnosed, especially in the southern Mediterranean countries. Dysmorphic modifications are one of the earliest symptoms of this disease [2]. Raising awareness about acromegaly and its dysmorphic syndrome in the general population and among physicians in the Mediterranean region could aid in the early detection of undiagnosed cases.

References

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management. We report a case of CD in a 14-year-old child whose diagnosis was confirmed only after 2 years.

**Observation**

This was a 14-year-old female patient with a family history of consanguineous marriage and personal history of nephrotic syndrome who presented with delayed stature, delayed puberty and obesity. On initial examination, she had Cushing’s syndrome with facio-truncular obesity, buffalo hump, spontaneous bruising, and purple stretch marks. Her Weight was +2SD, her height was -4SD, with BMI of 33.5 kg/m2. Tanner score was A2P2S2R0. The diagnosis of ACTH-dependent Cushing’s syndrome was made in view of an abolished cortisol cycle, an elevated CLU of 182 mg/24h and a low post-braking cortisol level of 140 ng/ml with an elevated ACTH of 97 pg/ml. Investigations to decide between a central origin and ectopic ACTH secretion were initially discordant. In favor of CD: Positive desmopressin test, elevation of Cortisolaemia of 30% higher, and ACTH of 20% higher, no carcinoid tumor on thoracic CT scan and no pathological fixation on Octreoscan. Negative strong braking (Cortisol level at 170 ng/ml) and hypopituitary-pituitary MRI without abnormalities were in favor of ectopic ACTH secretion. A second hypophysial-pituitary MRI was performed 6 months after the diagnosis of CS, showing a right anterolateral microadenoma of 3.4×5 mm with a small dehiscence of the sellar floor. There was no evidence of multiple endocrine neoplasia. Thoracoabdomino-pelvic CT scan showed bilateral adrenal hypertrophy predominantly on the left. The patient received a preparation with ketoconazole and then was operated: A complete excision of the friable microadenoma and all the surrounding parenchyma was passed without incidents. Immediately postoperatively, the patient presented with ketonuria and then was stabilized. An osteoarthrogenic breach was surgically repaired in a second stage. She presented panhypopituitarism and was substituted with Lthyroxine and hydrocortisone. Currently, at one and a half years post-operatively, the patient retains signs of hypercorticism with faciotruncal obesity. The 24 h cortisol level is lower than 2 mg/ml confirming cortisotropic insufficiency, a key biological marker of remission.

Discussion/Conclusion: Our case illustrates the diagnostic and therapeutic difficulty of CD in an adolescent girl. Since the cure rate is lower than in adults with a higher risk of recurrence and a shorter median recurrence time, a long term follow-up and a cardiovascular, metabolic and bone assessment in our patient is crucial.

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**EP845**

**Clinical, biological and radiological particularities of acromegaly: Experience of the Endocrinology Department of the EPH Bologhine of West Algiers**

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**Introduction**

Acromegaly is caused by chronic hypersecretion of GH and IGF-1. Chronically elevated GH and IGF-1 levels lead to a complex spectrum of symptoms.

**Objectives**

To describe the clinical, hormonal and radiological profile of acromegaly at the time of diagnosis.

**Materials and methods**

Retrospective study including 67 patients hospitalized in the Endocrinology Department of the EPH Bologhine.

**Results**

There were 40 men and 27 women (Sex ratio M/F:1.48), the average age at the time of diagnosis of the patients was 43 years, a partial or total anteropituitary insufficiency was found in 38,8% of the cases. This was global in 10.4% and partial in 28.35%. 7.4% of the patients had intestinal polyps, 2 of the 67 acromegalic patients had a thyroid cancer neoplasia and a colonic adenocarcinoma. Metabolically, 15% of the patients had diabetes mellitus Radiologically, a macroadenoma was found in 83.5% of cases, a microadenoma in 13.43% of cases. Hyperplasia was noted in one patient. In one case the pituitary gland was normal and the etiological investigation in search of an ectopic secretion was negative.

**Conclusion**

Our results agree with the data described in the literature, although acromegaly is more frequent in women. An early diagnosis is necessary in these acromegalic patients.

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**EP846**

**Case report: Kallmann syndrome associated with a non-functional pituitary microadenoma**

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**Introduction**

Kallmann syndrome (KS) is a rare disorder. It is now designated as olfactogenital dysplasia with an association between agenesis of the olfactory bulbs and hypogonadism. The association of KS with a pituitary microadenoma has not been well described in the literature.

**Case report**

It’s a 16-year-old and 6 months, admitted for evaluation of a micropenis, he has as ATCDS an orchidopexy performed at the age of 3 years, infertility in the maternal uncle. During the interrogation a growth retardation was noticed from childhood, anosmia since the age of 7 years. The clinical examination revealed a a eucnachoid body proportion Body mass index (BMI) of 24.52 kg/m², gynecomastia without galactorrhea. Tanner scale: G1P2. He had micropenis (stretched phalalus length 3.5 cm). Hormonal assays identified a hypogonadotropic hypogonadism profile with total testosterone 0.58 ng/ml, luteinizing hormone 0.1 IU/ml and follicle-stimulating hormone 1 IU/ml, prolactin (PRL) and the cortisol blood test are within normal limits. She had normal Thyroid function Karyotyping showed 46XY pattern. MRI of the brain showed hypoplasia of the olfactory bulb, especially on the left. MRI also revealed a 4 mm pituitary microadenoma.

Androgen replacement is planned for patient.

**Discussion**

We report a case of a rare association of KS with a non-functional pituitary microadenoma. KS is an isolated form of hypogonadotropic hypogonadism in combination with a defect in sense of smell. It is due to defects in olfactory structures (bulbs, grooves, tracts) and altered migration of GnRH-secreting neurons into the preoptic and hypothalamic regions. The patient’s clinical presentation seems to be concordant in the literature, with the classical association of hypogonadotropic hypogonadism and anosmia. MRI is highly valuable in evaluating suspected KS. Data suggest that, in hypogonadotropic hypogonadism, MRI being a non-irradiating technique, should be the first radiological step for investigating the pituitary gland as well as abnormalities of the ethmoid, olfactory bulb and tracts. The central finding in the present case is the MRI finding of a non-functioning pituitary microadenoma in association with KS. This association has been previously reported by Bola et al. in their MRI assessment of 120 male patients with idiopathic hypogonadotropic hypogonadism.

**Conclusion**

Olfactory MRI imaging may aid in the diagnosis of KS in patients with suggestive clinical findings. Pituitary adenoma is a rare association with the KS. This emphasizes the need to image the pituitary region in KS patients to assess for hypoplastic pituitary malformations or adenomas incidentaloma.

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**EP847**

Acromegaly revealed by pituitary apoplexy : a case report About 2 cases

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**Introduction**

Pituitary apoplexy is a rare endocrine emergency that can occur due to pituitary infarction or hemorrhage. There are conflicting data regarding the type of pituitary adenoma prone to apoplexy. Prolactinomas seem to have the highest risk. We report 2 cases of apoplexy of a somatotopic adenoma not medically treated.

**Case 1**

Patient aged 45 years, with a history of chronic headaches, hospitalized in the emergency room for management of a meningeal syndrome with violent headaches associated with vomiting, a significant decrease in visual acuity, exophthalmos and ptosis of the left eye. The patient was treated with antibiotics and underwent a brain scan which returned normal. In front of the observation of a dysmorphic syndrome typical of acromegaly, she was referred to the endocrinology department where the diagnosis of acromegaly was confirmed biologically, the pituitary imaging revealed a necrotic pituitary adenoma. The evolution was marked by a recurrence of the macroadenoma 6 years later.
EP847
Chronic diarrhea: the diagnostic process
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Introduction
Neuroendocrine tumors (NETs) are a heterogeneous group of rare neoplasms that originate from endocrine cells with the ability to secrete amines and hormonal polypeptides. Pancreatic neuroendocrine tumors (PNETs) can be functional or non-functional. Functional PNETs secrete common hormones such as gastrin, insulin and glucagon and much less frequent hormones such as vasoactive intestinal peptide (VIP). Their clinical characteristics depend on the peptide secreted. It is estimated that up to 10% of all PNETs being associated with MEN1.

Case report
We present the case of a 45-year-old woman who came to the emergency department with diarrhea, dehydration and electrolyte disorders (severe hypokalemia and hypercalcemia). The patient reported ~5 daily episodes of diarrhea without mucus or blood for 7 months while the last month she mentioned an increase to ~15 daily episodes of diarrhea with fatigue, polydipsia and polyuria. Due to the hypercalcemia, further testing was compatible with the diagnosis of primary hyperparathyroidism. 99 Tc-sestamibi scanning for diagnostics in a population of patients with the sporadic and family IAH anamnesis. Objective was to study features of clinical semiology, their value for differential diagnostics in population of patients with the sporadic and family IAH anamnesis.

Conclusion
We report the case of a 60-year-old female patient with secondary amenorrhea at the age of 38 years, neglected and never explored, and who installed after surgery for intestinal obstruction on colonic tumor, a polypus with polydipsia with 4 nocturnal awakenings and estimated input-output of 4 liters per day. The first-line workup was without abnormalities. The hypothalamic-hypophyseal MRI showed a 17 x 13 mm tumor that corresponds to a craniopharyngioma. This craniopharyngioma was complicated by a panhypopituitarism with 8 clock cortisol : 15 ng/ml, FT4 : 0.63 mUI/ml and hypogonadotropic hypogonadism profile with low FSH, LH and estradiol. The patient was put on Desmopressin with a good improvement of the polyuro-polydipsic syndrome. She was also put on Hydrocortisone and Levophyroxine.

Discussion and conclusion
Craniopharyngioma is a benign, slow-growing epithelial tumor of embryonic origin, originating in the pituitary stem or pituitary gland and developing in the sellar and/or suprasellar region. It is characterized by its considerable potential for extension, its tendency to recur, and its adhesions to surrounding structures.

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EP850
Polyuoro-polydipsia syndrome revealing a craniopharyngioma in a 60-year-old female patient following a surgery
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Introduction
Cranioopharyngioma is a benign, slow-growing epithelial tumor of embryonic origin, originating in the pituitary stem or pituitary gland and developing in the sellar and/or suprasellar region. It is characterized by its considerable potential for extension, its tendency to recur, and its adhesions to surrounding structures.

Case report
We report the case of a 60-year-old female patient with secondary amenorrhea at the age of 38 years, neglected and never explored, and who installed after surgery for intestinal obstruction on colonic tumor, a polypus with polydipsia with 4 nocturnal awakenings and estimated input-output of 4 liters per day. The first-line workup was without abnormalities. The hypothalamic-hypophyseal MRI showed a 17 x 13 mm tumor that corresponds to a craniopharyngioma. This craniopharyngioma was complicated by a panhypopituitarism with 8 clock cortisol : 15 ng/ml, FT4 : 0.63 mUI/ml and hypogonadotropic hypogonadism profile with low FSH, LH and estradiol. The patient was put on Desmopressin with a good improvement of the polyuro-polydipsic syndrome. She was also put on Hydrocortisone and Levophyroxine.

Discussion and conclusion
Craniopharyngioma is a rare and benign epithelial tumor of the central nervous system, affecting mostly children. It is rarely observed in adults. Its diagnosis remains late despite the development of imaging techniques resulting in significant morbidity and poor survival. This is why it is essential to take each symptom seriously.

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EP849
Features of a clinical flow and diagnostics of patients with the family amanessis of inactive adenomas of hypophysis (IAH)
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Objective was to study features of clinical semiology, their value for differential diagnostics in population of patients with the sporadic and family IAH anamnesis.

Materials and methods.
71 IAH patients with intracellar adenoma of a hypophysis. Patients with IAH were divided into two alternative groups: the 1st group - 50 (70.4 %) patients with environmental factors without the burdened family anamnesis and 2nd - 21 (29.6 %) with the burdened family anamnesis, including with a panmmiksiya - 9 (2.7 %) and an inbriding - 12 (16.9 %) patients. Average patients age was 18-70 years (44.5±3.85 years). At the same time the greatest number of the arrived IAH patients to fall on age from 35 (23.9 %) to 40 (25.4 %) years and to a lesser extent be elderly to 30 (18.3 %) and 55 (9.6 %) and is more than years that will be coordinated with literary data. It should be noted that at patients of 2-group with hereditary IAH signs is more often than patients of 1-group - without hereditary signs prevail frequency of clinical signs, such as sexual violations - 26.5 %, decrease in sight - for 40.2 %, headaches - for 26.5 %, doubling in eyes - for 15.0 %, visual discomfort - for 12.5 %, olfactory violations - for 19.8 %, vegetative crises - for 12.3 %, duration of a disease among women 5-20 years - for 12.3 and 24.6 %, but to a lesser extent till 20 and more than 21 years - for 23.2 and 15.2 %, and among men of such difference it is not revealed. Frequency of complaints in 1-group on visual violations it is revealed, decrease in visual acuity at IAH patients with a tumor to 10 mm at 10 % surveyed, to 20 mm - 70.0 %, with huge - 100 %, at patients of 2-groups - 50.0 %, 87.5 % and 72.7 %. At patients with the family it is IAH the main clinical symptoms of a disease associate: visual, sexual, headaches, vegetative crises, climax come aged till 20-25 years, and time of establishment of the diagnosis - 10-20 years. - adenomas > 10 mm which progress quicker, in huge adenomas, with the heavy course of a disease more often come to light, than at patients from the single is IAH - the IAH family form and development of clinical symptoms at early age should be object of diagnostic screening.

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EP848
Chronic diarrhea: the diagnostic process
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Introduction
Neuroendocrine tumors (NETs) are a heterogeneous group of rare neoplasms that originate from endocrine cells with the ability to secrete amines and hormonal polypeptides. Pancreatic neuroendocrine tumors (PNETs) can be functional or non-functional. Functional PNETs secrete common hormones such as gastrin, insulin and glucagon and much less frequent hormones such as vasoactive intestinal peptide (VIP). Their clinical characteristics depend on the peptide secreted. It is estimated that up to 10% of all PNETs being associated with MEN1.

Case report
We present the case of a 45-year-old woman who came to the emergency department with diarrhea, dehydration and electrolyte disorders (severe hypokalemia and hypercalcemia). The patient reported ~5 daily episodes of diarrhea without mucus or blood for 7 months while the last month she mentioned an increase to ~15 daily episodes of diarrhea with fatigue, polydipsia and polyuria. Due to the hypercalcemia, further testing was compatible with the diagnosis of primary hyperparathyroidism. 99 Tc-sestamibi scanning for...
Reproductive and Developmental Endocrinology

EP851

Eunuchoid skeletal proportions in male hypogonadism: a comparative analysis of anthropometric measures between men with congenital hypogonadotrophic hypogonadism (CHH) and Klinefelter Syndrome (KS)

Sara De Vincentiis1,2,3, Rossella Corleto1,2, Alessio Bellelli1,2, Soran1, Abigail Knell1, Tharu Tharakan2, Axel Cayetano-Alcaraz2

Background
Patients with CHH and KS have eunuchoid body proportions of the skeleton compared to normal male subjects, characterized by tall stature, and reduced upper-to-lower segment ratio (U/l). V ice versa, steroids exposure deeply differs between CHH and KS at puberty, with both testosterone and estradiol being very low only in CHH. At present, body skeletal proportions comparison between CHH and KS is not available.

Aim
To compare anthropometric measurements of adult male CHH patients to adult KS patients.

Methods
A prospective, cross-sectional, observational study was carried out. CHH patients were subdivided into 2 subgroups according to the timing of treatment start (testosterone replacement therapy [TRT] or gonadotropins): CHH1 CHH patients who started treatment late after 18 years; CHH2 CHH patients who started treatment on time before 18. All KS patients did not start TRT before 18 since KS do not usually delay puberty. The following anthropometric measurements were collected by using a digital scale and stadiometer (Seca gmbh&co®): height, weight, sitting height, total arm span. Legs length was obtained by subtracting sitting height from stature; U/l was calculated dividing sitting height for legs length.

Results
A total of 70 CHH and 45 KS age-matched patients were enrolled (mean age 33.7±13.7 and 33.5±13.7 years, respectively). CHH1 showed a longer arm span compared to CHH2 (P=0.001) and KS (P=0.003), and a shorter sitting height compared to KS (P=0.008). On the contrary, legs length was shorter in CHH2 compared to CHH1 (P<0.001) and KS (P=0.011). Accordingly, U/l and upper-to-height ratios were lower in CHH1 compared to CHH2 (P<0.001) and KS (P=0.0001). Furthermore, the arm span-to-height ratio was higher in CHH1 compared to CHH2 (P<0.001) and KS (P=0.008).

Conclusions
Under the same definition of eunuchoid body proportions, the traditional hallmark of male hypogonadism, more fine differences are observed comparing adult CHH to KS patients. CHH patients who delayed treatment showed longer arm length and lower U/l in comparison to CHH patients receiving treatment on time at pubertal age and KS. This suggests a different mechanism involved in the eunuchoid skeletal development between CHH1 and KS confirming a major role for estrogren/androgen deficiency in the former (leading to disproportional growth of both legs and arms due to delay in epiphyseal closure that could benefit from on time replacement treatment) and a possible role of genetic supernumerary X in the latter, displaying a disproportional growth only at the legs site since infancy.

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EP852

Investigating the prevalence of hypogonadism and associated cardiovascular risk of males presenting with infertility: Results from a diverse and multi-ethnic UK patient cohort

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Background
Hypogonadism is estimated to account for over 10% of male-factor infertility. However, due to conflicting data regarding the relationship between testosterone levels and sperm quality, hormone evaluation is not consistently requested during initial assessment of the infertile male. Hypogonadism is associated with cardiovascular disease (CVD) and has been linked to an increased risk of mortality. The aim of this study was to investigate the prevalence of hypogonadism and cardiovascular risk in a cohort of infertile men.

Methods
This was a single-centre retrospective analysis of all patients presenting with male-factor infertility between January 2015 and December 2020. Biochemical hypogonadism was defined as a morning serum testosterone level <10 nmol/l according to local reference range. Semen analyses were compared between hypogonadal and eugonadal males. Lipid-profiles were compared between both cohorts. Patient demographic and clinical data were used to calculate the Charlson Comorbidity Index (CCI) and QRISK2 scores.

Results
Of 855 patients, hypogonadism was present in 284 (33.22%) of patients. The median (IQR) testosterone level in eugonadal males was 15.5 (12.7-20.68), compared to 7.3 (5.25-8.60) in hypogonadal males (P<0.0001). A significantly greater proportion of hypogonadal males were found to be azoospermic compared to eugonadal males (57.6% vs. 42.2%, P<0.0001). Moreover, eugonadism was more prevalent amongst patients from a White-Background (30.6% vs. 20.1%, < 0.0001). Whereas hypogonadism was more common amongst patients from an Asian-Background (22.5% vs. 12.6%, P<0.0001). Accordingly, median testosterone levels were significantly lower in Asian males compared to white males (10.3 vs. 13.5, P=0.000162). A higher BMI was observed in hypogonadal males compared to eugonadal males (28.9 vs. 26.4, P<0.0001) and had significantly higher serum cholesterol (5.00 vs. 4.7, P=0.031), triglycerides (1.73 vs. 1.09, P<0.0001) and non-HDL cholesterol (3.90 vs. 3.49, P=0.001) compared to eugonadal males. However, HDL-Cholesterol levels were higher in males with normal testosterone (1.06 vs. 1.25, P<0.0001). Median QRISK2 scores were significantly higher in hypogonadal males than eugonadal males (1.40% vs. 1.10%, P=0.0004). A significantly greater proportion of hypogonadal males had a CCI score of 1 compared to eugonadal males (15.1% vs. 7.2%, P=0.0002).

Discussion and Conclusions
This study demonstrated a high prevalence of hypogonadism within a cohort of infertile males compared to existing literature. Whilst an association between testosterone and sperm quality was not established, hypogonadism was shown to be associated with raised lipid parameters and an increased risk of CVD. All infertile men should undergo endocrinological evaluation and follow-up to mitigate the risks of dyslipidaemia and CVD.

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EP853

Hereditary syndromes in children with short stature

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Short stature is a clinical sign noted in genetic syndrome. Purpose

Molecular genetic characterization of children with short stature.

Methods
The study involved 7 patients 3-15 yrs (3 boys and 4 girls) with short stature. Full clinical and molecular genetic research (Whole Exome or Genome Sequencing) was conducted.

Results

SDS height was from -2 to -4. All patients had multiple stigmata of dysmorphismogenesis, autistic behavior disorders, mental and speech development delay. In boys KBG syndrome (heterozygous mutation in the ANKRD11 gene on chromosome 16q24), Wiedemann-Steiner syndrome (mutation in the KMT2A gene on chromosome 11q23.3), Coffin-Siris Syndrome, type VI (mutation in the ARID1A gene on chromosome 12q12) were diagnosed. In girls De Grouchy syndrome, Yunis–Varon syndrome (mutation in the FIG4 gene on chromosome 6q21) was diagnosed. Two children with pronounced skeletal deformities and growth retardation were diagnosed with Brooke’s syndrome.

Conclusion

Short stature in children combined with stigmata of dysmorphismogenesis, autistic behavior disorders, mental and speech development delay is it an indication for molecular genetic examination in order to diagnose rare genetic syndrome.

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EP854
The kiss of metabolism and reproduction: is kisspeptin the key?  
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Background
The relationship between energy balance and reproduction is U-shaped, meaning that both a negative and a positive energy balance have a detrimental effect on reproductive function. In a world increasingly burdened by the growing prevalence of obesity, we turned our attention to the negative extremity of weight, by exploring anorexia nervosa (AN) and constitutional thinness (CT) metabolic and reproductive features. Kisspeptin (kiss-1) is a relatively recently discovered neurohormone with implications in the onset of puberty, sex steroid metabolism, and brain sexualization. More recent data show a possible involvement of kisspeptin in the metabolic processes, with a role in regulating the homeostasis of blood glucose, insulinemia and appetite, as well as regulating fat deposits, but these still need confirmation in further studies.

Objectives
The aim of this study was to evaluate the particularities of the indicators of reproductive function and look for possible implications in this regard of the neurohormone kiss-1 in normal and underweight patients, with or without eating disorders such as AN. In particular, the study focuses on the role of kisspeptin in amenorrhea induced by dietary restriction in patients with AN.

Material and Methods
We included in this cross-sectional and observational study a cohort of 34 young female patients gathered in 4 similar-sized groups, as follows: AN and underweight, AN and normal weight, CT, and healthy, normal weight patients. Anamnestic, anthropometric and biological data were recorded, as well as the total fat percentage (TFP) data from the whole-body DXA scan.

RESULTS
Kiss-1 was significantly higher in patients with atypical AN subjects than in underweighted, typical AN patients (1.24±0.15 vs 0.96±0.17 ng/ml, P=0.03). No significant associations were found between kiss-1 levels and clinical-biological factors of reproduction, even though kiss-1 was significantly correlated with TFP throughout the cohort (P=0.03, r=0.365). Menses are significantly associated with the diagnosis of AN (r=0.625, P<0.001), weight (r=0.448, P=0.005), TFP (r=0.457, P=0.007) as well as with gonadotropins and thyroid hormones levels (FSH r=0.353, P=0.007, LH r=0.474, P=0.005, TT3 r=0.472, P=0.006, TT4 r=0.625, P<0.01).

Conclusions
Kiss-1 increases in atypical AN patients, who, despite their psychiatric diagnosis, have a normal weight and are not in such deteriorating physical health condition, probably in an attempt to maintain viable reproductive function for as long as possible. This result, together with the correlation of this neurohormone with TFP, sheds light on the involvement of kiss-1 in both reproductive and metabolic regulation of the study population.

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EP855
Maternal prolactin-levels in pregnancy and offspring body composition at 7 years. Odense Child Cohort  
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Background
Prolactin is associated with metabolic risk inside and outside of pregnancy. Maternal prolactin levels could be associated with offspring body composition.

Aim
To investigate if maternal prolactin-levels were linked to offspring body composition at 7 years of age.

Design
Prospective observational cohort study (the Odense Child Cohort).

Methods
Maternal fasting blood samples were assessed during 1st (prolactin) and 3rd trimester (prolactin and glucose). Prolactin ratio was defined as 3rd trimester/1st trimester prolactin. Offspring body composition at seven years of age was assessed by Dual-Energy X-ray Absorptiometry (DXA)-scan, BMI and waist circumference. A total of 854 mother-child-pairs were included. Gestational diabetes mellitus (GDM) was defined by WHO13-criteria (fasting glucose ≥5.1 mmol/l). Oral glucose tolerance test (OGTT) was performed around gestation week 28 in 180 women with risk factors for GDM and in 168 randomly included women. Multiple regression analyses investigated associations between maternal prolactin (continuous and quartiles) and offspring body composition stratified by offspring sex and models were adjusted for maternal age, parity and BMI.

Results
Median (quartiles) maternal age was 30 (27–33) years and pre-gestational BMI 24.5 (21.3; 26.5) kg/m². In boys (n=301), maternal prolactin-ratio (4th quartile) was positively associated with fat percentage (Adjusted β=0.09, P=0.02, and yxid fat percentage (Adjusted β=0.08, P=0.04). In boys born of mothers with risk of GDM (n=135), the association between maternal prolactin-ratio (4th quartile) and fat percentage (Adjusted β=0.13, P=0.026) and android fat percentage (Adjusted β=0.22, P=0.032) was attenuated. Maternal prolactin was not associated with body composition in girls.

Conclusions
Maternal prolactin-ratio was positively associated with fat percentage and android fat percentages in boys born of mothers at risk for GDM.

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EP856
Nijmegen breakage syndrome with unusual presentation: a case report  
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Introduction
Nijmegen breakage syndrome (NBS) represents a rare autosomal recessive disorder, characterized by severe chromosomal instability. It is caused by mutations in the NBN gene, which product, nibrin, belongs to the hMre11/hRad50 protein complex, critical for processing DNA double-strand breaks during mitotic and meiotic recombination. The hallmarks of NBS are growth retardation, microcephaly, premature ovarian failure (POF) in females, immunodeficiency and predisposition for malignancy.

Case report
A 9-year-old girl presented in the Department of Endocrinology Iasi with a history of two vaginal bleeding episodes and recurrent respiratory infections. Her clinical features were short stature (G=23 kg, T=127 cm, 1.78 SD >Sarcana), craniofacial dysmorphism with microcephaly, up-slaning palpebral fissures, long nose, sloping forehead, microglossia and Sutton’s nevi, no clinical signs for secondary sexual characteristics development, borderline intellectual ability, Biological tests were normal, but the hormonal assessment showed hypergonadotropic hypogonadism (increased FSH=69.9 µIU/ml and LH=13.3 µIU/ml and low estradiol < 20 pg/ml). The pelvic ultrasonographic (US) examination reveals small uterus and ovarian sizes, regardless of age, without ovarian follicles. The karyotype and MLPA for SHOX gene deletion were normal. The two episodes of vaginal bleeding were interpreted in a mild pelvic traumatic injury context (falling from the bicycle). Six months later, she developed extensive vitiligo lesions on her lower body. The suspicion for Nijmegen Breakage Syndrome was confirmed by the Sanger sequencing, which identified the mutation of the Nibrin gene (NBN) in exon 6: c.657_661delACAAA, in a homozygous state. When she was 12 years old, we started the treatment for pubertal induction with low doses of transdermic estradiol.

Discussions
NBS is caused by mutations in the NBN gene, which product, nibrin, belongs to the hMre11/hRad50 protein complex, critical for processing DNA double-strand breaks during mitotic and meiotic recombination. The hallmarks of NBS are growth retardation, microcephaly, premature ovarian insufficiency (POI) in females, immunodeficiency and predisposition for malignancy. Our case is an unusual presentation for the NBS – suspicion of precocious puberty with vaginal bleeding. In the literature, NBS is associated with premature ovarian failure. The pathomechanism of hypoplastic ovaries or streaks gonadal is explained by failure to form functional primitive germ cells. It is known that both a negative and a positive energy balance have a detrimental effect on reproductive function. In a world increasingly burdened by the growing prevalence of obesity, we turned our attention to the negative extremity of weight, by exploring anorexia nervosa (AN) and constitutional thinness (CT) metabolic and reproductive features. Kisspeptin (kiss-1) is a relatively recently discovered neurohormone with implications in the onset of puberty, sex steroid metabolism, and brain sexualization. More recent data show a possible involvement of kisspeptin in the metabolic processes, with a role in regulating the homeostasis of blood glucose, insulinemia and appetite, as well as regulating fat deposits, but these still need confirmation in further studies.

Objectives
The aim of this study was to evaluate the particularities of the indicators of reproductive function and look for possible implications in this regard of the neurohormone kiss-1 in normal and underweight patients, with or without eating disorders such as AN. In particular, the study focuses on the role of kisspeptin in amenorrhea induced by dietary restriction in patients with AN.

Material and Methods
We included in this cross-sectional and observational study a cohort of 34 young female patients gathered in 4 similar-sized groups, as follows: AN and underweight, AN and normal weight, CT, and healthy, normal weight patients. Anamnestic, anthropometric and biological data were recorded, as well as the total fat percentage (TFP) data from the whole-body DXA scan.

RESULTS
Kiss-1 was significantly higher in patients with atypical AN subjects than in underweighted, typical AN patients (1.24±0.15 vs 0.96±0.17 ng/ml, P=0.03). No significant associations were found between kiss-1 levels and clinical-biological factors of reproduction, even though kiss-1 was significantly correlated with TFP throughout the cohort (P=0.03, r=0.365). Menses are significantly associated with the diagnosis of AN (r=0.625, P<0.001), weight (r=0.448, P=0.005), TFP (r=0.457, P=0.007) as well as with gonadotropins and thyroid hormones levels (FSH r=0.353, P=0.007, LH r=0.474, P=0.005, TT3 r=0.472, P=0.006, TT4 r=0.625, P<0.01).

Conclusions
Kiss-1 increases in atypical AN patients, who, despite their psychiatric diagnosis, have a normal weight and are not in such deteriorating physical health condition, probably in an attempt to maintain viable reproductive function for as long as possible. This result, together with the correlation of this neurohormone with TFP, sheds light on the involvement of kiss-1 in both reproductive and metabolic regulation of the study population.

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Clinical and biochemical markers of premature ageing in young hypopituitary women with untreated hypogonadism

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Hypogonadotropic hypogonadism as a part of hypopituitarism can be a cause of persistent amenorrhea and hypofertrogeinemia in women of reproductive age as it is observed in postmenopause. We know that premature and early menopause leads to accelerated aging with such markers as decreased quality of life, phyco- emotional deprivation, dyslipidemia, bone mineral density and others. We hypothesized that untreated hypogonadism in young women with hypopituitarism could cause premature aging. Clinical symptoms, hormonal levels, lipid and mineral metabolism, BMI, BMD and quality of life (GHQ-28) were evaluated in young women with hypopituitarism (n=49, X±SD;31.1 y.o.), healthy age-matched young women (YW: n = 53, 24±23.28 y.o.) and middle-aged women with natural postmenopause (PM n = 50, 56±53.59 y.o.) were compared. Duration of amenorrhea and postmenopause was similar (median 5 and 6 years, P=0.9). Hypopituitarism group included patients with organic pituitary lesions, hypothryoidism and hypocortisolism were compensated. The prevalence of general, neurovegetative and psychoemotional symptoms was significantly higher in women with hypopituitarism than in YW though it was similar to PM. In contrast to YW the postmenopause vasomotor symptoms were observed less frequently in hypopituitarism. Concentrations of E2, T and DHEAS, total cholesterol, triglycerides, calcium and alkaline phosphatase as well as quality of life in women with hypopituitarism were not typical of YW but were comparable to PM. Frequency of increased BMI was higher in women with hypopituitarism (51%) than in YM (11%) and comparable to PM (48%). BMD in lumbar spine and femur was even lower in young patients with hypopituitarism than in postmenopausal women. Thus, clinical and biochemical abnormalities revealed in women with untreated hypogonadism at young age were similar in many aspects to those in postmenopausal women at middle/old age in spite of the age difference and various reasons for hypofertropenia. These findings could be considered as markers of premature ageing because the biological changes attributable to postmenopause occurred well in advance.

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Therapeutic management in transsexual women infected by VIH: a case study

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A 38-year-old transsexual woman, with no known drug allergies, active tobacco smoker, ICAT 2. As diseases of interest, stage A2 human immunodeficiency virus (HIV) infection with current negative viral load. Louis in 2012 treated. In treatment with Strid (elvitegravir 150 mg/ cobicistat 150 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 245 mg). She went to the Transsexual Persons Care Unit due to gender inconsistency since childhood with the adoption of the female role for years. She now expresses her desire to start hormonal and surgical treatment to try to accommodate her secondary sexual characteristics to the desired sex. After the directed anamnesis and carrying out of complementary tests according to the recommendations of the Assistance Process of Attention to Transsexual People in Andalusia, cross-hormonal therapy is started. Antiandro- genic treatment was prescribed with cyproterone acetate 50 mg/day and estrogenic treatment with estradiol valerate at progressive doses up to a final dose of 6 mg/day (maximum recommended dose). However, despite adequate adherence to treatment and the high doses of estrogen used, plasma levels of estradiol remained low. Given the suspicion of possible interaction between antiretroviral treatment and estradiol valerate, Internal Medicine was consulted, deciding to change treatment to Triumeq (dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg). Six months after the change in treatment, the target plasma estradiol levels were reached, even allowing the dose of estradiol valerate to be reduced to 4 mg/day. A prevalence of 19.1% of HIV-infected transsexual women is estimated. Several studies have associated the use of ritonavir-boosted protease inhibitors or cobicistat with a decrease in exogenous estrogen levels. The use of non-analog reverse transcriptase inhibitors (nevirapine, efavirenz) with decreased estrogen levels has also been described. Therefore, based on current evidence, the best option as antiretroviral treatment in transsexual women with cross-hormonal therapy could be a nucleoside reverse transcriptase inhibitor (such as abacavir, lamivudine) together with an integrase inhibitor (dolutegravir, raltegravir) without booster.

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EP860
A 20-steroid LC-MS/MS panel to investigate classical and backdoor pathways of androgen biosynthesis in the Leydig cells
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Background
The classical steroidogenic route to the synthesis of dihydrotestosterone in Leydig cells involves delta-5 and delta-4 precursors. Besides, the “backdoor pathway”, encompassing progesterone metabolites, is gaining increasing interest in fetal development and men pathophysiology. Nowadays, liquid chromatography/tandem mass spectrometry (LC-MS/MS) is the ideal technique to simultaneously quantify large panels of steroids with elevated sensitivity and specificity.

Aim
We developed and validated a LC-MS/MS method measuring 20 among androgens, precursors and metabolites pertaining to both the classical and the backdoor pathways in the steroidogenic mouse Leydig tumor cell line (mLTC1).

Methods
Steroidogenesis of serum-starved mLTC1 cells was induced by 100μM chorogonadotropin (hCG). Steroids released in 500μL cell medium were extracted with 2mL N-hexane:ethyl-acetate (8:2) spiked with 100μL internal standards in methanol. The organic phase was dried and samples were reconstituted with 100μL of 75% methanol before 10μL were analyzed. The platform included the Serie200 HPLC (Perkin Elmer) and the API-4000 QTrap (Sciex) operated in multiple reaction monitoring mode. 16O-Hprogesterone, 11-deoxycorticisol, 11-deoxycorticosterone (21OH-progesterone), testosterone, androstenediol, 17OH-progesterone, 17OH-pregnenolone, dehydroepiandrosterone, androstenedione, epitestosterone, dihydrotestosterone, 17OH-dihydroprogesterone, progesterone, androstanediol, androstanediol, pregnenolone, 5α-dihydroprogesterone, 17α-Hprogesterone, 11-deoxycorticisol and allopregnanolone were separated in 13-min gradient operated on a Luna C8 100x3 mm, 3 Å column, equipped with 4x2.0 mm guard column (Phenomenex), termostated at 45°C, using 100μM ammonium fluoride and methanol as mobile phases. Analytes were revealed by quantitative and qualitative transitions and quantified by isotopic dilution.

Results
Isobaric compounds were separated to ensure selectivity. The dynamic range was between 3 and 5 orders of magnitude. Functional sensitivity was between 0.012 and 38 nmol/L. Intra-assay and inter-assay imprecision and trueness, valued at low, medium and high levels, were below 9.1 and 10.0%, and within 93.4-122.0%, respectively. Recovery and matrix factor were within 55.6-101.4% and 76.4-106.3%, respectively. Levels (nmol/L) of 16H-progesterone (20.7 ± 4.2), 11-deoxycorticisol (0.924 ± 0.115), androstenediol (727 ± 89), 11-deoxycorticosterone (3.69 ± 1.9), testosterone (52.8 ± 10.1), 17OH-pregnenolone (0.58 ± 0.75), androstanediol (774 ± 164), epitestosterone (26.1 ± 4.4), dihydrotestosterone (9.61 ± 2.51), progesterone (4.79 ± 0.60), androstanediol (379 ± 80) and 17OH-allopregnanolone (4.30 ± 0.58) were within the measurement range. Levels of 17α-Hprogesterone (0.844 ± 0.107), androstanediol (21.5 ± 5.9) and 5α-dihydroprogesterone (0.791 ± 0.136) were slightly above the limit of detection, whereas other compounds were undetectable.

Conclusions
We validated a LC-MS/MS method including a broad number of androgens, precursors and metabolites. Medium secretion levels from mLTC1 cells were measured effectively for most of the steroids, however, levels of some neutral and delta-5 steroids were below method’s sensitivity. Nonetheless, we provided a powerful tool to simultaneously characterize the gonadal classical and backdoor steroidogenic pathways.

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EP861
Associations of serum AMH levels and hormonal, metabolic and cardiovascular parameters in adult men
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Background
Anti-Müllerian hormone (AMH) is well known for its association with ovarian follicular count and ovarian reserve in general as well as for its recruitment of primordial follicles in women. With an explicit decrease in menopause, it is mainly used for clinical questions from in-vitro-fertilisation to polycystic ovary syndrome. Interestingly, AMH levels in men are quite high during lifetime, but there is only few data about its relevance and potential effects in adult men. The aim of our study was to investigate and describe AMH levels in men in association with a number of hormonal, metabolic and cardiovascular parameters and whether there are links to physiological or pathophysiological functions.

Methods
We analysed data from the BioPersMed cohort (Biomarkers for Personalized Medicine), a prospective cohort of asymptomatic subjects at cardiovascular risk.

Clinical parameters, past medical history, AMH, hormonal profiles including androgens, fasting glucose and insulin values as well as oral glucose tolerance tests, lipid measurements including high-density lipoprotein (HDL) and low-density lipoproteins, inflammation markers such as C-reactive protein (CRP) and others were assessed as well as anthropometric parameters, DXA(dual energy X-ray absorptiometry)-derived body composition.

Results
Out of n = 1022 healthy volunteers, we identified 389 men (38% of the cohort) with an age 58 ± (-9 years. While AMH was BMI-dependent (P = 0.0113), and decreased slightly with age (P = 0.03), it was inversely associated with pituitary hormones LH (luteotropic hormone, P = 4.5e-5) and FSH (follicle stimulating hormone, P = 1.6e-10). The highest AMH quartiles showed an inverse association with C-peptide, but also HDL, while androgens or SHBG were not significantly different between groups, in contrast to pronounced differences of these parameters according to BMI categories.

Conclusion
AMH in men is an interesting, however neglected biomarker with a number of potential associations with hormonal, but also metabolic and potentially cardiovascular risk profiles. Its clinical value has to be determined in follow-up studies, but AMH in men might become an important health marker and needs further investigation.

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EP862
Hormonal profile in idiopathic male infertility
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Male infertility arises as a global public health in the context of the dramatic decrease in birth rates, within a complex picture of hormonal, genetic and epigenetic factors. However, the underlying causes of male infertility remain unknown in many cases. Our study included samples (n = 82, median: 34 years, range 20–55 years) obtained from men investigating couple infertility and from a normal control group (n = 11, median: 29 years, range 21–55 years). Blood and seminal fluid were harvested after 3–5 days of sexual abstinence. Hormonal profile was evaluated, including FSH, LH, testosterone, estradiol, inhibin B and prolactin. Exclusion criteria: Radiotherapy and/or pelvic chemotherapy (over the last 6 months), known genetic aberrations, endocrine diseases, urogenital infections, bilateral orchectomy, vasectomy and occupational exposure to harmful organophosphorous hydrocarbons, ionizing radiation, heavy metals.

Inclusion criteria: spemmic parameters according to WHO 2010 Standards (Word Health Organization, 2010). The infertile group was divided in three subgroups: azoospermia (AZO n = 23), oligoasthenozoospermia/severe oligoasthenozoospermia (OAS/AZOSS n = 14), oligoasthenoteratozoospermia/severe, oligoasthenoteratozoospermia (OAT/SATSS n = 41). The analysis of hormonal profile displayed statistically significant differences for FSH (P = 0.0003), LH (P = 0.0092), prolactin (P = 0.0434), and inhibin B (0.0003). Moreover, a significant difference between azoospermia and control group was noted regarding FSH/E2 ratio (median: 0.4532 ± 0.152; P = 0.00163). A similar
pattern was displayed by the FSH/E2 ratio between subjects with < 1 million spermatozoa/ml and control group (median: 0.420 vs 0.152; P = 0.00174). The motility/E2 ratio was significantly lower in the azoospermia group compared to the control group (median: 0.000 vs 2.064; P = 0.0034). Sperm concentration/E2 ratio displayed a significant difference between the selected groups vs the control group (median: Azo-0; OAS/OASS-63328; OATS-70998; control-1455000).

Investigating the LH/T and T/LH ratio, it was observed a significant difference between azoospermia and control group (median: 2.207 vs 1.097, P = 0.0094; respectively median: 0.373 vs 0.912; P = 0.0388). Subtle imbalances of reproductive hormones levels, revealed by disturbed evaluated ratios might be one of the causes of inappropriate sperm production mechanism. It appears that estrogen activity as reflected in the investigated ratios, is important with regards to proper fertility in males, since the spermatogenesis is modulated by estrogen at the level of HPG axis. In conclusion, investigated ratios could serve as a potential instrument in the diagnosis and management of male infertility, since these hormones cooperate to maintain the semen quality, stability and feedback control of the system.

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**EP863**

Does iron homeostasis influence gonadal axis in men with obstructive sleep apnea?

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Introduction
Obstructive sleep apnea syndrome (OSAS) is characterized by chronic inflammation. Hepcidin is an acute-phase protein involved in iron metabolism. Increase in hepcidin has been shown in OSAS. Testosterone probably exerts inhibitory effect on hepcidin levels and even trans iron and inflammation-mediated mechanism in chronic inflammatory state. On the other hand iron balance may influence gonadal axis. The aim of this study was to assess whether hypogonadism in OSAS could be associated with iron metabolism.

Material and Methods
We recruited 92 males. Mean age was 61 years old. Sixty nine were diagnosed with OSAS, based on polysomnography. This group was divided into two subgroups. First comprised of 45 eugonadal men (g1), while the second included 24 hypogonadal patients (g2). Control group consisted of 23 patients with normal testosterone levels and normal sleep pattern (g3). We measured multiple parameters, among them: serum testosterone, LH, CRP, insulin levels and iron balance parameters.

Results
We have found significant differences in testosterone (g1 > g2, g3 > g2; P < 0.0000), iron (g1 > g3, g2 > g3; P = 0.0378), CRP (g2 > g3; P = 0.0389), BMI (g1 > g3, g2 > g3; P = 0.0065), insulin (g2 > g1 > g3; P = 0.0153) and hemoglobin (g3 > g1, g2 > g3, P < 0.0000) between groups. There was a tendency toward statistically significant difference in hepcidin levels (g1 > g2, g1 > g3; P = 0.0513). On linear regression in a whole group testosterone level was inversely associated with hepcidin (P = 0.0152; β = -0.1804), insulin (P = 0.0024; β = -0.1409) and BMI (P = 0.0042; β = -0.3589). On multiple regression BMI and hepcidin were independent factors negatively influencing testosterone levels (P < 0.0009).

Conclusion
Changes in testosterone in men with OSAS might be at least partially attributed to hepcidin concentration. Metabolic factors such as insulin and BMI negatively influence gonadal axis. The exact mechanism of potential mutual relationship between iron homeostasis and gonadal status in men with OSAS remains to be elucidated.

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**EP865**

A new, accurate and time-saving, two-step intracavernosal injection procedure to diagnose psychological erectile dysfunction

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Background
The recognition of the erectile dysfunction (ED) pathogenesis is essential to identify the appropriate ED management. Since vascular ED (vED) could be a manifestation of a systemic arterial damage, the watershed in the ED diagnostic framework is the discrimination between psychological (pED) and vED. However, reliable tools to directly diagnose pED are currently lacking.

Aim of the study
To identify which parameters could predict pED. Moreover, we suggest a new intracavernosal injection (ICI) procedure to optimize the ED diagnostic work-up.

Methods
A retrospective, real-world analysis was carried out including all men who underwent ICI procedure at the Andrology Unit of Modena (Italy) from 2018 to 2021. Data about previous medical history and ED characteristics were collected. A first ICI procedure with 5 µg of prostaglandin E-1 (PGE-1) was performed. In
Effect of testosterone on body composition - randomised placebo-controlled study in hypogonadal men with uncontrollable type-2 diabetes

Objective
The objective of the study was to assess the effect of intra-muscular testosterone on body composition in men with hypogonadism and poorly controlled type 2 diabetes.

Research design and methods
This is a randomised double-blinded placebo-controlled add-on trial of intramuscular testosterone undecanoate administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase 1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase 2 was an open-labelled phase for 6 months and patients on placebo moved randomly assigned to either treatment or placebo arm for 6 months of TRT. Patients in the treatment group continued. Body composition was measured by dual energy X-ray absorptiometry (DEXA scan).

Results
Mean age of the cohort was 59 years. Baseline characteristics were comparable between active/placebo groups. Only 48 patients had DEXA scans both at baseline and at 6 months. Limb fat mass and percentage fat significantly correlated strongly and inversely with total testosterone(TT), calculated free testosterone (cFT) and bioavailable testosterone(cBT) and there was no correlation with limb lean mass. There was strong inverse correlation between total fat mass, total fat percentage and truncal fat percentage with TT, cFT and cBT(P<0.05). Truncal fat mass correlated inversely with TT and cBT but did not correlate significantly with cFT. There was no significant correlation between lean mass and TT, cFT or cBT. These correlations remained significant after correcting for age, BMI and SHBG in linear regression model. There was a significant reduction in left leg fat mass after 6 months of TRT. There was no significant difference in either the fat mass or lean mass between the active and placebo group elsewhere including truncal area. There were no significant changes in either fat or lean mass before and after 12 months of treatment with testosterone in the active group.

Conclusions
Testosterone levels strongly and inversely correlates with fat mass and has no correlation with the lean mass. There was significant reduction in left leg fat mass after 6 months of TRT. There were no significant changes in any other body composition at 6 or 12 months and it suggests that these changes may take more than a year to show positive changes.

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The FSH administration to men with idiopathic infertility improves sperm DNA fragmentation index together with testosterone serum levels increase

Objective
The background is that FSH is regulated in both men and women, but little is known about its role in spermatogenesis. The aim of this study was to determine whether FSH administration improves sperm DNA fragmentation index and testosterone serum levels in men with idiopathic infertility.

Methods
A prospective, observational study was conducted on 201 infertile men who presented to our fertility center with a primary夫妇 infertility for more than 1 year. The patients were randomly assigned to receive either FSH or placebo for 12 months. The primary outcome measure was the percentage of sperm with DNA fragmentation index below 50%. Secondary outcomes included sperm count, motility, morphology, and testosterone levels.

Results
Out of the 201 patients, 106 were treated with FSH and 95 were treated with placebo. The percentage of sperm with DNA fragmentation index below 50% was significantly higher in the FSH group compared to the placebo group (P<0.001). There was also a significant increase in sperm count, motility, and morphology in the FSH group compared to the placebo group (P<0.05). Testosterone levels were also significantly higher in the FSH group compared to the placebo group (P<0.05).

Conclusions
These findings suggest that FSH administration can improve sperm DNA fragmentation index and testosterone serum levels in men with idiopathic infertility. Further studies are needed to determine the long-term effects of FSH administration on fertility outcomes.

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efficacy are still far from being detected. While pregnancy rate remains the strong outcome in couple infertility management, the identification of reliable, and possibly early, markers of therapeutic response to FSH in males is mandatory. Randomized controlled clinical trials (RCTs) on the topic focused, on the seminiferous component, not considering the potential involvement of the testosterone-secreting compartment.

Aim of the study
The evaluation of the potential relationship between testosterone serum levels and semen quality measured through sperm DNA fragmentation (sDF) index before and after FSH administration in male idiopathic infertility.

Methods
A retrospective post-hoc re-analysis was performed on raw data of RCTs in which idiopathic infertile men were treated with FSH and both testosterone serum levels and sDF were reported among primary and/or secondary endpoints. Additional data regarding couple infertility history, age, anthropometric variables, FSH treatment scheme and semen variables were included in a single dataset.

Results
Two RCTs (Colacurci et al. 2016 and Simoni et al. 2016) were included accounting for 148 patients (median age 37, 25-52 years). After three months of FSH administration, a significant increase was observed in FSH levels (P<0.001), inhibin B (P=0.012), sperm concentration (P=0.003), total sperm number (P=0.021), progressive motility (P<0.001) and normal sperm morphology (P<0.001). Moreover, an overall sDF index reduction was confirmed after treatment (P=0.002). SDF resulted significantly inversely related to sperm concentration both at baseline and after FSH treatment (Rho -0.325, P<0.001 and Rho -0.316, P=0.001, respectively). Interestingly, sDF index after treatment showed a significant inverse correlation with testosterone serum levels (Rho -0.327, P=0.002). Multivariate stepwise linear regression analyses using sDF index as dependent variable identified testosterone as a predictor for sDF index change (P=0.005). Similarly, logistic regression analysis highlighted testosterone and SHBG levels as predictive of sDF reduction after FSH administration (P=0.043 and P=0.005, respectively).

Conclusion
Combining raw data of published RCTs investigating FSH administration to idiopathic infertile men, a significant improvement of conventional semen parameters together with a reduction in sDF were confirmed. Intriguingly, a potential correlation between testosterone serum levels and sDF was highlighted for the first time, opening a completely unexplored way in the identification of potential early predictors of FSH therapy response in male idiopathic infertility.

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EP869
Procoagulant imbalance in male hypogonadism and effect of short-term testosterone replacement therapy
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Introduction
The effects of testosterone on coagulation have not yet been clarified. In particular, it is still controversial whether male hypogonadism, or testosterone replacement therapy (TRT), may slightly increase the risk of venous thromboembolism, in particular during the first months of therapy. This study aimed to assess the hemostatic balance in hypogonadal men before and after short-term TRT, compared to healthy controls.

Methods
Thrombin generation assay (TGA) was performed in 38 hypogonadal men (10 primary hypogonadism, 19 organic central hypogonadism, 9 functional hypogonadism) at baseline (ETP 217±3.288 nM/min) and during TRT (2166±3.301 compared to controls (1947±2.73, P<0.001 and P=0.001), with no significant change over 6 months in hypogonadal patients (P=0.82). Similar results were observed when thrombomodulin was added to TGA. The ETP-ratio was comparable in hypogonadal patients before (0.68±0.23) and after TRT (0.68±0.20, P=0.73), and in controls (0.61±0.20, P=0.17 and P=0.13). Thrombin peak did not change from baseline to six months (P=0.29); however, it was significantly higher than controls only at baseline (P=0.03). ETP was inversely associated with total testosterone concentrations at baseline (r=-0.44, P=0.008) but not when on TRT.

Conclusion
A procoagulant imbalance is observed in hypogonadal men. This does not appear to involve the FVIII-PC axis and is not modified by short term testosterone therapy. Further studies are needed to clarify which coagulation factors drive the procoagulant imbalance, whether longer TRT can normalize it, and if platelets or endothelial cells are affected as well.

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EP870
Combined omic analysis revealed autism-linked NLGN3as new candidate gene associated to GnRH neuron development and disease
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References

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EP871

Endometrial cell-type-specific disease signatures and endometrial organoids in polycystic ovary syndrome

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Introduction

Polycystic ovary syndrome (PCOS) is the leading cause of female infertility and is associated with high degree of comorbidities including type 2 diabetes and endometrial cancer. Hyperandrogenemia is a hallmark of PCOS and contributes to endometrial-related dysfunctions, including implantation failure and miscarriage. Whether cellular heterogeneity contributes to the functioning of the endometrium is not previously studied. Therefore, the aim is to reveal cell-type-specific disease signatures in the endometrium in women with PCOS at the single-cell level and to validate the role of molecular targets in endometrial organoids (EOs).

Method

Single nuclei were extracted from frozen endometrial biopsies collected from women with PCOS (n = 12) and healthy controls (n = 5) at cycle day 7-10. The nuclei RNA libraries were prepared following the 10x genomics protocol allowing us to sequence ~10,000 cells per sample and ~20,000 reads per cell. Sequencing data is processed using Cellranger count for further data integration, quality control and analysis with the Seurat package. In parallel, 3-dimensional (3D) EOs are established from fresh endometrial biopsies that are enzymatically digested and collected at cycle day 7-10. The cells are resuspended in Matrigel droplet and organoids are generated and maintained in a defined medium. Following several passages, EOs are cryopreserved to create a biobank to be used for future functional analyses of identified molecular targets by single-cell RNA-sequencing, immunofluorescence microscopy and Seahorse metabolic analysis.

Results

Single-nuclei were extracted from 17 endometrial samples, 12 from women with PCOS and 5 from healthy controls for 10x snRNA-sequencing. Our initial bioinformatic analyses show that the endometrial tissue of women with PCOS has a distinct single-cell transcriptomic profile, with cell-type specific differentially expressed genes that differ from the healthy controls. The EO protocol has been established and EOs from four women with PCOS have been cryopreserved with cell-type specific differentially expressed genes that differ from the healthy controls.

Conclusion

This rigorous mapping of endometrial tissue samples will increase the understanding of the cellular complexity and dysfunction and will be linked to phenotypic features in women with PCOS. By successive formation of 3D PCOS-EOs, we can further study cellular and molecular mechanisms causing PCOS-specific endometrial dysfunction.


EP873

Gender affirming hormonal treatment in Danish transgender persons. A nationwide register-based study

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Background

Gender affirming hormonal treatment (GAHT) is for many a cornerstone of transgender care. National data regarding use of hormonal treatment by transgender persons are limited.

Aim

To assess use of GAHT in transgender persons. Design

National register-based cohort study in Danish transgender persons followed from 2000 until 2018. The main outcome measure was redemption of GAHT. Persons with an ICD-10 diagnosis code of “gender identity disorder” (CGI-cohort) and persons with legal sex change but without diagnosis (CPR-cohort) were included. In the CGI-cohort, transgender women were defined by prescription of estrogen and/or antiandrogens and transgender men were defined by prescription of testosterone after study inclusion. Discontinuation of GAHT was defined as no


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redemption of GAHT ≥ 13 months or shift from feminizing to masculinizing hormone treatment, or vice versa.

Results
The cohort included 2770 transgender persons (n = 1700, CGI-cohort and n = 1070, CPR-cohort). The median age (interquartile range) at study inclusion was 26.0 (17.3) years for persons assigned male at birth (n = 1437) and 22.5 (10.4) years for persons assigned female at birth (n = 1333). In the CGI-cohort, the redemption rate for GAHT in transgender women increased from 4.0 (95% CI: [3.1; 5.2]) events per 100 person in year 2000-2005 to 20.5 [17.7; 23.6] between 2014 -2018. In transgender men, the event rate of GAHT increased from 4.2 [2.8; 6.2] to 18.9 [16.4; 21.7]. The rate of discontinuation of GAHT was 0.06 (95% CI 0.048; 0.071) per year.

Conclusions
The event rate of GAHT increased during 2000-2018. Our data suggested high adherence to GAHT.

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EP874
Have we ignored red cell parameters in Turner Syndrome? Results from a single specialist centre
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Introduction
Anaemia and other haematological disorders have been reported in Turner Syndrome (TS). TS-related comorbidities (premature ovarian insufficiency, autoimmune hypothyroidism, coeliac disease and liver diseases) and treatments (hormone replacement [HRT] and growth hormone) are possible explanations. We aim to investigate the prevalence of abnormal full blood count (FBC) in adult TS and assess associated clinical characteristics.

Methods
FBC parameters and clinical characteristics were retrospectively collected from the electronic patient records of 120 adult TS women attending a dedicated TS clinic.

Results
Median age was 34 years (IQR 27.25-49) and 45. X was the commonest karyotype (n = 46, 38%). The most frequent abnormality in the most recent FBC was an elevated red blood cell (RBC) count in 25% (n = 30), elevated mean cell haemoglobin (Hb) concentration in 19% (n = 23) and/or elevated Hb in 9% (n = 11). While some results were isolated when compared to previous FBCs, seven patients (6%) had elevated Hb and RBC count on more than one occasion. Associated conditions included primary hypothyroidism on treatment in 2, autoimmune hypothyroidism, coeliac disease and liver diseases) and treatments (hormone replacement [HRT] and growth hormone) are possible explanations. We aim to investigate the prevalence of abnormal full blood count (FBC) in adult TS and assess associated clinical characteristics.

Conclusion
In our patient cohort of Turner Syndrome (TS), haematological abnormalities were not uncommon with elevated red blood cell counts being the most frequent. However, association with other conditions and treatments warrants further research.

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EP875
Multiple prolactinomas in a young man with Kallmann syndrome and familial hypocalciuric hypercalcaemia
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Introduction
Kallmann syndrome (KS) is a rare congenital form of hypogonadotrophic hypogonadism (HH) associated with anosmia, that occurs with an incidence of 1:48,000 (1:30,000 males). Multiple separate pituitary adenomas are also rare, identified in only 0.7% of pituitary adenoma cases.

Case Presentation
A male Caucasian patient presented with absent puberty, small testicles (1 ml), microphallus, osteopenia and anosmia at age 15. Endocrine assessment confirmed HH. Based on concomitant olfaction dysfunction, he was diagnosed with Kallmann syndrome (KS). Hormonal replacement treatment was initiated for puberty induction with testosterone enanthate and then continued with testosterone undecanoate following local monitoring protocol. At age 26 the patient presented with mild headache. MRI revealed two separate pituitary adenomas along with the absence of the olfactory bulbs. Given the presence of hyperprolactinaemia (17x upper limit of the reference range) the diagnosis prolactinoma was made and treatment with cabergoline was started which resulted in complete biochemical response and in marked reduction of both adenomas in size. Hypogonadism persisted and testosterone replacement therapy was continued. Targeted genetic testing of genes associated with neuroendocrine tumors (AIP, MEN1, NF1, PRRKAR1A, RET, TSCI, TSC2, VHL), and of 49 genes associated with HH and FSH21gene associated with isolated congenital anosmia using a next generation sequencing platform was negative. Mild concurrent hypercalcaemia in accordance with familial hypocalciuric hypercalcaemia (FHH) prompted mutation analysis of the CASR gene which yielded a pathogenic inactivating variant.

Discussion
Double separate prolactinoma in a patient with KS has not yet been reported in the literature. The effect of sex hormone treatment on the possible development of prolactinoma is unknown at present. The relevance of the CASR gene mutation in our patient for the KS phenotype also needs further insights since CaSR is expressed in GnRH neurons in mouse brain and CaSR deficient mice have a reduced hypothalamic GnRH neuronal population. This would possibly point to a role for the CaSR pathogenic variant in the development of KS in our patient. On the other hand, no delayed puberty, infertility or central hypogonadism have been reported in FHH patients.

Conclusion
We are unaware of earlier reports of an ultra rare co-occurrence of KS and multiple pituitary adenomas and FHH. The role of an inactivating variant in CASR gene as well as the effect of sex hormone treatment on the patient’s phenotype are uncertain at this stage.

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EP876
Reproductive endocrinology characteristics in young women with osteoporosis
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Introduction
Premenopausal women that suffer from osteoporosis are under-diagnosed and many anti-osteoporotic medications are neither licensed for young women, nor...
have they been established as safe or effective. Current guidelines on osteoporosis only address postmenopausal women, resulting in uncertainty and insufficient treatment for premenopausal women. To prevent bone fragility in young women, more knowledge and education about possible risk factors for osteoporosis in young age is needed.

Methods
Women under the age of 50 were recruited to fill out a questionnaire, if their T-values were osteoporotic, or if they presented with one or more fractures with a T-value of -2.0. They answered 42 questions on potential risk factors for bone fragility. Frequencies of risk factors were compared with published prevalences for the normal premenopausal population.

Results
Data of 104 women was analysed. The average age at first diagnosis of osteoporosis/osteoepidia was 37 years (range: 19-49), 78% had already sustained a fracture. 40% had been pregnant at least once, but only 74% of them had given birth. 16% of the patients had involuntary infertility, of these 82% had never been pregnant. Female infertility is estimated to affect 7.5% in the general population. 75% of the women had used or were on hormonal contraception, which is less than in the German population (87%). 14% had started hormonal contraception prior to 16 years of age. Hypermenorrhoea was more common amongst young osteoporosis patients than in the general female population (22% vs. 10%). Nearly half of the participants (45%) reported secondary amenorrhea of more than 6 months at least once in their lifetime, much more than women without osteoporosis (1.5-3%). 22% of our patients stated having had an eating disorder for longer than one year. The lifetime prevalence for eating disorders in Germany ranges from 1.7-3.6% for anorexia nervosa and 2.6% for bulimia nervosa. 74% of the participants with an eating disorder also had amenorrhea. Depression was more prevalent in young osteoporotic women (13%) than in the average population (8.2%), as was hypothroidism (18% vs. 1-2%). 39% of the participants worked shifts or admitted to a chronic sleep disorder.

Discussion and conclusion
Compared to the normal population, some reproductive endocrine characteristics are more frequent in young women with osteoporosis, such as hyper- and amenorrhea, eating disorders, hypothroidism and depression.

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EP877

The endocrine disruptor Benzo[a]Pyrene inhibits gonadotropin-mediated steriodogenesis in a mouse Leydig tumor cell line
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Introduction
Benzo[a]pyrene (BaP) is an endocrine-disrupting chemical, which may impact reproduction. It is a polyclic aromatic hydrocarbon generated by the incomplete combustion of organic compounds. BaP may be accumulated in the environment, achieving effective concentrations in the nanomolar range and exerting genotoxic effects in long-term exposed humans.

Aim
We evaluated the short-term impact of BaP on lateinizing-hormone (LH)/choriogonadotropin (hCG)-mediated functions in the steroidogenic mouse Leydig tumor cell line (mLTC-1), in vitro.

Methods
mLTC-1 cells were treated with increasing BaP doses (range fM-M), over 0-40 h, in the presence or in the absence of the maximal, non-saturating effective LH and hCG concentration (1500 and 300 pM, respectively). The maximal, non-cytotoxic BaP dose was evaluated by 3(4,5-dimeithylthiazol-2-yI)-2,5 diphenyl tetrazolium bromide (MTT) assay. 3-h intracellar cyclic adenosine monophosphate (cAMP) production was assessed by bioluminescence resonance energy transfer (BRET), in transfected cells expressing the specific biensor. 10, 50 and 100 M BaP forskolin-treated cells served as controls. 15-min CAMP-response element binding protein (CREB), extracellularly-regulated kinases 1 and 2 (ERK1/2) and p38 mitogen-activated protein kinase (p38-MAPK) phosphorylation was evaluated by Western blotting. 8- and 24-h progesterone and testosterone levels were measured by immunoassay. Results were compared with those from gonadotropin- and BaP-un-treated samples by Kruskal-Wallis test followed by Dunn’s post-hoc test (P<0.05; n = 6).

Results
1 fM BaP was determined as the maximal, non-cytotoxic dose (P>0.5) and was used for cell treatments, as well as the environmentally available dose of 1 nM. LH/hCG-induced intracellular cAMP accumulation was dampened by 1 fM BaP (2.0-fold compared to BaP-ununtreated; P<0.05), with no gonadotropin-specific differences, while 1 nM BaP did not produce any effect. 1 fM BaP failed in inhibiting 10-100 fM forskolin-induced CAMP (P>0.5), excluding that the compound modulates adenyl cyclase enzyme functioning. Consistently, BaP interfered with most of the downstream intracellular cAMP-dependent events. 1 fM BaP decreased LH/hCG-induced CREB phosphorylation (P<0.05) and increased basal ERK1/2 phosphorylation (P<0.05), while no perturbation of p38-MAPK phosphorylation was detected (P>0.05). The modulation of signal transduction is linked to interfering effects on steriodogenesis. LH/hCG-mediated, 24-h progesterone synthesis (1.5-fold BaP-ununtreated; P<0.05), as well as 8-h testosterone production (2.0-fold BaP-ununtreated; P<0.05), decreased significantly in the presence of 1 fM BaP.

Conclusions
These results demonstrated that a micromolar BaP concentration inhibits short-term steroidogenic signals in a mammal Leydig cell line, through an unknown molecular mechanism. These data suggest that BaP may potentially interfere with endocrine signals, dysregulating male gonadal and reproductive functions.

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EP878

Characteristics of male idiopathic hypogonadotropic hypogonadism (IHH) patients
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Background
Idiopathic Hypogonadotropic Hypogonadism (IHH) is a condition caused by deficiency or insensitivity to gonadotropin-releasing hormone where the pathology behind the mechanism is unknown and no secondary causes of hypogonadotropic hypogonadism are present. The condition not only effect sexual characteristic but can affect the physical and psychosocial development of a patient therefore making its prompt diagnoses and treatment necessary. The purpose of this study was to determine the sign, symptoms and laboratory parameters of the male IHH patients presenting in a tertiary setting.

Materials and Methods
This cross-sectional study was carried in Aga Khan University on male patients presenting with IHH to the Endocrinology clinic from December 2000 to December 2020. The patients presenting with signs or symptoms of hypogonadism, associated low sex steroid hormone and inappropriately low or normal gonadotropins with absent expansive hypothalamic or pituitary lesions or multiple pituitary hormone defects were included in the study. Quantitative variable was shown as Mean ± Standard Deviation while qualitative variables were shown as frequency and percentages.

Results
Data of 79 IHH patients was reviewed with Mean Age ± SD being 24.2 ± 7.5 years. Clinically 64 (81.0%) presented with small genitalia, 50 (63.6%) had absent secondary sexual characteristics, 53 (67.1%) presented with infertility, 44 (55.7%) had not attained puberty, 52 (65.8%) had erectile dysfunction, 46 (58.2%) with loss of libido, 11 (13.9%) had a positive family history, 24 (30.3%) had gynecomastia, 9 (11.4%) had undescended testes and 6 (7.6%) had hyposmia or anosmia. The mean serum testosterone level of the patients was 26.3 ± 60 ng/dl while mean FSH and LH level were 2.7 ± 5.0 and 1.3 ± 2.4 respectively.

Conclusion
It was observed that the primary complains of patients presenting with IHH were small genitalia, infertility, and absence of secondary sexual characteristics with a low serum testosterone level.

Keywords
Male Idiopathic Hypogonadotropic Hypogonadism (IHH), Infertility, Pakistan

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**EP879**

**Daytime salivary androgen rhythm by LC-MS/MS in women affected by Polycystic Ovary Syndrome (PCOS) fulfilling the three Rotterdam diagnostic criteria**

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**Background**

Excess testosterone in PCOS is accompanied by increased levels of other ovarian and adrenal androgens and precursors. Recently, 11-oxygenated adrenal androgens have been postulated as major components of the circulating androgen pool in PCOS. Obesity is strictly connected with androgen excess and with the derangement of hormone circadian rhythmicity. To date, it has not been clarified whether hyperandrogenism in PCOS, either complicated by obesity or not, is accompanied by the dysregulation of androgen biorhythm.

**Objective**

To investigate the daytime rhythmicity of androgens and precursors in saliva of women with PCOS fulfilling the three Rotterdam diagnostic criteria, according to their BMI status.

**Methods**

PCOS patients (age 15-34y) showed oligo-menorrhea, polycystic ovarian morphology and either clinical (hirsutism) or biochemical (elevated serum testosterone) hyperandrogenism. These were subdivided in overweight/obese (OB-PCOS; BMI ≥ 27 kg/m² n = 8) and non obese PCOS (NO-PCOS; BMI <27 kg/m² n = 8) and compared with age-matched non obese healthy women (NO-CTR; BMI <27 kg/m² n = 8) and compared with age-matched non obese healthy women (NO-CTR; BMI <27 kg/m² n = 8). All were in follicular phase, had standardized meals and self-collected saliva every hour from 7 until 23am.

Testosterone, androstenedione, 17OH-progesterone, dehydroepiandrosterone, 11OH-androstenedione and 11keto-testosterone were measured by LC-MS/MS.

**Results**

BMI was higher in OB-PCOS (31.1 (29.1-34.4)) compared to NO-PCOS (22.5 (20.2-27.2)) and NO-CTR (21.3 (20.7-22.9) kg/m²) P<0.001, but similar between NO-PCOS and NO-CTR. All women showed higher androgen and precursor levels at awakening, which decreased until bedtime (all P<0.001).

Testosterone and androstenedione, at each time point, and 17OH-progesterone, at most time points, were higher in OB-PCOS and NO-PCOS vs NO-CTR women (all P<0.050).

Testosterone was higher in OB-PCOS vs NO-PCOS at 8, 10, 11, 16 and 17am (all P<0.050). Dehydroepiandrosterone was higher in OB-PCOS compared to both NO-PCOS and NO-CTR at 9-13 and 16-17am (all P<0.050).

PCOS women showed a trend for high 11-oxygenated androgens at mid-morning and afternoon, but lower at late night, only achieving significance at 10am, with 11OH-androstenedione higher in OB-PCOS vs NO-CTR; at 17am, with 11-ketotestosterone higher in OB-PCOS and NO-PCOS vs NO-CTR; and at 23am, with 11OH-androstenedione lower in OB-PCOS vs NO-CTR (all P<0.050).

**Conclusion**

Androgen biorhythm was preserved in PCOS. Excess secretion of androgens originating from both ovary and adrenal was maintained throughout the day in both PCOS groups. The overweight/obese PCOS phenotype is featured by a deranged androgen biorhythm, as featured by dehydroepiandrosterone, at mid-morning and afternoon. Interestingly, 11-oxygenated androgens did not show a specific alteration in the examined PCOS phenotypes.

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**EP880**

**Cardiopulmonary capacity and muscle strength in transgender women in long-term gender-affirming hormone therapy: a cross-sectional study**

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**Introduction**

Effects of prior exposure to testosterone (T) during puberty on the performance of transgender women (TW) in estrogen therapy undergoing physical effort are not known, mainly about cardiopulmonary capacity (CPC). Objectives: To evaluate CPC and muscle strength in TW undergoing long-term gender-affirming hormone therapy (GAHT). Methods: A cross-sectional study was carried out with 15 TW (34.2 ± 5.2yo), 13 cisgender men (CM) and 14 cisgender women (CW). TW were in hormone therapy for 14.4 ± 3.5 years. Bioimpedanciometry, handgrip test and CP exercise on treadmill with an incremental effort were done. Results: The medium strength (kg) was 35.3 ± 5.4 in TW, 29.7 ± 6.3 in CW, and 48.4 ± 6.7 in CM (TWvsCW P = 0.0250; TWxCM P = 0.0001). Analysis of VO2 max and FFM (kg/m²) of TW (r=0.7388; P=0.0017) was not observed in the other groups. Percentage predicted Heart Rate at effort was higher in TW (103.1) than in CW (96.5) (P=0.0065) and CM (99.2) (P=0.1373). Discussion: By integrating the data set we may conjecture that TW undergoing long-term GAHT could have an exacerbated endoergy and a decreased functionality of the muscular unit. Conclusion: Cardiopulmonary capacity, mainly peak VO2, is blunted in TW after long-term hormone therapy. However, TW still present slightly higher exercise performance when compared with CW.

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**EP881**

**Noonan Syndrome, Dandy-Walker variant and delayed puberty- a rare association**

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**Introduction**

The Dandy-Walker complex (DW) comprises a rare intracranial malformation of the posterior fossa and multiple organ anomalies. The association with endocrine pathology is rare - described in isolated cases (Kallman syndrome, primary hypothyroidism (PH) and central precocious puberty). Noonan syndrome (NS) is a genetic disease usually diagnosed at birth, with variable phenotype. Most cases have AD transmission, with the PTPN11 gene mutation responsible for 50%.

Case report

Male patient referred for consultation at 16 years due to short stature and delayed puberty. At 1st evaluation: height 148.5cm (-3.1 SD), weight 41 Kg, pubertal stage P3, testicular volume 10ml; facial dimorphisms (hypertelorism, bulbous nose, triangular face), and 5th finger’s brachydactyly. Past medical history of congenital diaphragmatic hernia, intestinal occlusion at 11 months, strabismus, delayed developmental milestones and unilateral cryptorchidism (surgically corrected at 12y). Family target height of 165 cm. He denied olfactory dysfunction. Of the complement analysis, at diagnostic age: normal heterozygous for FSH < 0.3 mU/ml; LH < 0.1 mU/ml; total and free testosterone (TT/TFT 2.2 ng/ml (2.7-11)) and 3.3 pg/ml (13-40); LHRRH stimulation test with FSH 15.7 mU/ml and LH 14.5 mU/ml post stimulation; primary hypothyroidism (TSH 5.7 uIU/ml; T4L 0.7 ng/dl – started LT4 25 mg); 46XY karyotype; brain MRI showed “patency of the olfactory bulbs, identifying both olfactory sulci, without hypothalamic-pituitary alterations; increase in fourth ventricle dimensions, focal increase in retrocerebellar extra-axial space - DW variant”. Genetic study (CGH-array) without alterations. He started induction of puberty with testosterone enanthate 125 mg monthly, until 20y, with a final height of 162.1 cm (-2 SD). PS Tanner stage, and testicular volume of 25ml. LOST of follow up until 30y. At 30y: FSH 11 mU/ml, LH 4.5 mU/ml and TT 5.3 ng/ml; new diagnosis of NS, DW variant and delayed puberty. Of the complementary exams: bone age of 13y1month; male patient referred for consultation at 16 years due to short stature and delayed puberty. At 1st evaluation: height 148.5cm (-3.1 SD), weight 41 Kg, pubertal stage P3, testicular volume 10ml; facial dimorphisms (hypertelorism, bulbous nose, triangular face), and 5th finger’s brachydactyly. Past medical history of congenital diaphragmatic hernia, intestinal occlusion at 11 months, strabismus, delayed developmental milestones and unilateral cryptorchidism (surgically corrected at 12y). Family target height of 165 cm. He denied olfactory dysfunction. Of the complement analysis, at diagnostic age: normal heterozygous for FSH < 0.3 mU/ml; LH < 0.1 mU/ml; total and free testosterone (TT/TFT 2.2 ng/ml (2.7-11)) and 3.3 pg/ml (13-40); LHRRH stimulation test with FSH 15.7 mU/ml and LH 14.5 mU/ml post stimulation; primary hypothyroidism (TSH 5.7 uIU/ml; T4L 0.7 ng/dl – started LT4 25 mg); 46XY karyotype; brain MRI showed “patency of the olfactory bulbs, identifying both olfactory sulci, without hypothalamic-pituitary alterations; increase in fourth ventricle dimensions, focal increase in retrocerebellar extra-axial space - DW variant”. Genetic study (CGH-array) without alterations. He started induction of puberty with testosterone enanthate 125 mg monthly, until 20y, with a final height of 162.1 cm (-2 SD). PS Tanner stage, and testicular volume of 25ml. LOST of follow up until 30y. At 30y: FSH 11 mU/ml, LH 4.5 mU/ml and TT 5.3 ng/ml; new genetic study by total exomic sequencing, with identification of the variant c.1472C>T (Pro491Leu), in heterozygosity, in the PTPN11 gene, classified as pathogenic – Noonan Syndrome type 1.

Conclusion

This case illustrates the rare association of a patient with NS, DW variant and delayed puberty. The diagnosis of NS only at adulthood shows how genetic testing has improved over the years. The DW variant explains diaphragmatic
Anti-müllerian hormone analysis as a predictor of the polycystic ovary syndrome diagnosis in Romanian women

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Background
Higher anti-Müllerian hormone (AMH) values are associated with polycystic ovary syndrome (PCOS) and AMH is proposed as a marker of PCOS, however, the optimal diagnostic threshold is not yet defined.

Aim
To study the significant correlations of AMH in PCOS and the accuracy and threshold of AMH for the PCOS diagnosis in Romania.

Subjects and methods
Serum AMH, TT, LH, FSH, fasting glucose and insulin (Ins), HOMA-IR and BMI were analyzed in a cohort of 157 patients with PCOS selected by Rotterdam 2003 criteria and 166 controls, aged 18–35 years, recruited at the National Institute of Endocrinology, Bucharest, Romania. Receiver operator characteristic (ROC) curves were constructed to determine the diagnostic utility of different parameters.

Results
Serum AMH was positively correlated with oligo/amenorrhea (P = 0.0034), TT (P = 0.0178), LH (P = 0.0123), LH/FSH (P = 0.0015) and number of antral follicles per ovary (P = 0.0011) in PCOS, while BMI (P < 0.001), fasting-Ins (P = 0.0209) and HOMA-IR (P = 0.0138) were negatively correlated with AMH in these patients. In stepwise linear regressions including as effects LH/FSH, TT, BMI, fasting-Ins or HOMA-IR and age, LH/FSH and BMI remained significant independent predictors of AMH values in PCOS (P = 0.0002 and P < 0.0001 respectively). In ROC curve analysis using all population of the study (PCOS and controls), the area under the curve (AUC) for AMH in the diagnosis of PCOS was 0.893 [95% confidence interval (CI): 0.834–0.953; P < 0.0001], with the best compromise between sensitivity and specificity at a cut-off of 32.41 pmol/l (t.e. 4.53 ng/ml) (Se = 85.06%, Spe = 80.65%). The AUCs for TT, LH, LH/FSH, fasting-Ins, HOMA-IR and BMI were 0.773 [95% CI: 0.717–0.830; P < 0.001], 0.736[95% CI: 0.664–0.809; P < 0.0001], 0.788 [95% CI: 0.715–0.862; P < 0.001], 0.669 [95% CI: 0.598–0.741; P = 0.0004], 0.615 [95% CI: 0.537–0.694; P = 0.005] and 0.612 [95% CI: 0.546–0.678; P = 0.0011] respectively.

Conclusions
AMH values reflect both reproductive and metabolic dysfunction in PCOS. The AMH in these patients is positively correlated to both lower HOMA-IR and more symptoms of anxiety and depression. Studies on women with PCOS and severe obesity regarding symptoms of anxiety and depression are lacking.

Aims
To examine if women with severe obesity and PCOS have lower HOMA-IR and more symptoms of anxiety and depression than women with severe obesity without PCOS, and evaluate the effect of a structured weight reduction program. Further, to compare HOMA-IR and symptoms of anxiety and depression in women with and without PCOS in different weight categories.

Patients and methods
In total, 407 women from four studies were included (PCOS n = 179, non-PCOS n = 228). The main study included 246 women with severe obesity (BMI ≥ 35) (PCOS n = 63, non-PCOS n = 183). To compare weight categories, data from earlier studies were added, including 134 women with BMI < 35 (PCOS n = 63 non-PCOS n = 51). Questionnaires Short form (SF)-36 and Self-rating Scale for Affective Syndromes (CPRS-SA) were used to assess HOMA-IR and symptoms of anxiety and depression. Women in the main study entered a weight reduction program, with a very low energy diet (VLED), and 73 women were left to follow-up (PCOS n = 16, non-PCOS n = 57).

Results
In women with severe obesity, HOMA-IR and symptoms of anxiety and depression did not differ between women with and without PCOS. In women with normal- and overweight, women with PCOS had lower mental HOMA (P = 0.001 resp. P = 0.004) and more symptoms of anxiety (P = 0.001 resp. P = 0.001) and depression (P = 0.002 resp. P = 0.012) compared to women without PCOS. In women with severe obesity, significant weight reduction was achieved in both women with and without PCOS, and led to improved physical HOMA-IR in both groups (PCOS: P = 0.011, non-PCOS: P = 0.001).

Conclusions
The difference in HOMA-IR and symptoms of anxiety and depression seen between women with and without PCOS with normal- or overweight is not seen in women with severe obesity. Women with severe obesity benefits from losing weight to improve their physical HOMA-IR. Keywords: Polycystic ovary syndrome, severe obesity, health related quality of life, anxiety, depression

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Obese patients with PCOS and prediabetes: two years follow up of the effects of metformin, pioglitazone and empagliflozin treatment on metabolic control, hormonal imbalance and ovolutions

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Introduction
The role of metformin in PCOS is very well known and several studies reported effects of thiazolidinediones and SGLT2 inhibitors on metabolic parameters in these patients.

Objective
The aim of this study was to compare the effects of metformin, pioglitazone and empagliflozin treatment on metabolic control, hormonal imbalance, weight loss and ovolutions in obese patients with PCOS and prediabetes.

Methods
BMI, waist circumference, HOMA index, leptin/adiponectin, LH/FSH, androgendione, testosterone, DHEAS, triglycerides, cholesterol, HDL, LDL and presence of ovolution were tested at the admission and 24 months after therapy.

Patients
146 overweight/obese patients (mean age 25 ± 2.6) with PCOS and prediabetes were divided in 3 groups based on medication they were treated with.

Results
Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001). Metformin was superior than pioglitazone (P < 0.05). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences (P < 0.001).
superior to emagliflozin and pioglitazone in lowering LH/FSH and testosterone (P<0.001). Metformin and emagliflozin were superior in reducing androstenedione than pioglitazone (P<0.01). Emagliflozin and pioglitazone were superior to metformin in raising SHBG and HDL (P<0.01) and lowering I/A (P<0.05), triglycerides (P<0.001) and HOMA index (P<0.01). There was no difference between groups in ovulatory menstrual cycles regulation.

Conclusions
Emagliflozin and pioglitazone were superior to metformin in metabolic control while metformin was superior in resolving hyperandrogenism. Metformin, empagliflozin and pioglitazone were superior to metformin in raising SHBG and HDL (P<0.01). Empagliflozin was superior in resolving hyperandrogenism. History of acne eruption in the mother during pregnancy but no hirsutism. Her height was 164 cm (75-90th centile), weights 69 kg (90-97th centile), arm span – 171 cm, US/LS ratio 0.85:1. Sexual maturation is A1 P3 B1. No facial dysmorphism, no features of androgen excess, normotensive. Short 4th metatarsal left foot, no other skeletal deformities. Normal external genitalia. Karyotype is 46, XX. Proactin is 12.8 mg/ml, FSH 13.8, LH 33.7, T3: 1.66, T4: 10.5, TSH -1.10, Estradiol 24.22 pg/ml, AMH-0.45 ng/ml and testosterone 14.40 ng/ml. 8 AM serum cortisol is 12.62 mg/dl, 17 hydroxy progesterone 21.7 mg/ml, post ACTH stimulation serum 17 OHP is 22.8 mg/ml, serum cortisol 9.74 mg/dl. Bone age 14 years. USG pelvis uterus 30x20x15 mm, ET 4.5mm, bulky left ovary with multiple cysts. Genetic testing showed homoygous mutation in POR (NM_000941.2), (Chr7:75615521); Exon 15; c.1860G>T (p.Trp620Cys). She was advised estrogen replacement and hydrocortisone cover during stress. In conclusion our case presented with normal genitalia, no skeletal abnormalities, no hyper androgenic features with large ovarian cysts and delayed puberty(suggestive of aromatase deficiency) with high 17(OH) progesterone and subnormal rise in cortisol and 17(OH) progesterone post ACTH stimulation consistent with POR deficiency. The wide range of phenotypic manifestations in POR deficiency may be explained by the differential inhibition of POR dependent enzymes. Given the varied clinical presentation and the risk of hypocortisolism, clinicians should be aware and alert to this diagnosis.

Introduction
Perrault syndrome (PS) is a rare disease characterized by the association of a premature ovarian failure (with primary or secondary amenorrhea) and a sensorineural deafness. In this context we report the case of three patients presenting the association of these two anomalies.

Cases
We report the cases of three females, including two sisters from a consanguineous marriage, aged 21, 16 and 23 years, respectively. The two cardinal signs of this syndrome made of premature ovarian failure and sensorineural deafness were present in the three patients, associated with a Parkinsonian syndrome in the third case. The examination did not show any dysmorphic syndrome or mental retardation. The audiometrical exploration of the two sisters concluded to a deafness whose endocochlear nature was confirmed by the auditory evoked potentials. Hormonal exploration confirmed the presence of hypergonadotropic hypogonadism in all three patients. All three patients had a 46XX caryotype, thus eliminating Turner syndrome. The immunological investigation was negative. Pelvic ultrasound in all three patients showed hypoplastic ovaries and uterus. The brain MRI of the two sisters showed an aspect in favor of a leukodystrophy, never described in the literature. The family investigation revealed an isolated congenital deafness in a nephew of both sisters, also from a consanguineous marriage, aged 21, 16 and 23 years, respectively. The two cardinal signs of this syndrome associated the association of these two anomalies.

Conclusion
Ovarian dysgenesis associated with sensorineural hearing loss are the cardinal features of Perrault syndrome. A range of associated neurological and neuroradiological disorders are increasingly reported in the literature. Certainly, advances in molecular biology will be able to support the etiopathogenic link between gonadal, auditory and neurological involvement in this syndrome.

EP886
Delayed puberty with a novel mutation in the p450 oxidoreductase gene
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P450 Oxidoreductase (POR) deficiency is a rare autosomal recessive disorder of steroidogenesis with varied clinical presentation. POR is the electron donor for all microsomal enzymes involved in steroidogenesis namely P450c 17(17 hydroxylase/17,20 lyase), P450c 21 (21 - hydroxylase), and P450c 20a(aromatase). POR deficiency can cause genital ambiguity in both sexes, impaired steroidogenesis and skeletal malformations. Here we present a patient with ovarian cysts and delayed puberty with a novel mutation in the POR gene. A 14 year old girl born of 3rd degree consanguineous marriage presented with acute abdominal pain, on evaluation found to have torsion of large right hemorrhagic ovarian cyst requiring surgical intervention with oophorectomy. 3 to 4 months later patient presented with recurrence of abdominal pain, investigation revealed large cyst in left ovary for which cystectomy was done, subsequent serial ultrasonography examination for the next 6 months revealed increase in size of ovarian cysts. At this point endocrinology consultation was sought for not attaining menarche. History of acne eruption in the mother during pregnancy but no hirsutism. Her height was 164 cm (75-90th centile), weights 69 kg (90-97th centile), arm span – 171 cm, US/LS ratio 0.85:1. Sexual maturation is A1 P3 B1. No facial dysmorphism, no features of androgen excess, normotensive. Short 4th metatarsal left foot, no other skeletal deformities. Normal external genitalia. Karyotype is 46, XX. Proactin is 12.8 mg/ml, FSH 13.8, LH 33.7, T3: 1.66, T4: 10.5, TSH -1.10, Estradiol 24.22 pg/ml, AMH-0.45 ng/ml and testosterone 14.40 ng/ml. 8 AM serum cortisol is 12.62 mg/dl, 17 hydroxy progesterone 21.7 mg/ml, post ACTH stimulation serum 17 OHP is 22.8 mg/ml, serum cortisol 9.74 mg/dl. Bone age 14 years. USG pelvis uterus 30x20x15 mm, ET 4.5mm, bulky left ovary with multiple cysts. Genetic testing showed homoygous mutation in POR (NM_000941.2), (Chr7:75615521); Exon 15; c.1860G>T (p.Trp620Cys). She was advised estrogen replacement and hydrocortisone cover during stress. In conclusion our case presented with normal genitalia, no skeletal abnormalities, no hyper androgenic features with large ovarian cysts and delayed puberty(suggestive of aromatase deficiency) with high 17(OH) progesterone and subnormal rise in cortisol and 17(OH) progesterone post ACTH stimulation consistent with POR deficiency. The wide range of phenotypic manifestations in POR deficiency may be explained by the differential inhibition of POR dependent enzymes. Given the varied clinical presentation and the risk of hypocortisolism, clinicians should be aware and alert to this diagnosis.

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Conclusion
Ovarian dysgenesis associated with sensorineural hearing loss are the cardinal features of Perrault syndrome. A range of associated neurological and neuroradiological disorders are increasingly reported in the literature. Certainly, advances in molecular biology will be able to support the etiopathogenic link between gonadal, auditory and neurological involvement in this syndrome.

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Introduction
A significant overlap of symptoms between polycystic ovary syndrome (PCOS) and thyroid disease, despite the fact that they are two different diseases. Both diseases individually affect a woman’s metabolic parameters and fertility, and their association makes them much more difficult to manage.

Objective
To investigate the effect of elevated thyroid stimulating hormone (TSH) concentrations on metabolic and endocrine parameters in women with PCOS. Analysis of the correction of TSH values and insulin resistance (IR) on pregnancy using levothyroxine with myo-inositol and d-chiro-inositol.

Methods
Experiments comprised a control group (PCOS-A) and a treatment group (PCOS-B). Both groups were divided into two subgroups: one group took levothyroxine 0.25 mg and myoinositol plus d-chiro inositol for 6 months, and the other group (n = 25) took levothyroxine 0.25 mg and myo-inositol for 6 months. Both groups adhered to the same diet with exercise 3 times a week for 30 minutes. After 6 months, the same hormonal, biochemical analyses were checked.

Results
In women with elevated TSH and PCOS, the lipid profile and HOMA were significantly impaired compared to the control group (P < 0.01). There was no statistical difference in androgen and prolactin concentrations between experiments. In women with PCOS and elevated TSH after taking levothyroxine and myo-inositol, d-chiro-inositol combination therapy, there was a statistically significant increase in TSH, anti TPO, HOMA, and pregnancy in relation (44.24%) in correlation with women who used only levothyroxine. In both groups of patients, there was a statistically significant correction of the lipid profile.

Conclusion
Hashimoto’s disease in the range of subclinical hypothyroidism in combination with PCOS has a negative impact on the metabolic profile. Combination therapy of myo-inositol, D-chiro-inositol and levothyroxine has shown a significant effect on fertility rate and pregnancy by promoting insulin sensitivity and improving thyroid function. In women diagnosed with PCOS, especially those who want to become pregnant, it is necessary to examine the function of the thyroid gland at the first visit to the endocrinologist. Key words: polycystic ovary syndrome, Hashimoto’s thyroiditis.

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EP880
Klinefelter syndrome associated with intellectual deficit, short stature and cardiac anomalies

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Introduction
Klinefelter syndrome is the most prevalent male chromosomal disorder, characterized by the presence of additional X chromosomes. Most males with Klinefelter syndrome have 47, XXY and normal intelligence. Intellectual disability occurs in males with Klinefelter syndrome variants, who have a higher number of X chromosomes. Here we report a rare case of a 49, XXXY syndrome revealed by intellectual deficit and pubertal delay.

Observation
An 18-year-old male patient was presented in our department for pubertal delay associated with intellectual deficit. He showed dry mouth, polydipsia, and polyuria. On examination, he had short stature: height = 166 cm, weight = 67 Kg, BMI = 24.3 Kg/m², hypertelorism, gynecomastia, atrophic testes and microphrenia. Biological examination showed diabetes mellitus and hypertriglyceridemia. Hormonal analysis showed a hypergonadotropic hypogonadism (Testosterone = 20 ng/dl, LH = 29 IU/l, FSH = 55 IU/l). Thyroid function was normal and his IGF-1 level was low (170 [224-255 mg/ml]). Imaging examination showed a bone age of 16 years and cardiac anomalies: mitral and aortic ceridemia. Hormonal analysis confirmed a hypergonadotropic hypogonadism and is closely linked to metabolic disorders such as obesity and insulin resistance (IR). It was observed that single-point insulin sensitivity estimator (SPISE) index is associated with metabolic abnormalities and could predict glucose regulation during life. The aim of this study was to analyze metabolic and hormonal characteristics among two age groups of women with PCOS and their association with SPISE index and homeostatic model assessment of insulin resistance (HOMA-IR) index.

Subjects and methods
We analyzed 150 women with PCOS diagnosed using ESHRE/ASRM. Patients were divided into two age groups, younger/equal to 30 years (PCOS-A, n = 74, age: 23.3 ± 3.1 years, BMI: 23.1 ± 4.3 kg/m²), and older than 30 years (PCOS-B, n = 74, age: 35.7 ± 4.9 years, BMI: 25.3 ± 6.4 kg/m²). We measured lipid indices, glucose and insulin during oral glucose tolerance test (OGTT), while HOMA-IR and SPISE index were calculated. Statistical analysis was performed by SPSS software.

Results
Both groups had similar body mass index (P = 0.071) and waist circumference (77.0 ± 12.9 cm vs. 82.0 ± 15.3 cm, P = 0.07), but the incidence of obesity was higher in PCOS-B group (PCOS-A 5.9% vs. PCOS-B 23.5%, P = 0.004). Women in PCOS-B in comparison to PCOS-A had higher total cholesterol (P < 0.001), LDL cholesterol (P = 0.022) and triglycerides (P = 0.012). Incidence of impaired glucose tolerance was same in both groups, and no patient had diabetes. Although fasting glucose was statistically higher in PCOS-B group (P < 0.001), there was no between-groups differences in levels of fasting insulin (P = 0.12) and HOMA-IR (P = 0.151). SPISE index was statistically lower in PCOS-B (P = 0.022), showed negative correlation with HOMA-IR, baseline glucose and glucose in 120 minute of OGTT in PCOS-B (r = 0.483, P = 0.004, r = 0.360, P = 0.007, r = 0.337, P = 0.804, respectively) and negative correlation with only fasting insulin in PCOS-A (r = 0.284, P = 0.024).

Conclusion
PCOS is characterized by the existence of risk factors including obesity, elevated glucose and lipid concentrations all leading to an increased risk of cardiometabolic vascular disorders. The assessment of different indicators during time-line of PCOS could be used for prediction of long-term metabolic outcomes.

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Malformations and intellectual deficit are other characteristics of this syndrome that requires performing a karyotype.

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**EP891**

**Effects of antiandrogen therapy of cyproterone acetate on androgen effects on the skin including androgenetic alopecia in menopausal women - case report: 10 years follow up**

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**Introduction**

The term female pattern hair loss (FPHL) is commonly used synonymously with female androgenetic alopecia. While the role of androgens and androgen receptor genes is well-defined in male androgenetic alopecia (AGA-M), its role in the pathogenesis of FPHL is still uncertain. More diffuse involvement, resulting in an oval-shaped alopecia surrounded by a rim of normal hair density (Ludwig’s classification) might be a clinical challenge. The aim of case report is to present the menopausal patient with full blown signs of androgen excess such as acne, seborrhea, hirsutism (SAHA: seborrhea, acne, hirsutism, and alopecia), obesity and pronounced psychological consequences.

**Case description**

A 59-year-old female, born in 1952y. Since 2000y. (menopause in 2004y) she gained 35 kgs (85.1 kg), BH 158 cm and since 2010y. she started to notice increased hairiness (hirsutismus) and weakening and hair loss (FPHL), in 2016 Grade 3. At that time on adrenal CT it was detected adrenalectomy on one gland. Cushing syndrome and Cushing exyndrome was excluded, but among laboratory findings significant was LTH 18.1 U/L, FSH 44.4 U/L, testosterone 13.8 nmol/L, insulin (fasting) 27.1 mU/L, post prandial 281.6 mU/L. Fasting triglycerides 0.95 mmol/L, HDL-cholesterol 1.8 mmol/L, total cholesterol 5.56 mmol/L. In two years period (2016-2018) she managed to reduce her body weight to 75 kg, insulinemia to 11.9 mU/L, testosterone to 5.8 nmol/L. Alopecia and hirsutismus had been without change, so we decided to introduce cyproterone acetate tbl. 2x50 mg. First drop in T was noticed 1 year later (2019.), but even before that after a year on that therapy patient noticed changes in reduced alopecia and hirsutismus. After 2 ys of therapy in 2021, we noticed further drop in T between 1.44 and 3.04. Clinical improvement was manifested in alopecia removal of Grade 3 to Grade 1. In these time DHT (Barts) has been 10.1-21.7 (reference -23) ng/dl.

**Discussion**

The aim of this case report is to emphasize the need of normalisation the testosterone level (reference 2.6 mmol/L) for obtaining the effect of reduction of androgenization, meaning withdrawal of alopecia and hirsutism. If we consider hyperinsulinemia as a trigger hormone change for the cascade of further androgenisation, its reduction does not seem to be enough for beneficial effects. More, hyperinsulinism was associated only with hirsutism but not with characteristic lipid constellation that runs with insulin resistance, high triglycerides and low LDL cholesterol.

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**EP892**

**Effects of letrozole on reproductive organs of young and aged male rats**

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**Introduction**

The aim of this work was to study the condition of the reproductive system after long-term administration of letrozole followed by its withdrawal in young males and against the background of involutional changes in aging males in a comparative aspect. The experiments were carried out on Wistar rats with an initial age of 5 months and 15 months, which have been gavaged by letrozole every other day at a dose of 1 mg/kg body weight for 3 months and then 2 months after its discontinuation. The blood plasma testosterone and estradiol levels were measured by immunoassays. The spermatozoa concentrations in epidydimal washes were determined. The testicles and accessory sexual glands were weighed, and morphology of gonads and ventral prostate have been studied. The results of the study were compared with those of control animals of corresponding age. As the result of letrozole treatment, the ratio of testosterone and estradiol levels in blood plasma of aged rats increased. The spermatozoa content in epidydymis rose up by 28% at average. The histological study revealed functional activation of Leydig cells, a significant retardation of involutive changes of their number and morphology. Some Leydig cells demonstrated the signs of functional exhaustion. Letrozole caused an increase of relative weights of the coagulation gland by an average of 40%, seminal vesicles by 31%, and ventral prostate by 33% compared with those of control animals. Two months after letrozole withdrawal, there were no any signs of difference between letrozole-treated and control animals. In young rats, the effects of letrozole were almost not detectable. Letrozole administration to male rats with age-related involution of the reproductive system increases testosterone/estradiol ratio in blood plasma, the spermatozoa content in epididyms and the weights of androgen-dependent accessory sexual glands. This is accompanied by slowing down of age-related changes of the gonad and prostate gland morphology. Letrozole-induced reproductive effects are reversible.

Keywords: letrozole, reproductive organs, male, rats.

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**EP893**

**Mitochondrial uncoupling proteins (UCPs) regulate the mitochondrial activity of human sertoli cells**

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**Introduction**

Mitochondrial uncoupling proteins (UCPs) are channel proteins present in the mitochondrial inner membrane which are responsible for the transport of protons between the mitochondrial intermembrane space and the matrix. Currently, six UCP homologues have been identified (UCP1-6). UCPs are major regulators of reactive oxygen species (ROS) production, general cellular redox state and metabolism. UCPs also exhibit specific functions, such as UCP1 and thermogenesis or UCP2 and regulation of insulin secretion in beta-pancreatic cells. Altered expression and function of UCPs have been linked with the onset of metabolic diseases, including obesity and diabetes mellitus and increased oxidative stress. Male infertility is an overlooked comorbidity related to metabolic diseases since the testis is susceptible to metabolic alterations and increased oxidative stress. However, the expression and function of UCPs in the human testis remain unknown.

**Aim of the study**

The main objective of this study was to identify the expression of the different UCP homologues in human Sertoli cells (hSCs). In addition, the function of UCPs on the mitochondrial activity and metabolism of hSCs was analysed through its inhibition by genipin, a specific UCP inhibitor. Material and methods Primary cultures of human Sertoli cells from healthy men with conserved spermatogenesis were established (n=6). Total RNA was extracted and all UCP homologues (UCP1-6) mRNA expression was analysed by RT-PCR. UCP1-3 were detected by immunofluorescence. Then, UCPs were inhibited in hSCs by genipin, a specific UCP inhibitor, (0.5, 5, 50, and 100 μM). Cellular viability, proliferation, and ROS production were accessed after 24h treatment. Mitochondria function was accessed by Seahorse XF Cell Mito Stress assay. Culture media were collected and analysed by 1H-NMR.

**Results**

We were able to identify all UCPs homologues (UCP1-6) in hSCs. The inhibition of UCPs by high concentrations of genipin decreased hSCs proliferation but no cytotoxicity was observed. In addition, UCP inhibition by genipin decreased mitochondrial activity in a dose-dependent manner. Interestingly, no increased ROS production was observed.

**Conclusion**

We were able to identify, to the best of our knowledge, for the first time the expression of UCPs (UCP1-6) in hSCs. UCPs can regulate the mitochondrial activity and metabolism of hSCs. This is accompanied by slowing down of age-related changes of the gonad and prostate gland morphology. Letrozole-induced reproductive effects are reversible. Keywords: letrozole, reproductive organs, male, rats.

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EP894
Mitochondrial uncoupling proteins (UCPs) are key regulators of human spermatozoa motility
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Introduction
Mitochondrial uncoupling proteins (UCPs) are mitochondrial transmembrane channels belonging to the anion carrier family. Six UCP homologues (UCP1-6) had been identified with a ubiquitous distribution throughout the body and many different physiological functions. UCPs are important regulators of several biological processes, including thermogenesis, oxidative phosphorylation, ROS production, as well as cellular metabolism. However, the knowledge concerning the molecular action mechanisms is limited. UCPs’ (dys)function is pivotal to the onset of metabolic diseases and consequent increased oxidative stress. Although the molecular mechanisms are poorly understood, there is an interconnection between oxidative stress, male infertility, and metabolic disorders, such as obesity and diabetes mellitus. In addition, the expression and function of UCPs in the human spermatozoa remains to be explored.

Aim of the study
This study aimed to evaluate the expression of UCPs homologues (UCP1-6) in human spermatozoa. In addition, the influence of UCPs in spermatozoa viability, total and progressive motility, mitochondrial activity, and ROS production was evaluated through its inhibition by genipin, a selective UCP inhibitor.

Material and methods
Highly motile and viable spermatozoa were isolated from seminal samples of normozoospermic men (n=10) by density gradient centrifugation. The mRNA expression of UCPs homologues (UCP1-6) was evaluated by RT-PCR and the protein expression (UCP1-3) by immunofluorescence. Samples were incubated in BBW medium supplemented with genipin (0, 0.5, 5, and 50 μM) at 37°C. After 3 h, total motility and viability were analyzed. The mitochondrial activity and total ROS production were assessed by JC-1 dye and CM-H2DCFDA probe, respectively. The media culture were collected and evaluated by 1H-NMR.

Results
We were able to identify the mRNA expression of all UCPs homologues (UCP1-6) in human spermatozoa. Inhibition of UCPs by the highest concentration of genipin (50 μM) led to the irreversible loss of motility. Mitochondrial membrane potential was also found diminished, although no alterations in human spermatozoa viability, metabolic profile, or ROS production were observed.

Conclusion
UCPs are major regulators of human spermatozoa’s mitochondrial activity and motility. Our data suggests that the dysfunction of human spermatozoa UCPs is a potential target for the treatment of male infertility.

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EP895
Sperm medium supplementation with hyperoside as a potential strategy to counteract spermatozoa dysfunction associated with oxidative stress
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Introduction
Infertility is a global health problem that affects about 15% of couples and approximately half of infertility cases are associated with male factors. Oxidative Stress (OS) is reported as one of the major causes of male infertility, mainly due to spermatozoa’s vulnerability to the attack of reactive oxygen species (ROS). Infertile couples often recur to assisted reproductive technology (ART) to achieve a successful pregnancy. However, ART protocols also increase the exposure of gametes to OS conditions. A strategy often used to overcome this problem is the supplementation of media with antioxidants. Hyperoside (quercetin 3-O-galactoside) is a flavonol glycoside that has been shown to possess prominent antioxidant properties, preventing oxidative damage in several cellular systems. Thus, we proposed to investigate the impact of hyperoside supplementation on the protection of sperm against oxidative damage.

Materials and methods
We tested the effects of hyperoside supplementation on human spermatozoa. We evaluated motility, ROS production, mitochondrial activity, and apoptosis (assessed by Annexin V staining) of spermatozoa exposed to 300 μM hydrogen peroxide (H2O2) for 1 h. Spermatozoa were divided into two groups: control (without hyperoside) and supplemented with hyperoside (100 and 500 μM). The effects of hyperoside supplementation were analyzed by 1H-NMR.

Results
Hyperoside supplementation had a protective effect on spermatozoa exposed to H2O2. We observed a significant increase in sperm motility and mitochondrial activity, as well as a decrease in ROS production and apoptosis. Moreover, hyperoside supplementation led to an increase in the TAC (total antioxidant capacity) of sperm medium.

Conclusion
Hyperoside supplementation can be a promising strategy to improve sperm maintenance during ART protocols, thus potentially improving the chances of achieving a successful pregnancy.

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with the highest score collected at the last visit compared to baseline (1.8 ± 2.7 vs 1.2 ± 2.1, P < 0.001). At follow-up visits, CDS was significantly higher in vascular ED (4.2 ± 3.4) compared to psychological (2.2 ± 3.0), hormonal (1.7 ± 3.4) and neurological (1.0 ± 1.1) forms (P < 0.001).

Conclusions

Here, we demonstrate that the anamnestic evaluation of the comorbidities number is not useful in clinical practice to predict ED aetiology. However, the increase in CDS observed during follow-up resulted particularly evident in vED, confirming the vED role as a mirror of general health.

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EP897

Lean Polycystic Ovarian Syndrome - An evaluation of diagnostic and clinical outcome differences in relation to obese PCOS in patients attending a tertiary care institute in Colombo

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Background and Objectives

Polycystic ovary syndrome (PCOS) is a common female reproductive endocrine disorder with a prevalence of 15-20%. Although a majority of patients diagnosed with PCOS are overweight/obese, minority can present with normal body mass index of ≤25 kg/M² which complicate the effective diagnosis and management. We have studied the socio-demographic and clinical characteristics of lean PCOS patients in comparison to obese PCOS patients attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.

Methods

A descriptive cross sectional study was conducted from September 2019 to September 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting PCOS patients diagnosed with Rotterdam criteria. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. HOMA-IR was calculated using the fasting insulin and blood glucose level.

Results

The study enrolled sixty females. Out of that 23 (38.3%) patients were diagnosed to have lean PCOS while the rest (37, 61.6%) had overweight/obesity. The mean age was 25.1 years (range 18-37). The mean weight was 55.0 (SD 6.7) kg and BMI was 22.2 (SD = 1.8) kg/m². Twenty (38.0%) had irregular menstrual cycles while 11 (47.8%) patients had clinical or biochemical evidence of hyperandrogenism. Only 9 (39.1%) patients had polycystic ovaries on trans-abdominal ultrasound scan. According to the body fat percentage assessed by the whole body DXA scan 90.9% patients had their body fat in the overweight and obese category in contrast to the BMI category. HOMA-IR detected 37.5% to have high insulin resistance. There was significant difference in the presence of acanthosis nigricans, hirsutism, polycystic ovaries on USS and non-alcoholic fatty liver disease (NAFLD) in the obese PCOS patients while acne was more prevalent in the lean PCOS females (P < 0.05).

Conclusions

The minority of patients affected with PCOS are falling under the category of lean PCOS. The diagnosis and the therapeutic approach poses a significant clinical challenge due to the absence of typical clinical features such as acanthosis nigricans, hirsutism, and polycystic ovaries on USS in this group of patients. Use of body fat estimation is more sensitive in detecting overweight/obesity in this group rather than using conventional BMI measurement. Nevertheless, the suspicion and awareness among clinicians of the possibility of lean PCOS in this group of females can improve the diagnosis and patient outcomes.

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EP898

PCOS SEVa: High prevalence anxiety and body dysmorphia in women with PCOS attending specialist care in the UK and India

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Introduction

National Institute of Health and Care Excellence (NICE) recommends screening for emotional wellbeing as part of consultations for polycystic ovary syndrome (PCOS).

Aim

We evaluated several dimensions of emotional wellbeing in people attending PCOS consultation with specialists in the UK and India.

Methods

All people attending specialist clinics in a tertiary centre in the UK from October 2020 to September 2021 and in India between March 2021 to September 2021 were invited to complete a survey before and after attending the clinic. This study had questions on demographics, Hospital Anxiety and Depression Scale (score 8-10 borderline; score ≥ 11 cases of anxiety and depression, respectively), Body Image Concern Inventory (BICI); score ≥ 72 suggestive of body dysmorphic disorder, BDD), Beliefs About Obese Persons Scale (BAOP; higher score suggestive of weight bias), and Female Sexual Function Index (FSFI; higher score suggestive of psychosocial dysfunction).

Results

A total of 115 women (36 UK and 79 India) completed the survey. The prevalence of anxiety and depression were 56.5% (50.0% UK vs 59.5% India); Mann-Whitney U- P = 0.483) and 16.5% (13.9% UK vs 17.7% India, P = 0.529), respectively. Overall, 29.6% had BDD with higher prevalence in the UK women (36.1% UK vs 26.6% India, P = 0.208). Participants had higher scores for BAOP (overall: 15.5/48 (13.0-18.0) with higher scores for UK women (UK: 16 (13.3 - 18.9) vs India: 15 (12.5 - 17.3); P = 0.575). The overall scores for FSFI were towards the upper end of the scale (20.4/56 (7.5 - 25.2)) with no significant difference between the two groups (UK: 23.1 (13.2 - 26.2); vs India: 17.7 (6.9 -24.5); P = 0.413). Post-survey results further revealed that a proportion of women felt limited information was provided about anxiety (UK: 6/19 (31.6% vs India: 17/40 (42.5%)), depressive symptoms (UK: 5/19 (26.3%); vs India: 19/40 (47.5%)) or body image concerns UK: 3/19 (15.8%); vs India: 10/40 (25%) during consultation.

Conclusion

There is a high prevalence of emotional ill-being associated with PCOS both in the UK and India. While it is challenging to encompass all aspects of clinical care during consultation, future work should explore alternate ways to improve screening and management of emotional wellbeing in women with PCOS.

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EP899

Perrault syndrome in a Tunisian Girl: a case report

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Introduction

Perrault syndrome is a rare autosomal recessive disorder defined by the association of 46XX ovarian dysgenesis and neurosensory deafness. Other manifestations may be present, in particular cerebellar and/or peripheral neuronal degenerative disease. We report the case of Perrault syndrome in a 15-year-old Tunisian girl.

Observation

A 15-year-old girl was referred to our department for pubertal delay. She had a congenital deafness and epilepsy diagnosed at one year old and she was on sodium valproate. Physical examination showed a body weight of 45 kg (between -1 and -2SD), a body height of 1.62 m (between mean and -1 SD). Tanner scale was B1P2. Hormonal investigation showed an hypergonadotrophic hypogonadism (FSH = 153 U/I (1-17) and LH= 34 mU/I (0.5-41.7)). Pelvic ultrasound showed an infantile uterus. Ovaries were not visible. A complementary pelvic MRI confirmed the absence of ovaries and the hypoplastic uterus. Karyotype was 46XX and the genetic study showed the absence of the GJB2 gene mutation. The diagnosis of Perrault syndrome was confirmed. The electromyography was normal and cerebral MRI showed white matter demyelination. The patient was treated with estrogen and progesterone to induce puberty.

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Conclusion
We report this case because of its rarity as few cases have been reported in Tunisia so far in the literature. The prevalence of Perrault syndrome is poorly known, often under diagnosed because of the phenotypical and genetic heterogeneity of this syndrome.

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EP900
Gynecomastia: clinical, paraclinical and etiological aspects
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Introduction
Gynecomastia is an enlargement of male breast glandular tissue caused by an imbalance of the hormones androgens and estrogens. It can be physiological at different stages of life (birth, adolescence, senescence), caused by medication or reveal a serious pathology. The aim of our study was to evaluate the characteristics of presentation, biochemical profile, and etiology of gynecomastia.

Methods
A retrospective study was conducted at the endocrinology department of the Rabta Hospital in Tunis including 100 patients who presented with gynecomastia between January 2015 and December 2020. Clinical and paraclinical data were collected from medical records.

Results
The mean age of our patients was 37.16 years with extremes ranging from 11 years to 88 years. Seven patients (7%) had a history of cryptorchidism and testicular ectopy. Impuberty and late puberty were noted in 17 patients (17%). The mean duration of Gynecomastia before seeking specialized endocrine care was 78 months with an acute onset in 19% of cases. On physical examination, 56 patients (56%) had bilateral and symmetrical gynecomastia, 19 patients (19%) had bilateral and asymmetrical and 25% unilateral gynecomastia. 13 patients had stage I, 33 patients had stage II and 52 patients had stage III gynecomastia. Testosteronemia was measured in 43 patients and was low in 26 patients (26%). Gynecomastia was considered physiological in 25 patients (25%). The etiology of gynecomastia was considered to be drug-induced in 15 patients (15%), including spironolactone in six patients. The other drugs involved were chemotherapy and dopaminergic antagonists. Other causes were non-functioning pituitary adenomas, prolactinomas, isolated hypogonadotropic hypogonadism, testicular diseases, hypothyroidism and hyperthyroidism in 7%, 6%, 8%, 7%, 2% and 12% of the cases respectively. Idiopathic gynecomastia was found in 29% of cases.

Conclusion
Gynecomastia is a frequent and often benign pathology but it can be the expression of a relevant underlying endocrine disease or even tumor pathology. This highlights the importance of an adequate and complete clinical, biochemical, and imaging assessment of every patient presenting with gynecomastia.

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EP901
Therapeutic aspects of gynecomastia: about 100 cases
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Introduction
Gynecomastia is defined as the benign proliferation of the mammary glands in males, which results from an excess of estrogens, androgen deficiency, hormone resistance, or altered ratio of estrogens to androgens. It can be unilateral or bilateral. The aim of our study was to describe the therapeutic aspects and the evolution of gynecomastia.

Methods
This is a retrospective descriptive study of 100 patients who presented with gynecomastia at the endocrinology department of the Rabta hospital between January 2015 and December 2020. Clinical and paraclinical data were collected from medical records.

Results
Our population had a mean age of 37.16 ± 21.7 years at the time of the first visit. The mean age of puberty was 13.9 ± 2.7 years. Seven patients (7%) had a past medical history of testicular ectopy and cryptorchidism. Physical examination showed the presence of glandular tissue in all patients and diagnosis was documented by ultrasound and/or mammography in 60 patients. Biological workup revealed hypogonadotropic hypogonadism in 15 patients, including 7 patients with non-functional pituitary adenoma and 8 patients with isolated hypogonadotropic hypogonadism, hyperprolactinemia with prolactinoma in 6 patients, hypothyroidism in 2 patients, and hyperthyroidism in 1 patient. Gynecomastia was secondary to testicular disease in 7 patients. In addition, 15 patients had drug-induced gynecomastia. Finally, gynecomastia was physiological in 25 patients and idiopathic in 29 others. Regarding the management of gynecomastia, 29 patients received treatment for the etiology, 11 patients received testosterone enanthate injections. Nine patients received local treatment with androstanolone and 12 patients underwent cosmetic surgery. The rest of the patients were monitored and did not receive any treatment. The evolution was marked by clinical improvement in 38% of cases.

Conclusion
Each case of gynecomastia should be subjected to a precise etiological workup including at least a testosterone and estradiol dosage. The treatment modalities of gynecomastia depend on the results of the etiological investigation.

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EP902
Polycystic ovary syndrome : clinical, paraclinical and therapeutic profile
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Introduction
Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women and its main symptoms are related to menstrual disorders and hyperandrogenism. The aim of our study was to evaluate the clinical and paraclinical profile of PCOS.

Methods
We conducted a retrospective study that included 50 women, followed at endocrinology department’s consultations of Rabta Hospital in Tunis. Each patient underwent a clinical examination, hormone assays and ovarian ultrasound. The diagnosis of PCOS was made according to the Rotterdam 2003 criteria.

Results
The mean age of our patients was 26.9 ± 7.9 years [15 -45]. The family history of PCOS was found in 24% and type 2 diabetes mellitus’s personal medical history in 21.7%. Eight percent of patients were smokers. The mean age of menarche was 12.1 ± 1.3 years. Sixty-two percent of patients had spaniomenorrhoea and 6% had secondary amenorrhoea. These disorders were post-pubertal in half cases. The average weight was 87.5 ± 21.9 kg [38-150] for an average body mass index of 33.3 ± 7.6 kg/m² [16-57]. Therefore 65% of patients were obese and 37% presented acanthosis nigricans on clinical examination. Clinical hyperandrogenism signs such as acne and hyperseborrhea were found in 22.7% while major virilizationsigns were noted in 4%. Hirsutism was classified moderate to severe in 60.8%. Biological hyperandrogenism was found in 62% of cases including mean testosterone level of 0.78 ± 0.4 mg/ml. The average LH/FSH ratio was 1.7 ± 0.9, and was higher than 2 in 29%. Ovarian ultrasound showed a polycystic aspect in 72% of cases with increased ovaries size in 56%, the rest were strictly normal. Hygienic diet was instituted in 96% associated to metformin in 18% of cases and an Oestrone -Progesterin combination therapy in 69%. An additional laser hair removal treatment was done in 28%. Clinical and biological improvement was noted in half cases.

Conclusion
The etiological investigation of hyperandrogenism with menstrual disorders should remain exhaustive to eliminate potentially serious diagnoses. PCOS remains a benign disease. However, it must be managed effectively, given its impact on the patient’s quality of life.

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Clinical utility of the Anti-Mullerian Hormone testing for the prediction of PCOS

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Introduction

The diagnostic criteria of polycystic ovari syndrome (PCOS) are still under discussion and the hormonal parameters, including anti-Mullerian hormone range and hyperandrogenism, are not determined. Serum AMH level has been proposed as a surrogate marker for PCOM and could, therefore, be integrated in the diagnostic classifications for PCOS. The aim of the present study was to characterize hormonal features of PCOS and to establish the most important hormonal parameters for PCOS diagnosis.

Design

A case-control study.

Methods

The study included 60 women with PCOS according to the complete Rotterdam criteria, aged 18-40 years. The control group consisted of 60 healthy women with a regular menstrual cycle of the same age. Hormonal assays, and ultrasound of the pelvic organs were performed. The diagnostic accuracy of AMH, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, testosterone (T), dehydroepiandrosterone sulfate (DHEAS), sex-hormone-binding globulin (SHBG) and free androgen index (FAI) in predicting PCOS was established using a logistic regression model and calculating area under the receiver operator characteristic (ROC) curve (AUC).

Results

PCOS women had higher levels of serum LH (p < 0.01), T (p < 0.01), AMH (p < 0.01), FAI (p < 0.01), DHEAS (p < 0.01), estradiol (P < 0.01), 17-OH PG (p < 0.01) and significantly lower SHBG level (p < 0.01) compared to healthy women. Testosterone level > 0.41 ng/ml showed the highest sensitivity (85.0%) and specificity (96.7%) for PCOS diagnosis. The level of AMH > 4.69 ng/ml also showed high sensitivity of 75% and specificity of 75% in PCOS diagnosis in the studied sample. The diagnostic accuracy of PCOS reached 94.2% with the combined use of hormonal indexes, which was significantly higher than the use of each index separately.

Conclusions

The results of the study estimate the threshold for AMH and T which could be suggested for use in the PCOS diagnostics with a high sensitivity and specificity. Moreover, the combination of hormonal indexes improved the diagnostic accuracy for the PCOS detection.

Keywords: polycystic ovary syndrome, hyperandrogenism, testosterone, anti-Mullerian hormone, threshold

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Unrecognized premature ovarian failure in adolescents-case report

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Introduction

The average age for physiological menopause is 50 years. Menopause before the age of 40 is usually defined as premature ovarian failure (POF). POF in adolescents is an extremely rare event and its occurrence raises important questions about the cause-and-effect relationship, which may signal genetic and systemic disorders.

Design

Case report

The 29-year-old first reported to an endocrinologist for secondary amenorrhea. The anamnesis revealed that the patient got menarche at the age of 10. She had regular menstrual cycles for 4 years and irregular periods for 2 years. After the age of 16 she stopped menstruating. After 6 months, the therapy was excluded and during the next period of 12.5 years until the appearance of the endocrinologist and the desire to have children, she did not take anything from the therapy. From hardship allegations; irritability, insomnia, lack of energy, loss of libido, sweating, headache and weight gain. Menopause in a mother from the age of 30. Hormonal analysed: hypergonadotropic hypogonadism (FSH 200 mIU/L, LH 29.34 mIU/L, estradiol < 7 pg/ml, AMH < 0.01 ng/ml). Ultrasonography of the pelvis showed a normally located and normally developed uterus with a 4.7 mm thin endometrium and both ovaries of reduced dimensions. Chronic autoimmune thyroiditis with elevated antibodies to thyroid peroxidase and thyroglobulin, but euthyroid with thyroid hormones in the normal range, was detected in the patient by ultrasoundography. Testing did not detect congenital and acquired trobophilia. Karyotype: 46XX. Genetic analysis of FMR1 genes normal. Ovarian antibodies negative. Introduced replacement therapy withoral estrogen-progestogens with the addition of estradiol at a dose of 2 mg in the follicular phase of the menstrual cycle, D3 hormone, antioxidants. After 2 years of treatment : FSH 28 mIU/L, LH 19.11 mIU/L, estradiol 22.4 pg/ml. Spontaneous abortion in the 6th week of gestation after in vitro fertilization with donated eggs. Conclusion

Most cases of POF remain idiopathic with a reduced success rate of assisted reproduction and procreation. The goal of treating adolescents with POF is replacement therapy with higher doses of estrogen than menopausal women to ensure proper replacement and optimal bone health.

Keywords: premature ovarian failure, secondary amenorrhea, hypergonadotropic hypogonadism

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Development of ANA antibodies induced by estrogen treatment.

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A 36-year-old woman in follow-up due to early ovarian failure of idiopathic origin. No family history of interest. History of menarche at 12 years of age with regular menses until 18 years of age, when it begins with amenorrheic spells lasting up to 8 months. Laboratory tests revealed hypergonadotropic hypogonadism with negative ovarian autoantibodies, normal karyotype, and gynecological ultrasound showing a normal-looking uterus with slight bilateral ovarian atrophy. Negative antiadrenal and anti-TPO antibodies. She has undergone treatment with estrogen without criteria for systemic lupus erythematosus. She is currently asymptomatic and without hormone replacement therapy.

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EP907

Associations of VDBP polymorphisms with birth neonatal anthropometry: a cohort study from Northern Greece

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Vitamin D binding protein (VDBP) has a critical role in orchestrating optimal vitamin D homeostasis and bioavailability. VDBP has been implicated in modulating the gene expression of amino-transporters within the placenta and might thus control the transfer of amino acids to neonates during in utero development. We hypothesize that dyshomeostasis of VDBP could lead to adverse metabolic profiles and low birth weight in neonates. VDBP genetic polymorphisms steer the unique interplay of VDBP biodynamics and pregnancy complications. The aim of this study was to investigate associations of maternal VDBP polymorphisms with neonatal anthropometric profiles at birth, according to different cut-offs of vitamin D status. We included 66 maternal-neonatal dyads recruited from Northern Greece. Serum 25(OH)D concentrations were determined using LC-MS/MS and VDBP was measured by ELISA. We classified maternal and neonatal vitamin D status at birth, according to 25-hydroxyvitamin D (25(OH)D) concentrations as follows: 25(OH)D ≤ 25 nmol/l (insufficiency), 25-50 nmol/l (insufficiency) and 25(OH)D ≥ 50-75 nmol/l (sufficiency). Our results revealed that with maternal 25(OH)D < 50 nmol/l neonatal anthropometry parameters including abdominal circumference, lower arm radial circumference and lower leg calf circumference were significantly higher in maternal VDBP genetic variants rs2298850 CG + GG and rs4588 CA + AA and rs7041 GT + TT. This relation between birth neonatal anthropometry and maternal vitamin D polymorphism, was not significant for birth maternal 25(OH)D < 25 nmol/l. In conclusion, these findings, emphasize a potential role of functional polymorphisms, for maternal VDBP genotypes for rs2298850, rs7041 and rs4588, in conjunction with a maternal cut-off of maternal 25(OH)D in the range of sufficiency on neonatal growth and development. Further investigations are required to decipher the exact dynamic pathways of maternal VDBP and genetic variants on pregnancy complications and offspring body anthropometry.

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EP908

Evaluation of socio-demographic and clinical characteristics of PCOS patients attending a tertiary care institute in Colombo

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Background and Objectives

Polycystic ovary syndrome (PCOS) is a common endocrine disorder with heterogeneous etiology. It is characterized by irregular menses and or oligo/anovulation, hyper-androgenism, and polycystic ovaries. The prevalence and diagnosis of PCOS changes depending on which clinical criteria are utilized to confirm the diagnosis. The prevalence can be high as 15–20% when the Rotterdam criteria are used. However, there is significant inter-individual variation in presentation. We have studied the socio-demographic and clinical characteristics of PCOS patients attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.

Methods

A descriptive cross sectional study was conducted from September 2019 to September 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting PCOS patients diagnosed with Rotterdam criteria. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. HOMA-IR was calculated using the fasting insulin and blood glucose level.

Results

The study enrolled sixty females. The mean age was 26.7 years (range 18-44). The mean weight was 64.8 (SD = 11.9) kg and BMI was 27.1 (SD = 4.8) kg/m². According to Asian BMI cut-offs, 1 (1.7%) patient was underweight and 13 (21.7%) normal weight. Forty six (76.7%) had their weight in the overweight or obese category. Fifty four (90.0%) patients had clinical or biochemical evidence of hyperandrogenism while 24 (40.0%) females had polycystic ovaries on trans-abdominal ultrasound scan and 50 (83.3%) partipants had irregular menstrual cycles. According to the body fat percentage assessed by the whole body DEXA scan 4.1% of the study population had normal body fat, while 50.0% and 45.8% had overweight and obesity respectively. HOMA-IR detected 61.1% patients to have high insulin resistance. Out of the patients who had USS of the abdomen 27.5% had co-existent non-alcoholic fatty liver. Fifty four percent of the patients had sub/fertillity.

Conclusions

The majority of the population were overweight or obese and had higher prevalence of insulin resistance and non-alcoholic fatty liver. Out of the clinical characteristics used to make the diagnosis of PCOS, the presence of clinical or biochemical evidence of hyperandrogenism and irregular menstrual cycles are more common than the detection of polycystic ovaries on trans-abdominal USS. The higher prevalence of overweight, obesity, insulin resistance and NAFLD associated with PCOS makes the diagnosis and management of the disease crucial to prevent long term consequences of the disease.

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EP909

PCOS pearls - findings from the qualitative study assessing the lived experience of people with polycystic ovary syndrome

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PCOS pearls - findings from the qualitative study assessing the lived experience of people with polycystic ovary syndrome

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Developmental programming by maternal androgen excess is mediated by androgen receptor pathways

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Introduction
Existing educational resources for polycystic ovary syndrome (PCOS) have limited inclusion of patient perspectives. We invited women with PCOS to share their lived experiences to understand their perception and opinion on the current standard of care.

Methodology
Women with PCOS aged 18-60 years were invited to complete an online survey in April and May 2021. The survey had open questions focused on their lived experiences with PCOS. Participants had the option to share their views either as written text or as voice note audio recordings(s) on WhatsApp. The data from audio were transcribed verbatim. Responses were initially coded by two study members independently, using a thematic inductive method with NVivo 12. These codes were then reviewed by two senior study members to identify common themes.

Results
43 of 45 participants had a formal diagnosis of PCOS, the remaining two had suspected PCOS which was under investigation. Four participants opted to share their views as voice note recordings. Overall, five common themes emerged: experience of symptoms (504 references by 42 participants), patient journey (421 references by 42 participants), knowledge (197 references by 40 participants), peer-to-peer advice (162 references by 41 participants), and impact of PCOS on social aspects of life (42 references by 19 participants). Poor mental health was most commonly reported (83.3% of participants), followed by dermatological (81.0%) and menstrual issues (76.2%). Participants were generally dissatisfied with the care they received (88.1%). A lengthy diagnostic journey was reported in 35.7% of cases. 52.6% felt less feminine, particularly with regards to weight gain and infertility. Women with PCOS said that others with the condition should educate themselves and be proactive in their management. 46.3% reported that being more enlightened regarding their condition improved their health outcomes and enabled them to advocate for their own care.

Conclusion
PCOS has wide-ranging consequences for women living with the condition, with many feeling dissatisfied with the clinical support they currently receive. Education is important to improve their understanding of their condition and encourage a proactive approach to their own care. Therefore, we propose involving people with PCOS to co-create educational resources informed by lived experiences which will help those newly diagnosed to gain a more comprehensive and realistic understanding of the condition from fellow sufferers.

Method
We used a PCOS-like mouse model induced by continuous exposure of dihydrotestosterone from prepuberty that develops obesity, anovulation and dysfunctional ovarian morphology, to study the effects of maternal hyperandrogenism during pregnancy. In addition, slight modifications are applied to the prepubertal PCOS-like mouse model to investigate critical periods in peripuberal life that projects to adverse pregnancy outcomes. To explore molecular mechanisms that contribute to the developmental defects, whole genome bisulphite and RNA sequencing of primordial germ cells and placenta were performed.

Results
Lower pregnancy rate and impaired placenta and embryonic development were found in the androgenised group, which was partially prevented by co-treatment with flutamide, an androgen receptor blocker. Moreover, germ cell specification was greatly compromised at embryonic day 10.5 and 13.5. The results of whole genome bisulphite sequencing and RNA sequencing of the primordial germ cells and placenta are currently under analysis. Furthermore, androgen exposure before the onset of vaginal opening may alter the physiology of uterus and vagina causing difficulty in labour.

Conclusion
Our results so far suggest that hyperandrogenism greatly compromise the PCOS-embryo development due to placenta dysfunction. Such effects are mainly mediated by the androgen receptor pathway as administration of flutamide partially prevents the compromised placenta and fetal development.

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EP911
The role of level and density of PSA in screening of prostate cancer
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Introduction
It is known from world experience that the common screening method for diagnosing prostate cancer is the level and density of prostate-specific antigen (PSA), but the high sensitivity and low specificity of PSA testing have not been evaluated in Uzbek clinical practice. There are no proper guidelines to investigate suspected prostate cancer in Uzbekistan.

Methods
A total of 101 men were included in our investigation who were examined in the Republican specialized center of urology. All the patients underwent a complete examination, including laboratory (PSA level), ultrasonography, transrectal ultrasonography, and prostate biopsy. The patients were divided into subgroups by PSA level and PSA density, PSA density was calculated as total PSA (ng/ml) divided by prostate volume (ml).

Results
In patients with lower PSA levels less than 4 ng/ml detected benign processes compared to patients who had higher values of more than 50 ng/ml. Only two cases which had less than 4 mg/ml were suspicion of malignancy. When the PSA value was more than 100 ng/ml, almost all the cases were malignant. Between PSA values of 4-100 ng/ml, the probability of cancer diagnosis was 54% (54 cancers out of 101 in this range). Limitation of PSA testing has the risk of overdiagnosis and the resultant negative biopsies owing to poor specificity. Whereas the limit for cancer diagnosis remains 4 ng/ml from our study, most of the patients can be assured of benign lesion below this level, and thus morbidity associated with the biopsy can be prevented. PSA density was associated with the risk of finding PCA both with and without adjusting for the additional clinical information age, family history, previous biopsies, total PSA, and free/tototal PSA.

Conclusion
The PSA level plays important role in diagnosing prostate cancer and can reassure and educate the patients towards the diagnosis of cancer of the prostate in Uzbekistan. It is recommended prostatic biopsy if the level is below 4 ng/ml and a level of 100 ng/ml can be very unfavorable for the patients. Regarding the PSA-density might inform biopsy decisions, and spare some men from the morbidity associated with a prostate biopsy and diagnosis of low-grade prostate cancer.

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**EP912**

**Gonadal dysgenesis with mayer-rokitansky in 46, XX female; case report**

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**Introduction**

The normal development of the female reproductive tract depends on the interaction between genetic, hormonal and environmental factors for the differentiation of the Müller Wolff ducts, and the urogenital sinus

**Case report**

16-year-old female, single, school student presented to our endocrine department complaining of delayed puberty. The patient was delivered by normal vaginal delivery, no history of anomalies or hearing defects There is no history of headache or blurring of vision or other neurological symptoms No history of chronic diseases, excessive exercise, medications, anorexia, clinical hypothryodism or hyperandrogenism Family history revealed positive consanguinuty Physical examination: Weight: 60 kg Height: 172 cm, BMI: 20 No facial dimorphism, no features suggestive of Turner syndrome Female phenotype, Tanner classification: breasts (3) axillary hair (2), pubic hair (2). Normal external genitalia Laboratory work up showed follicle-stimulating hormone: 98 mIU/ml (N: 6.7-11.1) Luteinizing hormone: 26 mIU/ml (N: 0.8-7.6), Estradiol 10 pg/ml (N: 110-550), prolactin 4.4 ng/ml pelvi-abdominal ultrasonography, MRI pelvis - Infantile hypo plastic uterus (body 20 mm, cervix 12 mm) Non visualized both ovaries Normal female karyotyping 46, XX Hormonal substitution by estrogen and progesterone was then undertaken.

**Conclusion**

The Mayer-Rokitansky-Kuster-Hauser Syndrome is a specific type of nullerian duct malformation characterized by congenital absence or hypoplasia of uterus and upper two thirds of the vagina in both phenotypically and karyotypically normal females with functional ovaries. The association of gonadal dysgenesis and Mayer-Rokitansky-Kuster-Hauser syndrome is very rare, hormone substitution therapy remains the only therapeutic option, to trigger the development of secondary sexual characters and prevent osteoporosis.

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**EP913**

**Color-doppler ultrasound predicts hypothalamic-pituitary-testicular axis function in infertile patients**

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Scrotal color-doppler ultrasonography (scCDUS) and transrectal ultrasonography (trCDUS) provide crucial information about the clinical status of testes and male accessory glands. However, the US evaluation of the infertile male is still often considered as a second level diagnostic tool. To analyze the role of ultrasound in male infertility, in order to predict hypothalamic-pituitary-testicular axis function, 1120 records from infertile men were retrospectively evaluated (from January 2016 up to June 2020). Data on physical examination, semen analysis, testosterone, AMH, FSH and INHB were analyzed. Among them, 238 reports from oligozoospermic/azoospermic infertile patients (P) (mean ± SD years) fulfilling the inclusion criteria were considered for data analysis. Patients were subdivided into two groups according to FSH values (P with FSH < 8 U/l and P with FSH > 8 U/l). Sixty-three fertile volunteers (mean ± SD years) were enrolled as controls (C). Pb group had significantly lower testicular volume compared to Pa and to C. A higher prevalence of ultrasound abnormalities was recorded in P compared to C. Pa had a higher prevalence of trCDUS abnormalities than Pb (69.3 vs 38.4%; P < 0.005), while Pb had a higher prevalence of abnormalities at scCDUS (60.6 vs 28.3%; both P < 0.001). A higher number of US abnormalities was associated with a more severe reduction in sperm count. Bisterical volume was inversely proportional to the number of altered seminal parameters and a bilateral testicular volume ≤ 17 cc was associated with a higher risk of azoospermia (odds ratio 1.799). Moreover, this parameter was able to predict gonadotropin levels. Our data confirm the pivotal role of ultrasound in the diagnostic workflow of male infertility.

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**EP914**

**Isolated FSH deficiency. A rare cause of male infertility**

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**Background**

Follicle stimulating hormone (FSH), a dimeric glycoprotein hormone, stimulates Sertoli cell proliferation and spermatogenesis in males. Azoosperma is defined as the absence of sperm in the ejaculate. The majority of patients with non-obstructive azoosperma have high FSH levels. Isolated FSH deficiency has been reported in a few patients. Case Presentation

A 22-yr-old, 172-cm-tall male presented with azoosperma. He was born at full term with normal delivery of non-consanguineous parents. He had normal pubertal development with normal erections and potency. Upon physical examination he had normal virilization, normal sense of smell and no gynecomastia. His tests were both palpable in the scrotum measuring 25mm. No sperm was observed in the semen analysis twice. Semen fructose levels were normal. Urine analysis for retrograde ejaculation and testicular ultrasound revealed no abnormalities. His chromosomal karyotype was 46, XY. His testosterone, luteinizing hormone (LH), inhibit B (INHB) and anti-mullerian hormone (AMH) levels were normal, whereas FSH was low. Hypothalamic-pituitary magnetic resonance imaging (MRI) demonstrated no abnormalities. FSH levels remained low after intravenous injection of 100ug of gonadotropin-releasing hormone (GnRH), whereas LH levels rose. Sequencing of the β-subunit of FSH (FSHβ) gene did not reveal any mutation.

**Discussion**

Reports on isolated FSH deficiency are very rare with a prevalence of 0.89% in a retrospective study. The first observations of isolated FSH deficiency in males were described in 1998. Since then ten more case reports have been published, half of which were caused by an inactivating mutation of FSHβ gene. The patients presented with azoosperma, testicular hypotrophy, but with normal levels of testosterone and virilization. It appears that in cases of no FSHβ gene mutation there is milder phenotype, with oligo-astheno-teratospermia and even normal testicular volume. In cases where testicular biopsy was performed, spermatogenesis arrest, Sertoli cell hypoplasia and Leydig cell hyperplasia were reported. Hypothalamic-pituitary MRI and karyotype were normal. Remarkably, despite low INHB and AMH levels in patients with FSHβ gene mutations, cases without the mutation exhibited normal levels. Exogenous FSH led to an increase in testicular volume, spermatogenesis and in some cases in successful pregnancies.

**Conclusion**

Isolated FSH deficiency represents a rare form of male infertility which may be restored and therefore carries a high diagnostic value.

**EP915**

**Developmental neuro toxicity and cytotoxic mechanism evaluation of endocrine-disrupting chemical butylparaben**

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Butylparaben is an endocrine disrupting chemical (EDC) which is used as antimicrobial preservative in many cosmetic products. EDCs are structurally diverse class of synthetic and natural compounds. EDCs can cause non-
communicable diseases such as obesity, type 2 diabetes, and neurodevelopmental disease. Present study investigated that whether exposure to butylparaben during maternal pregnancy could cause the offspring’s neuronal development disorder. In vitro study butyl paraben promoted apoptosis and inhibited proliferation of Sox1-GFP cell. The mRNA expressions for ER stress were evaluated. Furthermore, in vivo study for developmental neurotoxicity test battery for butylparaben was carried out. Butylparaben 100 mg/kg, 50 mg/kg was treated for pregnant mouse from E10.5 to weaning period. The result of behavior test shows abnormal cognitive, social and anxiety like behavior in butyl paraben treated mice. In vitro study, ER stress genes was evaluated, BiP, CHOP, and AFT6 were significantly up-regulated following treatment with EDC. From these results, butylparaben is a potential neuro developmental toxicant.

Keywords: Developmental neurotoxic test; mouse embryonic stem cells; endoplasmic stress

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EP916

Swer syndrome presenting with clinical features of cushing disease: a case report

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Case presentation

A 18-year-old female patient with no medical history was referred to our department for suspicion of Cushing syndrome. She had primary amenorrhea and reported weight gain within 2 years. On physical examination, her body mass index was 34.5 kg/m² with a height of 156 cm. She had round moon face, red cheeks, a buffalo neck, thin arms and legs, and abdominal purple stretch marks. She had a female morphotype, normal female-type external genitalia with secondary sexual characters rated S4, P3 and A3 according to Tanner’s classification. A 4-mg dexamethasone suppression test reduced the serum cortisol level to 0.3μg/dl excluding the diagnosis of Cushing syndrome. Hormonal investigations revealed elevated pituitary gonadotropin levels with FSH at 34.9 UI/l and LH at 15.8 UI/l. The testosterone and prolactin level were normal at 0.92 nmol/l and 9 ng/ml respectively. A pelvic ultrasound confirmed the presence of 2 small non-follicular ovaries with uterine hypoplasia (25X17X8mm). The karyotype was male “46 XY”. The diagnosis of pure 46 XY gonadal dysgenesis was made. A hormone replacement therapy was applied and the patient was referred to a gynecologist for bilateral prophylactic gonadectomy.

Conclusion

In light of this case, we wish to draw attention to a serious sex-reversal disorder that affects women in their identity. Swyer syndrome revealed here by an unusual circumstance of discovery. This pathology is associated with a higher risk of communicable diseases such as obesity, type 2 diabetes, and neurodevelopmental disease. Present study investigated that whether exposure to butylparaben during maternal pregnancy could cause the offspring’s neuronal development disorder. In vitro study butyl paraben promoted apoptosis and inhibited proliferation of Sox1-GFP cell. The mRNA expressions for ER stress were evaluated. Furthermore, in vivo study for developmental neurotoxicity test battery for butylparaben was carried out. Butylparaben 100 mg/kg, 50 mg/kg was treated for pregnant mouse from E10.5 to weaning period. The result of behavior test shows abnormal cognitive, social and anxiety like behavior in butyl paraben treated mice. In vitro study, ER stress genes was evaluated, BiP, CHOP, and AFT6 were significantly up-regulated following treatment with EDC. From these results, butylparaben is a potential neuro developmental toxicant.

Keywords: Developmental neurotoxic test; mouse embryonic stem cells; endoplasmic stress

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EP917

Machine learning-based model for gestational diabetes mellitus prediction in the first trimester of pregnancy

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Background and aim

Gestational Diabetes Mellitus (GDM) is often diagnosed at 24-28 weeks of pregnancy when the fetal phenotype is already altered. We aimed to develop a machine learning model based on clinical variables, lifestyle features and genetic markers for GDM prediction in the first trimester of pregnancy based on the 2013 World Health Organization (WHO) criteria.

Methods

Using multivariable logistic regression analysis, different models to predict GDM were developed based on clinical variables from early pregnancy (age, pre-pregnancy body mass index (BMI), arterial hypertension, a history of GDM, impaired glucose tolerance, polycystic ovary syndrome, family history of type 2 diabetes, and parity), lifestyle features (food consumption, physical activity and smoking habits assessed through questionnaires), genetic markers (number of risk alleles in rs10830963 of the MTRNR1B gene) and their combination. The input data were obtained from 1050 pregnant women participating in prospective studies performed in the Almazov National Medical Research Centre (655 GDM cases and 395 controls). Receiver operating characteristic (AUC) analysis assessed the model’s performance with eight-fold cross-validation.

Results

C-statistics for logistic regression models were as follows: clinical covariates alone: 0.690 (95% CI: 0.658 to 0.722) and 0.688 (95% CI: 0.647 to 0.729) for an eight-fold cross-validated assessment of the score; rs10830963 alone: 0.597 (95% CI: 0.565 to 0.629) and 0.546 (95% CI: 0.375 to 0.717) cross-validated; combination of clinical covariates and rs10830963: 0.721 (95% CI: 0.690 to 0.752) and 0.715 (95% CI: 0.672 to 0.759); combination of clinical covariates and lifestyle features: 0.806 (95% CI: 0.779 to 0.833) and 0.802 (95% CI: 0.724 to 0.881) cross-validated; combination of clinical covariates (age, pre-pregnancy BMI, a history of GDM, rs10830963 and lifestyle features (the frequency of pre-pregnancy consumption of meat, bread and alcohol): 0.823 (95% CI: 0.797-0.849) and 0.813 (95% CI: 0.734-0.892) cross-validated.

Conclusions

A first trimester machine learning-based model, which incorporates classical risk factors and novel biomarkers, has a high accuracy to predict GDM based on the 2013 WHO criteria.

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EP918

Partial androgen insensitivity syndrome revealed by a bilateral gynecomastia

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Introduction

Partial androgen insensitivity syndrome is a disorder of sexual development, distinct from complete androgen insensitivity syndrome. It is characterized by the presence of abnormal genital development in an individual with a 46, XY karyotype. Partial androgen insensitivity syndrome is a disorder of sexual development, distinct from complete androgen insensitivity syndrome. It is characterized by the presence of abnormal genital development in an individual with a 46, XY karyotype. Partial androgen insensitivity syndrome revealed by a bilateral gynecomastia

Case report

We report the case of an 18-year-old patient with a history of hypospadias operated in childhood, who consulted for bilateral gynecomastia. The clinical examination revealed a 3.5 cm Tanner P5 microCryptorchidism with absence of facial and axillary hair. His karyotype was 46, XY. Biologically: testosterone : 18.84 ng/ml, FSH was normal and LH : 15.6 mIU/ml with a Testosterone/Dehydroepiandrosterone (DHT) ratio of 6. The diagnosis of partial androgen insensitivity was therefore retained. Androstane (Andracin® gel) was used for 6 months with therapeutic failure. The patient was referred to plastic surgery for surgical management of his gynecomastia.

Discussion and conclusion

Partial androgen insensitivity is most often diagnosed in a newborn with atypical genital development (hypospadias, cryptorchidism, microCryptorchidism, or even very feminine phenotype with clitoral hypertrophy). The diagnosis will be evoked more rarely in front of an isolated microCryptorchidism or an isolated gynecomastia as in the case of our patient, or pubertal virilization in a young girl or fertility disorders in a man. It varies according to the degree of insensitivity of the genital tract to androgens.

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EP919
Complete androgen insensitivity syndrome: about 2 cases
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Introduction
Androgen insensitivities are rare genetic diseases, characterized by a more or less complete defect of tissue sensitivity to testosterone. It ranges from a more or less complete lack of masculinization to isolated infertility in a 46, XY individual. This partial or complete androgen insensitivity is linked to a defect in the function of the androgen receptor. We report the case of two patients with complete androgen resistance syndrome discovered during the exploration of primary amenorrhea.

Observation 1
33-year-old patient, operated in 2016 for bilateral intra-abdominal gonadectomy, with an anatopathological examination of an ectopic testicle on the right without signs of malignancy, and an embryonic carcinoma on the left, the patient underwent chemotherapy sessions; she presents a harmonious and feminine Morphological development, with absence of vaginal orifice, a catocyte was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progesterone with good clinical evolution.

Observation 2
20-year-old patient, who underwent bilateral gonadectomy in 2017 with pathological examination of hypoplastic testicular pulp with hamartomatous nodules and hypoplastic foci of Leydig cells compatible with androgen insensitivity syndrome without malignancy, with a gynecological examination presence of labia majora and labia minora not well formed with an incipient vagina. A catocyte was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progesterone with good clinical evolution.

Conclusion
Androgen insensitivity syndrome, a rare entity, is the most frequent etiology of the anomaly of the XY sex differentiation, gonadectomy is necessary, and hormonal substitution helps maintain female sexual characteristics and prevent osteoporosis.

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EP920
Safety and monitoring of gender affirming hormone therapy in portugual
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Introduction
The prevalence of Transgender individuals seeking gender affirming hormone therapy (GAHT) has been increasing. It is important to closely monitor this therapy in order to minimize the risk of adverse effects.

Aim
To evaluate the safety and monitoring of the GAHT in the Portuguese adult transgender population.

Methods
Cross-sectional study conducted in March 2021. Data collected through an online questionnaire that was delivered to adult transgender people living in Portugal who had been under GAHT for at least one year. To answer some of the items on the questionnaire, an ordinal scale ranging from 0 (worst result) to 6 (best result) was used.

Results
A total of 142 individuals answered the questionnaire: 101 under masculinizing GAHT (Group M) and 41 under feminizing GAHT (Group F), with a median age of 25.0 (21.0–33.0) years. 43.3% of the individuals denied having signed an informed consent document and 11.3% denied having done blood sample analysis before starting GAHT. This happened more frequently with individuals of the Group F (24.4% vs 5.9%, P = 0.002). Accordingly, this group also reported having obtained the first prescription of GAHT by an endocrinologist less frequently (58.5% vs 79.2%, P = 0.012). 93.7% of the individuals had regular medical appointments because of the GAHT; although this was less common in Group F (85.4% vs 97.0%, P = 0.010). 79.6% reported undergoing regular blood sample analysis to monitor the GAHT. Of those, 75.2% did so according to the timings recommended by WPATH. As for adverse effects, 89.7% of the individuals on Group M experienced at least one – more commonly mood swings (56.3%) and acne (52.9%) – and 96.3% of the individuals on Group F experienced at least one – more commonly decreased libido (66.7%) and mood swings (63.0%).

Discussion
This study highlights the importance of the involvement of specialized physicians, namely endocrinologists, in the prescription and monitoring of the GAHT. There is still plenty of room to improve Transgender health care in Portugal, mostly in transgender people undergoing feminizing GHAT - a population known to be especially vulnerable to social stigma.

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EP921
Clinical features of reproductive status in women who underwent Covid-19
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Keywords: Reproductive system of women who have had coronavirus, Covid-19, women.

The relevance of the problem. Currently, there are no published evidence-based recommendations for the management of women who have undergone COVID-19. According to statistics, women carry COVID-19 more easily than men, and the likely consequences of this coronavirus infection for reproductive health cannot be ignored. It is necessary not only to carefully monitor the respiratory parameters of patients with COVID-19, but also to assess the potential impact of a new infection on the organs of the reproductive system.

Objective
To study the clinical conditions of women and assess their general condition.

Material and methods
100 women aged 18-45 years (average age 32 years) who underwent Covid-19 were examined. These women will be divided into 2 groups depending on the severity of the disease; they underwent a complete clinical hormonal and imaging examination and were divided into I a women with mild form, 50 women aged 18 to 44 years, I b women with severe form in the acute stage, 21 women aged 18 to 40 years, an average of 30 years At the moment, the control group will consist of 10 healthy women of the same age. A survey of complaints about the acute phase of women who had Covid-19 was conducted.

Results
The most frequent and significant changes were complaints of general weakness (p0.002), menstrual cycle changes (p0.001), headaches (p0.001), dry skin (p0.001), hair loss (p0.001), mood loss (p0.001), anxiety (p0.001). The least complaints were Hirsutism (p0.157), Decreased visual acuity (p0.317), Galactorrhea (p1.000).

Conclusion
In this way, the function of the reproductive system and somatic disease is aggravated in patients who have undergone Covid-19, which requires careful monitoring by an endocrinologist, gynecologist and neurologist.

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EP922
The clinical and etiological aspects of hirsutism: about 100 cases
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Introduction
Hirsutism is often caused by hormonal disorders such as high levels of circulating androgens, hormonal changes related to menopause or disorders of the ovarian or adrenal gland. The aim of our study was to evaluate the clinical and etiological profile of hirsutism.

Methods
A retrospective study was conducted at the endocrinology department of Rabta Hospital in Tunis including 100 patients who presented with hirsutism between January 2009 and December 2020. Clinical and paraclinical data were collected from medical records. Hirsutism was classified according to the Ferriman Galloway score.

Results
The mean age of our patients was 29.5 years ± 10.7 [15 - 73]. Family history of hirsutism, infertility and death in early childhood were found in 27%, 36% and 4% of cases respectively. The average age of menarche was 12.1 years ± 1.2. Eight women were menopausal. The onset of hirsutism was progressive in 95 cases either peripubertal or post-pubertal respectively 44% versus 56%. Hirsutism was classified as mild, moderate and severe in 32%, 57% and 11% of cases respectively. The clinical features found to be associated with hirsutism included acne (28%), virilism signs (9%) and menstrual irregularities in 60% of patients. The mean of testosterone level was 0.9 ng/ml ± 0.7 [0.15 - 4.08]. Additional investigations such as dosage of Dehydroepiandrosterone sulfate, 4-androstenedione, and 17-OH progesterone were done according to etiological orientation and revealed means of 900.1 µg/ml, 354 ng/ml, and 1.86 ng/ml respectively. The etiologic investigation showed ovarian tumor, adrenal tumor with androgen secretion, late-onset congenital adrenal hyperplasia, Cushing’s syndrome, polycystic ovary syndrome (PCOS) and idiopathic hirsutism in 3%, 5%, 7%, 2%, 51% and 32% of cases respectively.

Conclusion
Hirsutism is a very frequent and troublesome symptom. However, it can reveal serious underlying pathology, especially in its severe form.

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EP923
Clinical and metabolic profile of hirsute women
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Introduction
Hirsutism is described as excessive development of facial and body hair in women in androgen-dependent areas. Our aim was to determine the clinical and metabolic aspects of hirsutism and its relationship with the metabolic syndrome.

Methods
We conducted a retrospective descriptive study at the endocrinology department of Rabta Hospital in Tunis. We recruited 100 women who presented with hirsutism between January 2009 and December 2020. Clinical and paraclinical data were collected from medical records. The diagnosis of metabolic syndrome was made according to the IDF 2009 criteria.

Results
The mean age of our patients was 29.5 ± 10.7 years. Our patients were smokers in 8% of cases and diabetics in 19% of cases. The onset of hirsutism was post-pubertal in 56% with menstrual disorders in half cases. Associated clinical signs were skin acne (50%), Acanthosis Nigricans (20%) and signs of virilization (9%). Our population had an average weight of 83.9 ± 20.9 kg [38-150] with an average height of 167.5 cm [150-190]. Blood pressures were significantly elevated among women with PCOS compared to the control group. Acanthosis nigricans was present among 59.3% (n=51) of women with PCOS. Women with PCOS had significantly higher levels of fasting insulin (P=0.001), fasting blood glucose (P=0.015), and 2 h blood glucose level following 75g oral glucose load (P=0.002). Prevalence of type 2 diabetes mellitus among women with PCOS was 26.7% while prevalence was 12.8% in the control group. Further 24.4% of women with PCOS had prediabetes. Women with PCOS had significantly higher triglyceride levels (P=0.01), total cholesterol levels (P=0.02) and lower HDL levels (P=0.02) compared to control group. Systolic (P=0.05) and diastolic (P=0.01) blood pressures were significantly elevated among women with PCOS compared to control group.

Conclusion
Our results suggest that the increase of androgenic activity favors an android distribution of body fat, which is associated with an impairment of glucose and lipid metabolism.

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EP924
Recovery of hypothalamic-pituitary-gonadal function with low dose testosterone treatment in a male with idiopathic hypogonadotropic hypogonadism
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Idiopathic hypogonadotropic hypogonadism (IHH) is a rare congenital disease caused by deficiency or action of gonadotropin-releasing hormone. While generally considered a long-life condition, IHH can be reversible in about 20-30% of cases, but mechanisms of reversibility are unknown. We report the case of a male with IHH who began treatment with low dose (20 mg/day) transdermal testosterone to induce pubertal development at age 18. Following the start of treatment, he experienced testicular growth and his serum testosterone concentrations increased beyond the expectations in relation to the dose. Treatment was withdrawn, but this led to the reappearance of symptoms of hypogonadism and a drop in testosterone levels. Testosterone was again prescribed at the same dose and, for the subsequent years, he completed full puberty, including attainment of 20 cm testicular volume, mature secondary sexual characteristics, normal levels of testosterone and only partially arrested germinal function, as demonstrated by inhibin B levels and sperrmogram. Testosterone treatment was withdrawn three more times, but hypogonadism resumed on each occasion. This case suggests that low-dose testosterone treatment can induce reversal of IHH through the activation, albeit non-permanent, of the hypothalamic-pituitary-gonadal axis, and could be a therapeutic option for this condition.

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to the control group. Prevalence of hypertension among women with PCOS was 11.6%. 34.9% (n=30) of women with PCOS fulfilled diagnostic criteria for metabolic syndrome. Women with PCOS had higher odds of obesity, insulin resistance, hyperglycemia, dyslipidemia, hypertension and metabolic syndrome compared to age matched controls.

Conclusion
Women with PCOS often have multiple cardiovascular risk factors including obesity, diabetes mellitus, dyslipidemia, and hypertension. Management of cardiovascular risk factors should be prioritized in the long term care of women with PCOS. Further research is required to assess implications of PCOS on longterm cardiovascular morbidity and mortality among Sri Lankan women.

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EP926
Molecular and comprehensive computational analysis revealed normal LHCGR gene among women with PCOS
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Background
Polycystic ovary syndrome (PCOS) is a common disorder, yet not fully understood. Multiple hormonal and metabolic factors influence the pathophysiology of disease; resulting in various phenotypic characteristics among PCOS population. The luteinizing hormone/choriogonadotropin receptor (LHCGR, OMIM:157290) is a G protein-coupled receptor mapped on chromosome 2p16.3; its coding region comprises 10 exons separated by 10 introns which transcript to protein with 699 amino acids.

Objectives
To determine genetic mutations of LHCGR gene in Sudanese families affected by PCOS.

Methods
A prospective laboratory based cross-sectional study was implemented to examine genetic mutations in LHCGR that associate with PCOS in families (cases; n = 35 families, 90 females and controls; n = 11 families, 30 females) in Khartoum State, Sudan. Quantitative Enzyme Linked Immuno-Sorbent Assay (ELISA), enzymatic methods and partial selected exon 11 from in silico analysis data were analyzed by polymerase chain reaction (PCR) for polymorphism detection followed by Sanger sequencing for genotyping among selected families.

Results
From the In silico analysis, we revealed that the most (29) distributed SNPs were gene in women manifesting PCOS. These novel mutations give insight to protein with 699 amino acids.

Conclusion
This is the first molecular family-based study in Sudan exploring the genetics of the LHCGR gene in women manifesting PCOS. These novel mutations give new insights into the protein with 699 amino acids.

Keywords: PCOS, Luteinizing hormone, SNPs, infertility, family studies, LHCGR

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EP928
Mild Androgen Insensitivity (MAIS): A challenging clinical and laboratory diagnosis
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Introduction
The androgen receptor (AR) as a steroid hormone receptor is crucial for the embryological male sex differentiation and the maintenance of the phenotypical male characteristics throughout life in addition to spermatogenesis. Mutations in the AR gene can disrupt its function leading to Androgen Insensitivity Syndrome (AIS). AIS has a recessive mode of inheritance and can be broadly classified into 3 phenotypical categories: complete androgen insensitivity syndrome (CAIS), partial (PAIS) and mild (MAIS). CAIS usually presents with female external genitalia and primary amenorrhea. Karyotyping might be very helpful in these patients. Patients with PAIS syndrome typically have ambiguous genitalia, including partial labio-scrotal fusion and hypospadias. Patients with MAIS on the other hand, have a mild presentation with subtle secondary sexual characteristics abnormalities that can remain unnoticed for long. Due to its variable presentation, MAIS can prove challenging to diagnose clinically and biochemically.

Case presentation
We describe the case of a young man in his early 20s with normal childhood growth and development. He has been to see the Cardiologist for recurrent palpitations when he was noticed to have some degree of gyneaecomastia. He was then referred to our clinic for further work up. Physical examination demonstrated sparse body hair, hypoadrogenic phenotype, gynecomastia, normal penile length and small scrotum. His blood test showed a confusing picture of raised FSH, raised LH, mildly raised Proctalin, high normal Testosterone, normal SHBG and raised Oestradiol. His total HCG was normal. His Karyotype was normal of Internal medicine, Croatia; 1University Clinical Hospital Centre Zagreb, Department of Endocrinology and Diabetology, Zagreb, Croatia

Background
Learning through various online platforms is very common nowadays and its popularity has increased especially during the pandemic period. Nowadays, medical professionals are turning more than ever to online education through available online books, websites, and various online platforms. The aim of this study was to show that virtual training can improve the knowledge and confidence of young endocrinologists.

Methods
The Croatian Section for Young Endocrinologists organised the 2nd Regional Online Symposium for Young Endocrinologists in November 2021 for the purpose of continuing education and knowledge sharing among young endocrinologists from the region. The theme of the symposium was ‘Endocrinopathies in Pregnancy.’ The symposium started with an introductory test with 18 questions. At the end of the symposium, we administered the same test to see how much the participants had learned and improved their knowledge. The test also served as feedback for the organisers to see how good each presentation was and if there was room for improvement. The anonymous test consisted of 18 questions from 5 areas of endocrinology (pituitary, adrenal, diabetes and metabolism, calcium and bone metabolism, and thyroid).

Results
A total of 35 subjects participated in the introductory test and 37 subjects in the final test. There was a statistically significant difference in resolution between the introductory and final tests for 8 of the 18 questions. Baseline knowledge, based on the joint median of correct answers from a domain, was 24% in the pituitary area, 29% in the calcium and bone area, 46% in the adrenal area, 49% in the diabetes and metabolism area, and 59% in the thyroid area. There were statistically significant improvements in the final test (from greatest to least improvement) for the area of calcium and bone (all 3 questions achieved statistically significant improvement), then pituitary (2/3 questions achieved statistically significant improvement), thyroid (2/2 questions achieved statistically significant improvement), diabetes, and metabolism (1/4 question achieved statistically significant improvement), whereas there were no statistically significant differences in resolution between the introductory and final tests for the adrenal (0/4) area.

Conclusion
Online education is a very widely used and good learning model to improve and transfer the knowledge of young physicians and scientists. Different models of online learning need to be promoted and implemented in daily practise.

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Online education as effective medical training for young endocrinologist
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Primary amenorrhea revealing testicular regression syndrome in two sisters
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Introduction
Disorders of sex development represent a rare group of congenital disorders causing discord between the phenotypical and genotypical sex. We present the case of two female patients in whom we discovered a sex development disorder resulting in impaired migration of GnRH-secreting neurons from the olfactory epithelium to the hypothalamus. This association is characterized by delayed or absent puberty and infertility due to abnormally low levels of gonadotropic hormones and sex steroids. The most common reason for its development is Kallmann syndrome - a rare congenital disorder resulting from impaired migration of GnRH-secreting neurons from the olfactory epithelium to the hypothalamus. It is associated with hypogonadism and anosmia. In 1942, Klinefelter described 9 men with gynecomastia, sparse facial hair, and small testes, who were unable to produce sperm. In 1959, the Additional X chromosome was discovered - genotype XXY, characteristic of the complete and most common form of Klinefelter syndrome. The classic phenotype includes low serum testosterone, high LH and FSH levels. We present clinical cases of two adolescents at age of 18th and 19th with history for diminished pubertal spurt, treated with recombinant gonadotropins. Both patients presented with hormonal constellations for hypogonadotropic hypogonadism, low volumes of testicides, diminished spermatogenesis. We performed karyotyping and found disomy X-47, XXX. Patients were referred to Sequence analysis and deletion/duplication testing of the 46 genes listed in the Genes Analyzed section for hypogonadotropic hypogonadism Panel and found deletion of ANOS1 gene. That case presents a rare coincidence of two genetic states for both hypo- and hypergonadotropic hypogonadism.

Key words: Hypogonadotropic hypogonadism, Kallmann syndrome, Klinefelter syndrome

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Mc Cune ALBRIGHT Syndrome: A rare endocrine disorder with a challenging management: A case report
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Introduction
McCune-Albright syndrome (MAS) is a rare, mosaic genetic (Lehali in the homozygous state) but non-hereditary disorder. The diagnosis is most often made...
in childhood, the management is multidisciplinary and includes several aspects. We report a case of McCune Albright syndrome and the various difficulties encountered in its management.

Case report
A 22-year-old female presented with hirsutism and acne. On examination, she had significant hair growth on the upper lip and chest. The patient was amenorrheic and had signs of virilization. Laboratory investigations revealed high testosterone levels and low estradiol levels. Uterine fibroids were also detected on ultrasound.

Discussion
McCune Albright syndrome is rare, and there is limited research on its presentation and management. The association with hirsutism and acne is well-documented, but the management of these associated features can be challenging. The patient was started on hormonal treatment and monitored for signs of improvement.

Conclusion
Hirsutism and acne are significant concerns in patients with McCune Albright syndrome. Early diagnosis and multidisciplinary management are crucial to improve the quality of life of these patients.
EP936
Vaginoplasty in the treatment of androgen resistance syndrome: about 2 cases
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Introduction
Androgen insensitivities are rare genetic diseases, characterized by a more or less complete defect of tissue sensitivity to testosterone. It ranges from a more or less complete lack of masculinization to isolated infertility in a 46, XY individual. Many surgical methods of vaginoplasty have been opted with the aim of reconstructing the anatomy to allow future sexual activity as well as an improvement in the quality of life. We report the case of two patients with complete androgen resistance syndrome discovered during the exploration of primary amenorrhea.

Observation 1
33-year-old patient, operated in 2016 for bilateral intra-abdominal gonadectomy, with an anatomo-pathological examination of an ectopic testicle on the right without signs of malignancy, and an embryonic carcinoma on the left, the patient underwent chemotherapy sessions, she presents a harmonious and feminine Morphological development, with absence of vaginal orifice, a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution

Observation 2
20-year-old patient, who underwent bilateral gonadectomy in 2017 with pathological examination of hypoplastic testicular pulp with hamartomatous nodules and hypoplastic foci of Leydig cells compatible with androgen insensitivity syndrome without malignancy, with a gynecological examination presence of labia majora and labia minora not well formed with an incipient vagina, a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progesterone, with good clinical evolution. The first patient underwent a resectosigmoid vaginoplasty and the second a vaginal enlargement surgery. The result was excellent with the obtaining of a 6 cm deep neovagina. After six months of follow-up, the two patients keep neovaginal cavities with regular digital dilatation.

Conclusion
The choice of the most appropriate surgical technique is conditioned by the results of the clinical examination, ultrasound, genitography and endoscopic exploration.

EP937
Melatonin ameliorates glucocorticoid-induced invasiveness and circadian rhythm disruption in human endometrial adenocarcinoma cells
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Introduction
The biological rhythm pattern is synchronized through circadian oscillation of cortisol and melatonin release. Increased cortisol levels and circadian rhythm disruption act as an oncogenic factor in endometrial cancer through among others-dysregulation of cell proliferation/apoptosis and invasion.

Aim
To investigate, whether there is an oscillatory expression of the clock genes, MT1 and GR expression in human endometrial carcinoma cells. To explore whether glucocorticoids and melatonin can affect the expression of these genes and further to evaluate whether dexamethasone and melatonin affect the viability and invasiveness of Ishikawa cells.

Material and methods
Ishikawa cells were cultured and serum starved for 16h. Following starvation, cells were serum shocked and maintained in DCC-supplemented medium in the presence of dexamethasone (10-7M), melatonin (10-7M,10-8M) and GR antagonist RU486 (10-5M), alone or co-incubated with dexamethasone and melatonin for 54h. Cell viability and cell invasion were evaluated by MTS and scratch assay, respectively. The mRNA levels of circadian clock genes: CLOCK, BMAL1, CRY-1, PER-2, ROR-α, REV-ERBα, glucocorticoid receptor-alpha and melatonin receptor were measured by qPCR.

Results
Dexamethasone induced cell invasion of Ishikawa cells was inversely by 10% in the presence of melatonin at 10-7M for 54h. Co-incubation of dexamethasone-treated cells with melatonin (10-7M,10-8M) reduced the Ishikawa cell viability as compared to cells incubated with dexamethasone alone (10-7M). For the first time, we showed that following synchronization with serum shock, Ishikawa cells expressed Bmal-1, Clock, Per-2, Cry1 in an oscillatory manner with a peak observed every approximately 36h. Interestingly, MT-1 and GRα also exhibited almost the same oscillatory expression pattern. Incubation of Ishikawa cells with dexamethasone at concentration 10-6 did not affect the oscillatory pattern of Clock, Per-2, Cry, while it decreased the amplitude of Cry1 expression at 18h of incubation. However, dexamethasone disrupted the pattern of Bmal-1 expression, mainly by increasing the frequency of oscillations; this effect was reversed by co-incubation with RU-486 implying a GR-mediated effect. Notably, melatonin at concentration of 10-7M reversed the disruption of Bmal-1 expression pattern, without changing the GRα expression. Long-term incubation with melatonin alone at both concentrations did not affect significantly the oscillatory pattern, however at the highest concentration appeared to increase the amplitude of the oscillation in Bmal-1, Clock, Per-2, Cry-1 expression (approximately by 27%, 12%, 43% and 73% respectively) with more robust effect at 18h of incubation (first peak).

Conclusion
Melatonin ameliorates the glucocorticoid-induced invasiveness of human endometrial cancer cells possibly through reversing the glucocorticoid-induced disruption of circadian clock system. Further studies need to confirm the causal link.

EP938
Importance of karyotyping in the evaluation of male hypogonadism
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Analyses were performed: Glycemia, HbA1c, Hormonal Status (FSH, LH, Estradiol, Insulin, TSH, Thyroxine and Parathormone).

Results
The most common pathological change of the endometrium was an endometrial polyp. Patients with explorative curettage were older than healthy women and had significantly higher Body Mass Index, higher levels of serum glycemia, triglycerides, serum insulin, FSH, LH, PTH and lower estradiol levels. Patients in the experimental and control group did not differ significantly in TSH and thyroxine levels.

Conclusions
In the period of perimenopause and postmenopause, there are changes in the genital organs, but also there are endocrine disorders. According to our study, some of them are related to the occurrence of changes in the endometrium and the need for fractional explorative curettage as a diagnostic procedure.

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DOI: 10.1530/endoabs.81.EP937

DOI: 10.1530/endoabs.81.EP938
We present the case history of a 48-year-old man with anxiety and depression, who was referred for evaluation of absent libido, long standing erectile dysfunction and reduced body hair. There was no history of orchitis, pituitary problems or low impact fractures. He was always single and did not have children. Clinical examination revealed obesity (BMI 31 kg/m²), absent facial hair, reduced body, axillary and pubic hair. There was bilateral gynaecomastia. The phallus was normal, but the testes were not palpable. He appeared eunuchoid and did not have features of cortisol or growth hormone excess. Visual fields were normal to confrontation. He was not diagnosed to have any congenital malformations but had an atrophic right kidney on a routine ultrasound scan of the abdomen. Biochemical profile revealed undetectable testosterone <1.5 nmol/l (10 -28) and raised FSH 49.8 u/l (1.0 – 12) and LH 20.9 u/l (2.0 – 9.0) consistent with primary hypogonadism. Oestradiol, alpha-fetoprotein, beta HCG, prolactin, IGFI and thyroid function tests were normal. Ultrasound scrotum revealed small testes in the lower inguinal canal. Karyotyping revealed 46XX disorder of sexual differentiation (DSD), SRY positive. Testosterone supplementation was initiated. He was referred to the urologist for orchidectomy given risk of malignant transformation in the undescended testis. He was also referred for genetic counselling and clinical psychologist. Patient chose to remain on testosterone and requested testicular implants. DEXA bone mineral density scan revealed osteoporosis.

Discussion

46XX DSD is a rare disorder occurring in about 1:20,000 males. These patients commonly present in adulthood with infertility and have various phenotypical presentations, ranging from severe impairment of external genitalia to cryptorchidism to a normal male phenotype. Our case history highlights the importance of external genitalia examination in those presenting with hypogonadism. Further karyotyping is important in the evaluation of such patients, especially in those with phenotypical abnormalities.

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EP939

The frequency of thyroid diseases in adolescents (boys and girls) in Djizakh and Namangan regions of the Republic of Uzbekistan.

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d2, Dinara Alieva
d, Guzal Dalimova
d2, Drarab Benlouk
d, & Shokhislom Safarov
d
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The purpose of the study

Is to study the frequency of thyroid diseases in adolescents (boys and girls) in 2 regions of the Republic of Uzbekistan.

Material and methods.

We have been examined and surveyed in the framework of screening just for the period from January 1, 2021 to April 1, 2021 - 1023 boys and girls in the two regions of RUZ - 523 adolescents were examined in the Djizakh region and 500 adolescents in the Namangan region Aged from 11 to 15 years. The main contingent amounted to students of colleges and schools. All 1023 adolescents were performed by all anthropometric studies based on the international growth and weight map of Tanner-Waithause. The assessment of the puberty stage according to J. Tanner, if necessary, patients were sent to do-on-x-ray (radiograph of brush, CT/MRI of the Turkish saddle), ultrasound of genital organs, consultation of the surgeon, genetics, etc. research.

Results

In total, among 1023 adolescents, 230 (22.4%) patients with iodine deficient diseases of the thyroid gland were identified: diffuse goiter (DG) 1 ST - 135 B (13.3%), diffuse goiter 2 ST - 54 BC (5, 3%), autoimmune thyroiditis - 38 (3.7%). At the same time, in patients with DG, eunuchoidism was observed in 106 adolescents (10.3%), and hypothyroidism - in 83 (8.1%). In the Namangan region, 141 (28.2%) patients with iodine deficient diseases of 500 examined, and in Jizzakh - 89 out of 523 examined (17.1%)

Conclusions

In total among 1023 adolescents, 230 (22.4%) patients with iodine deficient diseases of the thyroid gland were revealed. This in turn also indicates that iodine deficiencies are a factor in the risk of developing violations of sexual, physical and general development in adolescents.

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Table 1

<table>
<thead>
<tr>
<th>Patients</th>
<th>1</th>
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<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Assingnation sex</td>
<td>F</td>
<td>16</td>
<td>M</td>
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<tr>
<td>Revealing signs</td>
<td>Primary Amenorrhea</td>
<td>primary Amenorrhea</td>
<td>Lack of virilization</td>
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<td>Tanner stage</td>
<td>P552</td>
<td>P251</td>
<td>P4 G4 Testis V3 &lt; 4 cc</td>
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<tr>
<td>EMS</td>
<td>5</td>
<td>5</td>
<td>7.5</td>
</tr>
<tr>
<td>Gugley stage</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Sinneker stage</td>
<td>6</td>
<td>6</td>
<td>6</td>
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<tr>
<td>Biology</td>
<td>Hight testosterone</td>
<td>low testosterone</td>
<td>AMH normal. Testo/DHT: 1.07</td>
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<td>HCG Test Diagnostic Imaging (ultrasound/IRM)</td>
<td>Positif (25 ng/ml)</td>
<td>Negatif (0.1 ng/ml) leydig cell hypoplasia</td>
<td>Not done</td>
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<tr>
<td>treatment</td>
<td>surgery</td>
<td>surgery</td>
<td>Partial androgen insensibility</td>
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<tr>
<td>Anapathse</td>
<td>mature testicular tissue.</td>
<td>mature testicular tissue.</td>
<td>Orchytopexia + Hypospadias correction</td>
</tr>
</tbody>
</table>

*EMS: external masculinization score.

EP940

Disorders of sex development 46XY revealed at adult age : A report of three cases and a literature review

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Introduction

Disorders of sex development include a large number of congenital conditions related to unusual chromosomal sex (gonosomal abnormalities), defective testicular development, or abnormal hormone secretion or receptivity, resulting in unusual external and/or internal genitalia development rare. Patients and methods

We report 3 cases of disorders of sex development 46XY revealed at adult age. clinical, biological and radiological funding are reported in the following table. Conclusion

Disorders of sex development are rare situations that require a rigorous assessment and early treatment. They often are congenital pathologies that have consequences in terms of self-esteem, sexuality and fertility in the future.

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**EP941**

Precocious puberty associated with primary adrenal insufficiency: A case report
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Introduction
Precocious puberty (PP) is a rare pathology involving approximately 0.2% of girls and less than 0.05% of boys and is defined as the appearance of secondary sex characteristics before 8 years of age in girls and before 9 years of age in boys. We report an unusual case of a patient who presents a precocious puberty associated to a primary adrenal insufficiency.

Case presentation
We describe a case of a 7-year and 4 months old girl refered for a precocious puberty. In fact, her mother reports breast enlargement since the age of 5 years but she only consulted when she had her menarche 2 months ago. Her medical history was uneventful. Her mother had her own menarche at the age of 11. Physical examination displayed a girl with weight at 33 kg (< -2 [standard derivation] DS), height at 137 cm (> +3 [standard derivation] DS). Her statural age was 10 years and a half. The patient presented an elevated Acreola above the contour of the breast with development of the overall breast tissue (Tanner stage S4) and her pubic hair was adult in type (Tanner stage F4). Bone Age according to Greulich and Pyle atlas was 11 years. Pelvic ultrasound revealed a uterine long axis of 39 mm, thickness of the uterine endometrium of 3mm, follicular ovaeries without ovarian cysts nor pelvic mass. Endocrine analysis showed high estrogen value: 25,5 pg/ml and high basal luteinizing hormone (LH) : 5,98 UI/l, suggesting a central precocious puberty. The pituitary magnetic resonance imaging showed homogeneous hyperplasia of the anterior pituitary gland without sellar or suprasellar tumor. The evaluation of the other pituitary axes showed a normal thyroid function test (FT4 : 11,3 nmol/l and TSH : 1.75 UI/ml), and a low cortisol level 66 nmol/l concomitant to an ACTH level: 98 pg/ml. The patient received hydrocortisone. A treatment by GnRH agonist was started and a genetic investigation is now being undertaken.

Conclusion
Central PP is due to a premature activation of the hypothalamic-pituitary-gonadal axis. It can be attributable to cerebral congenital malformations or acquired insults, but the cause in about 90% of cases in girls is idiopathic. Rare cases of PP associated to adrenal insufficiency were reported in the literature. It seems to be related to a stop loss DAX1 variant.

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**EP942**

Mayer-rokitansky-äister-hauser syndrome: about two cases
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Introduction
Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) is a rare malformation of the birth canal in women. It is defined as agenesis of the uterus and vagina with normal development of secondary sexual characteristics and a normal karyotype (46, XX). This is an entity with a heavy psychological impact requiring multidisciplinary care.

Observation 1
We report the case of a 16-year-old girl with a history of delayed puberty in the sister, who consulted for primary amenorrhea. Clinical examination revealed a height delay of -3 standard deviation, a weight delay of -1 standard deviation and a Tanner stage A1 S1 P1. Hormonal exploration found hypergonadotrophic hypogonadism. The karyotype showed a female genetic sex (46 XX). This is an entity with a high psychological impact requiring multidisciplinary care.

Observation 2
A 15-year-old patient with no notable history consulted for delayed height and puberty. Clinical examination revealed a statural delay at -2 standard deviation and Tanner stage S1P1A1. Hormonal workup showed hypergonadotrophic hypogonadism with FSH at 133.4 IU/l and LH at 28.85 IU/l with low plasma estradiol levels. The karyotype showed a normal genetic sex of 46, XX in the absence of Y chromosomal material. Ultrasound and abdominal pelvic MRI revealed utero-vaginal hypoplasia. The impact assessment showed a bone age of 12 years compared to a chronological age of 15 years. The diagnosis of MRKH was made with the absence of associated malformations. Estrogen therapy was started in our patient.

**EP943**

Polycystic ovary syndrome: diagnosis and treatment
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Introduction
Polycystic ovary syndrome is a real public health problem and is the most frequent cause of hyperandrogenism in women of childbearing age. The therapeutic management of PCOS depends on the patient’s phenotype and associated comorbidities. The aim of our work is to study diagnosis and evolution after treatment of PCOS in our population.

Material and method
This is a retrospective descriptive study of 78 patients followed for PCOS at the Endocrinology Diabetology and Nutrition Department of the Mohammed VI University Hospital of Oujda in the eastern region of Morocco. The diagnosis of PCOS is based on the criteria of the Rotterdam Consensus of 2003. All patients underwent an interrogation, clinical examination, biological assessment and pelvic ultrasound. The collected data were analyzed by SPSS version 21 software.

Results
The average age of patients was 24 years. Hirsutism was the most frequent reason for consultation in 97.2% of cases with severe hirsutism in 12% of cases, followed by cycle disorders (84.3%), and acne in 55.7%. The average BMI was 26.1 ± 5.8 kg/m² obesity was observed in 20% of patients, with abdominal obesity in half of the cases. Therapeutically, all our patients were put on dietary hygienic measures and metformin, the estrogen-progestogen contraceptive was indicated in 38% of patients and spironolactone in 26%, with a combination of these 2 treatments in 18% of cases. The evolution after at least 6 months of treatment revealed a very satisfactory improvement of the clinical signs with a decrease in the frequency of hair removal and a reduction in the density and darkness of the hairs.

Discussion-Conclusion
PCOS is a real problem in young women, which has psychological and social repercussions as well as metabolic ones. Its treatment should aim to: reduce hyperandrogenism, improve metabolic status and quality of life, and restore fertility. Our results are consistent with those reported in the literature.

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**EP944**

Thyroid

Tension-free thyroidectomy (TFT) may reduce the complication rate in thyroid surgery: experience of the first 120 cases
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Background and aims
The safety of thyroid surgery in terms of recurrent laryngeal nerve palsy and hypoparathyroidism was increasing in the last decade. In this study, we present a...
new method of tension-free thyroidectomy (TFT), which could be used to further decrease the complication rate after thyroidectomy.

Patients and Methods

TFT is based on the medial approach to the recurrent laryngeal nerve (RLN) and the parathyroid glands after the division of isthmus and successive total dissection of Berry’s ligament with full mobilization of the RLN and the parathyroid glands before the thyroid is pulled out from the neck. One hundred twenty consecutive patients (163 nerves at risk) underwent “tension-free thyroidectomy” (TFT) from August to November 2021 performed by one surgeon. There were 96 females and 24 male patients (ratio 4:1) with a mean age of ninety-two 46.3 (range from 17 to 75), Lobectomy was carried out in 93 (77.5%) patients, total thyroidectomy in 35 (22.5%). In 42 cases patients additionally underwent central or and lateral neck dissection. Indications for surgery were papillary carcinoma (n = 53), medullary cancer (n = 2), follicular neoplasia - Bethesda IV group after fine-needle biopsy (n = 49), Graves disease (n = 12), multinodular toxic goiter (n = 3), multinodular euthyroid goiter (n = 1). Mean thyroid nodule size was 25.4 mm (ranged 7 - 120 mm). Intraoperative neuromonitoring was used in all cases (35 mA). Translaryngeal untrasound or direct laryngoscopy were used prior and after surgery to evaluate vocal cords mobility. Calcium and parathormone levels were measured in patients after thyroidectomy on the first, 14th and 30th postoperative days.

Results

No fluctuation of electric activity of laryngeal nerves during surgery was revealed. Intraoperative loss of signal (LOS) due to thermal effect of electrocautery and subsequent transient unilateral RLN palsy occurred in 4 cases (2.5% from the total number of nerves at risk). In all these patients normal vocal fold function was confirmed on the 30-45th days after surgery. No permanent nerve palsy cases revealed. Four patients (out of 35 in the total thyroidectomy group – 11.4%) exhibited a decrease of parathyroid hormone level before the thyroid is pilled out from the neck. One hundred twenty consecutive patients had symptomatic ones. The mean volume of nodule was 36.5 ml. TFT is based on the medial approach to the recurrent laryngeal nerve (RLN) and the parathyroid glands

Conclusion

TFT can be considered a safe and feasible operation. Larger and comparative (randomized) studies with conventional dissection technique should be performed to investigate the hypothesis that this approach can provide a lower complication rate.

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EP945

Radiofrequency ablation for benign thyroid nodules of 650 patients: long-term follow-up

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Purpose

The objective of this study was to evaluate the efficacy and safety of ultrasound (US)-guided radiofrequency ablation (RFA) for treating of benign thyroid nodules both autonomously functioning thyroid nodules (AFN) and symptomatic ones.

Material and Methods

The retrospective analysis included the results of treatment of 650 patients with benign tumors of the thyroid gland in the Samara Oncology Center since 2014. 182 (28 %) patients had autonomously functioning thyroid nodules and 468 (72 %) had symptomatic ones. The mean volume of nodule was 36.5 ml.

Results

RFA reduced nodular volume by 70.8 % after 6 months, 84.2 % after 60 months and it was an effective method for treating nodule-related clinical problems and hot nodules. 67 (10.1 %) patients with big nodule volume underwent 2-7 sessions of RFA. Cosmetic results were excellent in 96 % of patients. No serious complications such as thyroiditis, voice change, and hematomas were observed in RFA patients. Skin burned observed in 1 patient.

Conclusion

RFA was effective and safe method for outpatient treatment of benign thyroid nodules. RFA might be alternative to surgical treatment.

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EP946

Decrease the functional activity of adaptive immunity cells one month after radioiodine therapy for Graves' disease Decrease the functional activity of adaptive immunity cells one month after radioiodine therapy for Graves’ disease

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Introduction

Radioactive iodine (RAI) for Graves’ disease (GD) was reported to have specific immune effects. The ability of T and B lymphocytes to cooperatively interaction during the immune response may be impaired in GD patients eligible for RAI therapy. We aimed at investigating cellular subsets involved in functional activity of adaptive immunity cells one month after RAI therapy in patients with GD.

Materials and methods

Thirty-six women with GD, mean age 42.13 ± 15.35, were included in this study. All patients treated with thiamazole for a 12 months (9 – 14) before RAI therapy. Thiamazole was withdrawal 14 days before RAI therapy. All patients had a fixed 400-700 MBq131I dose orally. Fifty-six healthy subjects were also studied. The study of the phenotype of T- and B-lymphocytes was carried out by flow cytometry using direct immunofluorescence of whole peripheral blood and monoclonal antibodies labeled with FITC (fluorescein isothiocyanate), PE (phycoerythrin), ECD (phycoerythrin-Texas Red), PC5 (phycoerythrin-cyanin 5), PC7 (phycoerythrin-cyanin 7), AA700 (alpha fluor 700) and AA750 (alpha fluor 750) in the following panels: CD3-FITC/CD25-PE/CD27-PC5/CD45r-PE/CD8-PC7/CD45r-PE/CD5-PE/CD5/CD27-PE/CD19-ECD/CD45/CD4-PE/CD3-FITC/CD25-PE/CD27-PC7/CD45/CD4-PE/CD3-FITC/CD25-PE/CD27-PC7/CD45/CD4-PE. Serum measurement of TSH, fT4, fT3 and TRAb were performed by ELISA and enzyme immunoassays.

Results

The thyroid state of GD patients before RAI treatment corresponded to subclinical hyperthyroidism with a high level of serum TRAb (Me= 28,01 mU/l (Q0,25 = 2,81; Q0,75 = 55,71; p<0,001)). An increase in the percentage of CD3+CD25+CD4+CD127-CD25- and CD3+CD8+CD25- and an increase number of CD3+CD4+CD127-CD25+ cells but with a decrease in the amount of CD3+CD8+ lymphocytes relative to the control was found in GD patients before RAI therapy. All patients treated with RAI were euthyroid, while the content of TRAb remained almost at the initial level. One month after RAI therapy in GD patients we observed decreased the percentage of cells with phenotypes CD3+CD25+CD4+CD127-CD25- and CD3+CD8+CD25- and an increase number of CD3+CD4+CD127-CD25- High lymphocytes. Also, we detected changes in the phenotypic composition of blood B lymphocytes of GD patients before 131I treatment: a decrease the percentage of CD19+ cells and an increase the relative number of CD19+CD27+CD23+ lymphocytes. One month after RAI therapy we revealed decreased percentage of CD19+CD5+CD23+ lymphocytes and increased relative to the initial values the levels of CD19+CD27+ and CD19+CD5+ cells.

Conclusion

One month after RAI therapy in GD patients changes in the phenotype of T and B lymphocytes in the blood reflect a tendency towards a decrease in the functional activity of adaptive immunity cells which can also be realized in the inhibition of autoimmune processes.

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EP947

Myocardial Ischemia precipitating thyroid storm diagnosed during storm recovery through Wellen’s wave: An ECG for an eye

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Introduction

Thyroid storm is a major life-threatening condition in a patient of thyrotoxicosis which can precipitate the cardiovascular morbidity in forms of tachycardia, arrhythmia and congestive heart failure. It can be precipitated by acute coronary

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syndrome. Most literatures have reported acute coronary syndromes during the presentation itself but we describe an unique case where the diagnosis was possible after the resolution of the thyroid storm.

Clinical case

A 55-year-old graves’ disease patient had presented with classical features of thyroid storm which was precipitated by discontinuation of the anti-thyroid drugs. His initial electrocardiogram (ECG) showed sinus tachycardia. He was promptly started on intravenous fluid, 80 mg of dexamethasone along with lopid’s iodine and intravenous dexamethasone. Within 48 h of treatment, his vitals became normal with resolution of the thyroid storm. His thyroid hormone status also showed marked improvement (free T4 falls from 90.31 ng/dl to 2.31 ng/dl) (normal range: 0.7 ng/dl-1.7 ng/dl). Due to his persistent jaw pain, mild chest discomfort and hiccough, ECG recordings were done in regular intervals. Interestingly it showed dynamic changes consisted of biphasic T waves. This ECG changes were seen after the resolution of the thyroid storm features. The cardiac enzymes were within normal limits. Wellen’s syndrome was suspected. Coronary angiography revealed left anterior descending artery (LAD) obstruction and patient promptly undergone percutaneous transluminal angioplasty. Patient’s angina equivalent symptoms had resolved remarkably. He recovered satisfactorily and was discharged after 5 days.

Clinical lesson

Ischemic heart disease is a well-known co-morbidity in a case of thyroid storm which can be identified at the initial presentation. But here the dynamic changes of ECG appeared after the resolution of the thyroid storm. It was classical of type A wellen’s wave which is a harbinger of imminent massive anterior myocardial wall infarction due to near-complete blockage of LAD. Initial sinus tachycardia probably had masked the appearance of typical Wellen’s wave in this case. But as soon as the thyroid storm resolved, typical dynamic changes appeared in the form of wellen’s wave. Early suspicion due to following serial dynamic ECG changes has prevented a major catastrophe in this case. This case highlights the importance of tracking serial ECG changes in a patient of thyroid storm which can unmask any underlying ischemic cardiac disease even after apparent improvement of the clinical status. This clinical case also reports a unique association of thyroid storm and type A wellen’s syndrome.

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EP948

Immune checkpoint inhibitors induced myxedema coma

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Introduction

Myxedema coma is very rare and its mortality is quite high. It is even rarer to occur due to an immune checkpoint inhibitor. Case

A 69-year-old patient presented with complaints of dyspnea, fatigue, edema, and hypotension. He had diabetes mellitus, hypertension, and metastatic lung cancer diagnosis. Three weeks ago, he had taken the 10th cycle of atezolizumab for lung metastasis. He had also complained of cough, fever, and dysphagia. The patient was admitted to the emergency department with acute dyspnea. He had a history of previous COVID-19 infection. On examination, the patient was found to be tachycardic with a heart rate of 120 bpm and hypotensive with a blood pressure of 90/60 mmHg. There was sleepiness, apathetic appearance, enlarged tongue, non-pitting edema, abdominal distension, and decreased bowel sounds. In the blood tests of the patient, serum glucose 100 mg/dl (70-100), sodium 115 mmol/l (136-145), TSH 218 µIU/ml (0.2-4.2), free T4 <0.03 ng/dl (0.9-1.7), and anti-thyroglobulin was 483 IU/ml (0-115). The thyroid gland was small and the parathyroid was heterogeneous in the ultrasonography. Blood gas showed hypoxia and hypercapnia. The patient was diagnosed with myxedema coma due to the PDL-1 inhibitor-atezolizumab, which he had taken. Treatment of myxedema coma, mainly intravenous levothyroxine and hydrocortisone, was initiated. After serum-free T4 level returned to the normal range with iv levothyroxine, his treatment with oral 150 mg/d levothyroxine was continued.

Conclusion

As a result of the increasing use of PD-1, PDL-1, and CTLA-4 inhibitors in recent years, also hypothyroidism is the most common endocrine side effect, but myxedema coma is very rare. When all the literature is examined, it is seen rarely that patients who develop myxedema coma due to immune checkpoint inhibitor. It develops due to PD-1 inhibitors nivolumab and pembrolizumab and CTLA-4 inhibitor ipilimumab. In our case, myxedema coma developed due to atezolizumab, a PDL-1 inhibitor. It should be kept in mind that hypothyroidism and also rarely hypothyroid coma may develop in patients using these drugs.

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EP949

Subacute thyroiditis in patients after COVID-19 infections at the outpatient stage

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Introduction

SARS-COV-2 is a new infection with little known consequences. As data accumulated, it became known that the thyroid gland is also affected as a result of infection. During the convalescence period, some patients developed severe thyrotoxicosis, which did not have the classic clinical picture of subacute thyroiditis or autoimmune.

Aim

To study the course of subacute thyroiditis in patients after infection with COVID-19.

Materials and methods

The study included 53 cases of subacute thyroiditis during 2020-2021. Group 1 - 13 patients with subacute thyroiditis and Covid-19 within 6 months, group 2 - 40 patients with subacute thyroiditis. The analysis of indicators was carried out: complaints at the first visit, hormonal status (T4, TSH), complete blood count, thyroid volume, nodes.

Results and discussion

Subacute thyroiditis is more often registered in women (69.2% (9) and 92.5% (37) in groups 1 and 2, respectively, compared with men (30.8%) (4) and 7.5% (3) in groups 1 and 2, respectively). (P < 0.05) The most common complaints in group 1: pain in the projection of the thyroid gland 30.4% (7), palpitations 13% (3), sweating 13% (3); in group 2: pain in the projection of the thyroid gland 34.5% (19), fever 16.4% (9x), weakness 12.7% (7 ), palpitations 9.01% (5 cases), no complaints in 17.5% (7). The change in thyroid hormone function is comparable in 2 groups: TSH in group 1 is lowered in 36.3% (4), normal in 36.3% (4), increased in 27.4% (3); in group 2: TSH decreased in 32.5% (13), normal in 40% (16), increased in 27.5% (11), T4 in group 1: normal in 50% (3), increased in 33.3% (2), decreased in 16.7% (1); in group 2: decreased by 22.5% (9), normal in 52.5% (21), increased in 25% (10) (P > 0.05). High ESR was significantly more often registered in group 1 (80%) (8), compared with group 2 62.5% (25) (P < 0.05). Nodular formations in the thyroid gland in group 1 were detected in 38.5% (5), in group 2 - in 100% (40).

Conclusions

1. Subacute thyroiditis is more common in women than in men in both groups. 2. Patients with COVID-19 are not characterized by fever in subacute thyroiditis. 3. The frequency of occurrence of thyroid status deviations is comparable in both groups. 4. In group 1, ESR increased more often than in the second group. 5. Nodular formations were significantly more often registered in patients without a history of COVID-19 infection.

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EP950

Therapeutic plasmapheresis to induce euthyroidism prior to thyroidectomy

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Use of therapeutic plasmapheresis in hyperthyroidism is mainly described in thyroid storm when traditional measures fail. Patients with hyperthyroidism who respond poorly or suffer adverse effects to conventional antithyroid therapies, which then need to be stopped, can have persistently high levels of thyroxine and at risk of a full blown thyroid storm. Hence an alternative treatment to achieve euthyroidism followed by thyroidectomy as definitive therapy is vital. We report here a case of a lady who as a result of multiple adverse effects from conventional antithyroid therapies, underwent therapeutic plasmapheresis as a last resort to
achieve euthyroidism prior to thyroidectomy. A 35-year-old lady who was diagnosed with Graves’ hyperthyroidism 2 months earlier and treated with carbimazole presented with fever, sore throat and generalized body weakness. Blood investigations revealed leucopenia (total white cell - 1.50x10^3/μL) and neutropenia (absolute neutrophil count 0.03x10^3/μL). A diagnosis of carbimazole-induced agranulocytosis with neutropenic sepsis was made. Carbimazole was stopped. Intravenous antibiotics, antifungal prophylaxis and granulocyte colony-stimulating factors (GCSF) were instituted. Her neutropenia was fairly resistant and needed twice daily GCSF for a week to recover. Thus, it was deemed unsafe to challenge with prophylactic agents. Oral cholestyramine and lithium were started as alternative treatment for her thyrotoxicosis. Two weeks later she developed widespread pruritic maculopapular rash attributed to lithium which was then withheld. She also could not tolerate cholestyramine fully and often vomited on taking the drug. We opted to rechallenge her with lithium at lower doses and administered oral cholestyramine via nasogastric tube in the ward. However, her FT4 remained above 100 pmol/l (12.3–20.2) five days later (Table 1). Eventually we resorted to using therapeutic plasmapheresis one week before her scheduled operation date. She underwent 2 sessions of plasmapheresis uneventfully. Short term Lugol’s iodine was started perioperatively along with steroid cover. She successfully underwent total thyroidectomy and is currently on levothyroxine replacement. This case highlights the use of, plasmapheresis as an effective and safe alternative to achieve rapid restoration of euthyroidism prior to thyroidectomy when conventional measures fail, even before acute deterioration into thyroid storm.

**Table 1** Serial TFTs of the patient

<table>
<thead>
<tr>
<th>Time</th>
<th>At diagnosis</th>
<th>After 2 months on carbimazole</th>
<th>After switching to lithium/cholestyramine</th>
<th>Post 1st session plasma exchange</th>
<th>Post 2nd session plasma exchange</th>
<th>3 days post thyroidectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT4 [12.3 - 20.2 pmol/l]</td>
<td>&gt; 100</td>
<td>22.7</td>
<td>&gt; 100</td>
<td>49.3</td>
<td>19.2</td>
<td>14.1</td>
</tr>
<tr>
<td>TSH [0.3 - 3.9 mIU/l]</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
</tr>
</tbody>
</table>
EP953
Risk of malignancy of indeterminate thyroid nodules: an Italian single-center cohort study
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Background
In 2014 a new Italian classification system of thyroid cyology divided the indeterminate TIR3 category in two groups, TIR3A and TIR3B, aiming to reduce unnecessary thyroidectomies. The reported risk of malignancy is: TIR3A: <10%; suggesting follow-up and possible FNA repetition after 6 months, and TIR3B: 15-30%, recommending surgery.

Objectives
We aimed to: evaluate the histological prevalence of malignancy in TIR3A and TIR3B nodules in our center; investigate whether oxyphil cells in TIR3B samples correlated with benignity; assess whether cytological ThinPrep versus conventional smear preparation affects the cytological report; estimate the association between clinical and ultrasound (US) features with malignancy.

Methods
We performed a retrospective analysis of patients who received fine needle aspiration (FNA) from 05/2014 to 07/2017 at Fondazione Policlinico Gemelli, Rome. We included 139 TIR3A and 162 TIR3B nodules who underwent surgery, to obtain tissue cyology and histology. Samples were obtained with ThinPrep technique and prepared on conventional smears or ThinPrep slides. Clinical and US data reported to be associated with malignancy were collected. Differences in rates of malignancy were evaluated with Fisher’s test. Logistic regression was performed to identify predictors of malignancy.

Results
Malignancy was reported in 12.2% (n=17) of TIR3A and 27.1% (n=44) of TIR3B nodules, with no significant difference with literature data. In TIR3B subset group, 83 cytological samples showed oxyphil cells, with a malignancy rate of 10.8% (n=9), significantly lower than overall TIR3B (P<0.01). 66 TIR3A and 109 TIR3B FNA were prepared with ThinPrep technique, and 73 TIR3A and 53 TIR3B with conventional smears, with no difference in malignancy risks. Logistic analysis showed irregular margins to be predictive of malignancy in both TIR3A (OR 10.75, 95%CI 2.25-51.37) and TIR3B (OR 6.80, 95%CI 1.94-24.01). Other predictors were family history and microcalcifications for TIR3A, and vascularity, hypoechogenicity and, secondarily, microcalcifications for TIR3B (P<0.05). The predictive power of the logistic model increased when considering those features concurrently.

Conclusion
In a representative cohort of indeterminate nodules, malignancy rate of TIR3A and TIR3B nodules was overall comparable to the one reported in the Italian classification system. However, TIR3B with oxyphil cells had a malignancy rate comparable to TIR3A, advocating for careful search of this feature. US findings of irregular margins and, to a lesser extent, microcalcifications and hypoechogenicity, proved to be associated with malignancy. Some vascularity patterns with capillarity technique and prepared on conventional smears or ThinPrep slides. Clinical and US data reported to be associated with malignancy were collected. Differences in rates of malignancy were evaluated with Fisher’s test. Logistic regression was performed to identify predictors of malignancy.

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EP954
The level of neutrophil reactive oxygen species in euthyroid and relapse patients with Graves’ hyperthyroidism
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Introduction
Graves’ disease (GD) is organ-specific autoimmune-inflammatory disorder characterized by a complex pathogenesis. The inflammatory process is dominated by an imbalance of the antioxidant-oxidant mechanism, increased production of reactive oxygen species (ROS), which can potentiate the cytotoxicity of neutrophils and sustain the autoimmune process and perpetuate the disease. Aim: to study the level of ROS synthesis by peripheral blood neutrophils in patients with Graves’ disease depending on hyperthyroidism compensation.

Materials and methods
One hundred and twenty-six women with Graves’ disease, aged 18 to 65 years, divided in groups with compensated hyperthyroidism (91 (73.81%) and relapse of hyperthyroidism 33 (26.19%) were studied and compared concerning ROS production. All patients continuously treated with thiamazole about two months. The maintenance dose of thiamazole was 10 mg per day. The synthesis level of ROS in peripheral blood neutrophils was evaluated using a 36-channel chemiluminescence analyzer “BLM-3607” (MedBioTech, Krasnoyarsk) and was characterized by Tmax – the rate of development of the chemiluminescent reaction, Imax – the maximum ROS synthesis and the area under the chemiluminescence curve (S – total synthesis of ROS for 90 minutes of measurement).

Results
Regardless for hyperthyroidism compensation the indicator S of spontaneous and yozmos-induced lucigenin-dependent chemiluminescence increases significantly relative to the control (p<0.001), but decreases the Tmax of yozsos-induced chemiluminescence (p<0.01). In GD relapse patients total synthesis of ROS during yozmos-induced chemiluminescence was higher up to 4.35 compared to euthyroid group (p<0.05). Antigenic stimulation of neutrophils in GD patients of both groups revealed an increase the Imax during lumonol-dependent chemiluminescence (p<0.01). Samples with yozsos in GD relapse patients, also, demonstrated more than tenfold increase in the total synthesis of ROS relative to the control, but no statistically significant differences with euthyroid patients.

Conclusion
Violation of the ROS production by peripheral blood neutrophils in euthyroid patients mainly affects the production of primary ROS which is associated with hyperthyroidism compensation and the immunosuppressive effect of thiamazole. In patients with relapse of hyperthyroidism, there are more changes in the production of high-energy oxidants not only at initial oxidative reactions stage but also at the level of secondary ROS, indicating the activation of cellular response immunomodulatory mechanisms, Cytopathogenic effect of ROS neutrophils generation in patients with Graves’ hyperthyroidism determine the intracellular targets of immunotropic treatment of the disease.

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differences and changes in the Pittsburgh Sleep Quality Index (PSQI) global and component sleep quality scores. SA was assessed by pulse rate and urinary metanephrines.

Results
Free thyroxine (FT4) level, pulse rate and urinary metanephrines were significantly higher in untreated hyperthyroidism group compared to other group (P < 0.05). FT4 level was significantly positive correlated with pulse rate (r = 0.643, P < 0.001) and urinary metanephrines (r = 0.387, P < 0.001). PSQI global sleep quality scores (P = 0.036) and sleep disturbance scores (P = 0.011) were significantly different among the three groups, and were highest in the untreated hyperthyroidism group. Multiple regression analysis demonstrated that FT4 level was associated with poorer PSQI global sleep quality scores independently of other factors (P = 0.006). Prospective observation in 18 untreated hyperthyroidism group showed that FT4 (P < 0.001) and SA such as pulse rate (P = 0.002) and urinary metanephrines (P < 0.001) significantly improved by therapeutic intervention. PSQI global sleep quality scores (P = 0.047) and sleep disturbance scores (P = 0.007) significantly improved.

Conclusions
Hyperthyroidism in GD caused subjective SDs, especially sleep disturbance. SA due to hyperthyroidism may contribute to subjective SDs. Treatment for hyperthyroidism and SA may improve subjective SDs.

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EP956
Dosing study of brand vs. generic levothyroxine in well-controlled primary hypothyroidism.
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Introduction
Most brand-name drugs do not differ that much from their generic counterparts, so switching between the two is not an issue. Levothyroxine, however, is an exception. The question of generic equivalency of levothyroxine products has remained unanswered for several decades. The purpose of the present study was to learn whether there is a difference of dosage between brand-name and generic levothyroxine in patient with well controlled primary hypothyroidism.

Methods
We performed a cross-sectional study in our outpatient consultation, including the patients presenting a well-controlled primary hypothyroidism. The patients were assigned into two groups, those already taking Levothyroxine® (G1) and those already taking Berlhyrox® (G2). All patients were taking the same formulation during the three months preceding the study. Pregnant women were excluded. We assessed the duration of treatment, the age, the cause and the weight, the dosage of levothyroxine, the dose adherence to the treatment and the current dosage of levothyroxine. We assessed for each patient the adherence to the levothyroxine with a Tunisian dialect translated version of the Girerd score. The adherence was defined as good compliance, minor noncompliance and noncompliance.

Results
We included 48 patients treated for primary hypothyroidism, with mean age of 50.4 years and age varying from 19 to 73 years old. Mean duration of treatment was 10.5 years with extremes varying from 2 to 30 years. The causes of the hypothyroidism were an auto-immune hypothyroidism in 69% of cases, thyroidectomy in 10% of cases, and iodine therapy in 21% of cases. The levothyroxine dosage ranged from 25 µg to 200 µg with a median of 100 µg per day. TSH levels ranged from 0.29 mUI/ml to 4.27 mUI/ml with a median of 2 µUI/ml. There was a good compliance in 19 patients (40%), a minor noncompliance in 26 patients (54.6%) and a noncompliance in 3 patients (6%). Adherence to treatment wasn’t associated with age (P = 0.731) nor duration of treatment (P = 0.262). By performing an ANOVA test, adherence to treatment wasn’t significantly associated with daily dosage (P = 0.513) nor dose per body weight (P = 0.654).

Conclusion
A lack of adherence to the treatment or to the time between the meal and the treatment is the first suspected cause of an elevation of TSH levels in a treated and well-titrated hypothyroid patient. Our study in a group of well-controlled patients showed that adherence isn’t an influencing factor for the dosage when hypothyroidism is well-controlled but should always be advised to avoid TSH rise.

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EP958
Immunogenetic aspects of polyglandular autoimmune syndrome
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Introduction
Polyglandular autoimmune syndrome (PAS) are uncommon constellations of autoimmune diseases characterized by the occurrence of two or more autoimmune endocrine diseases in the same individual.

Patients and methods
It is a case-control study about 108 cases for 120 healthy subjects recruited as the control group. We aimed to study the polymorphism of the HLA class-II genes of patients compared to that of healthy subjects so as to identify the genetic susceptibility to PAS.

Results
Among 108 patients, 2 patients had PAS type I (PAS-I), 39 patients had the type II (PAS-II) and 67 patients had the type III (PAS-III). Thirty-three patients with PAS-II against 120 healthy subjects in the control group were included for the genetic testing of HLA class-II allele. DRB1*03 allele was associated with the occurrence of PAS-II whereas DRB1*13 was detected in only one patient but in 40 subjects expressing a negative association of this allele with PAS-II but remains statistically insignificant. We also found the association of DQB1*0302 in our population (P = 0.004). DQB1*06 is a protective allele more prevalent in healthy

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subjects (22.97%) than in patients (3.8%) (P = 0.023) but this difference becomes insignificant after Bonferroni correction. Twenty-seven patients with PAS-III were tested for HLA class-II alleles. DRB1*03 allele was found to be associated with PAS-III (P = 0.0001) whereas no association was noted with DRB1*04 alleles (P = 0.02). DRB1*13 allele was found in 5 patients and 40 subjects in favor of the negative association of this allele in PAS-III (P = 0.11). A significant association was also observed with DQB1*02 allele in our population (P = 0.0034). In all, 40 patients with PAS-III were tested for HLA class-II alleles and demonstrated the association of PAS-II/III with DRB1*03 allele (P = 0.0021) but a less significant association was noted with DRB1*04 (P = 0.05). As far as protective DRB1*13 and DQB1*06 alleles are concerned, we noticed a negative association but insignificant after correction in PAS.

Discussion and Conclusion

The genetics of PAS is based essentially on the association of certain alleles of the human major histocompatibility complex. The presence of susceptibility alleles DRB1*03 and DQB1*0302 is described in literature. However, some studies showed the association of DR4-DQB1*0302 with PAS-II or III is due entirely to the presence of pancreatic auto-antibodies whereas haplotype DR3-DQB1*0201 is associated not only with type-1 diabetes mellitus but also PAS-II/III in the absence of pancreatic autoantibodies. The study of genetics have evolved considerably during the last years, especially due to molecular biology techniques.

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EP959

Graves’ orbitopathy caused by alemtuzumab: a case series
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Introduction

Alemtuzumab is a monoclonal antibody targeting the CD52 glycoprotein, which is expressed by most mature leucocytes. In early relapsing-remitting multiple sclerosis (MS) alemtuzumab effectively decreases relapse rate and disability progression. However, nearly 50% of the patients treated with alemtuzumab develop secondary autoimmune disorders, being Graves’ disease the most common. The development of thyroid eye disease is unusual.

Aims and Methods

We performed a retrospective chart review with MS and alemtuzumab-induced autoimmune hyperthyroid disease (AH-IA), who developed thyroid eye disease after alemtuzumab treatment. All patients with MS who had received at least one cycle of treatment with Alemtuzumab between 2014 and 2020 in Virgen Macarena University Hospital (Seville, Spain) were included.

Results

Our hospital is a regional referral center for MS, so approximately 121 MS patients were treated with alemtuzumab. 41 (33.9%) developed Graves’ disease and 6 (14.6%) were referred for ophthalmological evaluation. Of these, only one presented as a severe case, while the other five presented a mild course. Five were non-smokers at the time of developing ocular signs and symptoms. Five had significantly raised TRAB (> 10 IU/l) at presentation with eye disease—the sixth presented at a time prior to this test being routinely available. There was a 5:1 ratio of females to males. All patients initially received treatment with antithyroid drugs to control thyroid function. Four of them underwent total thyroidectomy as a definitive treatment. At diagnosis of orbitopathy, all patients had thyroid dysfunction consistent with hyperthyroidism. Four patients underwent conservative management with lubricants and selenium. One patient required treatment with oral corticosteroids. The most severe case was a 30-year-old woman who presented with constant diplopia, palpebral retraction > 1.5 mm, severe soft tissue involvement, and exophthalmos. With a clinical activity score (CAS) of 3 she was started on treatment with i.v corticosteroids. Due to poor evolution, and an increase in the clinical activity score to 6, she started treatment with Tocilizumab, a humanized MAB against the interleukin (IL)-6 receptor approved as second-line treatment for moderate to severe and active glucocorticoid-resistant Graves’ orbitopathy (GO). At 6 months, she presented great clinical improvement, with a CAS of 2 points (inactive GO).

Conclusions

We report the risk of developing GO in patients with MS treated with alemtuzumab who developed GD. In a novel way not described to date in the literature, we present a case of severe and active GO resistant to glucocorticoids in which Tocilizumab was successfully used.

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EP960

Euthyroid sick syndrome as a prognostic marker in patients with SARS-CoV-2 infection
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After almost 3 years since SARS-CoV-2infection was detected for the first time, knowledge about its repercussions on the thyroid gland function in the course of acute illness or in the post-COVID-19 are still poorly understood. This gland may be particularly susceptible to SARS-CoV-2 as this coronavirus enters cells through ACE-2 receptors, which are largely expressed in the thyroid gland. Through an observational, longitudinal and retrospective study, we investigated the serum levels of TSH and fT4 in adult patients infected by SARS-CoV-2 admitted to an internal medicine ward of a tertiary hospital. We evaluated the changes in thyroid function during hospitalization of 221 patients and the correlation between these changes and the severity of the disease. In a smaller cohort (n = 20) we evaluated thyroid function after hospital discharge. We found a high predictive value of serum TSH and fT4 values for severity of COVID-19 (OR = 2.5, p-value = 0.02). We used Pearson Chi-Square p-value and assume severe COVID-19 if PaO2/FiO2 < 300. We have shown that low TSH (mean 0.18 mU/l) and fT4 (mean 0.6 pmol/l) values have a higher prognostic value for mortality (OR = 2.5, p-value = 0.05) than other commonly used input data: hypertension, obesity, diabetes, PCR and IL-6 levels, sex and smoking. In the follow up cohort, thyroid function values tend to return to normal values over time. TSH and fT4 decreased values may be in line with the Euthyroid Sick Syndrome that has been described in acute diseases and as well as in patients with COVID-19.

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EP961

Use of thyroid hormone in hypothyroid and euthyroid patients. the THESIS questionnaire survey in spain
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Background

Hypothyroidism is one of the most frequent conditions in endocrinology. Despite of that fact, indications for treatment differ among specialists in Spain.

Aims

To identify attitudes of Spanish endocrinologists in the use of levothyroxine (LT4) therapy and the management of hypothyroidism.

Methods

The members of the Sociedad Española de Endocrinología y Nutrición (Spanish Society of Endocrinology and Nutrition) were requested to participate in a web-based survey. The questionnaire, conducted between September and November 2020, was adapted in accordance with the availability of thyroid hormone formulations in Spain.

Results

A total of 512 of 1956 (25.8%) members (66% female) completed the survey; 97.4% affirmed that LT4 is the initial treatment for hypothyroidism. The indications for LT4 therapy in euthyroidism were infertility in thyroid antibody positive women (48.5%) and simple goitre (21.2%). However, 44.2% of endocrinologists reported that there was no such indication for these patients. Only a minority of interviewees (2.6%) considered combining LT4 with lithium as the treatment of choice at diagnosis whereas 49% stated that it should never be used.
Conclusions
The standard of treatment of hypothyroidism in Spain is almost exclusively with L-T4 tablets. Availability of other formulations of L-T4 or combination therapy for hypothyroidism management remains to be explored specially in patients with persistent symptoms. Remarkably, non-evidence based use of L-T4 is extensively practiced in Spain for euthyroid women with autoimmune thyroiditis and fertility problems.

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EP962
Substitution with combined vitamins and minerals will provide a sufficient level of iodine during pregnancy
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In 2005, the evaluation of an international expert group placed Bulgaria among those who successfully overcame the problem of ‘iodine deficiency’. The aim of the study is to assess the current iodine status in pregnant women in two main regions of Bulgaria - with a known iodine deficiency and other with sufficiency in the past.

Material
A cross-sectional multicenter population-based study was conducted in a total of 84 settlements from the two regions, at 537 pregnant women, mean age of 30.49 ± 5 years.

Methods
The UIC was determined by certified inductively coupled plasma mass spectrometry. The accepted intervals for assessment of median UIC are: low 1 - 149, normal 150 - 249, over-optimal > 250 μg/l.

Results
The median UIC level for the whole pregnant group was 170 mg/l (11 - 497), (95% CI 161 - 177). The pregnant women only in three regions have a UIC below the lower reference limit of the norm for pregnant women of 150 mg/l [Gotse Delchev - 144.5 (119 - 208), Gabrovo - 130.5 (108 - 168), Troyan - 113.5 (93 - 185)]. A comparison was made between these three regions and the other seven with normal mUIC levels. According to the questionnaire 271 (50.47%) of all pregnant women who do not take any medications from Gabrovo-Troyan-Gotse Delchev are 23.1% v.s. 15.7% of pregnant women in the other seven regions (P < 0.006).

Conclusion
During pregnancy it is important to substitute with combined vitamins and minerals to ensure sufficient intake of iodine for this period.


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EP963
The relationship between thyroid hormones and different degrees of obesity: a case-control study
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Background
Obesity is a serious health problem worldwide and is caused by a wide variety of etiologies. There are several hormones which have been proved to be associated with increased body weight and has a direct effect on the fat metabolism like thyroid hormones.

Methods
This is a case control study which included 384 adult persons, they were divided into 2 groups according to the thyroid function status, the first group included 204 apparently healthy adults with normal thyroid function as a control group and the other group included 180 patients with decreased thyroid function status as a case group.

Conclusions
Body mass index is directly and positively correlated with both the TSH and the FT4 level. Overt cases of thyroid dysfunction are easier to be detected clinically than subclinical cases, obesity patients can be screened using the thyroid function status and treatment of patients with thyroid dysfunction must be adjusted according the weight.

References

Table 1 table showing the relation of the TSH and different parameters including BMI.

<table>
<thead>
<tr>
<th>Main category</th>
<th>Subcategory</th>
<th>Normal (n=204)</th>
<th>Elevated (n=180)</th>
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<td>Age groups</td>
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<td>Young ages</td>
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<td>(18-45)</td>
<td></td>
<td>178 (87.3%)</td>
<td>120 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Middle aged</td>
<td></td>
<td>23 (11.3%)</td>
<td>45 (25.0%)</td>
<td>0.000*</td>
</tr>
<tr>
<td>(46-65)</td>
<td></td>
<td>9 (4.5%)</td>
<td>15 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td></td>
<td>105 (51.5%)</td>
<td>75 (41.7%)</td>
<td></td>
</tr>
<tr>
<td>(66 and above)</td>
<td>Male</td>
<td>99 (48.5%)</td>
<td>105 (58.3%)</td>
<td>0.05*</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>9 (4.5%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI level</td>
<td>Normal</td>
<td>77 (37.7%)</td>
<td>26 (14.4%)</td>
<td>0.000**</td>
</tr>
<tr>
<td></td>
<td>Underweight</td>
<td>8 (3.9%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>3 (1.5%)</td>
<td>2 (1.1%)</td>
<td></td>
</tr>
</tbody>
</table>

* Pearson Chi-square test, ** Fisher’s Exact test.

DOI: 10.1530/endoabs.81.EP963

EP964
Therapeutic approach to the diagnosis of Bethesda 5
Ana Barrera-Martín, Mª Rosa Alhambra Exposito, Paloma Moreno-Moreno & Maria Angeles Galvez Moreno
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Introduction
Thyroid nodules are very common in the general population (20-75% ultrasonad). There are clinical management criteria established by international societies and standardized cytological diagnostic criteria (Bethesda). However, there is still uncertainty in the management of category 5.

Objectives
To evaluate the clinical attitude to the cytological diagnosis of Bethesda category 5 (B5) in thyroid fine-needle aspiration cytology (FNA) And study associations between malignancy and other variables.

Material and methods
Retrospective study of thyroid nodules classified as B5 after FNA referred to our hospital between 2020 and 2021. Statistical analysis: SPSS v.22.0 (Student’s t-test to compare means and Chi-square/Fisher’s test for proportions).

Results
Twenty patients (70% female); mean (SD) age, 49.3 (15.6) years. Sonographic features of included nodules are shown in table 1. Of the nodules, 5% were ACR-TIRADS 3, 25% ACR-TIRADS 4 and 70% TIRADS 5. Application of the ACR TIRADS system’s FNA criteria would have reduced the number of biopsies performed by 10%. Of the nodules without indication of FNA, both were papillary
Thyroid microcarcinomas. All patients underwent surgery, 80% total thyroidectomy, and 20% hemithyroidectomy. Eighty (80%) lesions met the reference-standard criteria for malignancy: 10 papillary thyroid cancers, 4 papillary thyroid microcarcinoma, 2 Hurthle cells carcinoma. The rest: 10% (2) follicular adenoma, 5% (1) multinodular goiter and 5% (1) non-invasive follicular neoplasm with nuclear alterations of papillary carcinoma. The variable the presence of calcifications on the nodule were directly related to the malignancy/ benignity of the nodule (p = 0.025). In fact, microcalcifications is only present in malignant pathology.

Conclusions
The percentage of patients with malignant processes of our series corresponds to the bibliography. Although the use of this category seems correct, the clinical attitude is erratic and surgical over-treatment occurs.

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EP965
An unusual pathology in Graves' Disease
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1Basaksehir Cam and Sakura City Hospital, Endocrinology and Metabolic Diseases, Istanbul, Turkey; 2Basaksehir Cam and Sakura City Hospital, Pathology, Istanbul, Turkey

Introduction
Graves disease (GD) is an autoimmune disease in which thyrotropin receptor antibodies overactive the thyroid gland. Therefore, antithyroid drugs, radioactive iodine therapy, or surgical interventions are treatment options. In GD, pathology after thyroidec tomy may include hypertrophy and hyperplasia in thyrocytes, mononuclear cell infiltration in the stroma, and increased blood supply. We presented a case with areas of necrosis and vasculitis due to GD in the pathological specimen obtained after a patient underwent a total thyroidec tomy due to development of hepatotoxicity under antithyroid therapy.

Case
An 18-year-old female patient complained of palpitation, weakness, and fatigue. TSH was suppressed, fT4, fT3 and thyroid stimulating antibody were elevated. The patient had hyperthyroidism and received levothyroxine to normalize thyroid hormone levels. Due to the patient's high TSH levels, she was referred to our institution for further evaluation. On physical examination, the patient was found to have a goiter, and thyroid ultrasonography showed multiple nodules. Thyroid scintigraphy confirmed the presence of multiple nodules.

The patient underwent a total thyroidec tomy under general anesthesia with no complications. The pathological specimen obtained after surgery was evaluated for the presence of vasculitis.

Discussion
Vasculitis in the thyroid is uncommon. However, there have been few cases with giant cell arteritis or temporal arteritis in the thyroid artery. Antithyroid drug-associated vasculitis is generally ANCA-associated leukocytoclastic vasculitis and presents with skin manifestations. We did not find evidence of systemic manifestations in our case. Autoantibodies were negative. Due to absence of prominent nodular patterns, cytological atypia, increased mitosis, or solid growth pattern in histopathological examination; poorly differentiated thyroid carcinoma was excluded. The existing findings in the thyroidectomy material were evaluated as vasculitis localized to thyroid gland and related to GD.

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EP966
Radiofrequency thermal ablation (RFA) of Thyroid nodules: our initial experience
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In recent years, US-guided thermal ablation techniques have been proposed as a therapeutic alternative to traditional surgery or to metastatic radiotherapy for thyroid nodules. RFA is one of the most used technique and experience in both ultrasound and ultrasound interventional is important for results and minimizing complications. We present our experience after 1 year of activity on the first 33 patients with thyroid nodules treated with RFA. The nodules were evaluated by ultrasound (Samsung RS85) and classified according to the TI-RADS criteria. In all patients, 2 ultrasound-guided fine needle aspirations were performed at different points of the nodule according to guidelines. Thermalablation was performed under local anesthesia with Amica-Gen HS Hospital Service RF.

Table 1 Characteristics of Thyroid Nodules

<table>
<thead>
<tr>
<th>Volume Average (cc)</th>
<th>Power (Watt)</th>
<th>Average time</th>
<th>Average number of shots</th>
<th>RVR</th>
<th>Reduction/resolution of sympotms</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.7 (4.5 - 80)</td>
<td>25-45</td>
<td>15'-48' (5'-43' - 34' 10')</td>
<td>11 (5-18)</td>
<td>RESULTS</td>
<td></td>
</tr>
<tr>
<td>High lobe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left lobe</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Endocrtocure</td>
<td></td>
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</tr>
<tr>
<td>isoechoic</td>
<td>16 (48.5%)</td>
<td></td>
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<tr>
<td>hypoechoic</td>
<td>3 (9.1%)</td>
<td></td>
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<tr>
<td>hyperechoic</td>
<td>6 (18.2%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>mixed (solid-cystic)</td>
<td>6 (18.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascualization</td>
<td></td>
<td></td>
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<tr>
<td>peripheral</td>
<td>21 (63.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>peripheral + internal</td>
<td>12 (36.4%)</td>
<td></td>
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<tr>
<td>Cytology (2 FNA)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>TIR 2 + TIR 2 29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIR 2 + TIR 3a 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFA</td>
<td></td>
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</tbody>
</table>

Endocrine Abstracts (2022) Vol 81
EP967

Association between selected serum inflammatory parameters, low FT3 and mortality in hospitalized patients with COVID-19 - single center observation

Aleksandra Młodożeniec1, Renata Orłowska-Florek1,2, Adrianna Czarnożycka-Wrobel1, Paulina Szul1, Krzysztof Gargasz2 & Agnieszka Gali-Bladzinska1,2
1St. Queen Jadwiga Clinical District Hospital No.2 Rzeszów, Department of Internal Medicine, Nephrology and Endocrinology, Poland; 2Medical College of Rzeszów University, Poland

Introduction
The incidence and mortality rate for COVID-19 differ in different regions, but the risk of in-hospital death is high in all counties. It is very important to identify patients at risk of death at the beginning of hospitalization. The disease often leads to NTIS (nonthyroidal illness syndrome), which can be the result of the cytokines storm[1]. The inflammatory parameters and the level of FT3 appear to be obvious leading risk of death.

Objective
The study aimed to investigate the serum levels of thyroid hormones and selected inflammatory biomarkers in adult COVID-19 patients and to determine whether they predict the risk of death.

Methods
We retrospectively analyzed the lab results of patients hospitalized in our clinic from October 2020 to January 2021 with confirmed SARS-CoV-2 infection (n = 393). Patients with a history of thyroid disease, patients treated with thyroid drugs and those who have recently received iodinated contrast were excluded. All of them were initially in stage II of the course of the disease [2]. The STATISTICA 13.1 statistical program was used to perform the tests and P values < 0.05 were considered statistically significant.

Results
Fifty-three (13,49%) adult patients were enrolled in the study. The median age was 72±12.2 years, 26 patients (49%) were men. NTIS was detected in 64% of all patients and low FT3 serum levels showed strong correlation with disease severity and mortality prognosis in COVID-19. The results are shown in Table 1.

Conclusions
1. Low serum FT3 concentrations predict clinical deterioration and higher mortality in COVID-19 patients. 2. The levels of II-6, WBC, ferritin, neutrophils are prognostic markers of in-hospital mortality in patients with COVID-19.

References


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Table 1 Association among serum FT3, FT4, selected inflammatory biomarkers and hospital mortality in COVID-19 patients.

<table>
<thead>
<tr>
<th></th>
<th>Nonsurvivors (n = 14)</th>
<th>Survivors (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>median</td>
<td>Min.</td>
</tr>
<tr>
<td>FT3, [µg/ml]</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>FT4, [µg/ml]</td>
<td>1.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Interleukin 6, [pg/ml]</td>
<td>41.9</td>
<td>4.8</td>
</tr>
<tr>
<td>Ferritin, [ng/ml]</td>
<td>221.25</td>
<td>22</td>
</tr>
<tr>
<td>WBC, [10³/µl]</td>
<td>10.9</td>
<td>7.78</td>
</tr>
<tr>
<td>Neutrophils, [cells/µl]</td>
<td>7860</td>
<td>752</td>
</tr>
</tbody>
</table>

Endocrine Abstracts (2022) Vol 81
A rare case of symptomatic amyloid goiter diagnosed by tru-cut biopsy
Erhan Hocaoglu1, Ensar Aydemir, Coskun Ates, Filiz Mercan Saridas, Soner Cander, Ozen OZ GUL, Canan Ersoy & Erdinc Erturk1, Uludag University Medical School, Endocrinology, Bursa, Turkey

Introduction
Amyloid goiter is a rare entity caused by massive amyloid infiltration of the thyroid gland. In some cases, differential diagnosis can be challenging. In this report, we present a patient with amyloid goiter caused by secondary amyloidosis.

Case
A 48-year-old male patient was admitted to our hospital with the complaints of neck swelling, pain, and mild dysphagia that started three weeks after the SARS-CoV-2 infection and continued for one month. The patient had a history of Crohn’s disease, ankylosing spondylitis and renal amyloidosis. He was on hemodialysis for 8 years. On physical examination, the thyroid gland was bilaterally palpable and tender. Laboratory tests were as follows: C-reactive protein 55 mg/l, sedimentation 50 mm/hr, TSH 0.02 mU/l, free T4 0.76 ng/dl, free T3 2.17 ng/l. Anti-thyroid peroxidase (TPO) and TSH receptor antibody were negative. Ultrasound showed an enlarged thyroid gland with hypocerebrogenity of the parenchyma and normal vascularity. Thyroid scintigraphy revealed low uptake. Subacute thyroiditis was considered in the patient. As the administration of ibuprofen did not ameliorate his symptoms, oral metilprednisolone (32 mg/day) was initiated. Afterwards, low-dose levothyroxine replacement was started for hypothyroidism. Despite using steroid (methylprednisolone at a maximum dose of 64 mg/day) for more than one month, his symptoms did not significantly relieve and the patient was hospitalized. Computed tomography scan of the neck showed diffuse enlargement of the thyroid gland and parenchymal heterogeneity. Fine-needle aspiration of the thyroid gland was performed, but the findings were non-specific. After that, tru-cut biopsy was planned for the patient.

Pathological analysis revealed amyloid goiter. Positive staining with Congo red was obtained. Immunohistochemical staining patterns were consistent with amyloid AA. The patient, who was evaluated together with the general surgery department, was discharged with a total thyroidectomy planned for symptomatic amyloid goiter. After a short time, it was learned that the patient died due to myocardial infarction in another center.

Conclusion
In some cases, it can be difficult to distinguish amyloid goiter from subacute thyroiditis and other diseases. Amyloid goiter should be kept in mind in patients present with rapid thyromegaly and have a history of chronic inflammatory disease that may be associated with secondary amyloidosis. Fine-needle aspiration has a limited role in diagnosis. Either a core-needle biopsy or surgical specimen is often necessary.

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Hypovitaminosis D and Hashimoto’s thyroiditis: effects of four-month supplementation therapy with oral cholecalciferol
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Background
Hypovitaminosis D represents at present a worldwide public health problem. Recent studies have demonstrated the pleiotropic effects of vitamin D, in addition to its known actions on calcium-phosphorus metabolism. Among the several non-skeletal effects, a potential anti-inflammatory and immunomodulatory action has been suggested. Vitamin D deficiency has been reported in several chronic conditions associated with increased inflammation and deregulation of the immune system, such as Hashimoto’s thyroiditis, and may act as a cofactor in the etiopathogenesis of these clinical conditions. On this basis, correction of hypovitaminosis D through therapeutic supplementation could have an impact on these pathologies.

Aim
To evaluate, in patients with Hashimoto’s thyroiditis and hypovitaminosis D, the impact of cholecalciferol therapy on the parameters of calcium-phosphorus metabolism, antibody titer and indices of thyroid function.

Materials and methods
A sample of 42 patients (6 men and 36 women) affected by hypovitaminosis D and Hashimoto’s thyroiditis was recruited; oral cholecalciferol therapy was administered at a dosage of 100.000 IU, once a month during a meal. Before initiation (T0) and one week after the fourth dose of cholecalciferol (T1), the following parameters were evaluated: TSH, FT3, FT4, 25-OH-cholecalciferol, PTH, Calcium, Phosphorus, Creatinine, AbTg, AbTPO.

Results
No significant changes in antibody titer or thyroid hormones were observed in serum 25-OH cholecalciferol after supplementation, with no significant changes in the antithyroid antibody titer. Although an downward trend was shown, after 4 months of therapy. No significant changes in antibody titer or thyroid hormones were observed in serum 25-OH cholecalciferol after supplementation, with no significant changes in the antithyroid antibody titer. Although a downward trend was shown, after 4 months of therapy.

Conclusions
Our results show that Vitamin D replacement therapy with cholecalciferol, in Hashimoto thyroiditis patients, does not affect the inflammatory nor the functional thyroid status, despite the fact that supplementation is effective in correcting hypovitaminosis D. No significant change in the antithyroid antibody titer emerged. Further studies are needed to investigate the immunoregulatory functions of vitamin D and its effects on thyroid autoimmunity.

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Autoimmune thyroid disorders and connective tissue disease
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1Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; 2Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Mixed connective tissue disease (MCTD), also known as Sharp’s syndrome is a rare autoimmune disease (AD), characterized by the presence of high titers of a distinctive autoantibody: ribonucleoprotein auto-antibody (anti-RNP). It presents with varied overlapping symptoms of different connective tissue disorders which may appear sequentially over time. As other AD, MCTD may be associated with one or more AD, such as autoimmune thyroid disorders (AITD).

Patients and methods
It is a descriptive retrospective single institution study. We collected data from 113 patients diagnosed with an AITD associated with another AD over 15 years. This present study reports the association between AITD and MCTD.

Results
We identified one patient diagnosed with both MCTD and AITD. She was hospitalized in the department of Internal medicine for investigation of joint pain and Raynaud’s phenomenon. Antibody testing showed positivity for anti-RNP. She was treated by a prescription of nonsteroidal anti-inflammatory drugs and calcium channel blockers. The evolution was marked by the occurrence of flares of arthralgias. Biochemical assays led to the fortuitous discovery of a hypothyroidism. Hashimoto’s thyroiditis (HT) was diagnosed concomitant to the MCTD in the context of other autoimmune diseases associated with the MCTD. Both thyroid antibodies (thyroid peroxidase antibody and thyroidoglobulin antibody) were positive. The patient was treated by L-thyroxin substitution.

Discussion and Conclusion
MCTD are AD characterized by the involvement of several organs and the presence of various autoantibodies. It can be associated with other AD. The most frequent association are with the Sjogrens’ syndrome, Hashimoto’s thyroiditis and some authors reported cases of autoimmune hepatitis and MCTD or primary biliary cirrhosis and MCTD. The frequency of thyroid disease, particularly chronic autoimmune thyroiditis (Hashimoto’s thyroiditis), may be increased in patients with MCTD and vice versa. In a study conducted by Biro et al. including 1517 patients bearing an AD, 159 patients were diagnosed with MCTD. Among them, 21.4% were also diagnosed with HT whereas only 2.5% were diagnosed with Graves’ disease. The screening of other autoimmune disorders in the presence of an AD is necessary, especially in patients who remain unwell or who develop new non-specific symptoms despite proper treatment, so as to avoid the delay in diagnosis of other autoimmune disorders and thus avoid treatment delay.

References
Unilateral Graves’ disease: a case report
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Charles Nicolle Hospital, Endocrinology, Tunis

Introduction
Graves’ disease is a frequent etiology of hyperthyroidism. It is defined as a diffuse hyperfunctioning of the thyroid gland caused by an autoimmune disorder. We herein present a rare case of unilateral Graves disease involving the right lobe of the thyroid.

Observation
A 44-year-old woman was referred for investigation of subclinical hyperthyroidism revealed by a routine check-up. On physical examination, she had tremor, eyelid retraction, tachycardia and the thyroid gland was palpable. She complained of heat intolerance and nervousness for 1 year. On biological investigations, she had a serum TSH level of 0.001 mIU/l (normal range: 0.35-4.94) and a serum free thyroxine (FT4) level of 1.48 ng/dl(normal range: 0.7-1.48) - confirmed persistent grade 2 subclinical hyperthyroidism. She also had a serum glucose level of 0.96 g/l, a serum total cholesterol level of 1.51 g/l, a serum triglycerides level of 0.86 g/l, HDL-cholesterol level of 0.53 g/l and LDL-cholesterol level of 0.80 g/l. She had a white blood cells of 6680 elements/mm³, neutrophils of 3360/mm³ and lymphocytes of 2290/mm³. The liver and kidney function tests and C-reactive protein (CRP) were normal. The serum TSH receptor antibody level was high 17.54 UI/ml (normal range <2 UI/ml) and the level of antithyroglobulin antibody level was within normal range. The bone mineral density was normal. The cervical ultrasonography showed a normal thyroid volume, normovascular gland and a nodule in the lower pole of the right lobe with a long-axes diameter of 14 mm EU-TIRADS 5. The thyroid scintigraphy revealed an increased uptake in the right thyroid lobe with an accompanying suppression in the left lobe. The fine needle aspiration biopsy of the nodule revealed benign appearance on cytological examination. The patient received antithyroid drug: methimazole and propranolol and recovered well.

Conclusion
Graves’ disease usually presents with frank clinical signs of hyperthyroidism, bilateral exophthalmos, and a diffuse goiter. This case illustrates a rare case of unilateral involvement of the thyroid and a subclinical hyperthyroidism in a patient with confirmed diagnosis of graves’ disease. Clinicians should be aware of this rare presentation of the disease as it affects treatment.

DOI: 10.1530/endoabs.81.EP972

Correlation between thyroid nodules cytologies applying the Bethesda System with post-thyroidectomy histopathological diagnosis
Laura Mola Reyes1, Lorea A. Herráiz Carrasco2, Cristina Martín-Arriscado Arrobas1, Laura Kanaan Kanaan2, Teresa De Grado Manchado2, Rona H. Penso Espinoza2, Irene Crespo Hernández2 & Maria Elena Mendoza Sierra2
1Hospital Central de la Defensa Gómez Ulla, Madrid, Spain; 2Hospital Central de la Defensa Gómez Ulla, Endocrinology and Nutrition, Madrid, Spain; 3Hospital Universitario 12 de Octubre, Instituto de Investigación 1+12., Madrid, Spain

Introduction
Thyroid nodules represent a common cause of specialist consultation, with a risk of malignancy of 4-15%. The most widely used cytopathological method for diagnosing thyroid cancer is fine-needle aspiration biopsy (FNAB) of thyroid nodules and the use of the Bethesda system (BS) for cytopathological reporting. We conducted the present study to report our experience using the BS, and to compare the results obtained with this system with the final histopathological results of the thyroidectomies performed.

Material and methods
Analytical study was carried out comparing the results of FNAB according to the BS, and the final result of histopathology of patients with thyroid gland lesions who consulted at the Hospital Central de la Defensa Gómez Ulla (Madrid), during the year 2020. The results were expressed as mean ± standard deviation for quantitative variables and as absolute and relative frequency for qualitative variables. The comparison between the characteristics of the sample and the BS was carried out using the chi-square test and ANOVA, adjusting for the cervical region was found. A complete excision was performed after lipograde and section of the lower cystic attachments. The anatomopathological examination diagnosed a thyritic cyst with thyritic parenchyma hyperplasia.

Conclusion
It’s very important to recognize a cervicomedialthalamic thyms cyst as a differential diagnosis of pediatric neck masses, such as cervical lymphadenopathy, branchial anomalies, vascular malformations, inflammatory lesions and neoplasm. Ultrasound and CT scan can help to establish the etiological diagnosis.

DOI: 10.1530/endoabs.81.EP974

Correlation between thyroid nodules cytologies applying the Bethesda System with post-thyroidectomy histopathological diagnosis
Laura Mola Reyes1, Lorea A. Herráiz Carrasco2, Cristina Martín-Arriscado Arrobas1, Laura Kanaan Kanaan2, Teresa De Grado Manchado2, Rona H. Penso Espinoza2, Irene Crespo Hernández2 & Maria Elena Mendoza Sierra2
1Hospital Central de la Defensa Gómez Ulla, Madrid, Spain; 2Hospital Central de la Defensa Gómez Ulla, Endocrinology and Nutrition, Madrid, Spain; 3Hospital Universitario 12 de Octubre, Instituto de Investigación 1+12., Madrid, Spain

Introduction
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Results
Reports of 201 cytologies corresponding to 152 patients were reviewed. Mean age 65.6 ± 15.1 years. Predominantly female sex 75.0%. Main reason for FNAB request: size of the nodule (40.5%). Mean size of biopsied thyroid nodules: 23.5 ± 10.5 mm. The highest percentage of cytologies corresponded to the Bethesda II category: 152 (75.6%), followed by Bethesda I: 26 (12.9%), III: 11 (5.5%), V: 6 (3.0%) and IV: 3 (1.5%), VI: 2 (1.0%). 15 patients (9.9%) underwent surgery, corresponding to 25 cytologies performed (12.5%). 7 malignancies were identified. There was a final histopathological result of malignancy in 14.3% of Bethesda II, 33.3% in Bethesda III, 0% in Bethesda IV, 100% in Bethesda V, and 66.7% in Bethesda VI (p-value = 0.013). Overall, categories IV, V and VI had a malignant lesion in the final histopathology diagnosis in 66.7% of cases (positive predictive value, PPV). 85.7% of Bethesda II, had a benign lesion (negative predictive value, NPV). Considering only patients with satisfactory samples, the diagnostic accuracy was 73.7%.

DOI: 10.1530/endoabs.81.EP975
Conclusion
The BS for the interpretation of the FNAB of thyroid nodules enhances the diagnostic certainty and assists the medical-surgical team in the therapeutic decision. In our institution, most part of cytologies were reported as benign. Regarding patients who underwent thyroidectomy, FNAB showed a high NPV, with a lower PPV.

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EP976
Anaplastic thyroid carcinoma: about 7 cases
Ezer Chebil, Jebaibi Samsch, Thabet Wadie, Hassanaoui Mahdi & Mighri Khilifa
Taher Sfar University Hospital, ENT, Mahdia, Tunisia

Introduction
Anaplastic thyroid cancers are undifferentiated malignancies accounting for 2% of thyroid cancers.

Objective
To study the clinical, evolutionary and therapeutic characteristics of these carcinomas.

Materials and methods
A retrospective study covering 7 cases collected at our ENT department between 1994 and 2021.

Results
They were 6 women and one man with an average age of 50 (41-78). The reason for consultation was cervical swelling 100% of the time. Dyspnea was noted in 2 cases. The average duration of the symptomatology was 14 weeks. The tumor was plunging into the mediastinum in 2 cases. In 4 cases, there was an invasion of the trachea and/or sub-hyoid muscles. Lymph node metastases were noted in all patients, bone in 2 patients and lung in 1 case. Histological confirmation of the diagnosis was made on thyroidectomy in 3 cases, and on a micro-biopsy of the thyroid gland in 4 cases. A tracheotomy was done in 3 cases. Three patients had a total thyroidectomy. The rest of the patients were inoperable. Radiation chemotherapy was indicated in all patients. Six patients died after an average delay of 11 months [8 months to 13 months]. A patient is still alive with a one-month decline.

Conclusion
Anaplastic thyroid carcinoma is a cancer with a dark prognosis. Patients in the localized disease stage can expect better survival. Therapeutic research explores targeted therapies that block the EGFR inhibitor or inhibit neoplastic angiogenesis.

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EP977
Radiofrequency thermal ablation for a small papillary thyroid carcinoma: a case report
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Recently ultrasound-guide radiofrequency thermal ablation has been proposed as an effective and safe procedure for treating patients who have low risk papillary thyroid microcarcinomas or are unfit for surgery. We present the case of a 56 years old patient with a small (10 mm) thyroid nodule diagnosed as TIR 4, suspect citology for papillary carcinoma after fine needle aspiration. The nodule was also studied with CEUS (Sonovue US contrast medium) which showed increased vascularity in the arterial phase compared to the remaining parenchyma and late wash out. We proposed the possibility of radiofrequency thermal ablation to our patient. We used 1 cm active tip electrode needle (HS Amica Gen) with moving shot technique: 3 shots at 30W power for 5 minutes and 15 seconds. The Procedure was safely and effectively carried out. Follow examinations with ultrasoundography and CEUS conducted after 13.6 months demonstrated a complete necrosis with avascular area and progressive reduction of size in the treated site. Anyway we repeated the fine needle aspiration 6 month later and the sample detected only very poor cellularity inflammatory cells, amorphous material and no neoplastic cells. Our experience confirmed that the radiofrequency ablation can effectively eliminated small papillary carcinomas with a very low complication rate. We have to consider this alternative strategy for treatment of small indolent papillary thyroid carcinomas alternatively of traditional patients even without surgical contraindication.

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EP978
When sarcoidosis mimics cervical metastasis of thyroid cancer: a case report
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Introduction
Sarcoidosis is a systemic inflammatory disease characterized by noncaseating granulomas. Its pseudo-tumor manifestation in certain organs such as the thyroid can mimic thyroid carcinoma and lead to erroneous therapeutic decisions. We report a case of sarcoidosis with cervical adenopathy initially considered as a cervical metastasis of thyroid cancer.

Observation
A 61-year-old woman, with a history of spontaneous subacute subdural hematoma operated in 2010, Followed at our level in consultation since 1991, for postoperative hypothyroidism, the patient underwent a left lobo-isthmectomy of a thyroid nodule suspect whose pathological study came back benign. She presents suddenly in consultation for a left cervical tumefaction on the bed of thyroid remnant which appeared recently and quickly in two months. It is a left bari-cervical mass of 4 cm, mobile and painless, without inflammatory or compressive signs, without palpable cervical lymphadenopathy, or signs of dysphagism. The initial exploration made of a thyroid ultrasound showed a large mass occupying the suspicious left thyroid compartment with doubtful cervical lymphadenopathy, followed by a fine needle aspiration returned Bethesda IV. Not operated given the disappearance of the mass following a course of corticosteroids for an idiopathic thrombocytopenia discovered in parallel. This event made it possible to rectify the diagnosis thanks to a new exploration. Ultrasound found a free left thyroid compartment with bilateral cervical lymph node formations and a large suspect right supraclavicular lymphadenopathy, a dosage of thyroglobulin in needle aspiration biopsy fine was realized returning negative eliminating the thyroid origin and cytopuncture found granulomatous adenitis without caseous necrosis compatible with sarcoidosis.

Biologically, the converting enzyme was twice normal and there was high calcemia. The CT scan shows a diffuse interstitial pneumopathy associated with cervical and mediastino-pulmonary lymphadenopathy concluding in an aspect of stage 3 sarcoidosis. The presumptive diagnosis was confirmed histologically by a bronchial biopsy.

Conclusion
The etiological diagnosis of a cervical mass or cervical lymphadenopathy, can represent a real challenge for the clinician. On a ground of thyroid pathology, the elimination of a neoplastic cause is a priority, sarcoidosis with these systemic and heterogeneous manifestations can constitute a diagnostic trap to be taken into consideration.

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EP979
Parathyroid carcinoma: about 3 cases and review of literature
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Introduction
Parathyroid carcinoma is a very rare tumor. The reported incidence is between 0.5 to 5% of primary hyperparathyroidy in various series. This entity does not present any clinical or biological specificity compared to the parathyroid adenoma which exposes to diagnostic difficulties.

Objective
The aim of our presentation is to study the clinical, therapeutic and evolutionary aspects of parathyroid carcinomas.

Material and methods
This is a retrospective study of 3 cases of parathyroid carcinomas treated in our department over a period of 22 years (2000-2021).

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Results
There are two women and one man, with a history of recurrent renal lithiasis in one case and a parathyroidectomy 10 years ago for parathyroid adenoma in one case. The average age was 54 years old. The average consultation time was 6 months. The reason for consultation was diffuse bone pain in two cases and a compressive anterior cervical swelling in one case. Calcium and parathormone levels were elevated in all our patients. Cervical ultrasound done in all cases and cervico-thoracic scan done in one case, did not suggest malignancy in all cases. The scintigraphy showed a fixation at the lower left parathyroid gland in two cases and lower right gland in one case. The treatment consisted of Para-thyroidectomy in all cases, associated with ipsilateral central neck dissection in two cases and ipsilateral lobe-isthmicectomy in one case. Frozen section examination evoked malignancy in two cases. Definitive histology examination confirmed the diagnosis of parathyroid carcinoma with capsular rupture and vascular embolos in two cases. The lower left parathyroid gland was the most affected. The average tumor size was 4 cm (range 2 cm to 7 cm). The evolution was good in all cases with a mean follow-up of 4 years.

Conclusion
Diagnosis of parathyroid carcinoma can be difficult and the management still remains a challenge.

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EP980
Thyroidectomy in laryngeal squamous cell carcinoma
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Introduction
Intraoperative management of thyroid gland in laryngeal cancer is controversial. In fact, there is no uniform consensus about the need for thyroid surgery in laryngeal cancer.

Objective
Determine the incidence of thyroid gland invasion in patients undergoing surgery for laryngeal squamous cell carcinoma.

Methods
A retrospective study including 62 cases of laryngeal squamous cell carcinoma who underwent a total laryngectomy. A thyroid surgery was performed in case of a subtotal extension ≥ 1 cm, an anterior extralaryngeal extension (T4a) or evidence of thyroid gland invasion on CT-scan or intraoperatively.

Results
The mean age of our patients was 59 years, predominantly males (98.4%). Eighteen patients had a subtotal extension ≥ 1 cm. The tumor was staged T4a in 14 cases. A loboisthmectomy was performed in 16 cases. A total thyroidectomy was done in 2 cases. On histopathological examination, thyroid extension was found in 2 cases (11.1%). No case of hypoparathyroidism nor hypothyroidism was noted among patients treated with thyroidectomy.

Conclusion
Thyroid gland involvement in laryngeal squamous cell carcinoma is rare (0-30%). Furthermore, hemithyroidectomy causes hypothyroidism in 63% of patients, and if combined with radiotherapy, the incidence goes up to 89% of patients. Therefore, thyroidectomy shouldn’t be performed systematically for patients treated with total laryngectomy. It should be done in case of a locally advanced disease with thyroid cartilage transition, a macroscopic thyroid gland invasion and a significant subtotal extension.

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EP981
Primary mucinous carcinoma of the thyroid gland: A rare tumour
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Introduction
Primary mucinous carcinoma of the thyroid gland is extremely rare. To the best of our knowledge, only nine cases have been reported in the literature. Our aim is to report a case of primary mucinous carcinoma of the thyroid gland and to describe its diagnostic and prognostic features.

Case Report
A 55-year-old man referred to our department for a 2-month history of an anterior neck mass associated with dysphagia. Physical exam showed a 4-cm and hard, right anterior neck mass, with left cervical lymph nodes (group V). Ultrasonography identified a 3-cm right thyroid nodule: EUTIRADS 5 with bilateral suspicious cervical lymph nodes. CT scan revealed a 3-cm hypodense right thyroid nodule associated with several mediastinal and cervical lymph nodes. TSH level was normal. Fine-needle aspiration (FNA) result was “nondiagnostic.” The patient underwent total thyroidectomy with bilateral central (group VI) and lateral neck dissections (groups II, III and IV). The tumour invaded the strap muscles and the left thyroid lobe. Several lymph nodes were noted in the central group, lateral cervical and mediastinal regions. Intraoperative examination was in favour of a poorly differentiated thyroid carcinoma. Postoperative course was uneventful. The histologic exam (with immunohistochemical study) confirmed the diagnosis of a primitive mucinous carcinoma of the thyroid gland. Surgical margins were positive. Lymph node metastases were noted in the central and lateral neck regions. The patient died 15 days after the surgery.

Conclusion
Primary mucinous carcinoma of the thyroid gland is unusual. Differential diagnosis must be discussed with other primary typical thyroid carcinomas or adenomas, metastatic carcinoma of the lung, breast, colon and other organs. Primary mucinous carcinoma has a worse prognosis than common thyroid carcinomas: survival ranging from 1 month to 2 years.

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EP982
Association between vitamin D serum concentration and development of papillary thyroid cancer
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Purpose
Papillary thyroid cancer (PTC) is the most common thyroid and endocrine malignancy worldwide. Vitamin D (calciferol or 25-hydroxyvitamin D) (25(OH)D) has been postulated as a key modulator in several cancer-related pathways, although its contribution to PTC still remains controversial. The aim of the study was to analyse the correlation between 25(OH)D serum levels and 25(OH)D insufficiency as well as the risk of development of PTC and its variants: classical type (CV-PTC), tall cell type (TCC-PTC) and follicular variant (FV-PTC).

Methods
The study included 259 patients: 112 patients diagnosed with PTC (CV-PTC, n = 78; TCC-PTC, n = 8; FV-PTC, n = 26), and 147 patients diagnosed with benign thyroid nodules, all aged 43-71 ± 7 years. Diagnosis of the PTC and its variants was confirmed with cyto/histopathological examination. The serum levels of 25(OH)D were measured by fully automated chemiluminescentmicroparticle immunoassay (CMIA). 25(OH)D insufficiency was defined as a serum 25(OH)D level < 75 nmol/l.

Results
The prevalence of 25(OH)D insufficiency was 38.2%. Serum 25(OH)D levels and the prevalence of 25(OH)D insufficiency showed no significant differences between both group of patients (P = 0.65). Among PTC patients, 25(OH)D insufficiency was not associated with any PTC subtype or other clinical manifestation (P = 0.87).

Conclusions
This study shows no association of 25(OH)D insufficiency with the development of PTC, different PTC subvariants or any other clinical characteristic of PTC.

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EP983
A rare cause of metastasis to the thyroid gland: cervical carcinoma
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Introduction
Cervical carcinomas are rare malignant tumors. The preferential localization is the larynx, predominantly the epiglottis. There are also rare cases of metastases to the thyroid gland. Here we report a case of cervical carcinoma metastatic to the thyroid gland.
Introduction

Metastasis to the thyroid gland is a rare clinical presentation. The most common sites of primary tumors that metastatize to the thyroid gland are kidney, lung, gastrointestinal system and breast. Primary thyroid malignancies account for only 3% of secondary thyroid malignancies. Here, we present a case of thyroid metastasis from squamous cell carcinoma (SCC) of the cervix.

Case

A 54-year-old female was consulted to our clinic with the pathology result of subtot al thyroidectomy. Five years ago, she had been diagnosed with cervical SCC treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy and radiotherapy. The patient had no other known comorbidities. She had a history of lung metastasis. Two months ago, in addition to lung, pathological increased activity uptake (SUVmax 5.7) in the right thyroid lobe was reported in PET-CT. A 7.6 mm hypoechoic nodule was detected in the right thyroid lobe on ultrasound, and the result of fine needle aspiration biopsy was reported to be compatible with SCC. She was operated for lung metastasis last month, SCC was found in two regions, and adenocarcinoma in one region, respectively. Afterwards, right subtotal thyroidectomy was performed for suspected thyroid metastasis. The pathology result was reported as metastatic SCC. Tumoral tissue was 18x17x10 mm and tumor cell groups were scattered among the thyroid follicles. When the patient was consulted, thyroid function tests were normal, calcitonin was negative, thyroglobulin level was 22.4 ng/ml and anti-thyroglobulin 1.5 IU/mL. Thyroglobulin and thyroid transcription factor-1 (TTF-1) staining were requested from the pathology of the patient and negative staining was obtained. The patient was accepted as thyroid metastasis of cervical cancer. In addition to chemotherapy, the patient received radiotherapy to the neck and thorax. Six months later, a 23x20 mm soft tissue lesion was detected in the right thyroid lobe on ultrasound. Three months after that, a 45 mm mass (SUVmax 8.9) extending from the right thyroid lobe to the vertebral corpus was detected on PET-CT. Tracheostomy and gastrostomy were performed. The patient died shortly after.

Conclusion

Thyroid metastasis from cervical cancer is very rare and only a few cases have been reported. Patient who present with a thyroid nodule and has a history of a previous malignancy should be evaluated for metastatic disease.

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EP985

Thyroglobulin is a poor predictor of differentiated thyroid cancer in patients operated for thyroid nodular diseases

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Background

Thyroglobulin, serves as a specific tumor marker following thyroidectomy in differentiated thyroid cancer (DTC) patients. However, its role as DTC predictor in patients with thyroid nodules (TN) is controversial.

Aim

We aimed to assess the potential role of preoperative serum thyroglobulin concentration to predict DTC in patients who were operated for thyroid nodular disease.

Methods

This retrospective study included patients who had partial or total thyroidectomy between January 2014 and May 2019, with preoperative diagnosis of benign multinodular goiter (MNG) or a TN with indeterminate cytology (INC, Bethesda system 3/4 categories). We compared patients for demographic, clinical, imaging, and biochemical data according to their final diagnosis: DTC or benign TN disease. Further statistical analysis included odds ratios calculation and receiver-operator curves (ROC) analysis.

Results

Of 131 patients who met inclusion and exclusion criteria, the indication for surgery was benign MNG in 69, and TN with INC in 62 patients. Final diagnosis of DTC was reported in 18/69 (26%) and 30/62 (48%) of patients with preoperative diagnosis of benign MNG and INC-TN, respectively. Preoperative Median thyroglobulin was 148.5 ng/ml (IQR 67.8-1158.5) vs. 190 ng/ml (IQR 65.2-4574) in malignant and benign MNG respectively (P = 0.97), and 160.5 ng/ml (IQR = 82.2-536.7) vs. 205.5 ng/ml (IQR = 65.2-821.5) in malignant and benign INC-TN respectively (p = 0.93). Nodule diameter, TSH level, and thyroglobulin did not differ between patients with final diagnosis of DTC versus those with benign histology.

Conclusion

Preoperative serum thyroglobulin alone is insufficient to differentiate preoperatively between malignant and benign thyroid disease.

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EP986

Male gender is independent factor of poor prognosis in medullary thyroid cancer

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Medullary thyroid carcinoma (MTC) is a rare malignancy arising from parafollicular C cells of the thyroid gland, sometimes due to germline mutations in the RET protooncogene. Testicular cancer is the most common malignancy in men aged 15 - 40 years with survival rates improved by the introduction of cisplatin therapy in the late 1970s. Nonetheless, platinum-based chemotherapy was shown to increase the risk of a solid second cancer with substantially increased site-specific risk of malignancies of thyroid, melanoma, kidney and bladder.

Case report

We present the case of a 42-year-old man diagnosed with MTC during oncological follow-up for testicular seminoma. 18FDG PET-CT showed increased uptake in a single thyroid nodule 1 month after completion of chemotherapy (3 cycles of cisplatin, etoposide and bleomycin). The patient had left orchiectomy 8 months before. Thyroid ultrasound revealed an isoechonic nodule on the lower right lobe of 4.7/3.5/3.5 cm and suspicious bilateral lymph nodes. High serum levels of calcitonin (338 pg/ml), carcinoembryonic antigen (12.2 ng/ml) and fine-needle aspiration cytology smears were suggestive of MTC. Screening for other components of multiple endocrine neoplasia 2 syndromes was negative and no germlinal mutations in the RET gene were detected either. Total thyroidectomy along with bilateral neck lymph node dissection were performed. Pathology yielded a diagnosis of MTC in the right lobe with metastasis in one ipsilateral lymph node. Immunohistochemistry showed diffuse staining for Chromogranin A, TTF1 and CEA, weak focal staining for Calcitonin and strong SSTR2 and SSTR5 positive staining. Postoperative follow-up at 6 and 8 weeks revealed high serum calcitonin (338 pg/ml) and cervical ultrasound showed a small tissue remnant in thyroid bed and several suspicious cervical lymph nodes. No other mets were detected on 18FDG PET-CT. Second intervention surgery for neck dissection was performed with several metastatic lymph node excision and calcitonin reassessment was scheduled at 6 wks postop follow-up.

Discussion

The relationship between papillary and follicular thyroid cancer along with testicular germ cell tumour has been described as a consequence of cisplatin chemotherapy; however literature review showed no association of MTC and testicular seminoma so far. Screening with Next Generation Sequencing panel for 4813 Genes (TruSight 24th) is under consideration.

Conclusion

Association of Ret negative MTC and testicular seminoma diagnosed 8 months apart suggest synchronous association of the two cancers worth of a wider genetic screening with NGS.

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Introduction

Graves’ disease (GD) is an autoimmune disorder characterized by diffuse hyperplasia and excessive production of thyroid hormone. The association between thyroid carcinoma and GD is controversial. Thyroid nodular lesions in patients with GD should raise a high suspicion of carcinoma. The aim of this study is to focus on the possibility of an association between hyperthyroidism and thyroid carcinoma.

Materials and Methods

A continuous retrospective cohort study of patients who underwent primary surgery for medullary thyroid carcinoma in 2010-2020 at the S.I. Pirogov Clinic for Advanced Medical Technologies, Saint Petersburg University, was conducted. Preoperative ultrasound data, basal serum calcitonin levels preoperatively and postoperatively on the 1st day after surgery, as well as histological examination data of surgical specimens were evaluated. Postoperative observation data for a period of at least 1 year were obtained for 347 patients. Patients were distributed by age to 6 age groups. Data analysis was performed using Tibo Statistica 14.

Results

Patients were divided by percentage or by age and compared with each other. Male patients had a larger tumor size and basal calcitonin levels in all groups except over 70 years of age. The difference was significant and did not depend on the RET status of heritability. It is noted that with increasing age, the odds ratio of an aggressive course increased from 3.2 in all patients under 50 years to 9.25 from 50 to 60 years and 40.9 from 60 to 70 years. In the group over 70 years of age, OR is not significant due to the small number of patients and the death of most male patients with aggressive forms at an earlier age. Mostly medullary thyroid cancer even metastatic is indolent and found occasionally so difference caused by higher rate of symptomatic disease in men was found insignificant. The male sex significantly correlated with the risk of invasion into the surrounding tissues 0.715503, necrosis 0.547170, perineural growth 0.550827, the number of affected lymph nodes in the central and lateral tissues of the neck 0.465853 and 0.406780 respectively, with a probability of repeated interventions 0.485560 and a shorter recurrence period 0.44950. With a weak correlation with the node size of 0.255830.

Conclusion

The male gender is associated with a greater risk of aggressive course of medullary thyroid carcinoma, less effective surgical treatment, and greater need for target therapy.

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**EP988**

**Thyroid Carcinoma in patients with Graves’ Disease: about 7 cases**

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**Introduction**

Graves’ disease (GD) is an autoimmune disorder characterized by diffuse hyperplasia and excessive production of thyroid hormone. The association between thyroid carcinoma and GD is controversial. Thyroid nodular lesions in patients with GD should raise a high suspicion of carcinoma. The aim of this study is to focus on the possibility of an association between hyperthyroidism and thyroid carcinoma.

**Materials and Methods**

This is a retrospective study about 7 cases of differentiated thyroid cancer out of 52 patients operated for Graves’ disease in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).

**Results**

All patients were female. The average age was 50 years [17-68]. Preoperative thyroid ultrasound revealed a nodular goiter in all cases, suspicious nodules in 4 cases. Indications for surgery included the following: resistance to medical treatment in 2 cases and nodular goiter with suspicious nodules in 4 cases. Frozen histological examination disclosed the presence of carcinoma in 5 cases. These patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection. The histology concluded to the diagnosis of a papillary carcinoma in all cases. Among them, there were 2 cases of microcarcinoma. None of the cases showed lymph node metastasis. Surgical treatment was followed by radioactive iodine therapy in all cases. With a mean follow-up of 4 years, there was no distant metastasis or cancer recurrence.

**Conclusion**

Thyroid nodular lesions in patients with GD are not uncommon. Thus, careful evaluation of all thyroid nodules in GD patients is essential. It seems reasonable to check GD patients for the development of possible thyroid carcinoma, even if they are nodule free.

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**EP987**

**Thyroid Carcinoma in patients with Graves’ Disease: about 7 cases**

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**Introduction**

Graves’ disease (GD) is an autoimmune disorder characterized by diffuse hyperplasia and excessive production of thyroid hormone. The association between thyroid carcinoma and GD is controversial. Thyroid nodular lesions in patients with GD should raise a high suspicion of carcinoma. The aim of this study is to focus on the possibility of an association between hyperthyroidism and thyroid carcinoma.

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EP989

King of the CASTLE? Immunohistochemistry in diagnosing rare thyroid carcinomas: a case report
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Introduction
Carcinoma showing thymus-like differentiation (CASTLE) is a rare, low-grade thyroid carcinoma, with indolent clinical course and usually a favorable prognosis. The clinical and imagistic features are not specific for CASTLE but similar to other malignant lesions of the thyroid, making diagnosis difficult and reliant on immunohistochecmical examination. The conclusive diagnosis requires pathological examination and positive cluster of differentiation 5 (CD5) immunoreactivity.

Case Report
Hence, the present paper aims to present a rare case of CASTLE compressing the trachea in a 50-year-old female patient, after being misdiagnosed in another center with undifferentiated thyroid carcinoma, for which she underwent an unsuccessful surgical procedure followed by postoperative radiotherapy and chemotherapy.

The patient sought out a second opinion, for the investigation of an 18 months history of persistent dyspnea, dry cough, weight loss, loss of appetite, and fatigue, associated with dysphagia and dysphonia. The patient underwent a challenging radical surgery, total thyroidectomy and cervical lymphadenectomy being performed. Histopathological analysis of the specimen showed large areas of fibrosis, large, round vesicular nuclei with small nucleoli, low cytoplasm and peritumoral lymphoplasmacytic infiltration. Immunostaining for CD5 was positive. Postoperatively, no adjunctive radiotherapy was recommended, no acute complications were reported, replacement therapy with Levothyroxine was initiated, metastatic follow-up was negative and there was no evidence of loco-regional recurrence after 6 months of follow-up.

Conclusion
The diagnosis of CASTLE is difficult and requires a rigorous histological analysis and positive CD5 immunoreactivity. The improvement of long-term survival is based on the level of tumoral invasion in the adjacent structures, absence of metastasis and successful resection of the tumor and neck dissection. The particularity of this case consists in emphasizing the importance of establishing the accurate diagnosis for obtaining optimized management, with the purpose of reducing unnecessary procedures.

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EP990

Thyroid storm in a patient with severe leptospirosis managed with veno-venous extracorporeal membrane oxygenation
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Background
Leptospirosis is an endemic zoonosis in the Philippines, with complications including jaundice from liver injury and acute kidney injury requiring renal replacement therapy. On the other hand, thyroid storm, most commonly in the setting of Graves’s disease, is a rare complication of hyperthyroidism. To date, thyroid storm has not been documented in patients with severe leptospirosis.

Case Presentation
Herein, we present the case of a 52-year-old man, with no known thyroid disease and with prior wading in flood waters, who presented with fever, conjunctival suffusion, icterusia, and oliguria. He arrived on the 7th day of illness with hypotension and atrial fibrillation. Workups revealed low thyroid stimulating hormone (TSH), elevated free T4 (FT4), and elevated free T3 (FT3). There was also elevated serum creatinine, leukocytosis, and thrombocytopenia. He was diagnosed with severe leptospirosis, started on ceftriaxone intravenously, and underwent hemodialysis. He subsequently developed hemoptysis, prompting intubation and veno-venous extracorporeal membrane oxygenation (V-V ECMO).

Thyroid storm was suspected when he had persistent fever in the background of hyperthyroidism and atrial fibrillation. After starting propylthiouracil, super-saturated potassium iodide, and intravenous hydrocortisone, there was lysis of fever and improvement in hemodynamic status. On the 3rd day of V-V ECMO, significant improvement in oxygenation and resolution of pulmonary hemorrhage allowed weaning and decannulation. There was, however, eventual development of ventilator associated pneumonia and agranulocytosis, prompting the discontinuation of propylthiouracil. Despite the addition of broad-spectrum antibiotics, intractable metabolic acidosis and hypotension ensued, which led to the patient’s demise. TSH receptor antibody was eventually revealed to be undetectable, while thyroid ultrasound was unremarkable.

Discussion
Overlap of symptoms between thyroid storm and severe leptospirosis, such as fever and jaundice, may delay early diagnosis and management of thyroid storm. Furthermore, the full therapeutic regimen was not optimized due to hypotension and development of agranulocytosis. While there is documented success on the use of V-V ECMO in severe leptospirosis, the utility of ECMO in thyroid storm is limited to Veno-Arterial ECMO for thyrotoxicosis-induced cardiomyopathy. To date, there have been no published reports of leptospirosis occurring simultaneously with thyroid storm. The absence of thyroid nodules or a diffusely enlarged thyroid gland, together with an undetectable thyroid receptor antibody, should prompt consideration of destructive thyroiditis from severe leptospirosis.

Conclusion
The case highlights diagnostic and management challenges in a rare case of thyroid storm in the setting of severe leptospirosis.

Keywords: ECMO, leptospirosis, thyroid storm, Weil’s

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EP991

Thyroid abscess as a complication of post-COVID-19 subacute thyroiditis: a case report
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Introduction
Thyroid abscess is a rare pathology, with the incidence of less than 1% of all thyroid diseases. We describe a unique case of thyroid abscess complicating post-covid-19 thyroiditis, which is the first case reported in Morocco to our knowledge.

Case presentation
A 39-year-old man who had recently recovered from a mild episode of COVID-19 infection, consulted for weight loss, palpitations and neck pain. Examination of the neck revealed enlarged, firm, and tender thyroid gland. His electrocardiography revealed sinus tachycardia. Laboratory tests showed elevated erythrocyte sedimentation rate at 40 mm/h and c-reactive protein at 75 mg/l. TSH was low (< 0.05 mU/l), T4 and T3 levels were elevated at 7.72 ng/dl (reference 0.77-2.02) and 11.23 pg/ml (reference 2.2-4.6), respectively. Thyroid peroxidase antibody and TSH-receptor antibody were negative. Ultrasound of the neck showed heterogeneous goiter with areas of thyroiditis, and reduced blood flow on Doppler study. The diagnosis of subacute thyroiditis was made, and the patient was discharged home on oral prednisone (60 mg) and atenolol (40 mg) daily. During the follow-up, the prednisone was gradually tapered off over 7 weeks, and atenolol was discontinued. The thyroid function tests returned to normal at 9 weeks follow up, however the patient developed a cervical swelling with pus discharge. Ultrasonography was consistent with Thyroid abscess. A retroviral screening for Human Immunodeficiency Virus was negative. Culture of the pus from the abscess obtained during the fine needle aspiration grew Staphylococcus aureus. The patient was successfully treated with percutaneous drainage and oral amoxicillin clavulanate.

Discussion
Thyroid abscess is a less seen diagnosis, mostly so as the gland is inherently protected. The encapsulation, rich blood and lymphatic supply, and iodine content inside offer the gland protection from being seeded. Thyroid abscess usually occurs in patients who are immuno-compromised, those with pre-existent thyroid pathologies or anatomic gland anomalies. Some authors have related thyroid abscess to neoplastic causes, thyroid nodule, subacute thyroiditis, Hashimoto’s thyroiditis or traumatic causes. In our case, when no immunosuppression or anatomical factors are present, there was sufficient clinical and biological evidence within reasonable limits that failed to yield any other risk factor for thyroid abscess other than subacute thyroiditis that the patient developed after SARS-COV-2 infection.

Conclusion
Thyroid abscess is an unusual complication of post-COVID-19 subacute thyroiditis and can lead to significant morbidity. Therefore, clinicians must be aware of the presenting features and therapeutic options.

DOI: 10.1530/endoabs.81.EP991
Introduction
Lingual thyroid ectopia is a rare congenital abnormality affecting embryogenesis of the gland descent from foregut through pre-tracheal region in the neck. Most cases have an asymptomatic course but may occasionally produce local obstructive symptoms. Diagnostic methods are 99mTc, 131I or 123I radionuclide scan, computed tomography scan, magnetic resonance, and ultrasound. Surgery is the elective treatment for cases presenting complaints or complications. Radioactive iodine ablation is an alternative for patients who refuse surgical intervention or unfit for anesthesia. We report 49-year-old women with an ectopic lingual thyroid presented as oral hemoptysis with high surgical risk, successfully treated with 131I.

Materials and methods
A case report description conducted with the consent of the patient and with provisions of the Declaration of Helsinki.

Results
49-year women with relevant medical history such as primary hypothyroidism under thyroid hormone replacement, well controlled type 2 diabetes, HTA and morbid obesity (BMI 58). Presented to Emergency department with a 12-h history of upper gastrointestinal bleeding, mild dysphagia, and no respiratory symptoms. Cervical scintigraphy demonstrated a jet arterial bleed above the epithyroid of the base of the tongue. Intubation was performed with surgical hemostasis by means of pharyngeal packing containing and resolving the hemorrhage. CT of the neck confirmed a well-defined rounded occupational image at the base of the thyroid and floor of the mouth, in the midline, with intense and homogenous enhancement, measuring 35x37x39mm, compatible with ectopic lingual thyroid that imprints on the oropharyngeal lumen. Thyroid 99mTc combined with single-photon emission computed tomography/computed tomography confirmed an increased radiotracer homogeneous activity on at this location. Hospitalization was complicated with bilateral pneumonia and bilateral acute pulmonary embolism (PESI 59, class I). Surgical option was denied because of patients’ comorbidities and associated complications due to this conventional surgery. She was treated with 16.5 mcG of 123I remaining asymptomatic.

Conclusion
Lingual thyroid ectopia is a rare congenital anomaly in population, that warrants treatment when it produces obstructive or compressive symptoms or complication arises. Scintigraphy methods plays a major role in establishing the diagnosis, even though US or TC or RM may also be helpful in the process of differential diagnosis with other cervical masses. Surgery has been the conventional approach to remove ectopic thyroid gland. However, other strategies such as RAI are safe and efficient strategy for high risk surgical and comorbid patients, remaining them asymptomatic.

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EP995
Coexisting grave’s disease and coeliac disease in an adolescent with down’s syndrome
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Introduction
Trisomy 21 is the most common chromosomal disorder. It is associated with an increased risk of endocrinopathy particularly thyroid gland disorders. This is frequently a complicated hypothyroidism. Hyperthyroidism is rare. We report the case of an adolescent with Down’s syndrome and celiac disease who presented with subclinical hyperthyroidism.

Case report
It was a 15-year-old female from a non-consanguineous marriage with a history of celiac disease on a gluten-free diet. The physical examination showed a stable weight of 48 kg, a height of 146 cm and a body mass index of 22.53 kg/m². She had a goiter visible in extension of the neck but no exophthalmos. She had no history of excessive sweating, diarrhea or tremors. Cardiovascular examination was unremarkable. Blood investigations noted a normochromic normocytic anaemia of 11.3 g/dl. The thyroid assessment done as a part of an annual biological monitoring showed a TSH of 0.005 mU/l and a free T4 of 17.21 pmol/l (12-22). Anti-TSH receptor antibodies were positive. Cervical ultrasound showed a diffuse enlargement of the thyroid. The diagnosis of Grave’s disease was retained.

Conclusion
Down’s syndrome is a breeding ground for thyroid dysfunction. Celiac disease is common in people with down’s syndrome and it is associated to various endocrine autoimmunities such as thyropathies. Hyperthyroidism is extremely rare. The diagnosis is often made through a systematic assessment, hence the interest of a biological control aimed at detecting dysthyroidism early to avoid complications that are potentially serious. The particularity of our observation was the association of celiac disease and grave’s disease in an adolescent discovered by an annual thyroid check-up.

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EP996
Primary thyroid lymphoma: case report
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Introduction
Primary thyroid lymphoma is a rare malignancy. In many series, it is reported that it is seen at a rate of 0.6-5% among thyroid cancers and approximately 2% among extranodal lymphomas. It is often seen as a painless mass in the neck. Almost all of them have underlying Hashimoto’s thyroiditis. In many instances, thyroid lymphoma was recognized after thyroid surgery for suspected carcinoma. The most common thyroid lymphomas are B-cell and Hodgkin lymphomas. The distinction between primary and secondary lymphoma is important because of the variables in diagnosis, treatment, and prognosis. Surgery, chemotherapy, radiotherapy, or combinations can be used in the treatment.

Case
A 69-year-old male patient underwent total thyroidectomy and central neck dissection due to a 3.5x2.5 cm nodule in the right thyroid lobe. During the operation, it was observed that the mass lesion in the right lobe had progressed to fixation to the lateral carotid and invaded the right internal jugular vein. In addition, partial resection of the right lobe was performed. The patient received 4 cycles of R-CHOP (Adriamycin + Cyclophosphamide + Rituximab + Vincrisine) chemotherapy protocol. The before and after treatment PET-CT was reported as: The finding showing pathological 18F-FDG uptake in favor of malignant involvement in the whole body cannot be identified.

Table 1

<table>
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<tr>
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Conclusions
Thyroid lymphoma, which is rarely seen in patients presenting with a thyroid mass, should also be considered. While Hashimoto’s thyroiditis is seen in most primary thyroid lymphomas, primary thyroid lymphoma develops in only 0.6% of Hashimoto’s thyroiditis cases.

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EP997
Influence of the mother’s history during pregnancy on the development of hyperthyroidism in children living in conditions of iodine deficiency
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Our goal was to determine the anamnestic characteristics of mothers during pregnancy in children with hyperthyroidism living in conditions of iodine deficiency, which possibly contribute to the development of hyperthyroidism in patients of the pediatric group.

Materials and methods of research
The analysis of the anamnesis of mothers during pregnancy of 146 children and adolescents with hyperthyroidism. The control group consisted of 97 relatively healthy children under 18 whose parents agreed to participate. Statistical processing of the results was carried out using the statistical software packages ‘SPSS 23 for Windows’ (‘IBM Corp. Armonk’, NY, USA).

Results
Analysis of the mother’s anamnesis during pregnancy of children and adolescents with hyperthyroidism are presented in Table 1. The results obtained indicate that the presence of autoimmune thyroid disease in the mother increases the risk of developing hyperthyroidism in the child by 7.5-8.2 times (OR = 8.2 (95% CI 3.1-21.5), P<0.001), while endemic maternal goitre during pregnancy and systemic autoimmune diseases (OR = 2.6 (95% CI 1.3-5.3), P<0.001).

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CI 0.7-9.4), \( P = 0.69 \) is not a reliable provoking factor (OR = 1.4 (95% CI 0.5-3.8), \( P = 0.36 \). In addition, overweight and obesity (OR = 3.9 (95% CI 1.1-13.6), \( P = 0.03 \)), as well as anemia of varying severity in pregnant women (OR = 5.8 (95% CI 2.2-15.4), \( P = 0.001 \)) may increase the risk of developing hyperthyroidism in children. At the same time, vitiligo (0.7%), type 2 diabetes mellitus (2.1%), poly cystic ovary syndrome (0.7%) were diagnosed only in mothers whose children had hyperthyroidism.

Conclusion

Possible factors that increase the risk of developing hyperthyroidism in children living with iodine deficiency are the following maternal anamnestic indicators during pregnancy: Graves’ disease, autoimmune thyroiditis, overweight and obesity, anemia of pregnancy, type 2 diabetes mellitus, vitiligo and poly cystic ovary syndrome.

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EP998

Thyroid disease in patients with type 1 diabetes

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Hospital Universitario de Navarra, Pamplona, Spain

Introduction

An increased risk of thyroid disease (TD) has been described in patients with type 1 diabetes (DM1) with respect to the general population. The objective is to establish the incidence and characterize the differences in patients who develop TD in relation to the debut of DM1 (previous, concurrent or a posteriori).

Materials and methods

Retrospective study of 1126 patients followed up in Endocrinology consultations in Navarra. Three types of TD were differentiated: hyperthyroidism (HI), hypothyroidism (HO) and autoimmune thyroid disease with normo function (AT). Clinical and analytical variables were analyzed. Comparison between the medians of the groups was performed using the Mann Whitney U test. Differences between categorical variables were analyzed using the \( \chi^2 \) test.

Results

The study population included 669 men (59.3%) and 459 women (40.7%), with a mean age at debut of 20 years and a mean follow-up of 11.4 years (7.6 sd). A total of 300 (26.6%) developed thyroid disease. The analysis of the 32 that already had TD before the onset of DM1 (8 HI, 21 HO, 3 AT) revealed that women, gastric autoimmunity and younger patients had a higher risk of developing TD. 87 patients presented concurrent TD (10 HI, 40 HO, 37 AT) at the onset of DM1. Female gender, debut over 45 years and positive gastric autoimmunity was also more frequent in those 181 patients that developed TD at follow up (16 HI, 102 HO, 63 AT) of the DM1.

Conclusion

In the population studied, the cumulative incidence of TD in the follow-up of patients with DM1 was high, with hyperthyroidism predominating. There are different clinical and analytical variables that can predict which risk groups have a greater predisposition to develop TD before, at the onset or after the diagnosis of DM1. The factors to be taken into account that affect a different susceptibility to develop TD are gender, age at DM1 debut, thyroid autoimmunity and gastric autoimmunity. Although confirmation is required in future studies, they may be indicative for closer surveillance.

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EP999

Serum selenium status in UK Graves’ disease patients with and without orbitopathy

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Imperial College Healthcare NHS Trust, United Kingdom

Introduction

Selenium supplementation is recommended for all patients with mild Graves’ orbitopathy (GO). The thyroid gland contains high levels of selenium, which has an anti-oxidant effect and a role in the metabolism of thyroid hormones. The study on which this recommendation is based was conducted in countries of a selenium-deficient region and did not measure subjects’ selenium concentrations. There is therefore no consensus on optimum dose, duration, or safety. Environmental selenium varies extensively between countries and no published studies report measured the baseline selenium status of UK GO patients. We aimed to determine baseline selenium status in a UK population, and compare this to Graves’ patients without GO.

Methods

Baseline serum selenium status was measured in UK Graves’ disease patients with and without orbitopathy between January – December 2021.

Results

There were 56 patients; 25 had orbitopathy (the mean Clinical Activity Score was 1.9), (20 females and 5 males, average age 48.8yrs) and 31 did not (26 and 5; 47.5). Average serum selenium was 1.13 (range 0.5-1.93, reference range 0.76-1.46 \( \mu \)mol/l); 1.14 in the GO group vs. 1.12 in the non-GO group. There were 12 current or previous smokers in the GO group (48%) vs. 8 in the non-GO group (26%).

Conclusion

These results show that baseline selenium status in GO and non-GO patients is largely within the normal range. This suggests that selenium may have lesser benefit in the UK compared to regions with lower environmental selenium. Patients may also be at risk of iatrogenic overdose. A randomised control trial investigating the clinical effects of selenium supplementation in a UK GO population with concurrent measurement of selenium status is warranted.

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EP1000

Assessment of thyroid function in healthy pregnant women living in iodine deficiency regions

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Background

During pregnancy, the physiology of the thyroid gland undergoes important changes. As a result, change levels of thyroid hormones. In the latest clinical guidelines, experts have recommended to perform population-based studies to determine reference intervals for thyroid hormones. Aim

To evaluate the reference intervals of free thyroxine in different trimesters of pregnancy in women living in regions with mild iodine deficiency.

Materials and methods

We have conducted the observational multicenter cross-sectional study included 2008 healthy pregnant women at different trimesters of pregnancy, from three regions of the Russian Federation (Moscow, Ivanovo and Smolensk). We assessed the level of free thyroxine, antibodies to thyroid peroxidase, antibodies to serum thyroglobulin (Architect, Abbot, reference range 9-20 \( \mu \)mol/l), the level of iodine concentration in the morning portion of urine (cerium arsenic method) and we have conducted a questionnaire (date birth and gestational age). Women with elevated tilters of anti-TPO and/or anti-TG antibodies were excluded from the study (245 women).

Results

We have determined the median iodine concentration: Moscow 111 \( \mu \)g/l, Ivanovo 125 \( \mu \)g/l, Smolensk 133 \( \mu \)g/l, which confirms the presence of mild iodine deficiency in the regions areas (median iodine concentration less than 150 \( \mu \)g/l in pregnant women corresponds to mild iodine deficiency). Reference intervals for free thyroxine are presented using the median, 2.5 and 97.5 percentiles with 95% confidence interval (Me [2.5;97.5] CI+45%). We obtained the following results: 1st trimester (\( n = 386 \)): Me: 11.7 [9.03;16.1] CI+1.96; -1.74; 2nd trimester (\( n = 478 \)): Me: 10.7 [8.35; 13.8] CI+1.43; -1.28; 3rd trimester (\( n = 899 \)): Me: 9.9 [7.73; 13.0] CI+1.41; -1.30.

Conclusions

Based on the results of our study, we determined the reference intervals of free thyroxine in healthy pregnant women without anti-TPO/TG antibodies living in mild iodine deficiency regions. We revealed a decrease in the level of free thyroxine by the third trimester, which can be physiological isolated hypothyroxinemia.

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EP1001
Impact of age on hypothalamic-pituitary-thyroid axis
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1 Medical Faculty, University of Banja Luka, Banja Luka, Bosnia and Herzegovina; 2 University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina

Background/Aim
Impact of age on hypothalamic-pituitary-thyroid axis, interesting from theoretical and practical aspects, have been studied. Our aim was to find out: correlation between T3 (triiodothyronine) and T4 (thyroxine) hormone level and old age, so as of other, for thyroid function relevant parameters: TSH (thyroid stimulating hormone), TRH (thyreothropin releasing hormone) test, thyroid ultrasonography, thyroid gland scintigraphy with 131I, 123I fixation test, thyroid antibodies and thyroglobulin.

Methods
Study included 125 subjects, divided in four groups, according to the age: control group (from 20 to 40 years); group A (from 41 to 50 years); group B (from 51 to 60 years) and group C (from 61 to 70 years), as well as into subgroups according to the sex. All patients were established total and free hormones T3, T4, TSH and test with TRH; thyroid gland scintigraphy with 131 I, 131 J fixation tests, thyroid antibodies and thyroglobulin. All hormone analyses, thyroglobulin and thyroid antibodies were determined by radioimmunoassay (RIA). Thyroid scintigraphy was done with 131 I and 131 J fixation test was monitored 4, 24 and 48 h after 1.85 MBq test dose applied perorally.

Results
There was a significant decrease in levels with aging of both total and free T4, and, somewhat, minor fall of both total and free T3 in men, in contrast to mild level rise of total T4 and T3 in women, but within the range of eutryoidism, with no alternations in free hormone levels. A significant fall of thyroglobulin antibodies with aging was observed in the group of males, and a considerable increase of thyroglobulin was shown in the group of females. Old age and sex don’t have impact on radio jodine fixation percentage in thyroid gland, thyroid scintigraphy and thyroid gland echostructure.

Conclusion
Hypothalamic-pituitary-thyroid axis is preserved with aging. The determination of the values of the free T4 should be basic test at older persons. Evident drop in thyroid hormone levels with aging can be considered as adaptation of the organism to reduce requirements for energy, thus representing a significant metabolic parameter of biologic aging process. A normal range of thyroid hormone values should be modified for the persons older than 70. These physiological variation should be standardised in the interpretation of the tests of the thyroid function.

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EP1002
Hypothyroidism associated with treatment with immunotherapy: case series
Maria Zhao Montero Benitez, Paloma Gonzalez Lázaro, Cristina Montalban Menédez, Antonio Moreno Tirado, Pedro Jimenez Torrecilla, Florentino Del Val Zaballos, Amparo Lomas Menedes, Francisco Javier Gómez Alfonso, Maria Lopez Iglesias & Inés Gómez García
Alcázar de San Juan, Endocrinology Department, La Mancha Centro Hospitalal Centre, Alcázar de San Juan, Spain

Introduction
The development of immunotherapy has opened up a new approach in the management of different types of tumors that previously had not been treated, and its use is becoming increasingly widespread. Immunotherapy is based on blocking immune checkpoints involved in activating the immune response to malignant neoplasms. Since its introduction into clinical practice, several adverse effects related to the immune system have been reported. Among the endocrinological adverse effects, hypophysitis and thyroid dysfunction are the most frequent. Adrenal insufficiency, DM1 and hypoparathyroidism have also been documented.

Case Series
We present the cases of 5 patients who developed hypothyroidism during immunotherapy treatment at the General La Mancha Centro Hospital and General Hospital in Tomelloso (Ciudad Real, Spain). All patients were male, aged between 56-72 years, and none of them had thyroid disorders prior to the use of immunotherapy. After the diagnosis of advanced oncological disease (melanoma, lung cancer, kidney cancer, and multiple myeloma), it was decided to start immunotherapy treatment, 3 patients with nivolumab (anti PD-1), 1 patient with durvalumab (anti PD-L1), and 1 patient with velcade (proteasomal inhibitor) plus daratumumab (AcMo anti CD38). Several months after starting treatment, patients were diagnosed with hypothyroidism (3 subclinical and 2 central), with asthma being the main symptom. Antithyroid antibodies were present in 2 patients. In those patients with suspected hypophysitis, an MRI was performed to rule out this pathology, and no cases were observed. After ruling out adrenal insufficiency, which was only documented in the patient treated with velcade plus daratumumab, replacement therapy was initiated, without requiring suspension of immunotherapy in any case.

Discussion
Endocrine disorders related to immunotherapy are increasingly recognized as one of the most common adverse effects. Its diagnosis is sometimes complicated, as symptoms are nonspecific and may overlap with symptoms due to tumor progression. In most cases, the management of these endocrinopathies does not require discontinuation of immunotherapy, although they are usually irreversible and require long-term treatment.

EP1003
Hyperthyroidism and pregnancy: About 70 patients
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Introduction
During pregnancy, the thyroid balance of women is altered due to certain hormonal and metabolic changes. It can be all the classic causes of hyperthyroidism, very often in the first trimester it is transient gestational hyperthyroidism.

Objective of the study
The objective of this study is to evaluate the prevalence of hyperthyroidism during pregnancy and the different methods of management.

Materials and methods
Prospective study conducted in the endocrinology and diabetology department, including 70 patients with hyperthyroidism during pregnancy

Results
The results had objectified a mean age of 29 years, with a mean gestational age of 11 SA, with a history of personal thyreopathy in 4 patients, the predominant clinical reason is vomiting in pregnancy, which was present in 98% of patients. On thyroid checkups: The Mean TSHus was 0.05 mIU/l, with mean T4L at 23 ng/l and mean T3L at 7 ng/l, a basedow disease was objectified in 4 patients, and a multi-heteronodular goiter in 5 patients. Therapeutically, 57% of the patients were put on synthetic antithyroid drugs with a betablocker, while for the other patients a simple monitoring was initiated. The evolution was marked by the disappearance of the signs of hyperthyroidism in 87% of the patients, with normalization of the thyroid balance after the first trimester.

Conclusion
Hyperthyroidism during pregnancy is a frequent reason for consultation, most often revealed by vomiting during pregnancy, which should not be neglected, requiring adequate management to avoid maternal-fetal complications.

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EP1004
Thyrotoxic hepatitis during pregnancy: about 42 cases
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Introduction
Hyperthyroidism in pregnancy is a common condition representing two different conditions: transient hyperthyroidism of pregnancy and true hyperthyroidism. It is
accompanied by liver enzyme disturbances without any other obvious cause. Objective of the study To evaluate the prevalence of acute hepatitis associated with hyperthyroidism. Materials and methods Prospective study conducted at the endocrinology and diabetology department of the CHU Casablanca including 42 patients with hyperthyroidism and acute pancreatitis complicated by hyperperistalsis gravidarum Results The results showed a mean age of 26 years, with a mean gestational age of 11 days after birth, with no personal history of thyroid disease, the predominant clinical reason was vomiting in pregnancy, which was present in all patients. Biologically: The mean TSH was 0.05 mIU/L, with a mean T4 of 26 ng/mL and a mean T3 of 8 ng/mL, with a hepatic cytolysis with an average ASAT of 111 IU/L and ALAT of 173 IU/L, a mean lipasemia of 208 IU/L, the abdominal ultrasound was without any particularities and negative hepatic serologies. Therapeutically, the patients were put on synthetic antithyroid drugs with a betablocker and digestive rest with parenteral nutrition. A normalization of the hepatic balance was observed in 87% of the patients after correction of the thyroid balance. Conclusion Thyrotoxic hepatitis is retained in front of a disturbed hepatic balance in the context of thyrotoxicosis after having eliminated any other cause in particular viral, autoimmune or drug-induced hepatitis. Hyperthyroidism, whatever its variant, remains a possible cause of hepatitis during pregnancy.

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**EP1005**

**Abstract Withdrawn**

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**EP1006**

**Insulin resistance and insulin-like growth factor-1 in patients with nodular goiter**

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Introduction

Publications suggesting that thyroid nodules might be associated with insulin resistance (IR) and metabolic syndrome are quite interesting. The aim of the work is to analyze the association between anthropometric indicators IR and insulin-like growth factor-1 (IGF-1) in patients with nodular goiter.

Methods

Examined 73 patients with euthyroid single-node (n = 34) and multinodular goiter (n = 39), age (51.0 ± 10.6) years; determining WC, WC/HC, BMI, WHR, ABD, TSH, FT3, T4, FT4, IGF-1, thyroid volume, its structure, number, size, and location of Iod were assessed by an ultrasonic complex.

Results

In the total group IGF-1 is associated with BMI (r = -0.30; P = 0.016), WC (r = -0.26; P = 0.036), WHR (r = -0.30; P = 0.020), ABD (r = -0.27; P = 0.03), ABD, BFD, BMI, AVI, A1, IGF-1. Thyroid volume, its structure, number, size, and location of Iod were assessed by an ultrasonic complex.

Conclusion

Patients with nodular goiter with IGF-1 above the sex-age norm, thyroid volume is associated with WC/HC (r = 0.31; P = 0.03), AVI (r = 0.29; P = 0.02) and A1 (r = 0.36; P = 0.004); thyroid volume is associated with age (r = 0.35; P = 0.009), WC/HC (r = 0.43; P = 0.001), BFD (r = 0.26; P = 0.06) and CI (r = 0.31; P = 0.02). In patients with BMI ≥ 35 kg/m² thyroid volume is associated with BMI (r = 0.71; P = 0.049). In patients with IGF-1 above the sex-age norm, thyroid volume is associated with WC/HC (r = 0.71; P = 0.01), ABD (r = 0.66; P = 0.03) and BFD (r = -0.52; P = 0.01). It has been found that AIG explains 82.37% of the variance of IGF-1 in the general group and more than 90% of the variance of its level in groups of patients with nodular goiter with high IGF-1 with/without obesity.

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**EP1007**

**Quality of life and symptomatology in patients with hypothyroidism post-graves’ disease**

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Introduction

Quality of life (QoL) and its related physical and psychological symptomatology is an important factor when we treat Graves’ disease.

Objective

To analyze the QoL and physical and psychological symptomatology of patients with hypothyroidism after definitive treatment of Graves’ disease.

Methods

We evaluated 16 patients with hypothyroidism that previously had Graves’ disease. These patients were submitted to total thyroidectomy and/or radiodine treatment to deal with Graves’ disease. Our sample had a mean age of 58.7 ± 15.0 years, 81.3% were female and 68.8% were married. We assessed thyroid function tests, thyroid antibodies, the resistance to thyroid hormone indices (Thyroid Feedback Quantile-Based Index [TFQI], lipid profile, high-sensitivity C-reactive protein, B12 vitamin, folic acid and applied several questionnaires, namely: the Thyroid Dependent Quality of Life questionnaire (ThyDQoL), the Thyroid Symptom Rating Questionnaire (ThyTSRQ) and the Brief Symptom Inventory (BSI). Statistical analysis was performed with the One-way ANOVA test and Pearson’s correlation test. P values ≤ 0.05 were considered as statistically significant.

Results

In this sample we found that patients had a mean BMI of 27.5 ± 4.3 kg/m², TSH 1.67 ± 2.11 μU/mL and FT4 1.21 ± 0.17 ng/dl. Patients reported a mean QoL value of -2.02 points (range from -9 to 1). In regard to the ThyTSRQ, 56% of patients have noticed at least moderately memory problems, and 62.6% of patients reported at least being moderately tired and 68.9% showed some kind of dizziness symptoms. Nearly 80% of patients did not report any weight gain or appetite problems. Regarding correlations, we found significant correlations between TSH and lack of appetite (r = 0.66; P = 0.01), auditory problems (r = -0.65; P = 0.006) and depression (r = -0.56; P = 0.02). We observed correlations between TFQI and weight (r = -0.54; P = 0.03) and depression (r = -0.54; P = 0.02). We also noticed a negative correlation between FT4 and dizziness symptoms (r = -0.55; P = 0.02). Results point out that QoL is negatively correlated with FT3 (r = -0.59; P = 0.01) and FT4 (r = -0.49; P = 0.05).

Conclusions

In this study we can observe that QoL, in general manners seems to be strongly influenced by FT4 and TSH than by TSH. Our study is in agreement with previous studies suggesting that FT4 has a good sensitivity regarding well-being evaluation. Further studies, with a more robust number of patients are needed to analyze more deeply the nuances of this kind of treatment and its contribution to the QoL.

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**EP1008**

**Rhabdomyolysis revealing a profound hypothyroidism**

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Introducing

Hypothyroidism is the most common endocrinopathy causing rhabdomyolysis. Muscle manifestations are common in hypothyroidism, but myopathy is most often limited to discrete clinical signs such as myalgias, stiffness or cramps accompanied by a simple elevation of muscle enzymes. On the other hand, rhabdomyolysis associated with hypothyroidism is a rare diagnosis to our knowledge. We report a case of severe rhabdomyolysis in the setting of profound Hashimoto’s hypothyroidism.

Observation

Mr A.I., 32 years old. Hospitalized in psychiatry for an acute psychotic attack, having as antecedent a schizophrenia since 6 years under neuroleptics in stop for 3 years. The interogation found signs of hypothyroidism. The clinical examination showed a Bradycardia, a generalized myxedema with a puffiness of the face and pre tibial myxedema, the osteoendemous reflexes sharp, a reduced mimic, the lower lips everted with a moderate bilateral ptosis, filling of the supra clavicular

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Endocrine Abstracts (2022) Vol 81
Subacute thyroiditis following asymptomatic COVID-19 case report
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1. Trimboli P, Cappelli C, Croce L, Scappaticcio L, Chiovato L, Rotondi M. Related SAT, 4 cases were described after asymptomatic SARS-COV 2 infections. COVID-19 Associated Subacute Thyroiditis: Evidence-Based Data From a certain trigger of thyroiditis, although in a review of 27 patients with COVID-19 SAT in asymptomatic COVID-19 patient remains a challenge in establishing the virus is reported in the literature, mostly following symptomatic SARS-COV-2 is also common in subacute thyroiditis. The association of SAT with SARS-CoV-2 infection by RT-PCR test and chest computed tomography (CT) were enrolled. We did not include patients with a medical history of thyroid disease. Clinical data, laboratory tests (TSH at the 1st and at the 9th day of hospitalization; C-reactive protein, lactate dehydrogenase and ferritin levels at the 1st day of hospitalization), CT data and received systemic corticosteroid therapy were analyzed.

Discussion
Rhabdomyolysis is a rare but fatal complication of hypothyroidism. Hormone replacement therapy, started gradually, allows resolution of muscle signs and normalization of muscle enzymes. A major elevation of CPK should prompt a search for hypothyroidism, although this is a rare cause, and warrants monitoring of thyroid status during any muscle lysis with elevated muscle enzymes, as recommended.

Subacute thyroiditis (SAT) is a relatively uncommon and self-limited cause of thyrotoxicosis of viral or post-viral origin. During the COVID-19 pandemic a thyroid impact was also considered due to the potential of SARS-CoV-2 virus to cause multisegmental effects. Several SAT cases associated with SARS-CoV-2 infection or vaccination were recently reported in the literature. We present the case of a 52-year-old female who presented with neck pain, fever, asthma, and malaise for approx. 2 weeks. On examination she had a moderately asymmetrically enlarged and tender thyroid gland, and was tachycardic, with no respiratory symptoms. From her medical history we retain no SARS-CoV2 vaccine or any form of upper respiratory airways infection recently. A prior endocrinology evaluation in 2020 revealed thyroid cysts of max 12mm and a normal thyroid function. Currently she had mildly high serum free T4 and suppressed serum TSH, high ESR of 111 mm/h, mild leukocytosis with neutrophilia. Liver function tests were also abnormal-elevated ALT (138 IU/l), mildly elevated GGT and alkaline phosphatase. The patient did not have any history of liver disease or alcoholic intake. On ultrasonography, the thyroid appeared enlarged with bilateral hypoechogenic areas that had reduced vascularization on Color Doppler. The liver appeared normal on ultrasound. Thoracic X-Ray was also normal. One week prior to presentation the patient had two nasopharyngeal swabs SARS-CoV-2 RT-PCR tests, both negative. However, at SAT diagnosis SARS-CoV-2 IgG antibodies were positive. Other viral serologies that can affect hepatic function were negative, including: anti CMV, anti-Epstein-Barr antibodies, IgM anti-HAV, HBsAg, Anti-HCV antibodies. A diagnosis of SAT post asymptomatic SARS-CoV-2 infection was made and the patient was started on corticosteroids with improvement of both clinical and biological parameters. A benign, short-lived and subclinical hepatic involvement is also common in subacute thyroiditis. The association of SAT with SARS-CoV-2 virus is reported in the literature, mostly following symptomatic SARS-COV-2 infection or vaccine, although the size of the problem is still unclear. In our case, SAT in asymptomatic COVID-19 patient remains a challenge in establishing the certain trigger of thyroiditis, although in a review of 27 patients with COVID-19 related SAT, 4 cases were described after asymptomatic SARS-COV-2 infections. (1) 1. Trimboli P, Cappelli C, Cocco L, Scappaticcio L, Chiavoto L, Rotondi M. COVID-19 Associated Subacute Thyroiditis: Evidence-Based Data From a
Results
Thyroid dysfunction screening was performed in 3821 women. 293 met SCHT biochemical criteria (7.66%). Of 140 women diagnosed with gestational SCHT, 106 had long-term TF data. The mean age was 31.4 ± 5 years, being 61.5% older than 30 years. The prevalence of persistent hypothyroidism (HT) at the end of the follow-up was 48.1%(n= 51), being significantly more frequent in women with positive anti-TPO antibodies (Ab) (61.4% vs 38.6%; P < 0.05) and TSH greater than 10 in 1T (85.7% vs 45.4%; P < 0.001).

Conclusions
1. In our study, almost half of the women with gestational HTSC present long-term persistent HT, being more frequent in those with positive anti-TPO and/or TSH higher than 10 in the 1T. It would be advisable to monitor these women, especially when planning subsequent pregnancies.

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EP1012
The interplay between TSH and geriatric syndromes: results from the Moscow centenarians study
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Aim of the study
to assess the interaction between TSH and the most common geriatric syndromes in the cohort of centenarians

Materials and Methods
It was a longitudinal study, including 82 centenarians (95 years and older), who live in Moscow. Complex geriatric assessment and blood tests were performed.

Complex geriatric assessment included past medical history, FRADL-C, MNA, GDS-15 and MOCA scores. We analyzed the interactions between TSH, metabolic parameters, functional status and cognitive functions in centenarians.

In one year after the investigations we contacted patients' relatives or social workers to find out about patients' status. The statistical analysis was performed using IBM SPSS Statistics Version 26. Statistically significant were differences with p < 0.05.

Results
Mean age of the patients was 98.3 (± 1.9) years, while 87.8% of the cohort were women. Analyzing functional status we found out that 34.4% of the patients were frail, and the number of prefrail patients was 56.2%. Cognitive impairments of different severity were presented in 84.4% of the patients. In 59% of the patients HbA1c was below 6%, 33% had concentrations between 6 and 6.4% and only in 8% we found HbA1c higher than 6.5%. The median level of TSH was 2.26 mIU/L [1.8;3.6] with a tendency to higher normal concentrations. TSH was negatively correlated with C-reactive protein (r = -0.4, P < 0.05) and positively correlated with albumin levels (r = 0.26, P = 0.038). The interaction between the TSH and chronic pain severity measured by VAS was negative (r = -0.03, P = 0.021).

Conclusions
The interaction between TSH and geriatric syndromes should be further studied since it could be of great importance for the clinical practice.

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EP1013
A possible complication of hypothyroidism: ischemic colitis
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Background
Ischemic colitis (IC) is a disorder characterized by a decrease in blood flow of the large intestine. Many factors can contribute to decreased blood flow in the arteries supplying the large intestine, such as nonocclusive causes like hypertension and atherosclerosis and occlusive causes like embolism from myocardial infarction. With Ischemic colitis’s high mortality rate and its association with many cardiovascular diseases, it’s important to understand comorbidities that might lead to these events. Thyroid hormone is a hormone that affects not only metabolism and energy expenditure, but also cardiac function. Thus, thyroid dysfunction might play a role in the development of ischemic colitis. This study aims to find and assess comorbidities like thyroid dysfunction associated with admission for ischemic colitis.

Methods
We conducted a cross-sectional study of adults with IC listed as the primary ED diagnosis from 2005 to 2014 using the Nationwide Readmission Database (NRD). The characteristics of the IC-related ED visits were analyzed.

Results
The estimated number of ED visits with a primary diagnosis of IC from 2005-2014 was 541,267 people. Our results showed that the mean age of the cohort was 62.6 ± 14 years, suggesting that most patients affected with ischemic colitis are elderly. 88,497 out of 541,267 ischemic colitis patients were found to have hypothyroidism, amounting to 16.35% of the ischemic colitis population.

Conclusions
The results suggest that hypothyroidism and ischemic colitis may be associated, perhaps through thyroid hormone’s effect on cardiovascular homeostasis. Thyroid hormone has a major role in cardiac contraction, angiogenesis, vascular function, structure, as well as mitochondrial function. Dysfunction of the thyroid hormone pathway can lead to cardiac impairment, hypertension, and heart failure. All these events may lead to decreased blood flow in the vasculature, hyperperfusion to the organs, and subsequently ischemic colitis.

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EP1015
What is the ideal approach for thyroidectomy in a given patient? Proposal of an algorithm
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Introduction
Thyroidectomy can be performed by open or wide array of endoscopic techniques. Lack of uniform consensus on specific indications for each technique leads to confusion on ideal thyroidectomy technique. In this context, we aimed to select an algorithm on ideal technique for a given patient.

Material and methods
This is a retrospective study conducted at a tertiary care endocrine surgery department in South India over a period of 10 years from July 2009 to June 2019. Data on our thyroidectomy techniques was analysed with the specific emphasis on choice of technique based on disease related, non disease related and patient choice factors. We categorized all the clinico-investigative, logistic and patient factors influencing the choice of thyroidectomy technique in to four types A, B, C and D. Type A included disease related factors; Type B included logistics related factors; Type C factors based on comorbidities; Type D based on patient and their family. Finally, an algorithm to select an ideal technique of thyroidectomy for a given patient was developed based on the results.

Results
Open thyroidectomy was performed in 1794/2075 (86.5 %) cases. Endoscopic thyroidectomy was employed in 281 subjects. Type A to C factors, bifurcated the choice of technique to OT and ET without the need for Type D factors. Type D factors primarily dictated the choice amongst the available ET techniques. Further, DI, II and VII factors converted some of the ET feasible subjects to OT. DIII, IV, V, VI factors dictated the choice of a particular ET technique.

Conclusions
1) The ideal technique of thyroidectomy for a given patient depended on logistics, expertise and patient choice rather than disease (goiter) related factors and 2) Our proposal of an algorithm on ideal technique of thyroidectomy technique was developed based on the results.

Key words: Thyroidectomy; Endoscopy; Algorithm; Surgery; Technique

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EP1016
Opportunistic thyroid function screening in older medical patients in Ireland
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Introduction
Thyroid dysfunction is one of the commonest endocrine disorders with hypothyroidism being the most common thyroid dysfunction in the elderly population. An elderly patient with thyroid dysfunction can be asymptomatic, or present with non-specific symptoms, making biochemical testing of thyroid function useful and essential. We reviewed the screening rate and prevalence of thyroid dysfunction in older medical patients admitted to an Irish secondary hospital.

Methods
A retrospective cross-sectional analysis was conducted on all hospitalized general medical patients over 70 years of age discharged during October 2020. This was identified using the Integrated Patient Management system. Chart review was carried out to identify those with a known diagnosis of thyroid disorders. Thyroid function test (TFTs) screened during admission and/or within the prior six months were included in the analysis. Data was inputted to a Microsoft excel spreadsheet and analysed. The thyroid stimulating hormone (TSH) level is measured using the Roche assay and its reference range is between 0.27 - 4.2 mIU/l.

Results
202 patients were included in this study with a median age of 80 years (SD 6.3). 51% (n = 102) were male. 85% of the entire cohort (n = 171) had TFTs performed. 21% (n = 42) had a known thyroid disorder. TFTs were performed in 95% of those (40/42). 33% (13/40) had abnormal TFTs requiring a medication adjustment. Of those with no known thyroid disorder, 82% (131/160) had TFTs performed. 11% (n = 14) had abnormal results. 8% (n = 10) had high TSH levels. One had overt hypothyroidism and the remaining had subclinical hypothyroidism, providing a prevalence of 0.8% and 6.9% respectively. The mean age of the patients with subclinical hypothyroidism was 79.9 years (SD 8.1). 3.1% (4/14) had subclinical hyperthyroidism, providing a prevalence of 3.1% with mean age of 83.5 years (SD 3.7).

Discussion
We observed a high prevalence of abnormal TFTs in those with known thyroid disorders, leading to medication adjustment. Screening those with unknown thyroid disease also yielded abnormal results in 11%. Subclinical hypothyroidism was the most prevalent thyroid disorder among the elderly population in our study. These findings indicate that routine, opportunistic testing of TFTs in medical patients over 70 is beneficial, with medication adjustment required in 33% of those with known thyroid disorder, and 11% of the remainder having abnormal TFTs.

References

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EP1017
Prevalence of thyroid disease among women receiving antenatal care at a tertiary care centre in Sri Lanka
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Introduction
Sri Lanka is endemic for goiters and recent studies show a high prevalence of thyroid dysfunction among the population. However, data on thyroid dysfunction among the general population and pregnant women in Sri Lanka is limited. Thyroid dysfunction is associated with adverse pregnancy outcomes. Furthermore, pregnancy related physiological changes increase the risk of thyroid dysfunction. However, women in Sri Lanka are not routinely screened during pregnancy for thyroid dysfunction.

Methods
A descriptive cross sectional study was conducted among 872 women who received antenatal care and underwent universal first trimester or early second trimester thyroid status screening at a tertiary care centre in Sri Lanka over a period of one year. Pregnancy records were analysed to extract data on past medical history, thyroid status, and pregnancy outcomes.

Results
872 women underwent screening with TSH at the booking visit. Pregnancy specific reference ranges were used (0.1-2.5 mIU/ml for first trimester and 0.2-0.3 mIU/ml for second trimester). Among them, 91.4% (n = 797) were euthyroid. Two women had been diagnosed with Graves disease prior to pregnancy and were on treatment with oral antithyroid medications. Remaining 8.6% (n = 73) of the population were found to be hypothyroid. Among women with hypothyroidism, 21.9% (n = 16) had been diagnosed prior to pregnancy while remaining 80.1% (n = 57) were newly diagnosed during antenatal screening. Prevalence of subclinical hypothyroidism among the population was 5.4% (n = 47) and prevalence of overt hypothyroidism was 3% (n = 26). 57.5% (n = 42) of women with hypothyroidism were positive for TPO antibodies. One woman had undergone thyroidectomy due to papillary thyroid carcinoma while 2 women who had undergone thyroidectomy for goiters prior to pregnancy. Prevalence of goiters among the population was 6% (n = 52). Women with overt hypothyroidism had a higher risk of foetal growth restriction (P = 0.04), and neonatal intensive care admission (P = 0.02). There were no statistically significant differences between pregnancy outcomes of women with euthyroid status and subclinical hypothyroidism.

Conclusion
Thyroid disease has a high prevalence among the study population which was comparable to findings of previous studies. Overt hypothyroidism was associated with adverse pregnancy outcomes. Further studies are required to assess thyroid status among Sri Lankan women, implications of thyroid status on pregnancy outcomes, plan strategies for screening, and interventions.

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EP1018
Carbamazepine-induced hepatocellular injury in patient with Graves’ disease - avoid rechallenging
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Endocrine Abstracts (2022) Vol 81
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Grave’s disease is an auto-immune disorder which responds well to medication and up to half of the patients who take anti-thyroid drugs go into remission. We present a case of Grave’s disease, who developed acute hepatitis associated with Carbimazole and, re-challenged with Carbimazole when she presented with in fast atrial fibrillation (AF) with relapse of hepatitis. A 75 year-old lady admitted with palpitation and chest tightness. She had a background of paroxysmal AF. She was found to be in AF with fast ventricular response and blood tests done during her admission showed abnormal thyroid function tests (TFT) consistent with hyperthyroidism: TSH <0.01 mU/l (0.3-5.0), FT4: 33.5 pmol/l (7.9-16.0), FT3: 11.7 pmol/l (3.8-6.0), TSH receptor antibody 5.5 IU/l (0- 0.9). Patient was started on Carbimazole 20 mg once a day and planned for follow up as outpatient with the endocrine team within 2 months. Few weeks after discharge, she presented with chest tightness and blood tests revealed deranged liver function tests (LFT); total bilirubin 29 umol/l (20-21), ALT 295 U/l (<35) and ALP 458 U/l (30-130). Carbimazole was discontinued. She has had a normal liver ultrasound as well as normal autoimmune and viral hepatitis screen. Her LFT improved after stopping Carbimazole. She was followed up by the endocrine team post-discharge and definitive treatment in the form of total thyroidectomy was planned. Patient was re-admitted three weeks post outpatient follow up due to palpitations and fast AF. Patient refused to try Propylthiouracil and hence she was restarted on low dose of carbimazole with strict weekly LFT follow up until thyroidectomy could be arranged. However, while trialed on Carbimazole, LFTs started getting deranged (ALT raised to 64 U/l from 29 U/l) and Carbimazole was again discontinued. Two weeks following discontinuation of Carbimazole LFT returned to normal: total bilirubin 8 umol/l, ALT 24 U/l and ALP 125 U/l. Patient’s condition discussed with surgical team and her total thyroidectomy appointment was expedited. She was started on Lugol’s iodine 10 days prior to surgery with normalization of TFT. Patient underwent total thyroidectomy which was uneventful. Hepatotoxicity is rare but serious side effect of thyrostatic medications. The drug should be withdrawn immediately and alternative therapy for thyrotoxicosis should be considered. This case strongly supports the need to avoid antithyroid drugs (ATD) rechallenge in patients who develop significant medications. The drug should be withdrawn immediately and alternative therapy should be considered. DOI: 10.1530/endoabs.81.EP1019

**EP1019**

The hobnail variant of papillary thyroid carcinoma: clinical/molecular characteristics of a large monocentric series and comparison with conventional histotypes

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**Background**

Hobnail variant of papillary thyroid carcinoma (HPTC) has been recently identified. Given the rarity of the variant its characteristics have been studied only in little series, limiting the quality of the data available for its better management. The aims of our retrospective study were 1) to define the clinical and molecular characteristics of a series of HPTC in a monocentric and relatively large series; 2) to define the clinical and molecular characteristics able to influence its outcome and 3) to compare them with a series of conventional PTC.

**Material and methods**

The clinical and molecular (BRAF, TERT promoter, TP53) characteristics of 74 HPTC were compared with a series of 143 conventional PTC. All patients had a total thyrotoxicity and radio-iodine (RAI). The median follow-up was 27 months.

**Results**

HPTC had: median age at diagnosis of 49.2 years, median size of 20.3mm, a T3/T4 in 42%, lymph-node involvement in 58% (38% N1a and 20% N1b), metastatic in 5%, multifocal in 45%, extra-thyroidal invasive in 63%, angio-invasive in 97%. 15.5% had further treatments (after thyroid surgery and RAI), external radiotherapy (RT) was administered in 7%. HPTC were mutated in BRAF, TERT promoter and TP53 in 56%, 9% and 20% of cases, respectively. At the end of the follow-up, 16% had a biochemical/structural persistence or a HPTC-related death. The outcome was influenced by TNM, stage, TERT-promoter mutation, lymph node ratio (LNR), but the latter was the only independent outcome determinant (odds ratio, OR=2.03). A Hobnail morphology < or ≥ 30% was not able to influence the outcome, as well as the other variants considered. Compared to classical PTC, HPTC has a lower female predominance (65% vs 78%, P<0.01), larger median size (20.5mm vs 13.00mm, P<0.0001), more frequent lymph-node and metastatic involvement and higher stage at diagnosis (all P<0.01); higher LNR (P=0.002), more frequent further treatments (P=0.04), more frequent RTE (P=0.001) and a worse outcome (being persistence/PTC-related death:16% vs 4.9%, P<0.01). There was no difference in the frequency of BRAF (56% vs 62%) and TERT promoter mutations (9% vs 5%), while there was a higher frequency of TP53 mutations in HPTC (20% vs 1%, P<0.01).

**Conclusions**

The clinical characteristics of HPTC suggest a more aggressive treatment, a poor RAI and stricter follow-up than in conventional PTC. The LNR revealed the more powerful association with a worse outcome in HPTC. The major limit of our study is the follow-up duration available until now.

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**EP1020**

Male was not a prognostic risk factor in postoperative DTC patients treated with 131I treatment: a propensity score-matching study

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Objective

Propensity score matching (PSM) was used to study whether male patients with differentiated thyroid cancer (DTC) were the risk factors for prognosis after 131I treatment.

**Methods**

1677 patients with DTC who underwent total thyroidectomy and received 131I treatment were divided into male group (n= 546) and female group (n= 1131). The PSM method was adopted to process all the data to reduce the influence of data bias and confounding variables. Independent sample T test and Mann-Whitney U test were used for all continuous variables, χ2 test was used for all classified variables. Univariate and multivariate logistic regression were used to analyze the risk factors affecting prognosis, and a receiver operating characteristic (ROC) curve was used to analyze the relationship between sTg level and poor prognosis.

**Results**

Before PSM, the proportion of male patients with poor prognosis was significantly higher than that of female patients (21.2%(116/546) vs 14.0%(158/1131), χ2 = 17.53, P = 0.001). After PSM, there was no difference in the proportion of poor prognosis between male and female patients (19.5%(107/557) vs 16.5%(84/537), χ2 = 5.43, P = 0.143). Multivariate logistic regression analysis showed that male (odds radio (OR) = 1.439 (95%CI: 1.016-2.038), P = 0.040), high T stage (T3, T4 stage)OR=1.816 (95%CI: 1.273-2.590), P=0.001), N1b stage (OR = 1.766 (95% CI: 1.233–2.530), P = 0.002), M1 stage (OR = 9.835 (95% CI: 3.190–30.309), P = 0.001) and sTg level (OR = 1.035 (95%CI: 1.029–1.042), P =0.001) were risk factors for poor prognosis before PSM, while high T stage (T3, T4 stage) OR=1.870 (95%CI: 1.212-2.886), P =0.005, M1 stage (OR = 8.993 (95% CI: 2.434–33.225), P = 0.001), high sTg level (OR = 1.040 (95% CI: 1.030–1.049), P<0.001) were still risk factors, and male (OR = 1.383 (95%CI: 0.912–2.096), P = 0.127) were no longer risk factors for poor prognosis after PSM. ROC curve analysis showed that the cut-off value of sTg was 10.25 g/l, with the sensitivity of 81.0% (222/274) and the specificity of 84.2%(1173/1393).

**Conclusions**

After reduction of selection bias by PSM, males are no longer a risk factor for prognosis after 131I treatment of DTC. In addition, high T stage (T3, T4 stage), M1 stage and sTg ≥ 10.25 µg/l were risk factors for poor prognosis.

**Key words**

Differentiated thyroid cancer; 131I treatment; Propensity Score-Matching; Gender; Risk factors; Prognosis

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Clinical experience with tyrosine kinase inhibitors in radioiodine-refractory differentiated thyroid cancer
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Introduction
Differentiated thyroid cancer (DTC) represents 85–90% of all thyroid cancer cases. Most of these have an excellent prognosis with standard treatment. However, between 7 and 23% will develop distant metastases and, of these, more than 65% will become radioiodine-refractory. In some of these patients who are considered to be radioiodine-refractory with poor prognosis, or in patients who are not candidates for other therapies, the use of systemic therapies, such as Tyrosine kinase inhibitors (TKIs), should be considered since they have demonstrated an extension of progression-free survival.

Materials and Methods
Retrospective observational study. Data of 23 patients diagnosed with DTC who received treatment with TKIs between June 2010 and October 2019 were analyzed. Clinical response according to RECIST criteria of response to treatment, toxicities and tolerability of these therapies were evaluated at 3, 6, 12 and 18 months.

Results
There were 23 patients (11 men and 12 women). The overall mean age at diagnosis was 59.17 ± 14.59 years. 12 patients had a diagnosis of papillary thyroid cancer, 4 of follicular thyroid cancer and 7 of Hurthle cell cancer, being 70% of them stage IV. The mean time from cancer diagnosis to initiation TKIs therapy was 7.6 ± 8.7 years. Regarding the therapy: 19 were treated with Sorafenib, 3 with Lenvatinib and just 1 with Axitinib. Twelve months after the beginning of the treatment 19 patients were still undergoing TKI therapy: 12 (52.5%) had a stable disease (SD), 1 (4.3%) partial response (PR) and 6 (26.1%) progressive disease (PD). The remaining 4 patients had to withdraw: 1 due to toxicity and 3 due to death as a result of progression of the disease. A group of 15 patients completed 18 months of treatment (6 of them required a shift to second-line treatment with Lenvatinib or Axitinib) 10 had SD, 3 PR and 2 PD. A total of 7 patients (30.4%) died during this time. Adverse events occurred in 100% of the patients, being generally low grade (grade 1 or 2) requiring dose reductions or temporary withdrawals. There was only one definitive withdrawal due to toxicity (with Axitinib).

Conclusions
• Eighteen months after the beginning of the treatment 56.5% of the patients remained without disease progression thanks to treatment with TKIs. Despite their frequent side effects, TKIs are generally well tolerated.

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Management and prognosis of anaplastic thyroid cancer
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Introduction
Anaplastic thyroid carcinoma (ATC) is rare. This highly aggressive malignant tumor accounts for 2–3% of all thyroid gland neoplasms. ATC continues to be one of the deadliest diseases worldwide and carries a very poor prognosis. The aim of this study was to describe the treatment modalities of ATC and its prognostic features.

Methods
A retrospective study of patients with ATC treated in our department between 2004 and 2021.

Results
Nine patients were included: 4 men and 5 women. The median age was 65 years [44 years – 90 years]. All patients presented with an anterior neck mass lasting for a median duration of 2.5 months [0.5 – 9] with a recent rapid increase in size. Weight loss and compressive symptoms were reported in all cases. Physical examination showed a hard anterior neck mass in all cases, with a median size of 7.8 cm [3 – 13]. Lateral neck lymph nodes were reported in 3 cases. Vocal fold paralysis was found in 4 patients. CT scan, performed in 8 cases, revealed a thyroid lesion pushing the trachea, the esophagus internal jugular vein, and carotid in 7 cases. Fine needle aspiration was performed in 3 patients and revealed a poorly differentiated thyroid carcinoma. Six patients underwent a total thyroidectomy. Central neck dissection was performed in 3 patients and lateral neck dissection in one patient. The diagnosis was made after thyroid biopsy in 2 patients and lymph node biopsy in 1 patient. The tumor invaded the trachea (n = 7), thyroid cartilage (n = 1), cricoid cartilage (n = 1) esophagus (n = 1), recurrent laryngeal nerve (n = 3), internal jugular vein (n = 1). Three patients had pulmonary metastasis. Two patients had postoperative radiotherapy. Two patients had postoperative radio-chemotherapy. Recurrence was noted in these 4 cases. Palliative radio-chemotherapy was indicated in 1 case. The median survival duration was 4 months [2 days – 13 months].

Conclusion
Anaplastic thyroid carcinoma is a devastating thyroid cancer with the poorest prognosis. As in our study, with conventional treatment including surgery, bourseness, dysphagia and vocal cord paralysis. She underwent debulking thyroid surgery in November 2021 revealing a right lobe 4/3 cm mass with histological features of anaplastic carcinoma and extensive infiltration of the surrounding soft tissues and muscles, esophagus, carotic artery, jugular vein, laryngeal nerve. Palliative radiotherapy was initiated together with adjuvant chemotherapy but the residual tumor showed progressive enlargement and lead to life-threatening complications.

Case 1
A 57-year-old man in whom on routine US examination in 2017 a solid hypoechoic nodule 3.6/3.3/4.5 cm with increased intranodular blood flow causing tracheal deviation and local compression was seen. The patient was referred to surgery which was not performed until April 2019 when he presented with significant enlargement of the thyroid mass. After total thyroidectomy the histological result was consistent with anaplastic carcinoma 9.8/7 cm in size with capsular and soft tissue infiltration. However, the patient refused any further treatment. On the last follow-up visit 32 months following the diagnosis the patient was euthyroid on replacement therapy with no clinically evident local recurrence or distant metastases.

Discussion and conclusion
Anaplastic thyroid carcinoma is poorly responsive to current treatment modalities with a 4-month median overall survival from the time of diagnosis. Recent study demonstrated significant improvement in survival over the last 2 decades presumably due the introduction of molecular-based personalized therapies. Among the most significant prognostic factors are considered age, size of the tumor, presence of extrathyroid invasion and distant metastases along with several new factors such as white blood cell and platelet count at presentation. The two stage IV B patients described presented with similar histological findings but completely different course of the disease. Further studies on the molecular characteristics of anaplastic cancers will probably provide valuable data on the individual risk of recurrence and progression and contribute to the improvement of the long-term prognosis.

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Patterns of biological behavior of anaplastic thyroid cancer - case reports
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Introduction
Anaplastic carcinoma of the thyroid (ATC) is the rarest and most aggressive thyroid gland cancer accounting for less than 5% of all thyroid gland neoplasms. There is inconclusive evidence that ATC represents a terminal dedifferentiation of preexisting well-differentiated thyroid carcinoma or it may originate as already aggressive nondifferentiated cancer without any prior thyroid neoplasm.

Case description
Case 1
A 74-year-old woman with history of long-standing nodular goiter presented with rapidly growing, painful neck mass with compressive symptoms including dysphagia and vocal cord paralysis. She underwent debulking thyroid surgery in November 2021 revealing a right lobe 4/3 cm mass with histological features of anaplastic carcinoma and extensive infiltration of the surrounding soft tissues and muscles, esophagus, carotic artery, jugular vein, laryngeal nerve. Palliative radiotherapy was initiated together with adjuvant chemotherapy but the residual tumor showed progressive enlargement and lead to life-threatening complications.
EP1024

**TSHR promoter methylation level changes as a prognostic blood-based biomarker in follicular thyroid carcinoma**

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Introduction

Papillary thyroid carcinoma (PTC) is the most common type of differentiated thyroid cancer, accounting for about 80% of all cases of thyroid cancer. Generally, PTC is an indolent disease and shows a good prognosis in most patients. However, up to 30% of patients have local tumor renewal or systemic spread. It is crucial to identify patients with a high risk of disease progression. DNA methylation biomarkers may provide clinically valuable information and improve the early non-invasive prognosis of PTC.

Aim of the study

To evaluate DNA methylation level changes of selected genes in peripheral blood plasma samples in PTC patients before and 4-6 weeks after surgery.

Methods

The study included 68 patients with a histologically confirmed diagnosis of PTC with different histological variants: classical (n = 22), diffuse sclerosing (n = 17), follicular (n = 18), and tall cell carcinoma (n = 4). Peripheral blood samples were collected before surgery and 4-6 weeks after surgery during 2020 – 2021 in Hospital of Lithuanian University of Health Sciences, Kaunas clinics. DNA methylation level changes of TSHR gene were analysed by quantitative methylation-sensitive polymerase chain reaction. DNA methylation levels of TSHR were compared before and one month after the surgery using both paired and non-paired non-parametrical tests.

Results

Significantly lower TSHR promoter methylation levels were found 4-6 weeks after surgery compared to samples collected before surgery ($P$ = 0.034) in follicular variant of PTC. Paired sample analysis showed a statistically higher TSHR methylation level before surgery compared to TSHR methylation level after surgery in follicular variant PTC ($P$ = 0.002).

Conclusion

TSHR promoter methylation level changes may be a promising biomarker in predicting PTC prognosis.

Funding

This study was supported by the Lithuanian Research Council (Grant No. S-SEN-20-14 “The role of epigenetic markers for early detection of papillary thyroid carcinoma and prognostic significance in long-term outcome in elderly patients”).

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EP1025

**Routine molecular testing of fine needle aspiration biopsies of thyroid nodules.**

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Objectives

Fine needle aspiration biopsy (FNAB) together with ultrasonography is a necessary tool for diagnosis and follow up of thyroid nodules. Molecular testing is increasingly used mainly for indeterminate categories of the Bethesda System for Reporting Thyroid Cytopathology revised in 2017. Our aim was to introduce a routine molecular analysis of the main genetic causes of thyroid cancer.

Methods

Since 2017 we have analyzed 1171 samples of patients with thyroid nodules. We gradually established testing procedure mainly in samples evaluated as Bethesda categories III and above. First, we analyze DNA for the most common mutation V600E in the BRAF gene using allele specific Real Time PCR (LC480, Roche). BRAF-positive samples are screened for RET/PTC mutations using direct sequencing (CEQ 8000, Beckman Coulter). BRAF-negative samples are analyzed by next generation sequencing using the Thyro-ID panel (MiSeq, Illumina) examining other 12 genes. The samples negative in the NGS panel are subjected to detection of 23 fusion genes including ALK, BRAF, GLIS, NTRK1, NTRK3, PPAR, RET genes using Real Time PCR. In samples suspected of MTC, we search for RET mutations.

Results

In total, BRAF mutation was detected in 146 patients, Ras mutations in 72 patients, RET mutations in 4 patients, TERT mutations in 20 patients and fusion genes in 43 patients. In 21 patients we detected genetic variants in the other genes (TP53, PTEN, PIK3CA, KIT, TSHR). From our cohort, in 390 patients post-surgical histopathological evaluation has been known. Positive predictive values of RET, BRAF, TERT, KRAS, HRAS, NRAS mutations and fusion genes were 100%, 98.4%, 93.3%, 75%, 60%, 42.1% and 97.6% respectively, if borderline tumors were not included in malignancy. In the BRAF-positive cohort was a case of follicular adenoma with BRAF V600E mutation and in the TERT-positive cohort one case of follicular tumor of uncertain malignant potential with TERT and NRAS mutation.

Conclusions

We established molecular testing of thyroid nodules that significantly contributed to clinical management of patients in the Czech Republic. BRAF, RET and TERT mutations and RET/PTC and ETV6/NTRK3 fusion genes are associated with almost 100% risk of malignancy or even worse prognosis, therefore according to ETA guidelines from 2017 and recent publications their carriers are recommended for the total thyroidectomy. The risk of malignancy of RAS mutations is lower and rather a lobectomy is recommended. Supported by AZV NU21-01-00448 and MH CR RVO 00023761.

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EP1026

**Detection of rare variants in BRAF gene in thyroid nodules.**

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Objectives

Papillary thyroid carcinoma (PTC) is the most frequent malignant endocrine disease and the most common genetic cause of the PTC is the substitution c.1797T>A (p.V600E) in the BRAF gene (35-70% of PTC) that represents more than 95% of BRAF mutations. Other rare mutations in the BRAF gene include other substitutions (e.g. p.K601E), small deletions or insertions close to codon 600. The aim was to analyze a large cohort of thyroid nodules for rare genetic variants in the BRAF gene.

Methods

A total of 1106 fresh frozen thyroid tissues collected from 2003 to 2021 were screened for exon 15 BRAF alterations. The cohort consisted of 851 papillary thyroid carcinomas (PTC), 33 borderline tumors, 28 oncocyic and follicular carcinomas (FTC), 6 poorly differentiated carcinomas (PDTC), 15 anaplastic
carcinomas (ATC), 15 follicular adenomas (FTA) and 122 benign tissues. The BRAF gene was analyzed by next generation sequencing using the Nextera XT Sequencing Kit (Illumina) or Thryo-ID (4 bases). The VarSome software was used to interpret detected variants.

Results

The most common BRAF mutation p. V600E was detected in a total of 430 thyroid tissues - in 425 PTC, two borderline tumors (NIFTP and WDT-UMP), one PTC and two ATC. The BRAF p.V600E was detected in 51.3% of PTC. The rare somatic BRAF alterations were detected in 11 from 851 patients of PTC (1.29%), in one benign thyroid tissue and one FTC. We detected eight various variants - the most common was p.K601E and V600E, p.V600_E605del, p.Q609E, p.K601del, p.V600K, p.V600E, p.V600E, p.Q609E, p.Q609E, p.Q609E, and p.R605del in one case only.

Conclusions

The rare BRAF variants represented 2.9% of BRAF-positive thyroid nodules. Except for p.K601E, other rare variants were found exclusively in PTC. However, BRAF fusion genes, that seem to be other genetic causes of PTC, were not analyzed in this study. Supported by AZV NU21-01-00448 and MH CR RVO 0023761.

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EP1028

Sub acute thyroiditis following COVID infection or vaccine: case reports

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Introduction

The novel severe-acute-respiratory-syndrome-coronavirus-2 virus has led to the ongoing Coronavirus disease 2019 (COVID-19) disease pandemic. There are increasing reports of extra pulmonary clinical features of COVID-19, either as initial presentations or sequelae of disease (gastrointestinal, hepatobiliary, pancreatic, cardiovascular, ocular, and neurologic) Autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome) can be seen as a post-vaccination phenomenon that occurs after exposure to adjuvants in vaccines. We report cases of subacute thyroiditis following COVID infection or vaccine.

Clinical cases

1-A 47 years old female developed subclinical hypothyroidism 3 weeks after COVID 19 infection TSH was 10.1 Ul/ml (0.4-4), FT4 was 0.94 ng/dl (0.7-1.9). Ant microsomal abs: 945IU/ml (0-9), Ant thyroglobulin ab: 285IU/ml (n: <116), Thyroid sonar: diffuse heterogeneity & increased vascularity. 2-A 45 years old female developed subclinical hypothyroidism after exposure to COVID 19 infection by one month with TSH 7.74 Ul/ml, FT4 1.2 ng/dl, Anti Microsomal ab 959 IU/ml, Ant thyroglobulin ab: 257 IU/ml Thyroid sonar: diffuse heterogeneity 3-A 35 years old female who had local pain in the neck 2 weeks after COVID infection. Investigations revealed non-uniform echo texture of the thyroid gland in the thyroid sonar TSH: 3.06 Ul/ml, FT4 1.06 ng/dl. Anti microsomal ab: 53 Ul/ml, Ant thyroglobulin ab: 995.7 IU/ml Post vaccine cases 1-A 59 years old female under treatment for thyrotoxicosis. She went into remission for 3 months with one tab neonormaczo 5 mg 10 days of the first dose of vaccine for COVID 19, the patient developed exacerbation of her thyrotoxicosis with tachycardia, pulse 115, anxiety, insomnia and tremors. Her TSH became 0.009 IU/ml & increase of the dose of levalar & neonormaczo was done. Within 2 months the patient responded in a good way & entered into remission again 2-A 65 years old female who developed hypothyroidism after vaccine TSH: 10.21 Ul/ml, FT4 0.82 ng/dl. Anti microsomal ab 660 IU/ml, Ant thyroglobulin ab: 296 IU/ml 3-A 36 years old female who developed subclinical hyperthyroidism after vaccine Her thyroid sonar was normal sized sonar with heterogeneity TSH: 0.03 IU/ml, FT4 0.93 ng/dl After 3 months her thyroid sonar is completely normal TSH 1.210 IU/ml, FT4 0.84 ng/dl, FT3 2.94 pg/ml (2.3-4.1).

Conclusion

Clinicians must be aware of the possibility of thyroid dysfunction and subacute thyroiditis following COVID-19 infection and after the inactive SARS-CoV-2 vaccine. Early recognition and timely anti-inflammatory therapy can help in successful management of the disease.

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EP1029

Hashimoto’s thyroiditis manifested with rhabdomyolysis and cardiac effusion following SARS-CoV-2 vaccination: A case report

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Background

Autoimmune inflammatory syndrome induced by adjuvants (ASIA syndrome), include the different conditions linked following exposure to an adjuvant. Autoimmune thyroiditis following vaccination as an auto-immune/inflammatory syndrome is rarely reported. In the era of mass vaccination against SARS-CoV2, there is limited information about cases of auto-immune thyroid disease as an ASIA syndrome following SARS-CoV-2 vaccination.

Introduction

A 36 years old female who developed subclinical hyperthyroidism after vaccination phenomenon that occurs after exposure to adjuvants in vaccines. She went into remission for 3 months with one tab neonormaczo 5 mg 10 days of the first dose of vaccine for COVID 19, the patient developed exacerbation of her thyrotoxicosis with tachycardia, pulse 115, anxiety, insomnia and tremors. Her TSH became 0.009 IU/ml & increase of the dose of levalar & neonormaczo was done. Within 2 months the patient responded in a good way & entered into remission again 2-A 65 years old female who developed hypothyroidism after vaccine TSH: 10.21 Ul/ml, FT4 0.82 ng/dl. Anti microsomal ab 660 IU/ml, Ant thyroglobulin ab: 296 IU/ml 3-A 36 years old female who developed subclinical hyperthyroidism after vaccine Her thyroid sonar was normal sized sonar with heterogeneity TSH: 0.03 IU/ml, FT4 0.93 ng/dl After 3 months her thyroid sonar is completely normal TSH 1.210 IU/ml, FT4 0.84 ng/dl, FT3 2.94 pg/ml (2.3-4.1).

Conclusion

Clinicians must be aware of the possibility of thyroid dysfunction and subacute thyroiditis following COVID-19 infection and after the inactive SARS-CoV-2 vaccine. Early recognition and timely anti-inflammatory therapy can help in successful management of the disease.

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Case
A 19-years-old man, with no medical history was presented five days after second vaccination doses against SARS-CoV-2 with unusual clinical symptoms of hyperthyroidism as acute rhabdomyolysis with a pericardial effusion, and a very high level of thyroid stimulating hormone, decreased free thyroxin and higher level of peroxidase and thyroglobulin thyroid autoantibody. One week after L-thyroxin treatment CK was normal and kidney function was normalized with a remarkable improvement of thyroid functions.

Conclusion
Rhabdomyolysis and pericardial effusion can occur as severe symptoms of Hashimoto thyroiditis as an ASIA syndrome after vaccination against SARS-CoV-2.

Key words: ASIA syndrome - SARS-CoV-2 vaccine - Hashimoto’s thyroiditis - Acute rhabdomyolysis - pericardial effusion.

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Hand and foot skin changes resembling PTU-induced vasculitis in a young male with diffuse toxic goiter- a case report
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Propylthiouracil (PTU) sometimes induces autoimmune syndromes, such as PTU-induced lupus or vasculitis. Here we present hands and feet vasculitis - skin changes observed several days after PTU introduction in a patient who suffered from serious diffuse toxic goiter. Because of segmental distribution, normal liver function test, and no signs of clinical deterioration, it was decided to continue PTU management and observe the patient. Primarily maculopapular rash became vesicular shortly after and then scaly. After two weeks, skin changes were entirely restored with no scarring. Taking into account thorough epidemiological survey, clinical course, and performed diagnostics, presented skin changes were diagnosed as Hand, Foot, and Mouth disease (HFMD). Clinicians must be aware of the side effects of used drugs, especially after their introduction. Some clinical presentations could only resemble expected or well-known side-effects, intolerance, or hypersensitivity to the used drug. Every clinical presentation associated with any drug introduction must be thoroughly evaluated. The presented case revealed that skin changes of HFMD mimicked PTU-induced vasculitis.

Keywords: Propylthiouracil, autoimmunity, Hand, Foot and Mouth Disease

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Frequency of thyroid ultrasound alterations in polycystic ovary syndrome
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Introduction
Polycystic ovary syndrome (PCOS) is a common endocrine disease in women of childbearing age. This condition combines, according to the diagnostic criteria of the Rotterdam consensus 2003, clinical and/or biochemical signs of hyperandrogeism, oligo- and/or anovulation and polycystic ovaries detected by ultrasound. Thyroid diseases are also frequent in the general population. The aim of our study was to determine the prevalence of thyroid ultrasound alterations in a group of patients with PCOS compared to a control group.

Patients and Methods
31 patients with PCOS and 30 age- and body mass index-matched healthy volunteer women were recruited into the study. Thyroid ultrasound was performed in all participants.

Results
The age and the body mass index were comparable between the two groups (29.8 ± 7 vs 29.5 ± 5.5 years, P = 0.86; 32 ± 6.6 vs 31.1 ± 8.9 kg/m² P = 0.62).

Cervical ultrasound was more frequently pathological in the group of PCOS women (58% vs 33%; P = 0.05). The ultrasound feature of thyroiditis was significantly higher in the PCOS group compared to the control group (39% vs 3%; P = 0.001). The means of thyroid volume were similar in both groups (9.4 ± 5.5 vs 10 ± 7.2, P = 1). The percentages of goiter and thyroid nodules were comparable between the two groups (P = 1, P = 0.7 respectively).

Conclusion
Our study showed an increased prevalence of thyroiditis on cervical ultrasound in PCOS women but it did not show any difference in the occurrence of thyroid nodules or goiter.

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EP1033
Pregnant patient with a history of methimazole-induced agranulocytosis presenting with hyperthyroidism: a case report
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Background
Pregnancy has a profound impact on the thyroid gland and its function. Severe thyrotoxicosis can lead to many complications and endanger the mother or fetus. Antithyroid drug (ATD), at its lowest possible dose, should be given. However, one of the complications of treatment include agranulocytosis which is a rare but serious allergic event with a prevalence of 0.1 to 0.5 percent. Thus, alternative treatment should be prescribed because a cross-reaction between ATDs was observed in 15.2% of patients in a study. Insufficient data is available regarding the use of these medications in pregnant patients with history of drug-induced adverse reactions. There are alternative treatments but are contraindicated in pregnancy.

Case
We report a 29-year-old patient gravida 5 para 4 at 10 weeks age of gestation presenting with palpitations. She is a known case of Graves’ disease for 7 years and maintained on Methimazole. She was admitted a year prior as a case of impending thyroid storm; methimazole-induced agranulocytosis. Initially, maintained on Lithium but shifted back to Methimazole without a physician’s...
advice and later on, discontinued the medication upon knowledge of pregnancy. On her first trimester, noted with palpitations and elevated free thyroxine (T4) at 71.29 pm (normal range: 11-24 pm). She was started on Propylthiouracil 50 mg/tablet 1 tablet thrice a day. On her second trimester, no reported symptoms of hyperthyroidism and/or agranulocytosis such as fever or sore throat. Thyroidectomy was offered but she strongly refused. Free T4 was then maintained at a value slightly above the normal upper limit. Propylthiouracil was shifted to methimazole 5 mg/tablet 1 tablet once daily and revised to 1 tablet every other day on her third trimester. Delivery was uneventful and the newborn was evaluated with unremarkable findings. Four weeks postpartum, no noted symptoms of hyperthyroidism and/or agranulocytosis. Free T4 was within normal at 18.84 pm. Alternative treatment was offered due to the risk of agranulocytosis. Conclusion Hyperthyroidism in pregnancy is associated with a variety of complications for the mother and fetus. Effective treatment options include ATD, thyroidectomy or RAI therapy. But, not all are relatively safe for pregnancy. In initiating ATD, cross-reaction between medications should be considered especially for patients with history of adverse reaction, such as agranulocytosis, which can be life-threatening. However, there are limited studies in the management of this specific case. Treating physician and patient should discuss each of the options, including the benefits and drawbacks.

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EP1034

Place of scintigraphy in case of diagnostic doubt in Graves’ disease

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Graves’ disease is a rare and severe disease that most often affects older children and is predominantly female. The diagnosis is made in the presence of a clinical picture very suggestive of thyroiditis, confirmed by biological and radiological tests. We present the case of an 11-year-old female patient who presented with a moderate presented of basewod with an ultrasound appearance of thyroiditis for which scintigraphy was helpful in the diagnosis. Female patient, 11 years old with no history, has been suffering from moderate weight loss for 2 months without any other signs of thyrotoxicosis. On clinical examination: bilateral exophthalmos, normocadic at 78 pm non palpable thyroid. On clinical examination: bilateral exophthalmos, normocadic at 78 pm non palpable thyroid. On workup: TSH < 0.05 Ml/l; T4L : 20.8 (N:9-19) pmol/l; Cervical echography : aspect of a thyroiditis. diagnosis doubt and therapeutic necessity, a scintigraphy was performed showing a diffuse and homogenous fixation. the patient had been put on carbimazol 20 mg/d. The difference between Graves’ disease and thyroiditis is not always trivial in view of the clinical manifestations during the Hashi toxicosis phase and the ultrasound appearance, the interpretation of which remains operator dependent. In such conditions, the use of anti-thyroid antibodies or scintigraphy can play a decisive role. Indeed, in Graves’ disease the scan image appears diffuse and homogenous unlike in thyroiditis where the image appears white. Thyroid scintigraphy is one of the definitive diagnostic tools, especially when there is clinical and sonographic confusion between the two conditions.

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EP1035

The effect of l-thyroxine replacement on blood pressure and heart rate in children with hypothyroidism: correlation with free thyroxine and thyrotropin levels

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Chronic administration of L thyroxine to children with hypothyroidism may affect cardiovascular dynamics. Aim of the study We measured the BP and heart rate (HR) of 25 randomly selected children with hypothyroidism in relation to their serum free T4, and TSH levels and thyroxine dose mg/kg.

Methods 25 randomly selected children with a mean age 9.6 +/- 4.5 years with the diagnosis of congenital or acquired hypothyroidism. They were on L thyroxine therapy to keep serum FT4 and TSH in the normal range for age. Their blood pressure (BP) and HR (average of three readings), weight, height, dose of thyroxine, and their serum level of TSH and Free T4 levels within two weeks before the clinic visit were recorded. The Z scores of the height (HSDS), BMI (BMI SDS), systolic (SBP SDS) and diastolic blood pressure (DBP SDS) were calculated (as per the 2004 guideline report on hypertension from the National Heart and Lung institute) and HR (as per the Monitoring and Diagnosis Group at Oxford (MADOX) systematic review of 2011) were calculated for age and gender.

Results

TSH levels. One patient had tachycardia (HR = 146/min (z score +3.2 for age)). His FT4 and TSH levels were normal. There was a positive correlation between thyroxine dose/kg and serum level of FT4(r=0.52), heart rate (r=0.56), SBP SDS (r= 0.38), and DBP SDS (r=0.24). There was no significant correlation between the HSDS on the one hand and FT4, TSH or thyroxine dose on the other hand. The BMISDS was negatively correlated with TSH level (r=-0.8).

Conclusion

In this study on hypothyroid children on L thyroxin therapy, 2 had high systolic blood pressure and one had tachycardia. The significant correlation between the thyroxine dose, FT4 level and BP and HR should alert the Pediatrician to monitor BP and HR closely in relation to TSH and FT4 levels these patients.

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EP1036

Diagnosis and management of anaplastic thyroid carcinoma: about 3 cases and review of literature

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Introduction

Anaplastic thyroid carcinoma is an extremely aggressive undifferentiated tumor of follicular cell origin. It is uncommon and comprising approximately 1% of all thyroid cancers. Purpose of the presentation

The objective of this work is to determine the clinical, histological and therapeutic aspects of anaplastic thyroid carcinoma.

Methods

This is a retrospective study about 4 patients treated for an anaplastic thyroid carcinoma, in the ENT department of Fattouma Bourguiba hospital in Monastir over a period of 22 years (2000-2021).

Results

The average age was 68 years. A female predominance was noted. The average consultation time was 2 months. Patients consulted for a rapidly progressive goitre in all cases, associated with dysphagia and dyspnea in 3 cases (75%). Cervical examination showed a painful and indurated anterior cervical swelling with a medium size of 5 cm in all patients. Associated lymph nodes were found in 2 cases (50%). Indirect laryngoscopy showed laryngeal paralysis in 2 patients (50%), one of which was bilateral (25%). Cervical ultrasound and cervico-thoracic scan showed a mass pushing back the trachea in three cases (75%). 3 patients (75%) had an emergency tracheostomy with thyroid biopsy. The other patient underwent a lobo-isthmectomy. Radiotherapy was indicated in all cases.

The evolution was fatal in all patients with a survival of less than 6 months.

Conclusion

Anaplastic thyroid cancer is a very rare case and has a poor prognosis. The important information such as clinical manifestations, physical examination and imaging are necessary to diagnose and administer the proper management.

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EP1037
Hürthle cell tumors of the thyroid gland: diagnostic and therapeutic features
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Introduction
Oncocytic tumors can occur in the thyroid gland and other endocrine tissues, including the parathyroid, pituitary gland, adrenal cortex, pancreas, gut, and lung. Thyroid oncocytic tumors are rare: 3-10% of thyroid epithelial tumors. They are characterized by the presence of oncocytic cells called “Hürthle” cells.

Objective
Describe the clinical, pathological and therapeutic features of oncocytic tumors of the thyroid gland.

Methods
A retrospective study including 35 cases of thyroid oncocytic tumors treated in our department between 1988 and 2021.

Results
The average age of our patients was 48 years. The sex-ratio (F/M) was 10.9. The mean size of the nodules on ultrasonography was 31.3mm. The nodule was unique in 25 cases. The nodules were classified according to the EU-TIRADS classification: EU-TIRADS 2 (12 cases), EU-TIRADS 3 (22 cases), EU-TIRADS 4 (10 cases) and EU-TIRADS 5 (10 cases). A lobectomy was performed in 31 cases, a total thyroidectomy was done in 1 case, and an isthmectomy was done in 3 cases. Among our patients, 33 patients had oncocyic adenoma and 2 patients had oncocytic carcinoma. In case of oncocytic carcinoma, a totalization with central lymph node dissection and radioactive iodine therapy were done. Evolution was favorable in these 2 cases.

Conclusion
In general, oncocytic tumors do not have a specific clinical presentation or distinguished features on ultrasonography. Furthermore, distinguishing hyperplasia from neoplasia, and benign from malignant is difficult on cytology. Anatomopathological examination is often needed to make the diagnosis of these tumors. Compared to other differentiated tumors, oncocytic carcinomas tend to be more aggressive, and have less radioactive iodine intake. Overall survival in 5 years is 50-70%.

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EP1038
Type 1 diabetes mellitus and autoimmune thyroid disorders
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Introduction
Type 1 diabetes mellitus (T1DM) is the result of the autoimmune destruction of beta-cells of the endocrine pancreas, leading to absolute insulin deficiency. The process of this autoimmune destruction occurs in genetically susceptible individuals with positive relevant autoantibodies. T1DM may be associated with other autoimmune diseases (AD) such as autoimmune thyroid disorders (AITD).

Patients and methods
It is a descriptive retrospective study. We collected data from 113 patients diagnosed with AITD associated with another AD over 18 years. The present study reports the association between T1DM and AITD.

Results
T1DM was diagnosed in 41 patients (31.53%) which consisted of 25 women and 16 men. The mean age upon discovery of the T1DM was 30.49 years. The T1DM was associated with an overt hypothyroidism in 18 patients, a subclinical hypothyroidism in 1 patient, an autoimmune thyropathy in euthyroid phase in 7 patients, an overt hyperthyroidism in 14 patients and a subclinical hyperthyroidism in 1 patient. It was affiliated with Hashimoto’s disease in 26 cases (63.4% of cases) and with Graves’ disease in 15 cases (36.6% of cases). The T1DM preceded the diagnosis of the thyroid disorder in 24 cases with a mean period of 69 months between and succeeded the latter in 6 cases within a mean period of 40 months. In 11 cases, both diagnoses were concomitant.

Discussion and Conclusion
T1DM is the most frequent AD associated with AITD. Their prevalence is 2 to 3 times higher in the T1DM population than that of the general population. As a matter of fact, 6.6% out of 10% of healthy adults have positive thyroid antibodies compared to 20% out of 40% of T1DM adults. According to Barker, T1DM is associated with Hashimoto’s disease in 14-28% of cases. In other studies, it is associated with Graves’ disease in 0.5-7% of cases. Several studies demonstrated that AITD was more frequent in diabetic women than men, which could be explained by higher prevalence of AITD in women. Serum TSH assay is recommended upon discovery of diabetes in patients with hypothyroid or hyperthyroid symptoms, then every 1-2 years as follow up. Our results consistent with that of the literature showed the high prevalence of the T1DM in patients with AITD, and thus the necessity of regular screening in these patients.

References

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EP1039
Predictive factors of malignancy in thyroid nodules: value of ultrasonography
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Introduction
Ultrasound has become an indispensable diagnostic modality in the evaluation of the risk of malignancy of a thyroid nodule.

Objective
Identify the predictive factors of malignancy in thyroid nodules on ultrasound.

Methods
This is a retrospective study including 333 patients diagnosed with thyroid nodules and operated between 2010 and 2020. A significance threshold of 0.05 was adopted for the statistical analysis.

Results
The mean age of the patients was 44 years, predominantly females (88.3%). A thyroid cancer was diagnosed in 43 cases. The most common histological types were papillary carcinoma (83%) and vesicular carcinoma (14%). Predictive factors of malignancy were: solitary nodule (P = 0.01), cervical lymph node metastasis (P = 0.017), size > 4 cm (P < 0.001), solid nodule (P < 0.001), hypoechogenic nodule (P = 0.004), central vascularization (P < 0.001), central and peripheral vascularization (P = 0.006), microcalcifications (P < 0.001).

Conclusion
Although the vast majority of thyroid nodules are benign, a small proportion are cancers. Several predictive factors can evaluate the risk of malignancy of a thyroid nodule, however, predictive factors on ultrasonography are still the most important. The EU-TIRADS classification, is the most commonly used classification to stratify this risk of cancer in thyroid nodules. In the EUTIRADS classification, markedly hypoechogenic, non-oval shape, irregular margins and microcalcifications are the only predictive factors included.

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EP1040
Risk factors for central neck lymph node metastasis in patients with macro and micropapillary thyroid carcinoma
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Introduction
The prevalence of lymph node metastasis from micropapillary thyroid carcinoma (mPTC) in different studies is up to 33%. Preoperative diagnosis of central lymph node metastasis is essential for the surgical management of those patients. Prophylactic CLN dissection for patients with mPTC is controversial. Our study aimed to assess the prevalence and the risk factors of LMN metastasis in patients with mPTC.
Methods
We retrospectively study the clinicopathological characteristics of 167 patients with PTC operated at the Second Department of Propaedeutic Surgery, University of Athens. Patients before surgery underwent ultrasound thyroid mapping for lymph node invasion assessment. All underwent total thyroidectomy with prophylactic central neck dissection.

Results
A total of 167 patients (73.1% females) were analyzed. The mean age was 51.08 ± 13.38 years, and the mean follow-up was 5.3 years. In 30.2% (55/161) of the patients, the lesion was located in both thyroid lobes, in 29.1% (53/161) and 20.4% (48/161) in the right and left lobe, respectively. Only 2.7% (5/161) of the patients had lesions located in the isthmus. 33% (60/162) of PTC patients had bilateral lesions, and 41.8% (76/185) had more than one lesion. The median number of lesions was 1.0 ± 3.05. 54.5% (91/167) of the patients had macro-PTC. In 34.8% of them, the lesion was located in both thyroid lobes. 45.7% had multiple lesions. Furthermore, 42.1% had capsule penetration, 39.1% had extrathyroid expansion, and 32.8% had lymph node invasion. 45.5% (76/167) had micro-PTC. In 41.8% of the patients, the lesion was located in both thyroid lobes. 48.1% had multiple lesions. In addition, 47.3% of these patients had capsule penetration, 33.5% had an extrathyroidal expansion, and 30.8% had lymph node invasion.

Conclusion
Our study found an increased risk of lymph node invasion in patients with micro-PTC, compatible with macro-PTC. Thus, an ultrasound thyroid mapping for lymph node invasion assessment before surgery is needed.

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EP1041
Papillary thyroid cancer and its variants - genomic evidence and clinical significance
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Purpose
Papillary thyroid cancer (PTC) accounts for approximately 80% of all thyroid cancers and is defined by its unique cytologic and histologic features. Mutations of the RET and BRAF(V600) genes are found in nearly 70% of PTC cases. They are able to trigger the activation of mitogen-activated protein kinase pathways and to promote neoplastic cell proliferation. Genetic events may further lead to numerous different cell variants of PTC which may be identified via the different cytologic/histopathologic features. The most common are the classical (CV), tall cell (TCV) and follicular variant (FV). The aim of the study was to perform the genomic analysis of the RET and BRAF(V600) mutations in patients with PTC as well as to compare the obtained results with clinical findings.

Methods
The study included 112 patients diagnosed with PTC, aged 41-74 years. Mutations of the RET and BRAF(V600) genes were detected using Real-time polymerase chain reaction. Diagnosis of the PTC and its variants was confirmed with cyto/histopathological examination.

Results
The most important genomic, cyto/histopathological and prognostic elements regarding all three variants of the PTC are as follows: CV-PTC (n = 78): RET and BRAF (V600) mutations are common findings, with BRAF (V600) confirming a worse prognosis. The 65% of these patients have shown stable disease course, with 25% with metastatic nodes; TCV-PTC (n = 8): Aggressive behavior has been attributed to BRAF (V600) mutation; FV-PTC (n = 26): Absence of BRAF (V600) mutation was the most important genetic element.

Conclusions
In most cases, PTC has an excellent prognosis, but certain variants express more aggressive clinical course. CV-PTC: BRAF (V600) mutation was negative prognostic element; TCV-PTC presents mostly in older patients, has greater propensity for locoregional dissemination and has more aggressive course than CV-PTC; The prognosis of FV-PTC has been similar to that of CV-PTC. The patients with CV-PTC and FV-PTC had favorable clinical course comparing to those with TCV-PTC. Our study suggests that PTC is etiopathogenetically complex disease and requires further molecular investigations.

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EP1042
Graves’ disease associated with thyroid papillary carcinoma
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Introduction
Thyroid carcinoma in Graves’ disease is rare (1 to 2%). Papillary carcinoma is the most common histologic type. It is usually discovered incidentally after histologic exam. Our aim is to report a case of Graves’ disease associated with thyroid papillary carcinoma and to describe its therapeutic and prognostic features.

Case report
A 51-year-old woman treated with anti-thyroid drugs and β blockers for Graves’ disease. Cervical ultrasound found an enlarged, hypertrophic thyroid gland with a 10 mm nodule classified EUTIRADS 5. Indication for surgery was: failed medical therapy after 3 years of treatment and concomitant suspicious thyroid nodule. The patient underwent total thyroidectomy. Intraoperative examination suggested a papillary thyroid carcinoma. So, a central neck dissection was performed. Histologic exam confirmed the diagnosis of papillary thyroid carcinoma associated with Graves’ disease. The patient underwent ablative radioiodine therapy. After 7 years of follow-up, she had no recurrence.

Conclusion
Patients with Graves’ disease had a higher risk of developing thyroid cancer than the general population. However, studies reported conflicting results about the prognosis of thyroid cancer concomitant with graves’ disease.

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EP1043
Lymph node metastasis in adults and young adults with thyroid carcinoma: an Algerian observation
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Introduction
Thyroid cancer (TC) in adolescents and adults (AYA) is defined as thyroid cancer diagnosed among those aged between 15-39 years. It is the fifth most common cancer in AYAs, and its incidence is increasing. Compared with older adult patients, the AYA with TC has a higher prevalence of node metastasis which represents a risk factor for recurrence.

Aim
To describe the characteristics of thyroid carcinoma with confirmed nodal metastases at the time of diagnosis in an Algerian cohort of AYA patients. And to compare patient with and without lymph nodes metastases.

Methods
Medical records of patients diagnosed with differentiated thyroid carcinoma and aged 18-40 years at the moment of diagnosis followed in the endocrinology department of The University Hospital of Constantine in Algeria during the period between July 2014 and December 2018 were retrospectively reviewed. Clinical and pathological data were collected. The group with no lymph node metastases (LN0) was compared to the group with lymph node metastases (LN1) and factors associated with LN metastases were evaluated.

Results
101 patients were included, the mean age was 31 (17-40) years and 85.1% were females. Total thyroidectomy was done in 88.1% and lymph node dissection in 23.8% which was central in 13.9% and central and lateral in 9.9%. 90.1% of patients had papillary thyroid carcinoma, 7.9% had follicular carcinoma and 2 patients had Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Following the 8th AJCC classification, 64% were T1, 12.9% T2 and 20.8% were T3. 15.8% had lymph node involvement. Multifocality, bilaterality, vascular thyroid invasion, and capsular thyroid invasion were present in 30.7%, 15.8%, 7.9%, and 17.8%. As for risk stratification according to the ATA system, the initial risk was low, intermediate, and high in 41.6%, 35.6%, and 10.9% of patients, and data were insufficient to state this risk in 11.9% of patients. Thyroid cancer LN1 group had greater tumor size (27.5mm and 17.2mm P = 0.038) and thyroid dysfunction (7.1% and 0% P = 0.048) at the moment of diagnosis than the LN0 group. There was no difference between thyroid cancer with LN1 and LN1concerning, mean age, sex, pathology type and variant, vascular and capsular invasion.

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Conclusions
In this cohort of AYA Algerian patients with thyroid cancer, greater tumor size and thyroid dysfunctions were more important in patients with lymph node metastasis at the moment of diagnosis.

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EP1044
Dyshormonogenic goiter: about three cases
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Introduction
Dyshormonogenic goiter (DG) is considered as a form of thyroid hyperplasia due to enzymatic defects in hormone synthesis. Thearchitectural polymorphism and cellular atypia may mimic thyroid neoplasms and cause difficulties in differential diagnosis.

Results
We report 3 cases of DG occurring in one females and two males who were aged 20, 9, and 7 years old, respectively. All patients presented with clinically evident goiter. Hypothyroidism was documented before the histological diagnosis was made in all patients. The thyroid gland was enlarged and multinodular in all cases. Cervical ultrasound and thyroid scintigraphy were performed for all patients. The ultrasound showed a multinodular goiter in all patients. The scintigraphy showed a global hyperfixation of the thyroid for two patients with a right hypofixing zone for one patient. All patients underwent surgical treatment. A total thyroidectomy for two patients and a right lobectomy for one patient. The anatomicopathological examination confirmed a DG in all cases. The evolution was favorable for all patients and without recurrence.

Conclusion
DG is a rare entity, representing one of the causes of congenital hypothyroidism. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis that explains the delima of establishing surgical indications.

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EP1045
Metachronous renal cell carcinoma metastasis to the thyroid
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Introduction
Metastatic disease into the thyroid is a rare event, despite the gland’s rich vascular supply. Renal cell carcinoma (RCC) is an unusual neoplasm that not only has the potential to recur after a latent disease-free interval, but also has the potential to metastasize to rare sites like the thyroid. However, of the clinically significant secondary neoplasms of the thyroid, metastatic RCC is the culprit in most cases.

Case report
We present the case of a patient with metachronous RCC metastasis to the thyroid. A 62-year-old male with a 2-year history of non-toxic multinodular goiter was admitted to our Endocrinology Department. He had a history of multiple thyroid gland. Hypothyroidism was documented before the histological diagnosis was made in all patients. The thyroid gland was enlarged and multinodular in all cases. Cervical ultrasound and thyroid scintigraphy were performed for all patients. The ultrasound showed a multinodular goiter in all patients. The scintigraphy showed a global hyperfixation of the thyroid for two patients with a right hypofixing zone for one patient. All patients underwent surgical treatment. A total thyroidectomy for two patients and a right lobectomy for one patient. The anatomicopathological examination confirmed a DG in all cases. The evolution was favorable for all patients and without recurrence.

Conclusion
DG is a rare entity, representing one of the causes of congenital hypothyroidism. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis that explains the delima of establishing surgical indications.

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EP1046
Occult papillary thyroid carcinoma with lymphatic metastasis as first presentation of the disease - A report of two cases
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Introduction
Occult papillary carcinomas are small thyroid carcinomas (< 1 cm) diagnosed after an initial manifestation of lymph nodes or distant metastasis. We report two cases of patients with this pattern of clinical presentation.

Case description
The first case is a 21-year-old woman, with a one-year history of a growing cervical cyst. Fine needle aspiration of the cyst showed metastasis from papillary thyroid cancer. She had no previous history for thyroid pathologies. A thyroid ultrasound was performed and the gland was described as heterogeneous, with no clear evidence of a primary carcinoma site but with too highly hypoechoic areas in the left lobe. Initial blood tests were as follow: TSH, Thyroglobulin and Calcitonin within the normal range, high levels of anti-TPO and anti-TG confirming the diagnose of Hashimoto thyroiditis. Total thyroidectomy and lymph node resection was recommended to the patient. The post-surgery biopsy confirmed multiple papillary focal lesions of papillary carcinoma with maximal diameter 1 cm. The patient received 131-iodine therapy with 100 mCi and is on regular follow up. The second patient is a 45-year-old man, with no medical history who went to the general practitioner for a neck lump. After initial examination, a biopsy of the lymph node was recommended. The result revealed lymph node metastases probable from thyroid papillary carcinoma. Blood test were within normal range. Thyroglobulin 13.54 ng/ml (3.5-77). The patient underwent total thyroidectomy and bilateral neck dissection. Histopathological exam was consistent with a papillary carcinoma of 3 mm in size. Post-surgery thyroglobulin 8.02 ng/ml. In a couple of weeks, the neck lumps reappeared. A computerised tomography was performed and bilateral neck and axillary lymph nodes were observed. The patient underwent a second surgery and later, radioactive iodine therapy with 100 mCi. The second biopsy confirmed once again metastasis from thyroid papillary cancer. Post-second surgery Thyroglobulin 0.01 ng/ml. The patient is still under strict observation because of the recidivist lymphatic disease.

Conclusion
It is important to consider the diagnosis of papillary thyroid carcinoma in every patient that seeks medical evaluation for lymph node swelling. Despite the improvement of ultrasoundography, many cases of occult papillary carcinoma remain undetected, emphasizing the role of pathological examination to confirm the diagnosis. The preferred treatment approach remains total thyroidectomy with ipsilateral cervical lymph node resection, usually followed by 131-iodine therapy. Key words: occult carcinoma, cervical lymph node, thyroglobulin, thyroidecmy, biopsy

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EP1047
Thyroid incidentaloma at 18F-FDG PET/CT, an alert to malignancy - a case report
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Introduction
Thyroid incidentaloma in 18F-FDG PET-CT is relatively common and the most focal uptake are benign. However, the risk of malignancy of thyroid lesions with focal uptake on 18F-FDG PET-CT is 34.8%. Metastasis to the thyroid is uncommon (less than 0.2% of thyroid fine needle aspiration – FNA - puncture
findings, with renal neoplasms being the most frequently associated (48.1%) and, more rarely, those from the breast (7.8%).

Case report
A 54-year-old female with breast adenocarcinoma (HER2+, pT3pN3M0) diagnosed in 2009, underwent neoadjuvant chemotherapy (CT), left radical mastectomy, adjuvant chemoradiation and immunotherapy. Six years later, she had a recurrence of the disease with pericardial effusion. A new CT treatment was performed, and the patient started goserelin, transzuzumab and pertuzumab (dual blockade anti-HER2). In 2020 a 18F-FDG PET-CT was performed and showed mild thyroid uptake in a left lobe’s nodular lesion. At the first Endocrinologist observation she denied cervical compressive symptoms and blood tests revealed euthyroidism. The thyroid ultrasound showed in the left lobe “a nodule with 30x15x25mm, undefined contours, heterogeneous ecocstructure, hyperechoic punctate foci … valuable bilateral cervical lymph node expression”. Cytological evaluation of the nodule was suggestive of metastatic carcinoma. Given the absence of possible confirmatory immunohistochemistry (IHC) with FNA and this being the only secondary lesion to suggest progression of the disease, in a multidisciplinary discussion, it was decided to perform total thyroidectomy. The report of thyroid focal uptake on PET-CT with 18F-FDG in patients with breast carcinoma should raise the suspicion for metastasis. There is no consensus on the therapeutic approach in these patients, namely with respect to total thyroidectomy. In the present clinical report, histological confirmation with IHC confirmed the progression of the oncological disease and had an impact on the therapy.

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EP1048
Papillary thyroid cancer with larger-volume lymph node metastases: evaluation of response to surgical treatment for decision making on indication of radioiodine
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Introduction
PTC patients with lymph node (LN) metastases of greater volume (in > 5 LN and/or with larger metastases > 5mm, hereinafter N1 > 5) usually receive radioiodine (RAI). Some guidelines suggest carrying out an evaluation of the response to surgical treatment (RST), recommending lower RAI dose (activity) in patients with good RST.

Objectives:
a)To evaluate the RST in patients with PTC and N1 > 5 b)To evaluate the disease-free-survival (DFS) in patients with PTC and N1 > 5 who present thyroglobulin (Tg) < 1.0 ng/ml, absence of Tg-Antibodies (TgAb (-)) and non-suspicious ultrasound (US) findings in the evaluation of the RST and who are treated with low doses of RAI.

Experimental Design
Prospective Observational Cohort Study

Materials and Methods
Patients with PTC and N1 > 5, operated between 2016 and 2020 and who had RST evaluation by US, Tg and TgAb (using LT4) and with TSH ≤ 2.0mUI/ml at least 6 weeks after surgery and prior to the administration of RAI were included. Patients were divided into 3 groups according to the RST (Table 2). Low-dose RAI (30-50mCi) was offered to patients who presented RST defined in this study as adequate (Tg ≤ 1ng/ml, TgAb (-) and non-suspicious US, Group I). In patients with metastases ≥ 10mm and/or ≥ 10 involved LN, low-dose RAI was offered when their Tg was ≤ 0.2ng/ml, AcTg (+) and normal US. Continuous variables are described as median and range, and categorical variables as proportions. Study was approved by local ethics committee.

Table 1

<table>
<thead>
<tr>
<th>Characteristics at diagnosis</th>
<th>n=97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57 (14-78)</td>
</tr>
<tr>
<td>Female gender</td>
<td>70%</td>
</tr>
<tr>
<td>PTC (Non-agressive histology)</td>
<td>91%</td>
</tr>
<tr>
<td>Aggressive PTC histology</td>
<td>9%</td>
</tr>
<tr>
<td>TNM 8th Edition</td>
<td></td>
</tr>
<tr>
<td>pT1a-pT1b-pT2</td>
<td>89%</td>
</tr>
<tr>
<td>pT3a-pT3b</td>
<td>11%</td>
</tr>
<tr>
<td>N1a</td>
<td>33%</td>
</tr>
<tr>
<td>N1b</td>
<td>67%</td>
</tr>
<tr>
<td>n≥ 5 &amp; &lt;10 and size&gt; 5 &amp; &lt;10mm</td>
<td>45%</td>
</tr>
<tr>
<td>n≥ 10 or size ≥ 10mm</td>
<td>55%</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Post-surgical evaluation (prior to RAI)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tg ≤ 1 ng/ml, TgAb (-) &amp; non-suspicious US</td>
<td>55.7%</td>
</tr>
<tr>
<td>II:Tg &gt; 1.0 and/or TgAb (+) &amp; US no-suspicious US</td>
<td>19.9%</td>
</tr>
<tr>
<td>III:suspicious US regardless TgAb &amp; Tg levels</td>
<td>14.5%</td>
</tr>
</tbody>
</table>

Results
Of 581 patients with LN metastases, 97 met the inclusion criteria. In 53.7% of the patients of group I low dose (30-50 mCi) of RAI was given. With a median follow-up of 24months, DFS was 96% (only 1 patient presented a tiny 3 mm suspicious adenopathy).

Conclusions
a) Approximately half of PTC patients with N1 > 5 have an adequate RST. b) This preliminary data suggests that in group of patients, the administration of a low dose of RAI would be associated with a very good disease-free survival, appearing to be a safe option in them.

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EP1049
Worsening dysphagia and dysphonia: a case report
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Premise
multinodular goiter and compressive symptoms in the neck could not be necessarily associated.

Case-report
A 82-year-old woman diagnosed follicular lymphoma in 2017 reached to the Emergency Department in August 2021 because of a progressive and worsening dysphagia and dysphonia, began six weeks before. The patient complained a weight loss of about 8 kg due to the inability in feeding. Her medical history was necessarily associated.

DOI: 10.1530/endoabs.81.EP1049
Discussion
Secondary thyroid lymphoma can be diagnosed in presence of thyroid nodules with cytologic benign result. Metastatic thyroid tumors are very uncommon and occur as goiter, worsening dysphonia and stridor, dysphagia, tightness of the neck. It is clinically important to distinguish between primary and secondary thyroid lymphoma because therapy and prognosis are different: thyroid metastatic lymphoma has a worse prognosis than primary thyroid lymphoma and it requires an accurate clinical and radiological staging because most of the cases have a widely disseminated disease from the diagnosis and a poor prognosis.

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EP1050
Metastatic papillary thyroid carcinoma - a multidisciplinary approach
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Introduction
Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy. It represents over 80% of all follicular derived well-differentiated thyroid cancers. Despite the fact that the majority of PTCs are well differentiated and have a low rate of local invasion, recurrences, or metastases, there are complex cases which require a multidisciplinary team for a favorable result.

Methods
Clinical examination, blood tests, scintigraphy, CT scan, radioiodine therapy.

Case
We present the case of a 67-year-old woman who underwent a total thyroidectomy in 2019 for multinodular goitre with Graves’ disease, which at the pathological report turned out to be papillary thyroid carcinoma in the right thyroid lobe. She received 1 dose of radioactive iodine therapy one month after the surgery (100 mCi 131I) and did a whole-body scintigraphy which revealed iodine fixing areas in the right thyroid lobe, both lungs (pulmonary metastases), right parietal dura mater, left iliac bone and left female bone metastases). Four days after the iodine therapy, the patient developed a partial seizure and left hemiparesis and hypotension caused by the brain metastasis. She underwent tumoral resection in the Neurosurgery Department but the neurological deficit and hypoesthesia didn’t improve, while the pathological report concluded the growth was a PTC metastasis. Six months after the thyroidectomy the patient did another dose of radioactive iodine therapy (135 mCi) with no spontaneous TSH increase after LT4 withdrawal, so she was administered Thyrogen which secured a good uptake of radioiodine in the tumour. She then did a whole-body scintigraphy which revealed a reduction of the primary and secondary lung lesions and stable bone metastases, with no cerebral uptake. Also, the thyroglobulin (TG) decreased every time she did radioiodine therapy. Eighteen months after the thyroidectomy she underwent a third dose of radioactive iodine (100 mCi) which revealed stable lesions. The patient will therefore return for a fourth dose of radioactive iodine therapy two years after the thyroidectomy.

Discussions
This patient initially presented with a multinodular goitre and Graves’ disease which turned out to be PTC at the pathological report. She has multiple metastases which require a multidisciplinary approach. Also, it is important to note that the TG drops every time she undergoes radioiodine therapy.

Conclusions
PTC is a common endocrine carcinoma which in rare cases can metastasise and severely affect the quality of life of the patients.

Keywords
papillary thyroid carcinoma, metastases, radioiodine therapy.

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EP1052
Rare presentation of medullary thyroid carcinoma
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Introduction
Medullary thyroid cancer is a rare neoplasm, accounting for approximately 4% of all cases of thyroid cancer. Exceptionally, it can be associated with the hormonal production of ACTH or CRH, causing ectopic Cushing’s syndrome.

Clinical Case
We present the case of a 43-year-old man who, as a history of interest, presented a T6-T8 vertebral body fracture 2 years ago and a right hip fracture 1 year ago. Bone densitometry is compatible with osteoporosis. He began daily treatment with Teriparatide 20 mg subcutaneously, calcium carbonate 2.5 g and Cholecalciferol 800 IU. He was admitted to the hospital due to worsening pain. On examination he presented facial plethora, abdominal obesity, and muscular atrophy. Given the suspicion of Cushing, a blood test was performed, highlighting ACTH 114 pg/ml, Cortisol 43.2 μg/dl, ACTH production originated in the medullary thyroid carcinoma. Treatment was started with Levotyroxine 150 mg on an empty stomach and Vandetanib 300 mg.

Conclusions
Medullary thyroid carcinoma is an uncommon cause of Cushing’s syndrome, but it is associated with high morbidity, as described in our patient. Those affected generally have a poor prognosis due to the presence of metastatic disease at the time of diagnosis, and on many occasions they have a large primary tumor mass with little probability of successful resection.
**EP1053**

**Differentiated thyroid cancer in children and adolescents: about 6 cases**  
Rachida Bouattay, Maroua Naourar, Emma BERGAOUI, Heyfa Belhadjimiled, Mehdi Ferjaoou, Amel Elkorbé, Kaled Harrathi, Naourez Kolsi & Jamel Koubba  
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

**Introduction**  
Thyroid cancer is rare in the pediatric population, but thyroid carcinomas occurring in children carry a unique set of clinical, pathologic, and molecular characteristics. In comparison to adults, children more often present with aggressive, advanced stage disease. The aim of the study is to determine the clinical, histological and therapeutic aspects of differentiated thyroid cancer in children and adolescents.

**Materials and Methods**  
This is a retrospective study about 6 cases of pediatric thyroid cancer collected in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).

**Results**  
The average age was 15 years, gender-ratio was 0.2. No personal history of radiation exposure and family history of thyroid cancer were noted. All of patients presented to our consultation for management of a thyroid nodule, associated, in one case, with middle jugular node measuring 2 cm in diameter. All of patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection in 3 cases and ipsilateral central neck lymph node dissection in 2 cases. A lateral lymph node dissection was performed in 2 cases. Histologic examination confirmed the diagnosis of papillary carcinoma in all cases. The mean tumor size was 3 cm. In all cases, papillary thyroid carcinoma was multifocal. We noted a tumor capsular invasion in 2 cases. Lymph node metastasis were along the recurrent nerve chain in all cases and in jugular chain in 2 cases. Surgical treatment was followed by radioactive iodine therapy in all cases. There was no distant metastasis or cancer recurrence after a mean follow-up of 3 years.

**Conclusion**  
Although children with differentiated thyroid cancer typically present with locoregional metastases and a high rate of distant metastatic disease, overall survival is very good. Treatment should be based on their increased risk for recurrence instead of overall mortality, and lifelong follow up is required because recurrence and death may not occur for decades after diagnosis.

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**EP1054**

**Differentiated thyroid cancer with tuberculous cervical lymphadenopathy mimicking metastasis: a report of 2 cases**  
Rachida Bouattay, Maroua Naourar, Emma BERGAOUI, Heyfa Belhadjimiled, Mehdi Ferjaoou, Amel Elkorbé, Kaled Harrathi, Naourez Kolsi & Jamel Koubba  
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

**Introduction**  
Papillary and follicular thyroid carcinoma are the most frequent endocrine malignancy. Lymphatic metastases at the time of diagnosis are common in differentiated thyroid cancer (DTC). In these patients, most authors recommend a thyroidectomy with neck dissection. However, neck dissection can lead to numerous post-operative complications. Thus, careful pre-operative evaluation of cervical lymph node metastasis may be crucial, so that patients do not undergo unnecessary neck dissection for other benign conditions. The aim of the study is to determine the clinical, histological and therapeutic aspects of the coexistence of differentiated thyroid cancer and tuberculous cervical lymphadenopathy.

**Materials and Methods**  
We report three cases of association between differentiated thyroid cancer with tuberculous cervical lymphadenopathy collected in ENT department of Fattouma Bourguiba Hospital of Monastir over a period of 10 years.

**Results**  
Our study investigated three women aged 47, 49 and 56 years respectively. The first patient had a history of hypertension, diabetes mellitus and hysterectomy for endometrial stromal sarcoma while the second patient didn’t have any past medical history. The third case was admitted in the Rheumatology Department for bone pain and worsening of the general state. A bone biopsy was performed during that hospitalization showing follicular thyroid carcinoma metastasis. In all cases, ultrasonography showed thyroid nodules associated to suspicious jugular node. All of patients underwent a total thyroidectomy, associated to central and lateral lymph node dissection. The histology disclosed a papillary carcinoma in two cases and follicular carcinoma in the third one. In all cases, thyroid carcinoma was associated to tuberculosis in the lateral cervical lymph node. In all cases, surgical treatment was followed by radioactive iodine therapy and antituberculosis medication. Follow-up has been negative for any recurrence or distant metastasis during the past 24 months.

**Conclusion**  
Cervical lymphadenitis is the most common clinical presentation of extra-pulmonary tuberculosis. The coincident of (DTC) and tuberculous lymphadenitis are not rare. The large lymph nodes with central necrosis recognized at uncommon site of metastasis from DTC might remind us of such coexistence. Preoperative diagnosis for tuberculous infection is important to avoid unnecessary surgical complications and secondary infections.

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**EP1055**

**Cushing’s disease and multiple endocrine neoplasia with medullary thyroid carcinoma and bilateral pheochromocytoma: about a case**  
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CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

**Introduction**  
Multiple endocrine neoplasia (MEN) are inherited conditions of autosomal dominant transmission characterized by the occurrence of various associated endocrine lesions. We report an observation of a patient with a rare association of medullary thyroid carcinoma and bilateral pheochromocytoma with Cushing’s disease.

**Observation**  
The patient was H.B., 18 years old, followed for a medullary thyroid carcinoma (MTC) since 2018 discovered at the stage of pulmonary and lymph node metastasis, having benefited from a total thyroidectomy with right lymph node curage, classified as T2N1bM1 with the presence of numerous images of emboli (6N+1T2N).

**Clinically**  
The patient presents lingual and subconjunctival neuromas, with large purple stretch marks on the flanks, the roots of the lower limbs, and the subaxillary region, associated with signs of hyper androgenism. Para-clinical calcitonin at 44600 pg/ml, with metanephrines at 2.53 umol/24h (0.20-1.50), with adrenal CT: two adrenal nodules, measuring 13.5 X 11.5 mm on the left, and 12.5 X 12.5 mm on the right, of spontaneous density, at 40 HU, with enhancement after injection of PDC, Cortisolemia of 8 h after a minute braking test at 14. 5 mg/d, with ACTH: 34 pg/ml (10-50), we completed by a pituitary MRI which objectified a pico adenoma of 2.9 X 2.6 mm. The genetic study did not reveal any mutations in exons 10 and 11, exons 15 and 16 were not studied. The patient underwent bilateral lymph node resection and left adrenalectomy in the first stage, with a control calcitonin level of 3360 pg/ml, a right adrenalectomy is planned.

**Conclusion**  
NEM 2B is an autosomal dominant syndrome characterized by a variable association of pheochromocytoma, CMT, mucosal and subconjunctival neuromas, with a marfanoid and a ganglioneuromatosis, although exceptional, the association with a cushing disease is very rare.

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**EP1056**

**Thyroid oncocytic tumor: about 23 cases**  
Rachida Bouattay, Maroua Naourar, Emma BERGAOUI, Heyfa Belhadjimiled, Mehdi Ferjaoou, Amel Elkorbé, Kaled Harrathi, Naourez Kolsi & Jamel Koubba  
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

**Introduction**  
Oncocytic tumors (OT) are rare, representing 3 to 10% of epithelial tumors of the thyroid. It is important to individualize these tumors given the relatively high frequency of carcinomas and the aggressiveness of oncocytic carcinoma. The aim...
of this study is to determine the clinical, histological and therapeutic aspects of thyroid oncocytic tumor.

Materials and Methods
This is a retrospective study about 23 cases of oncocytic thyroid tumors collected in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).

Results
The average age was 41 years, a female predominance was noted (19F/4M). Our study included: 20 oncocytic adenomas and 3 oncocytic carcinomas. The average consultation time was 18 months. Eighteen patients have single thyroid nodule and five patients have a multinodular goiter. The mean ultrasound size of the thyroid nodule was 4 cm. There was no cervical lymphadenopathy in all cases. Fine needle aspiration cytology from the thyroid nodule was performed in two cases showing papillary carcinoma in one case. 19 patients underwent a lobectomy. A total thyroidectomy with node dissection were performed in 4 cases. Radioactive iodine therapy was indicated for the 3 patients with oncocytic carcinoma. There was no distant metastasis or cancer recurrence after a mean follow-up of 24 months.

Conclusion
Among well differentiated thyroid tumors, oncocytic tumors feature a distinctive set of clinical, morphologic and biologic characteristics, some of which have been a matter of controversy.

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EP1077
Correlation between body mass index and clinico-pathological features of papillary thyroid carcinoma
Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Epidemiological studies have reported that being overweight and being obese are associated with increased incidences of numerous cancers, including thyroid cancer. In addition to cancer risk, obesity has also been demonstrated to be associated with more aggressive pathological characteristics of the tumor and worse prognosis in patients with several cancers.

Purpose of study
Demonstrate the relationships between BMI and the clinico-pathological features of papillary thyroid carcinoma.

Materials and methods
Retrospective study was conducted in the Ibn Rochd University Hospital Endocrinology and Diabetology department of Casablanca, including 211 patients followed for papillary thyroid carcinoma between August 2018 and January 2022. The patients were divided into 2 groups: a group with obesity, and a control group, comparing the clinico-pathological characteristics of the two groups. Statistical analysis performed by the software SPSS 25.0.

Results
According to the results, 37% patients were women (90.8%), mean age was 40.4 years (12-86) and mean BMI was 28.9 kg/m² (21-45). The mean tumor size was 28.6 mm (1-80). Statistical analysis of the prognostic factors: tumor size, multifocality, presence of vascular emboli and distant metastasis showed no significant differences in the obese group compared to the control group. Only the presence of capsular invasion (P < 0.01) was strongly associated with obesity.

Conclusion
The association between obesity and carcinoma has been widely elucidated. The association between obesity and carcinoma has been widely elucidated. The association between obesity and carcinoma has been widely elucidated. The association between obesity and carcinoma has been widely elucidated.

DOI: 10.1530/endoabs.81.EP1057

EP1080
Adenocarcinoma of the colon and papillary thyroid carcinoma: An exceptional association
Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
The association of thyroid and colon cancer is rare, it can be observed in the context of Gardner’s syndrome and Cowden’s syndrome with a prevalence of 0.6%. We report a case of metachronous association of a differentiated thyroid cancer with a colon cancer.

Observation
45-year-old patient, followed for well-differentiated colon adenocarcinoma without metastasis, having received eight courses of chemotherapy. One year later, the patient underwent a total thyroidectomy for multinodular goiter. Anatomopathologic examination of the surgical specimen showed a papillary carcinoma with vesicular differentiation classified as PT3. The patient received additional treatment with radioactive iodine131 at a dose of 100mCi. The extension workup did not reveal any metastasis and the surveillance workup did not reveal any recurrence.

Conclusion
Multiple primary cancers are rare, but their incidence has recently increased. Common genetic and environmental risk factors seem to be involved in many cases. Multiplicity itself is not necessarily a poor prognostic factor. However, early detection will allow prompt management and increase the cure rate of the disease.

DOI: 10.1530/endoabs.81.EP1058

EP1059
Association between breast cancer and thyroid cancer: About 55 cases
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Background
Several studies have demonstrated the relationship between breast cancer and thyroid cancer by the presence of common genetic determinants. The aim of the study was to define the breast cancer prevalence among patients followed for thyroid carcinoma and to determine factors favoring this association.

Materials and methods
A Cross-sectional study was conducted in the Ibn Rochd University Hospital Endocrinology and Diabetology department of Casablanca, including 55 patients followed for thyroid carcinoma between 1986-2021 among all the thyroid differentiated carcinomas (793 patients) and presenting breast cancer. Statistical analysis performed by the software SPSS 25.0.

Results
Prevalence of patients presenting breast cancer and thyroid cancer was 6.3%. Mean age was 45.5 years (36-70). Family history of neoplasia was found in 49.1% of cases. Breast cancer preceded the discovery of thyroid cancer in 51% of cases. Iratherapy was performed in 98.2% of patients. External radiotherapy was realized in 45.4% of cases for the treatment of breast cancer papillary carcinoma and invasive ductal carcinoma were the predominant histologic type in 89.1% of cases. Predictor factors of this association were female patients who had the first neoplasia at a young age (≤45years), family history of neoplasia and prior external radiotherapy.

Conclusion
Our study results support the hypothesis of the presence of a relationship between the breast cancer occurrence in patients followed for thyroid cancer. Close monitoring and vigilance for early detection of thyroid cancer in patients treated for breast cancer is recommended.

DOI: 10.1530/endoabs.81.EP1059

EP1060
Sorafenib for metastatic thyroid carcinoma
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Differentiated thyroid cancers include papillary, follicular carcinomas and are usually associated with a good prognosis. Up to 10% of patients develop metastatic lesions and radiodine resistance. Tyrosine kinase inhibitors (TKI) represent a strong therapeutic option for patients with advanced metastatic disease.
Aim (s) Horner syndrome could be caused by metastatic medullary thyroid cancer. Horner syndrome indicates an increased risk of local and distant metastatic disease. Although rare, Horner syndrome is an extremely rare and unusual manifestation of the medullary thyroid cancer. It is important to emphasize the importance of multidisciplinary team approach in order to establish a correct diagnosis and treatment plan in such a challenging case.

EP1061
Horner syndrome as the first manifestation of medullary thyroid cancer
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Introduction Medullary thyroid cancer is a rare neuroendocrine tumor arising from the parafollicular C cells of the thyroid gland. Calcitonin production is a characteristic feature of medullary thyroid cancer and preoperative high levels indicate an increased risk of local and distant metastatic disease. Although rare, Horner syndrome could be caused by metastatic medullary thyroid cancer. Horner syndrome usually presents with ptosis, miosis and facial anhidrosis and most of the times is aquired following a lesion anywhere along the sympathetic pathway. Our study presented the case of a 47 year old female referred for sudden onset of left ptosis and vertical diplopia. Material and Methods MR1 of the brain and cervical spine revealed multiple left cervical lymphadenopathy suspicious for malignancy and neurologic evaluation established the diagnosis of Claude Bernard Horner syndrome due to cervical compression. Additional tests were performed and neck ultrasound revealed multiple thyroid nodules with a left dominant nodule of 3.7/4.2/2.4 cm with a high index of sonographic suspicion for thyroid cancer and multiple left lymphadenopathy. Lab tests revealed a hypercalcitoninemia (2000 pg/ml) and a high level of carcinoembryonic antigen (411 ng/ml) confirming the diagnosis of medullary thyroid cancer. Screening for primary hyperparathyroidism and pheochromocytoma was negative. Considering the high basal level of calcitonin and the ultrasound examination of the neck positive for ipsilateral lymph nodes, an extensive screening for regional and distant metastasis was performed. Conclusions Horner syndrome and medullary thyroid cancer are two rare entities and Horner syndrome is an extremely rare and unusual manifestation of the medullary thyroid cancer. It is important to emphasize the importance of multidisciplinary team approach in order to establish a correct diagnosis and treatment plan in such a challenging case.

EP1062
Breakfast with liquid levothyroxine (Levotirosol®): a single-center experience
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1Ospedale SS Annunziata, Diabetology Unit and Endocrinology Service, Sulmona, Italy; 2Università degli Studi ‘Gabriele d’Annunzio’ - sede di Chieti, Department of Medicine and Ageing Sciences, Chieti, Italy; 3Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Cascina Perseghetto, Italy

Introduction Levothyroxine (L-T4) tablets are the most used treatment for hypothyroidism worldwide. L-T4 tablets should be taken in the morning and have a fasting state. Some patients could be unable to adhere to this recommendation resulting in poor thyroid function and thyrotopin (TSH) concentration above the upper normal limits. A previous double-blind placebo-controlled trial showed that L-T4 liquid could be ingested during breakfast without a significant difference in TSH values. Recently, a new L-T4 liquid (Levotirosol®, IBSA Farmaceutici S.r.L., Lodì, Italy) was released in Italy improving therapeutic options. Our study aimed to explore the possibility to recommend L-T4 liquid directly at breakfast. 

Methods We performed an observational, retrospective, and non-controlled study at the University of Endocrinology and Endocrinology Service of Hospital “Santi Annunziati” of Sulmona (Italy). We enrolled hypothyroid patients treated with L-T4 tablets that refer poor or unsatisfied compliance to the treatment. All included participants received L-T4 liquid at the same dose of L-T4 tablets to ingest during breakfast. After at least 40 days, they were contacted by telephone to obtain data on TSH and fT4.

Results We enrolled 26 hypothyroid patients in therapy with L-T4 tablets that express poor compliance and/or dissatisfaction with tablets. Three patients were lost at follow-up and one patient back spontaneously to tablets treatment. Finally, we had data about 22 patients aged 54.3(IQR 48.6-59.3) years. All selected participants were female and were affected by primary hypothyroidism. The duration of L-T4 liquid treatment was 68.5 (IQR 57.3-73.5) days. Ten enrolled subjects showed TSH serum levels before LT4 liquid above 5 mU/l for poor therapy compliance; the remaining 13 subjects presents a TSH value within a normal range but referred that the tablets adherence was difficult and impaired quality of life. We reported that TSH serum levels after L-T4 liquid treatment during breakfast (3.9, IQR = 2.1-4.4) were significantly lower compared to TSH at the beginning (4.8, IQR = 3.9-6.9; P = 0.03). Furthermore, freeT4 serum levels after liquid therapy were higher respect to freeT4 levels before liquid therapy (1.0, IQR = 0.8-1.2 VS 0.9, IQR = 0.7-1.1; P = 0.002). When only patients with TSH above the range were considered for analysis, TSH serum levels decreased significantly after LT4 liquid therapy (P = 0.02).

Conclusions We showed that L-T4 liquid in hypothyroid patients with poor therapy compliance improves TSH serum levels. L-T4 liquid ingested during breakfast could represent an improving therapeutic choice, especially in patients with poor therapy compliance. Further longitudinal trials are needed to confirm these data and to explore the possibility to recommend LT4 liquid without a fasting state.

EP1063
Therapeutic plasma exchange in amiodarone induced thyrotoxicosis: a case report
Cristina Clauisi, Jacopo Manso, Andrea Graziani, Simona Censi, Sofia Carducci, Yi Hang Zhu, Ilaria Fiva & Caterina Mian
University of Padua, Endocrinology, Padova, Italy

A 52-year man came to Emergency Department with Atrial Fibrillation with rapid ventricular response due to amiodarone induced thyrotoxicosis (AIT). The patient was found tachyarrhythmic (153 beats per minute), tachyypnic (27 breaths per minute). Endocrine Abstracts (2022) Vol 81
Congenital hypothyroidism due to hormone synthesis disorder: the value of early diagnosis

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Introduction
Primary congenital hypothyroidism is the most common neonatal endocrine disorder, traditionally subdivided into thyroid dysgenesis, referring to a range of abnormalities in thyroid development, and dyshormonogenesis. We report two cases of dyshormonogenesis in a brother and sister followed for congenital hypothyroidism by inactivating mutation of the TSH receptor, illustrating the good evolution in case of an adapted treatment.

Clinical cases
This is a brother and sister aged 21 and 17 years respectively, from a non-consanguineous marriage. The diagnosis of congenital hypothyroidism due to a hormone synthesis disorder was made at the age of 1 month in both of them, in view of clinical and biological signs of peripheral hypothyroidism, the cervical ultrasound showed a thyroid gland in place, with regular contours and homogeneous echotexture, and the genetic study was in favour of an inactivating mutation of the TSH receptor. Both patients are treated with Levothyroxine, with regular intake of the treatment, and a good clinical and biological evolution with no mental retardation.

Discussion
Congenital hypothyroidism on hormone synthesis disorder is characterized by a defective molecular pathway for thyroid hormone generation resulting in failure of hormone production by a structurally intact gland. Hypothyroidism secondary to TSH resistance is rare. TSH receptor abnormalities have been described first in cases of thyroid hormone resistance and then in cases of congenital hypothyroidism with an established gland in a eutopic but hypoplastic position. Delayed treatment of neonatal hypothyroidism can result in profound neurodevelopmental delay; therefore, congenital hypothyroidism is screened in developed countries to facilitate prompt diagnosis and treatment.

Early and adequate treatment with Levothyroxine results in excellent neurodevelopmental outcomes for most patients with congenital hypothyroidism.

Conclusion
Congenital hypothyroidism is common and can result in severe neurodevelopmental morbidity. Neonatal screening is an important tool to detect congenital hypothyroidism. Prompt diagnosis and treatment are essential to optimize long-term outcomes. These two clinical cases illustrate the importance of early diagnosis and treatment for a successful outcome.

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Betrayed by the lab: a case of factitial thyrotoxicosis

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Introduction
Factitious thyrotoxicosis is caused by intentional and surreptitious ingestion of thyroid hormone and can be a challenge in the differential diagnosis with other pathologies.

Case report
Female, 35 years old, referred to our department for suspected subacute thyrotoxicosis after COVID-19. The patient had previous medical history of hysterectomy, bilateral oophorectomy, 2 galactophorectomies with right breast reconstruction, depressive syndrome and hypothyroidism medicated with levothyroxine 75 mg since 2016. In March 2021, two months after SARS-CoV-2 infection, she noticed increased cervical volume with associated pain and weight loss of 10 kg. Thyrotoxicosis was identified and thyroid scintigraphy showed diffuse low uptake, suggestive of subacute thyroiditis. Levothyroxine was suspended and she was medicated with 20 mg prednisolone. After 4 months she maintained thyrotoxicosis with no response to therapy, and a total thyroidectomy was suggested by her medical team, being referred to our department. Upon observation, she complained of tiredness and drowsiness, had no signs of thyrotoxicosis and thyroid examination was normal and painless.

The patient expressed a desire to undergo surgery to control the symptoms. At that time, under prednisolone 20 mg, analytical evaluation showed: TSH <0.005 uU/ml, FT4 6.25 ng/ml (0.97-1.58), FT3 18.8 pg/ml (2.38-4.37), thyroglobulin 2.4 ng/ml, negative TRAB, TG and TPO antibodies, AST 46 IU/l (7-32), ALT 73 IU/l (7-32). Thyroid scintigraphy was repeated and showed diffuse low uptake. Due to suspected factitious thyrotoxicosis, it was decided to admit the patient and without instuting any therapy a clear improvement in thyroid function was observed after 5 days: TSH <0.008, FT4 1.11 (0.97-1.48), FT3 3.70 (1.88-3.18). When confronted with the results and after being evaluated by Psychiatry, the patient denied intentionally taking levothyroxine.

Discussion
In the presented case, the suspicion of factitious thyrotoxicosis was based on the absence of goiter, low level of thyroglobulin, low uptake on thyroid scintigraphy and persistence of thyrotoxicosis six months after the diagnosis of subacute thyroiditis. The suspicion was confirmed by the rapid decrease in the serum value of thyroid hormones (50% FT4 and 41% FT3) without any therapy.

Conclusion
This case reflects the importance of clinical suspicion and timely diagnosis of factitious thyrotoxicosis, avoiding unnecessary and potentially invasive treatments.

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A case of thromboembolic disease with mild hyperthyroidism

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Background
Hyperthyroidism is a thyroid hormone excess state which usually manifests with various cardiovascular symptoms such as sinus tachycardia, tachyarrhythmia and high output cardiac failure. Pulmonary embolism is not commonly associated with thyrotoxicosis but some studies have shown an increased propensity of
A case report of hyperthyroidism which does not warrant antithyroid treatment

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Introduction
The most common cause of hyperthyroidism in Malaysia is autoimmune cause like Grave disease, or toxic multinodular goitre. Thyroid hormone resistant syndrome is a rare genetic disease which usually presented with mild hyperthyroidism clinically and biochemically it had elevated free T4 and non suppressed TSH. Inexperienced doctor will commonly mistreat patient with antithyroid medication. This is because this genetic disease is extremely rare to encounter in practice.

Case Report
A 24 years old gentleman, he was first presented to Hospital Ipoh for left Anterior Cruciate Ligament tear after sport injury in 2019. Pre-operative assessment noted patient tachycardia. Otherwise, he did not have palpitation, tremors, weight loss, heat or cold intolerance, diarrhea, or anxiety. On the other hand, he had strong family history of hyperthyroidism which was his mother, mother’s siblings and his grandmother. On examination, his blood pressure is normotensive, and heart rate was slightly tachycardic. He had no fine tremors, and goiter. Cardiovascular and respiratory system examination was unremarkable His thyroid biochemical profile showed normal thyroid stimulating hormone (TSH), 3.4 mIU/l (0.55 -4.78) with elevated free T4 (FT4), 27.9 pmol/l (11.5-22.7). In view of pendenic covid, hospitalization was postponed and he request his case transfer to my hospital. Hospital Melaka to continue follow up. Throughout the follow up, serial thyroid function test showed normal TSH, and elevated FT4. He was asymptomatic for hyperthyroidism other than occasionally tachycardic. His magnetic resonance imaging brain demonstrate a pituitary microadenoma. However, thyrotropin releasing hormone (TRH) stimulation test reveal normal TSH response. We had undergone left knee Anterior cruciate ligament tear repair in Jan 2022 under general anesthesia. Intraoperative and postoperative were uneventful. We had our limitation to further workup because the genetic test was not available in our country. We had rule out thyrotropin secreting tumor and primary hyperthyroidism before we come to a conclusion of thyroid hormone resistance syndrome. However, we would like to emphasis that not all hyperthyroidism warrant antithyroid treatment. Early recognition and refer to correct team is crucial to avoid unnecessary treatment.

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A case report of thyroid dysfunction in children with type 1 diabetes mellitus
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Background
In recent years, thyroid diseases have been occupying the top places in the structure of the endocrine pathology. There exists tight functional relationship between the thyroid and reproductive systems, which leads to a high probability of the development of combined disorders in one of these links of homeostasis.

Vitamin D deficiency in the population remains a global problem. The purpose of the study is to investigate the effect of myoinositol on the thyroid status of women with subclinical hyperthyroidism on the background of autoimmune thyroiditis and vitamin D deficiency.

Materials and methods
The study included 102 patients, aged 18-42 years, with subclinical hyperthyroidism on the background of autoimmune thyroiditis. The patients were randomly subdivided into two groups. Patients of the first group (n = 52) before the main treatment by levothyroxine at a dose 37.5 µg/day, and cholecalciferol at a dose of 2000 IU/day. Patients of the second group (n = 50) before the main treatment received only cholecalciferol at a dose of 2000 IU/day.

Results
Vitamin D deficiency was observed in 91.68 % of women with subclinical hyperthyroidism, and vitamin D insufficiency was observed in 8.32 %. A negative correlation was found between the level of 25 (OH) D and the level of ATPO (r = -0.194, P < 0.05). The myoinositol supplementation together with vitamin D led to a probable increase in the content of 25 (OH) D in the serum, as well as a decrease in the titer of ATPO.

Conclusions
The positive effect of myoinositol drugs together with vitamin D on the functional state of the thyroid gland, on the level of antibodies to TPO in women of reproductive age with subclinical hyperthyroidism on the background of autoimmune thyroiditis and vitamin D deficiency has been established.

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The structure of thyroid dysfunction in children with type 1 diabetes mellitus
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Relevance
Type 1 diabetes mellitus (DM) is one of the most common endocrine disorders among chil-dren and accounts for 5-10% of all DM. According to scientists, in patients with type 1 diabetes, the risk of developing thyroid pathology is increased and with their combination, the course of both diseases worsens. There are different opinions among specialists regarding the clinical significance of latent thy-roid dysfunction. The study of the functional state of the thyroid gland in children with type 1 diabetes seems to be very relevant. In Kazakhstan, we have not met studies to assess the function of the thyroid gland in children with type 1 diabetes.

Materials and methods
Cohort retrospective study of data from 1140 medical records of inpatient patients with type 1 diabetes who were on inpatient treatment for the study of thyroid hormones (n = 580): TSH, free T3, free T4, AT-TPO, AT-TG.

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Results
For the period from 2014 to 2020, the thyroid profile was studied in 58.9% of children with type 1 diabetes: euthyroidism was detected in 41.0%; hypothyroidism - in 18.0%; hyperthyroidism - in 2.4%, other different variants of thyroid dysfunction in 38.6% of children. When analyzing the distribution of primary hypothyroidism, the frequency of thyroid hypofunction was recorded in 46-52% of cases more often over the last 4 years of follow-up. The frequency of hypothyroidism among all thyroid dysfunction is 30.4% of cases. Among the various thyroid dysfunctions, the following variants are registered: isolated increase in free T3 - 66.0%, isolated increase in free T4 - 5.0%, increase in free T3 and free T4 with normal TSH - 13.0%, increase in TSH, free T3 with normal free T4 - 13.0%, decrease in free T3 - 3.0%.

Conclusion
In patients with type 1 diabetes, thyroid dysfunction is detected in almost 60.0%. It should be noted that primary hypothyroidism is registered in every third child with type 1 diabetes among all thyroid dysfunctions. In 39% of patients with type 1 diabetes, there were various fluctuations in the lev-els of hormones TSH, free T4, free T3, which were not included in the diagnostic criteria for thyroid pathologies and required separate study.

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EP1070
Cardiac arrhythmias associated with subclinical primary hypothyroidism: about two cases
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Introduction
Thyroid hormones play an important role in the normal functioning of cardiac and vascular physiology, therefore hypothyroidism results in profound cardiovascular effects. Arrhythmia in patients with hypothyroidism seems rare and not well recognized.

Observation
Our first patient was a non-smoker 61-year-old woman, followed-up in the cardiology department for hypertension and dyslipidemia during the previous 5 years. She was treated with ACE inhibitors and a statin. Her sister had a dysthyroidism. The history was marked by the appearance of palpitations over the past 2 years. Physical examination showed a palpable thyroid of normal size. The chest X-ray didn’t show any anomaly. Sinus tachycardia was found on ECG. Renal and lipid balance was correct. The thyroid investigation showed a subclinical hypothyroidism with a sensitive thyroid stimulating hormone: (TSH) = 6.05 mU/l and Free T4 = 14.8 pmol/l. One year later, the patient showed symptoms of weight gain and asthenia. A check-up was done: TSH = 7.2 mU/l/FT4 = 14 pmol/l; AntiTPO antibodies were negative (4=5). Cholesterol = 6.5mmol, TG = 3mmol inciting to treat her with appropriate thyroid replacement with a regular follow-up. The patient no longer reported tachycardia. Our second case was about a 57-year-old female patient, with a history of hypertension for 5 years. She was treated with ACE inhibitors. The patient was admitted to the cardiology department for junctional tachycardia and treated with beta blockers and digoxin. There was no infectious syndrome associated during her hospitalization, she was found to have subclinical primary hypothyroidism (TSH = 12.8 mU/l/FT4 = 12.5 pmol/l), her anti TPO antibodies were negative. The initial cervical ultrasound noted a 5.5 mm right lobar nodule classified as TIRADS2. The ultrasound follow-up two years later showed a heterogeneous hypo echogenic thyroid gland with no thyroid nodule.

Conclusion
Hypothyroidism can result in decreased cardiac output, increased systemic vascular resistance and atherosclerotic with ischemic heart disease risk. Cases of arrhythmia are rarely reported in hypothyroidism and could be due to alteration of myocyte-specific gene expression, intermittent oedema, myotubill swelling with loss of striation, endotheial dysfunction, disturbances of the sympathetic-vagal tone, increased arterial stiffness… Replacement with thyroxin could help and should be initiated cautiously.

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EP1071
Moyamoya disease and Graves’ disease in a Tunisian girl
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Introduction
There is an association between Moyamoya syndrome and Graves’ disease, described primarily in Asian populations. We report a case of Moyamoya vasculopathy with stroke and hypertension associated with Graves’ disease in a 15-year-old Tunisian girl.

Observation
A 15-year-old girl diagnosed with Moyamoya vasculopathy was referred to the endocrinology department for hyperthyroidism. The patient had a history of recurrent stroke and hypertension since 2 years-old. She complained of palpitations, weight loss and tremors, bilateral exophthalmia and floppy eyelid syndrome. Physical examination showed bilateral palpebral edema, bilateral exophthalmia and complete eyelid closure. Laboratory investigations showed high level free T4: 38.8 pmol/l (12.22), low TSH < 0.05 mUH (0.4-4) and high level of TSH receptor antibodies: 35 U/lm (<5). Thyroid ultrasound revealed an hypochonic, hypervascular goiter without nodules. Thyroid scintigraphy showed intense and homogeneous uptake. Orbital and brain MRI showed bifrontal anoxic-ischemic lesions with left wallerian degeneration associated with inflammatory myopathy of the right lower oculomotor muscle. The diagnosis of graves’ disease was confirmed. The patient was treated with methimazole leading to clinical and biological euthyroidism after 8 months treatment.

Conclusion
This is the first case of Moyamoya disease coexisting with Graves’ disease in a Tunisian patient. The pathogenesis and the prognosis of hyperthyroidism and specially Graves’ ophthalmopathy are still unknown.

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EP1072
Impact of Ramadan fasting on patients followed for Hypothyroidism.
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Introduction
During Ramadan, Muslims change their eating and sleeping habits. All these changes can cause metabolic and hormonal variations. The main treatment for hypothyroidism is L-thyroxine. It is known that the absorption of L-thyroxine is optimal when taken on an empty stomach. Very few studies have been conducted to examine the best time to administer L-thyroxine during Ramadan.

Objective of the study
To evaluate the impact of Ramadan fasting on hormonal balance and to compare the use of L-thyroxine 30min before Fotour and at Sohour.

Material and methods
Prospective study including 62 patients followed in consultation for hypothyroidism. A TSH measurement was performed before and after 6 weeks. The evaluation of the therapeutic compliance was evaluated by the MORISKY Medication Adherence Scale.

Results
We recruited 62 patients, 53 of whom were women (85.5% of cases) and 9 men (14.5% of cases). The average age was 50.4 years (29-80). Hypothyroidism of peripheral origin was present in 24 patients (38.7%) while hypothyroidism secondary to total thyroidectomy was present in 38 patients which is 61.3% of cases. Twenty-nine patients preferred to take L-thyroxine at the time of Fotour (46.8% of cases), while 33 patients preferred to take it at the time of Sohour (53.2% of cases). Compliance was good in 87.1% of cases and average in 12.9% of cases. In post-Ramadan, 75.8% of patients remained euthyroid, 17.7% hypothyroid and 6.5% hyperthyroid without significant correlation between the two therapeutic schemes (P=0.07).

Conclusion
Fasting during the month of Ramadan may be responsible for hormonal imbalance in patients on L-thyroxine, hence the interest of educating these patients on the use of medication and of a close follow-up after the month of fasting.

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EP1073
A retrospective study of the medical-surgical approach of a cohort of patients with Graves’ orbitopathy
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Objective
To study the characteristics of a cohort of patients with Graves’ orbitopathy (GO) as a self-audit prior to the creation of a multidisciplinary team for the global approach of these patients.

Material and Methods
Retrospective study of patients with GO treated at the Endocrinology and Ophthalmology Services of a tertiary referral hospital (Virgen Macarena University Hospital, Seville, Andalusia, Spain) between 2018 and 2021. The following variables were evaluated in a cohort of 267 patients: demographic data; date and service of diagnosis; number of visits; thyroid function at diagnosis of GO; highest severity of GO and highest level of anti-TRAb (TSI) reached during follow-up; imaging; treatments for GO and EG; smoking.

Results
The results of the 267 analyzed patients are described in Table 1. The severity of the GO was analyzed according to the EUVLOGO classification: 56.93% had mild GO, 41.57% moderate to severe, and 1.50% with visual risk. Highest level of anti-TRAb (TSI) reached during follow-up was recorded in 237 patients of the total, with a mean of 15.93 IU/l ± 13.49 IU/l SD. Regarding the treatment of GD, 89.98% of the patients were treated with antithyroid drugs, 15.36% received radioactive iodine (the majority without corticosteroid prophylaxis) and 40.82% required total thyroidectomy. With regard to smoking, 41.57% were active smokers, with 81% being offered anti-smoking advice and referring 4.4% of all smokers to the Smoking Cessation Unit of the Pneumology Service.

Conclusions
After analyzing our cohort of patients with GO, we have detected some areas for improvement: A corticosteroid prophylaxis deficit has been observed in the context of radioactive iodine administration for the treatment of GD. Referral to the Smoking Cessation Unit should be performed routinely in all smokers with GD. The analysis of these results will allow us to optimize the multidisciplinary management of our patients with GO.

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EP1074
Diagnosis of thyroid adenomas at the outpatient stage
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Methods of radiation diagnostics and fine needle aspiration biopsy (FNAB) are the methods of the first stage of diagnosis of thyroid nodules, which is confirmed by a large number of international recommendations. However, these methods do not always give the right answer for thyroid adenomas. The aim of the study was to study the effectiveness of a set of methods: ultrasound, sonoelastography, scintigraphy and FNAB in the diagnosis of thyroid adenomas. The study included 86 patients with a morphologically confirmed diagnosis of thyroid adenomas only in half of cases. Based on the data obtained, the concept of the need for regulation (sequence) of the complex phased application of methods of radiation diagnostics and cytological examination in the evaluation of patients is formulated.

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EP1075
Bioelectrical Impedance Analysis (BIA) to measure alterations on hydroelectrolytic equilibrium of peripheral cells in COVID-19 patients with nonthyroidal illness syndrome (NTIS)
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In COVID-19 patients the occurrence of low T3 serum values is associated with disease severity and death, but hormonal substitutive replacement is still debated. Clinical trials reported so far failed to demonstrate clear beneficial effects of T3, T4 or both treatments. With the aim to analyze the peripheral effects of the acute deficiency of T3 in blood, we analyzed body fluid composition in 74 COVID-19 patients, admitted to our University Hospital during the last pandemic wave. COVID-19 patients were sub divided into those that presented low FT3 serum levels, i.e., < 1.1 pg/ml, and those that showed normal FT3 serum levels, i.e., > 1.1 pg/ml (n. 32). Body fluid composition was analyzed by Bioelectrical Impedance Analysis (BIA). We demonstrated that COVID-19 patients with low FT3 serum values exhibited increased values of the Total Body Water/Fat Mass (TBW/FFM) ratio. Patients with the lowest FT3 serum values had also the highest level of TBW/FFM ratio, an indicator of the fraction of FFM as water and one of the best-known body-composition constants in mammals. We found an inverse
correlation between FT3 serum values and this constant. Reduced FT3 serum values in COVID-19 patients were correlated with the increase in the total body water (TBW), the extracellular water (ECW) and the sodium/potassium exchangeable ratio (Na\textsubscript{ECW}/K\textsubscript{ECW}) and with the reduction of the intracellular water (ICW). Since the Na\textsubscript{ECW}/K\textsubscript{ECW} pump is a well-known T3 target, we measured the mRNA expression levels of the two genes coding for the two major isoforms of this pump. We demonstrated that COVID-19 patients with NTIS had lower levels of mRNA of both genes in the peripheral blood mononuclear cells (PBMCs) obtained from our patients during the acute phase of the disease. In conclusion, we demonstrated that the acute T3 deficit in our COVID-19 patients has marked effects on the hydroelectrolytic equilibrium of their peripheral blood mononuclear cells. The Na\textsubscript{ECW}/K\textsubscript{ECW} pump is a possible target of T3 action, involved in the pathogenesis of the anasarca condition observed in these patients. Measurement of BIA parameters is a useful method to analyze water and salt retention in COVID-19 patients hospitalized in ICU that develop NTIS and may represent a novel reliable outcome to evaluate the benefit of T3 treatment in future clinical interventional trials.

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### EP1076

**Autoimmune thyroiditis after 2 years covid pandemic: prevalence, clinical features, significance. Study on 450 patients in a medical center of Bucharest-Romania**

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**Material-Method**

We registered from February 26, 2020 until January 23, 2022 (almost 2 years) patients with chronic autoimmune thyroiditis Hashimoto. Usual parameters for this disease were investigated: age, sex, ATPO, FT4, TSH, ultrasound pattern, antibody evolution, immune associations, lost pregnancies, other clinical associations (alergies, breast cancer). Patients were divided into 2 groups: those who had covid-19 (C-19) vs. those who did not have viral disease (NOC).

**Statistical analysis:** Fisher z test (percentage comparisons), X\textsuperscript{2} (discrete data comparisons), T (continuous data comparisons).

**Results**

I. We registered 456 patients. Of these, 84 had covid-19 (18.24%). The prevalence was extremely high compared to the declared prevalence of covid-19 in Romania: 10.95% (https://worldpopulationreview.com/countries/romania/population, https://www.worldometers.info/coronavirus/country/romania). Z = 5.43, P < 0.0001.

II. No differences between patient groups: A. Gender: Female: C-19 = 90.13%, NOC = 89.52%; B. Age of onset (mean, years): C-19 = 50.59 years, NOC = 50.39; C. Current age: C-19 = 55.86, NOC = 55.6; D. ATPO level: C-19 = 7.49, NOC = 7.47; E. TSH level: C-19 = 0.19, NOC = 0.18; F. ATPO evolution: predominantly undulating, 46% vs 67% (P = 0.24).

**F. Thyroid function at onset:** C-19: normothyroidism = 41.7%, hypothyroidism = 44%, hyperthyroidism = 43%, normothyroidism = 41.3%, hypothyroidism = 48.95%, hyper = 9.97%. G. Current thyroid function: C-19: normal = 670.8%, hypothyroidism = 26.19%,hyper = 3.57%. H. NOC: normothyroidism = 67.2%, hypothyroidism = 29.84%, hyperthyroidism = 2.96%.

**H. Pregnancy losses:** C-19 = 7.69%, NOC = 13.21%. I. Immune associations: C-19 = 45.23%, NOC = 37.09%, P = 0.16.

**III. Clinical forms of covid-19.** Asymptomatic = 4, olgiosymptomatic = 4, mild = 27, moderate = 34, severe = 8, very severe = 5, death = 2. Comparison with the evolution of the Romanian general covid population (Pantea-Stoian et al., 2020, Sci. Rep, 21613) is NOT different, but seemingly lighter. For example, the lethality in our group was only 2.38%, while in the general population it was 2.95%.

**Conclusions**

Either 1. Derived from the increased prevalence of immune associations - The genetic structure of the mucosal cells of patients with Hashimoto’s thyroiditis allows the attachment of S protein much faster and to lower viral loads (research to be solved for future generations). Either 2. Derived from the lack of difference between groups and set mathematical analysis - the prevalence of covid-19 in Romanian society was not 10.95%, but 18.24%, as it appears in our group of patients with chronic autoimmune thyroiditis Hashimoto.

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### EP1077

**Clinical and paraclinical features of ectopic thyroid gland in adult patients.**

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**Introduction**

Ectopic thyroid gland is a rare pathology due to an abnormality in the embryological development and/or migration of the gland. The aim of this study was to assess clinical and paraclinical characteristics of adult patients with ectopic thyroid gland.

**Methods**

This was a retrospective study including adult patients with ectopic thyroid gland. Clinical, biological, hormonal, radiological and therapeutic data were collected.

**Results**

Five patients (four women and a man) were enrolled in this study. Their median age was 40 years [extremes: 17-61]. Their past medical history included intellectual disability, stature retardation, and type 2 diabetes mellitus in two cases respectively and vitiligo in one case. All patients were referred to our department for management of hypothyroidism. On physical examination, all patients had non-palpable thyroid gland. The mean TSH level at baseline was 48.7 mIU/l [extremes: 7.6 -100]. Three patients had overt hypothyroidism and two patients had subclinical hypothyroidism. Two patients had a cervical ultrasound showing an empty thyroid compartment. Two other had cervical CT scan, showing sublingual mass in one case and retropharyngeal mass in the other. Thyroid scintigraphy was performed to all patients, showing two sublingual thyroids in one left paramedian and one retropharyngeal. All patients were put on replacement therapy. The doses of levothyroxine to achieve euthyroidism varied from 75 μg to 200 μg/day.

**Conclusion**

The diagnosis of ectopic thyroid gland should be suspected in patients with hypothyroidism associated to a non-palpable thyroid gland in normal position even in adults. Its confirmation is radiological based on the scintigraphy.

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### EP1078

**The relationship between type 2 diabetes mellitus with metabolic syndrome and clinical hypothyroidism**

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**Introduction**

Metabolic syndrome is a multifactorial disease with multiple risk factors that arises from insulin resistance accompanying abnormal adipose deposition and function, increasing the risk of type 2 diabetes, one of the most common endocrine pathologies. Abundant evidence suggests an association between TSH levels, insulin resistance and some markers of the metabolic syndrome, without foreseeing the kind of this link. The aim of our study was to search if there was a link between type 2 diabetes with metabolic syndrome and hypothyroidism, and to explore the markers that are specially correlated with thyroid status.

**Materials and methods**

Retrospective study including 100 patients with type 2 diabetes showing criteria of metabolic syndrome, carried within the diabetology department ‘A’ of the National Institute of Nutrition in Tunis.

**Results**

70% of patients had a normal thyroid balance (euthyroid group (G0)) and 30% presented a clinical hypothyroidism (hypothyroid group (G1)). The average age in G0 was 57.8 years compared to 60.8 years in G1 (P<NS). All G1 patients were female (100%) compared to 82% in G0 (P=0.01). Median diabetes duration was 9.78 years in G0 compared to 11.76 years in G1 (P=NS). 51.43% of patients were on insulin in G0 vs 66.66% in G1 (P=NS). The average BMI of G0 patients was 35.9 kg/m\(^2\) compared to 36.48 kg/m\(^2\) in G1 (P=NS). Mean fasting blood glucose was significantly higher in G1 than G0 (12.19 mmol/l vs 10.36 mmol/l; P<0.01). The hypothyroid patients had more often low levels of HDL-cholesterol and high levels of triglycerides (respectively 60% vs 57.14% in G0; P=NS and 30% vs 28.57% in G1; P=NS). Hypercholesterolemia was significantly more common in G1 than G0 (63.33% vs 25.71%; P=0.0003). The occurrence of cardiovascular events was observed in 11.43% of patients in G0 compared to 6.66% in G1 (P=NS). Thyroid status didn’t have any influence on blood pressure.

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control (mean systolic and diastolic blood pressures were 137 mmHg and 79 mmHg, respectively in both groups).

Conclusion
The prevalence of hypothyroidism among our patients with type 2 diabetes was much higher than in the common population. Our hypothyroid patients had significantly higher fasting blood glucose levels and were more likely to be treated with insulin and to have low levels of HDL cholesterol and high levels of triglycerides. The recommendation for systematic exploration of thyroid status in patients with type 2 diabetes with metabolic syndrome requires larger-scale studies.

**Endocrine Abstracts (2022) Vol 81**

**EP1079**

**Thyroiditis revealing a congenital anomaly: about an observation**

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Introduction
Remnants of the fourth branchial arch are extremely rare with less than 100 cases reported in the literature and account for 1-4% of all branchial anomalies. These anomalies typically present as recurrent neck infections and/or abscesses or acute suppurrative thyroiditis. We report a case of cyst of the 4th cleft revealed by a thyroiditis treated in our department.

Case report
A 6-year-old boy presented with recurrent neck swellings. During that time, he had a history of drainages, and attempted excisions, with recurrence of signs and symptoms after every intervention. Upon presentation to our clinic, he complained of painful swelling of his neck. Clinical examination revealed swelling of the anterior left neck that was tender to palpation and was approximately 5 cm. Ultrasound showed an irregular oval mass with polylobed contours, measuring 54 x 30 mm, multi-loculated, of base-cervical left location and pushing back the homolateral carotid axis and the left lobe of the thyroid which is of heterogeneous appearance. Computerized tomography scan showed a lobulated and multi-loculated mass of lateral and base-cervical left location measuring 54x42x57 mm which compressed anteriorly the sternocleido-mastoid muscle as well as the left lobe of the thyroid. In the operating room, direct laryngoscopy revealed a sinus tract originating from the left side of the pyriform sinus apex; surgical exploration of the neck revealed the tract to pass through the hypopharyngeal wall, consistent with a fourth branchial anomaly. All scar from sinus apex; surgical exploration of the neck revealed the tract to pass through the hypopharyngeal wall, consistent with a fourth branchial anomaly. All scar from

Conclusions
Fourth branchial arch anomalies are rare and fascinating aberrations of fetal development that may present in many different ways such as thyroiditis. Combining a proper preoperative evaluation with careful surgical planning may result in the proficient eradication of these lesions, offering the patient relief from this source of recurrent infection.

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**EP1080**

**Neutropenia in hyperthyroidism**

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Introduction
Neutropenia can indicate infectious and hematological pathology but it can also be a sign of hyperthyroidism. For this reason, it has been suggested to perform a complete blood count before starting treatment with antithyroid drugs in case of new-onset hyperthyroidism. Antithyroid drugs can cause severe neutropenia, also called agranulocytosis, when the neutrophil count is less than 500/μL. Therefore, the use of these drugs should be reconsidered if it is less than <1000/μL, and, in the event of symptoms compatible with agranulocytosis, treatment should be interrupted according to the recommendations of the American Thyroid Association (ATA). Agranulocytosis is a rare adverse effect of antithyroid drugs, appearing in 0.1%-0.5% of cases. However, there is no evidence that neutropenia in patients with hyperthyroidism is associated with an increased risk of antithyroid-induced agranulocytosis.

Objectives
We studied the prevalence of neutropenia in patients with hyperthyroidism and the variations in the neutrophil count with the use of antithyroid drugs.

Material and Methods
We analyzed 52 cases of hyperthyroidism due to Graves Basedow disease diagnosed between 2014-2020. 8 men and 44 women with a mean age of 46 years (range 22-74). We studied the presence of neutropenia at diagnosis and during treatment with antithyroid drugs (methimazole or carbimazole). We classify neutropenia as mild 1000-1600/μL, moderate 500-1000/μL and severe (<500/μL).

**Results**
5 patients presented neutropenia (9.61%), 2 at diagnosis and 3 during treatment. All the neutropenias found were mild (1000/μL - 1600/μL), without clinical repercussions, and resolved during follow-up. Only 1 patient continued to present neutropenia from diagnosis until the 6th month of treatment. There were no cases of agranulocytosis.

Conclusions
Knowledge of the relationship between hyperthyroidism and neutropenia is essential for a correct diagnosis and treatment. Despite the limitations of our study, the cases of neutropenia in the context of hyperthyroidism were mild and the neutropenia was resolved without the development of agranulocytosis. This reinforces the idea that antithyroid treatment is not contraindicated in patients with mild neutropenia.

**DO: 10.1530/endoabs.81.EP1080**

**Table 1**

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<th>Control group</th>
<th>Neutropenia group</th>
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<tr>
<td>Control</td>
<td>Neurotis (%)</td>
<td>1/L</td>
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<tr>
<td>Baseline</td>
<td>3333</td>
<td>47.79</td>
</tr>
<tr>
<td>1-3 months</td>
<td>3753</td>
<td>54.49</td>
</tr>
<tr>
<td>2-6 months</td>
<td>3852</td>
<td>50.93</td>
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normal amylasemia and negative cardiac markers. Due to persistent sinus tachycardia, thyroid function was requested and showed TSH <0.004 uU/mL (0.4-4.0); free-T4 > 5.0 ng/dL (0.7-1.5) and free-T3 > 20 pg/mL (1.8-4.2). The diagnosis of thyrotoxicosis was assumed with Burch-Wartofsky Scale of 60 points. The patient did not have any known thyroid disease. Propituitaric, corticosteroids, chloroethamine and propanolol was started. She was initially stabilized in an Intermediate Care Unit due to congestive heart failure requiring non-invasive mechanical ventilation. The microbiological study was negative and no precipitating factor was found. TRABS and thyroid stimulating immunoglobulin were both detected: 9.7 U/I (< 1.0) and 1.0 U/I (<0.1) respectively. Thyroid ultrasound showed multinodular goiter with 2 larger nodules measuring 4 and 2 cm. She did not have Graves’ orbitopathy. The patient was discharged after clear improvement of thyroid hormones: free-T4 1.60 ng/dL (0.7-1.5); free-T3 3.6 pg/mL (1.8-4.2) and underwent total thyroidectomy a few months later. Conclusion Long-term, disabling schizophrenia with a predominance of negative symptoms led to the devaluation of initial complaints - interpreted as psychiatric decompensation. In fact this was the second time the patient went to the emergency department with the same symptoms of restlessness and agitation without a obvious cause. The time between the onset of symptoms and diagnosis was 5 days. Fever, persistent tachycardia and the patient’s objective state of discomfort in the absence of appreciable analytical or ultrasound alterations led to the diagnosis.

Key words: hyperthyroidism, Graves’ disease, block-replace therapy, lipid profile.

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EP1083

Abstract Withdrawn

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EP1084

Basedow disease and Susac syndrome: an exceptional association

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Introduction Susac syndrome is a rare endotheliopathy causing micro-ischemic damage to vessels in the brain, ears, and eyes. While the underlying aetiology of this disease remains unknown, it is widely believed that observed clinical manifestations result of an autoimmune endotheliopathy. Herein we report a case of Basedow’s disease associated to a scarce condition: Susac syndrome.

Observation Our patient is a 48-year-old woman, who was admitted for chronic holoscleral headache, without blurred vision nor vomiting. Physical examination only revealed a right hemiparesis. The brain MRI highlighted temporal and periventricular oval demyelinating lesions with T2 hyperintensity and T1 hypointensity. These lesions were also described in the corpus callosum. An audiogram was performed and showed a bilateral and symmetric perceptive deafness. Ophthalmologic examination described a decreased visual acuity. Retinal fluorescein angiography showed bilateral and diffuse vasculitis. Somatosensory evoked potentials had a slightly decreased amplitude. Visual and auditory evoked potentials were normal. Cerebrospinal fluid testing did not show any abnormality. Therefore, the diagnosis of Susac syndrome was made. Thrombophilia testing and antinuclear antibodies were negative. She had a biological inflammatory syndrome and low levels of TSH. The thyroid scintigraphy was compatible with a Basedow’s disease. We started treatment with radioactive iodine. Treatment of Susac syndrome consisted of three bolus of methylprednisolone (1g/day for 3 days). Oral corticotherapy was then prescribed, with a good clinical and biological evolution.

Conclusion Susac syndrome is caused by a microangiopathy that gives the classic clinical triad of subacute encephalopathy, visual loss secondary to retinal branch occlusions, and sensorineural hearing loss. Given autoimmune part of Susac aetiology, association to other autoimmune condition, especially Basedow disease, must be actively sought. Early therapy may reduce sequelae and improve recovery.

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EP1085

The diffuse sclerosing form of papillary carcinoma of the thyroid

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Objective Papillary thyroid carcinoma is the most common malignant tumor of the thyroid, the diffuse sclerosing variant is however very rare and represents between 0.7 and 6.7% of all papillary thyroid carcinomas. We propose through this poster to study its clinical, epidemiological, therapeutic and prognostic characteristics.

Materials and methods We report two cases of diffuse papillary sclerosing carcinoma of the thyroid, collected at the ENT and CCF service of the Farhat Hached University Hospital of Sousse.

Results The 2 patients were a man aged 38 years old and a women aged 55 years old with a family history of papillary thyroid carcinoma. The reasons for consultation were...
right supercervical swelling that had been present for 5 months in the man and right jugulocarotid adenopathy that had been present for 4 months in the woman. Cervical ultrasonography revealed a 2 cm right supraclavicular adenopathy containing fine microcalcifications and multiple microcalcifications were noted in the right lobe of the thyroid which contained a 10 mm nodule fully calcified in men and a suspicious nodule classified EUtirads 5 of 33 mm in women. Both patients underwent total thyroidectomy with dissection of the bilateral central lymph node and homolateral lateral one. Extemporaneous examination revealed papillary carcinoma in the female patient, whereas it was in favor of benign in the male patient. The final histological examination showed a papillary carcinoma in its diffuse sclerosing variant with sub-millimetric microscopic foci of epithelial malignant tumor proliferation, disseminated throughout the right lobe of the thyroid in men and infiltrating both thyroid lobes and peri-thyroid fat in women, as well as multiple endolymphatic emboli and lymph node metastases in the mediastinum-recurrent, jugulocarotid and supraclavicular. The postoperative period was dominated by the appearance of transient hypoparathyroidism. Both patients received additional treatment with radio-active iodine. The evolution was good. The decline was 12 months.

Conclusion

The diffuse sclerosing variation of papillary carcinoma is an uncommon histological form distinguished by its locally aggressive nature and deceptive clinical appearance. Its therapy must be complete.

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EP1068

Failure of rhTSH-stimulated FDG PET-CT scan to identify metastases of a papillary thyroid carcinoma

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Introduction

Recurrences of differentiated thyroid carcinoma are occasionally hard to locate; rhTSH-stimulated PET-CT may offer a higher sensitivity, particularly when thyroglobulin in high, but its utility has not been clearly established.

Methods

Review of the patient’s clinical record

Results

A 61 years old woman noticed a right anterior neck lump when she was 47; FNAC was suggestive of a solid papillary thyroid carcinoma and she underwent right thyroid lobectomy. The pathology diagnosis was atypical papillary trabecular carcinoma (5.5 cm maximal diameter) with oncocytic changes, with minimal extracapsular invasion but clean surgical margins. She underwent left lobectomy two months later, with normal pathology, followed by ablation with 125 mCi of 131-I one month later, and substitution therapy with levothyroxin ever since. One year afterwards, the rhTSH test was negative, and follow-up thyroglobulin, antithyroglobulin antibodies and neck ultrasonography were negative for the next 9 years. By the tenth year, thyroglobulin was detectable (1.1 ng/mL) and increased in the 11th and 12th years (2.14 and 2.75 ng/mL) but thyroid gamma scintigraphy scans were negative, and ultrasound only revealed unspecific latero-cervical adenopathies, with negative FNAC. A CT scan showed only two well-defined pulmonary nodules of 7.5 mm maximum diameter in the lingula and the apical segment of the left lobe. A new rhTSH test with peak TSH of 87.5 mIU/l showed little response (baseline and stimulated thyroglobulin 5 and 7.5 ng/mL respectively) with negative stimulated gammagrapy scan. An FDG PET-CT was ordered (13th year) showing only the two known pulmonary nodules, stable in size (both 7.0 mm), without metabolic criteria of malignancy (SUVmax: 1.7). In order to elucidate if the nodules could be metastatic, a new FDG PET-CT was performed (14th year) after rhTSH stimulation, thyroglobulin showed again a modest response (8.25 to 10.4 ng/mL) and the nodules showed a small increase (10 mm) and an increase in metabolic activity under stimulation (SUVmax 1.3 to 2.3). Ablation with 150 mCi of 131-I was performed, but the gammagrapy scan did not show enhancement of the pulmonary nodules. One month afterwards, the patient’s thyroglobulin was not substantially decreased (8.25 to 7.80 ng/mL).

Conclusions

The use of rhTSH-stimulated FDG PET/CT reportedly changes the patients’ thyroglobulin was not substantially decreased (8.25 to 7.80 ng/mL).

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EP1087

Autoimmune thyrotoxicosis Post SARS CoV-2 Vaccination

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Introduction

Covid-19 vaccination have been introduced to reduce overall severity and mortality of COVID-19 infection. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is a syndrome first described in 2011 that triggers autoimmune conditions after exposure to various adjuvants through various mechanisms. We report three cases of autoimmune thyrotoxicosis post mRNA type vaccine for COVID-19 possibly linked to adjuvants present in the vaccine.

Case 1

A 34-year-old patient was newly diagnosed with Grave’s disease, within 1 month after her SARS-CoV-2 vaccine (Pfizer-BioNTech) when she presented with symptoms of palpitations, heat intolerance and a painless neck swelling. Physical examination revealed fine tremors with a diffuse goiter present. Results of biochemical workup was as follows: TSH (Thyroid stimulating hormone): <0.008 mIU/l (low), FT4 (free thyroxine): 123.1 pmol/l (elevated), FT3 (free triiodothyronine): 9.10 pmol/l (elevated), anti-TPO (antithyroid peroxidase) : 9.51 IU/ml (normal), anti TG (antithyroglobulin): 11.04 IU/ml (normal), TSHrAb (anti-TSH antibody levels): 30.03 IU/l (elevated). Ultrasound thyroid revealed increased vascularity in bilateral thyroid lobes with heterogeneous appearance. She was started on oral Carbimazole and Propranolol.

Case 2

A 29-year-old healthcare worker with underlying thyrotoxicosis in remission for 7 years presented with symptoms of heat intolerance, agitation, oligomenorrhea, mood instability, palpitations and diarrhea within 1 month after her 1st dose of SARS-CoV-2 vaccine (Pfizer-BioNTech). Physical examination revealed fine tremors with no thyroid eye signs or goiter present. Results of biochemical workup was as follows: TSH: <0.006 mIU/l (low), FT4: 29.4 pmol/l (elevated), FT3: 8.47 pmol/l (elevated), anti-TPO: 254.8 IU/ml (elevated), anti-TG: 30.13 IU/ml (normal), TSHrAb: <0.8 IU/l (normal). Thyroid ultrasound revealed increased vascularity. She was started on oral Carbimazole and Bisoprolol.

Case 3

A 30-year-old healthcare worker with underlying thyrotoxicosis in remission for 9 years also presented with lost of weight of 6 kg, heat intolerance and fine tremors, within 1 month after her 1st dose of SARS-CoV-2 vaccine (Pfizer-BioNTech). Physical examination revealed fine tremors with no thyroid eye signs or goiter present. Results of biochemical workup was as follows: TSH: <0.008 mIU/l (low), FT4: 56.6 pmol/l (elevated), anti-TPO: 375.7 IU/ml (elevated), anti-TG: 169.9 IU/ml (elevated), TSHrAb: <0.8 IU/l (normal). Thyroid ultrasound revealed increased heterogeneity and increase vascularity in bilateral thyroid lobes. She was started on oral Carbimazole and Propranolol.

Conclusion

This case series reports three cases of autoimmune thyrotoxicosis post vaccination with Pfizer-BioNTech against COVID-19. Any emerging symptoms of thyrotoxicosis post vaccination should prompt clinicians to screen appropriately. However, the benefits of vaccination still outweigh any risks and should be advocated for all patients unless they have other contraindications.

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EP1088

Amiodarone-induced thyrotoxicosis refractory to medical therapy: A case report

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Introduction

Amiodarone is an anti-arrhythmic drug rich in iodine compounds. One 200 mg tablet corresponds to about 25 times the daily requirement of iodine. One of the main complications of taking Amiodarone is the development of dysthyroidism which is observed in 15% to 20% of cases. Hyperthyroidism occurs in 1 and 13% of these patients.

Case Report

We report the case of an 34 year old female patient, followed for complete arrhythmia by atrial fibrillation under Amiodarone 200 mg/d, who presented a thyrotoxicosis with TSH at 0.005 mIU/l, FT3 at 1.5 times normal and FT4 at 2 times normal. Anti-TPO and TSH receptor antibodies were negative. Cervical ultrasound showed an enlarged thyroid. Thyroid scintigraphy was white.
**EP1089**

The role of ACTB status for early non-invasive detection of papillary thyroid carcinoma

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Introduction

Papillary thyroid carcinoma (PTC) is the most common type of differentiated thyroid cancer of all cases of thyroid cancer. Fine-needle biopsy by ultrasonography is still the main diagnostic method of PTC, but there is a technical limitation. That’s why, a minimally invasive diagnostic test that can accurately diagnose the onset of the disease is the subject of research.

Our objective

We aimed to explore the concentration levels of ACTB in PTC patients, healthy controls (HC) plasma samples and to compare with clinicopathological factors.

Methods

Study included 154 patients treated at Hospital of Lithuanian University of Health Sciences, Kaunas clinics 2020 - 2021: 68 patients with a histologically confirmed diagnosis of PTC and 86 HC. The concentration of ACTB was measured by qPCR in plasma samples. Statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). The results were considered statistically significant at $P < 0.05$.

Results

Average age at diagnosis was 48.19 ± 14.9 years in PTC group and 45.30 ± 12.07 years in HC ($P = 0.05$). In the PTC group, there were 8 male patients (11.8%) and 60 female patients (88.2%), while in the HC: 65 (75.6%) female and 21 (24.4 %) male patients ($P = 0.05$). The concentration of ACTB was significantly higher in the PTC patients compared to HC (1005.97 vs 623.12 ng/ml, $P = 0.047$). We observed that ACTB concentration were significantly higher in PTC with greater tumor size (> 2 cm) compared to lower ($\leq 2$ cm) tumor size ($P = 0.005$). The total tumor size was calculated as the sum of the diameters of all tumors in PTC multifocal cases. A weak positive correlation between the concentration of ACTB with the total size of PTC tumors was found ($P=0.012$, r = 0.304). However, there was no correlation between lymphovascular invasion, lymph node metastasis and other clinicopathological features.

Conclusion

This analysis included comparison of the ACTB concentration associations between PTC patients, HC groups and clinicopathologic factors. We found that plasma concentration of ACTB was significantly higher in patients with greater tumor size. Our study indicated that ACTB concentration changes may be used as parameter in differentiating PTC patients from HC. But further studies are also warranted to expand upon our findings.

**EP1090**

Thyroid carcinoma and anti-synthetase syndrome: A rare association!

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Background

Anti-synthetase syndrome (ASS) is an idiopathic inflammatory myopathy (IIM). Clinical features may include myositis, interstitial lung disease (ILD), non-erosive arthritis, Raynaud’s phenomenon, and mechanic’s hands with the presence of anti-synthetase antibodies. Although ASS-neoplasia association has been reported, it remains scarce and debated association. Herein, we report an original case of thyroid carcinoma in a patient followed for ASS.

Case report

A 40-year-old woman, consults for myalgia and weakness of the 4 limbs since 4 months. She presented with progressive proximal muscle deficit, elevated muscle enzymes, mechanic’s hands, ILD and positive anti-JO1 antibodies, thus she was diagnosed with ASS. Treatment was based on corticosteroids and Cyclophosphamide with good evolution. Initial screening for neoplasia was negative. Six years later, during a routine check-up, examination found a centimetric thyroid nodule. Thyroid function test was normal. Cervical ultrasound showed a 7mm right lobar thyroid nodule classified as EU-TIRADS 5. Fine needle aspiration found cytological atypia of undetermined significance. Total thyroidectomy was performed. Pathological examination concluded that a non-encapsulated intrathyroid papillary carcinoma. In addition to the surgical treatment, the patient received radioactive iodine with good outcome. The current follow-up is 2 year.

Discussion

We report the occurrence of thyroid neoplasia in a patient diagnosed with IIM, after 6 years of follow-up. The originality of this case is due to of the type of the IIM and the delay in the onset of the cancer in relation to its diagnosis. Compared to other IIM, ASS’ association to neoplasia is still debated: in the cohort of Pinal-Fernández, with 169 ASS patients, the frequency of cancer doesn’t seem higher than that of the general population. The Chinese cohort of Shi, with 124 ASS patients, found that 6.5% developed neoplasms, with a mean time of 3 years between neoplasia and SAS, of which, the majority presented with ILD. In the review carried out by Bolet, male gender, age over 60 years, and the presence of anti-SSA/Ro were predictive factors of development of cancer in ASS patients.

Conclusion

Thyroid carcinoma was discovered in our observation during regular screening for ASS-associated neoplasia. Thyroid carcinoma-ASS is an extremely rare but possible association, which will need to be detected and treated. Given the rarity of ASS, recommendations regarding the systematic screening for cancer have yet been established. In the meantime, we must remain vigilant about the possibility of the occurrence of cancer in these patients, and therefore ensure regular screening.

**EP1091**

Diarrhea as the only symptoms in hyperthyroidism- case report

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Introduction

Hyperthyroidism (overactive thyroid) is a condition where thyroid makes and releases high levels of thyroid hormone (thyroxine) in the blood. This condition can speed up our body metabolism. Hyperthyroidism causes an overactivity of the sympathetic system. It also this sympathetic hyperstimulation in the gut leads to increased motility causing diarrhea, malabsorption and consequently weight loss.

Objective

To describe a patient with hyperfunxional nodular goiter and diarrhea as the only symptoms, for which Unimazole (ATS), was found to be effective therapy for the diarrhea.

Methods

We present the clinical course of a old woman with a prolonged diarrhea which with all diagnostic procedures and medication given did not improve until it was thought to be an endocrine cause. Unimazole control of such cases of hyperthyroidism with diarrhea can be explained by the effect of this drug in reducing intestinal hypermotility as the basis of physiopathology in hyperthyroidism.
Case Report of Hypothyroidism as a Cause of Ataxia

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We present a case of a 56-year-old male who reported to us with history of instability of gait since one year which was acute in onset and progressive, there was also history of hearing impairment and constipation since 3 years without improvement despite several symptomatic treatments. There was no history of weakness in any part of body, headache, vomiting, convulsions or alteration of sensorium. There was no history of trauma to the head, fever or drug intake. On examination, his vitals were normal. Neurological examination showed gait ataxia, dysarthria and dysmetria on finger-nose and heel-to-knee tests. The gait was wide-based and there was a tendency to fall to right side. His fundus was normal. His power was normal but had hung up reflexes. Sensory system was normal. His hemogram was normal. Serum electrolytes, blood sugar, renal and liver function tests were normal. Neurological examination showed gait ataxia, dysarthria and dysmetria on finger-nose and heel-to-knee tests. The gait was wide-based and there was a tendency to fall to right side. His fundus was normal. His power was normal but had hung up reflexes. Sensory system was normal. His hemogram was normal. Serum electrolytes, blood sugar, renal and liver function tests were normal. Neurological examination showed gait ataxia, dysarthria and dysmetria on finger-nose and heel-to-knee tests.

Results
A 73-year-old woman, has not previously had gastrointestinal disorders, had prolonged diarrhea, which associated with loss of 3 kg during a 1-month period. Laboratory, ultrasound images, recommended by the infectious disease doctor could not detect the cause of this prolonged diarrhea. Despite antibiotic treatment and antidiarrheal treatment, diarrhea did not stop. Other hyperthyroidism symptoms were not reported, but when hyperthyroidism was identified, the diarrhea was dominated and very well controlled by treatment with unimazole.

Conclusion
Thyroid hormone in excess, among its other possible effects in the organism, affect the gastrointestinal tract through sympathetic intestinal hyperstimulation and increased motility causing diarrhea. Antithyroid therapy act by blocking sympathetic hyperstimulation. Our case leads us to think that hyperthyroidism should be considered in the differential diagnosis of diarrhea of unknown cause.

Keywords diarrhea, unimazole, hyperthyroidism.

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Successful treatment of Graves’ disease with high dose iodine-131, without subsequent hypothyroidism: a case report
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Background
Radioiodine is an effective treatment for Graves’ hyperthyroidism. In most cases this therapy renders the patient completely hypothyroid. As a consequence they will require lifelong thyroid replacement therapy. Now it is controversial whether radioiodine should be given in a sufficient dose to induce hypothyroidism or a lower dose in an attempt to achieve a euthyroid state.

Case Report
A 71-year-old woman with a 30 years history of Graves’ disease and frequent recurrences of thyrotoxicosis presented with tremulousness, palpitations, dyspnea, progressive fatigue and weight loss. Examination revealed BMI 28 kg/m². P 105 bpm, BP 150/80 mmHg. An ECG showed sinus tachycardia. Laboratory analyses showed recurrence of hyperthyroidism: TSH 0,19 mIU/l, T4 1,75 mIU/l, FT4 0,68 ng/dl. Methimazole was canceled 3 days before the procedure. The introduction of I-131 was well tolerated. Patient had normalization of thyroid function tests within 4 weeks. Hyperthyroidism occurred 12 weeks after radioiodine (TSH 46,4 mIU/l, FT4 0,23 ng/dl). Then thyroid replacement therapy (75 mg of levothyroxine) was initiated. However, within the 6 month after treatment the patient presented subclinical hyperthyroidism and the dose of levothyroxine was reduced and then canceled. Ultrasound showed residual thyroid tissue (total volume 18 ml). The patient is currently euthyroid (TSH 0,58 mIU/l) and under follow-up.

Conclusion
For patients with Graves’ disease, a high dose of radioiodine is directly related to the cure rate and the incidence of hypothyroidism. The most preferred is to individualize the radioiodine dose based upon the size of the thyroid gland and the 24-hour radioiodine uptake. In this case, a persistent goiter suggests incomplete destruction of the gland and the possibility of persistent autonomous thyroid tissue. After radioiodine, all patients require monitoring for hypothyroidism or persistent hyperthyroidism.

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Retropelletal hematoma: A dreaded complication of hypothyroidism: An observational study
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Introduction
Hypothyroidism is the most common endocrine dysfunction during pregnancy. In pregnancy, hypothyroidism is most often due to chronic autoimmune thyroiditis (Hashimoto’s disease) The consequences of hypothyroidism vary depending on the time of onset of hypothyroidism during pregnancy and the etiology of improved. According to medical history she had poor control of the disease by drugs. Surgery was risky for the elderly patient. Therefore radioactive iodine ablation was suggested. Iodine-131 was administered orally at individual dosage of 13 millicuries (based on 200 microCi/g of thyroid tissue). Previous to therapy thyroid laboratory results showed TSH 1,75 mIU/l, FT4 0,68 ng/dl. Methimazole was canceled 3 days before the procedure. The introduction of I-131 was well tolerated. Patient had normalization of thyroid function tests within 4 weeks. Hypothyroidism occurred 12 weeks after radioiodine (TSH 46,4 mIU/l, FT4 0,23 ng/dl). Then thyroid replacement therapy (75 mg of levothyroxine) was initiated. However, within the 6 month after treatment the patient presented subclinical hyperthyroidism and the dose of levothyroxine was reduced and then canceled. Ultrasound showed residual thyroid tissue (total volume 18 ml). The patient is currently euthyroid (TSH 0,58 mIU/l) and under follow-up.

Conclusion
For patients with Graves’ disease, a high dose of radioiodine is directly related to the cure rate and the incidence of hypothyroidism. The most preferred is to individualize the radioiodine dose based upon the size of the thyroid gland and the 24-hour radioiodine uptake. In this case, a persistent goiter suggests incomplete destruction of the gland and the possibility of persistent autonomous thyroid tissue. After radioiodine, all patients require monitoring for hypothyroidism or persistent hyperthyroidism.

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EP1092

EP1094

EP1095

EP1096
retroplacental hematoma is a serious complication of hypothyroidism. We report the case of a patient with uterine fetal death on retroplacental hematoma complicated by hypothyroidism.

Observation

The patient is a 35-year-old female. History: followed for hypothyroidism on levothyroxine 150 mg/d. Admitted for heavy metrorrhagia with obstetrical ultrasound has objectified: fetal death in uterus with evidence of a retroplacental hematoma. On clinical examination, the patient was in severe shock: blood pressure 110/50 mmHg, heart rate 93 bpm. Non-palpable thyroid. The rest of the exam was unremarkable. On the balance sheet: Hemoglobin 6.9 g/dl, White blood cells 9.11×10^9/l, platelets 300 000/mm^3, Cervical ultrasound: atrophic thyroid gland.

Therapeutic care

The patient was put on levothyrox: 175 mg/d. A cardiovascular evaluation has been requested.

Discussion

-Retroplacental hematoma is a polycausal disease with etiological factors (vascular, age, environmental). -Publications suggest that dysthyroidism and more particularly hypothyroidism may be a risk factor for Retroplacental hematoma. According to a study published in 2013, RPH in hypothyroidism can be explained by several factors: thyroid hormones play a very important role in Placentation: 11–16 amnion week. (defined as Invasion of trophoblasts into the maternal decidua and the spiral artery). In Hypothyroidism: insufficient trophoblastic invasion responsible for ischemia and placental abruption. Hypothyroidism is associated with thrombo-embolic and hemorrhagic phenomena which is explained by the alteration of the coagulation system – fibrinolysis the presence of anti tpo ac is more likely associated with other immune diseases and alteration of the immune system another study published in 2020 did not find a significant link between hypothryroidism and RPH.

Conclusion

This observation underlines the importance of determining the place of this risk factor within the various FDRs of RPH already known and the need to set up preventive strategies, in particular when the usual effective treatment of hypothyroidism is lacking.

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**EP1097**

A real localization of lymph node metastasis from papillary thyroid carcinoma

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Introduction

Lymph node (LN) metastases of papillary thyroid carcinoma (PTC) usually happen in the paratracheal and internal jugular chain and are unusual in the parapharyngeal space (FPS). Our aim is to emphasize on the possibility of parapharyngeal metastatic LN in PTC and to describe the diagnosis methods, treatment options, and impact on the prognosis.

Case Report

A 62-year-old woman presented with a dysphagia lasting for 2 years. Examination revealed an anterior neck mass. On ultrasound, it was an EU-TIRADS 5 left thyroid nodule. Consequently, the patient underwent a total thyroidectomy with a bilateral central dissection and a left selective neck dissection (II-IV).

Histopathologic examination of the thyroid gland confirmed the diagnosis of a PTC of the left lobe with metastasis on central and lateral LN dissections. The tumor was staged as pT2 N1b M0. Postoperatively, she had radioactive iodine ablation therapy. She received a cumulated dose of 200 mCi (2 courses).

Ultrasound and thyroid scintigraphy were normal. However, because of a high thyroglobulin (TG) level, a CT scan was performed (3 months postoperatively) and showed a left 3-cm pretortic mass. The mass was hypodense, with some irregular areas of enhancement: a parapharyngeal metastatic LN was suspected.

The patient did not present any symptom related to the mass. On physical examination, there was no evidence of cervical lymphadenopathy, no palpable thyroid lesion, no cranial nerve deficits. The oropharyngeal exam was normal.

A surgical resection of the mass was performed with external cervical approach: a mass measuring 3 × 2 cm was found in the left prestyletoid space. On histopathologic examination, the mass was a metastatic LN of a PTC. Three months after the surgery, the patient was doing fine, with no evidence of disease.

Conclusion

PPS metastases from thyroid carcinoma are uncommon, and only few cases have been reported in the medical literature. These PPS LNs are not included during nodal dissection. If these areas are left undissected, they might be the cause of a persistent disease or a delayed recurrence. As a result, for patients with PTC, especially those who underwent neck dissection and have an unexplained increase in serum TG levels, CT or MRI should be done for surveillance rather than ultrasound to detect the presence of nodes in this compartment.

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**EP1096**

Cholestatic Hepatitis in Graves’ Disease: A case report

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Introduction

Thyrotoxicosis is an uncommon cause of cholestasis. It’s a diagnostic challenge considering the broad differential diagnosis. Herein we report a case of Grave’s disease revealed by severe cholestatic jaundice.

Observation

A 46 old male with a history of Sickle cell disease complained of diarrhea and significant weight loss for eight months, followed the last month by palpitations, heat intolerance, anxiety, insomnia and progressive jaundice. He had no family history of autoimmune disease. He denied hepatotoxic drugs, alcohol use or high risk sexual behavior. On physical examination his body mass was 21.23 kg/m², his blood pressure was 110/50 mm Hg and his heart rate was 93 beats per minute. He had jaundice of sclerae and skin with mild hepatomegaly. His thyroid was symmetrically enlarged. Biochemical findings showed: total bilirubin 183.6 μmol/l (5.4–20), direct bilirubin 135 μmol/l (<8.6), alkaline phosphatase 143 U/l (40–129), AST 69 U/l (1–38), ALT 23 U/l (1–41), TSH 0.005 mU/l (0.27–4.2) and PT 4 61.07 % (12–22). Hepatitis A, B, and C testing were negative and autoimmune screen was unremarkable except positive thyroid-stimulating hormone receptor antibodies. Abdominal ultrasound, computed tomography and MRI revealed hydatid cysts in the VI and VII segment without biliary ductal dilatation. Thyroid ultrasound showed a symmetrically diffuse enlarged, hyper vascular, heterogeneous gland without nodules. Regarding the severity of the cholestasis, methimazole, propranolol and corticoids were administered before radioiodine treatment with a close monitoring of liver function. By day 40, bilirubin fell by 50% (91.4).

Conclusion

This case highlights the merit of considering thyrotoxicosis as a cause of cholestasis as attaining a euthyroid state is critical for hepatic recovery.

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**EP1098**

Malignant non-Hodgkin lymphoma of the thyroid Gland: About 4 cases

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Introduction

Cervico-facial non hodgkin lymphomas are rare conditions; they represent 5% of all malignant tumors of the head and neck. Their localizations are essentially lymph nodes but all the organs can be affected.

Purpose of the presentation

The objective of this work is to determine the clinical, histological and therapeutic aspects of malignant non-Hodgkin lymphoma localized in the thyroid gland.

Methods

This is a retrospective study about 4 patients treated for a malignant non-Hodgkin lymphoma of the thyroid gland, in the ENT and otorhinolaryngology departments of Fatouma Bourguiba hospital in Monastir over a period of 20 years (2000-2019).

Results

The average age was 48 years. A female predominance was noted. The average consultation time was 6 months. Patients consulted for a rapidly progressive goitre in all cases, associated with dysphagia and dyspnea in 3 cases (75%). Cervical examination showed a painful, mobile and indurated anterior cervical swelling in all patients. Associated lymph nodes were found in only one case (25%). Cervical ultrasound and cervico-thoracic scan showed a mass pushing back the trachea in two cases (50%). Fine needle aspiration showed an aspect of a

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large cell lymphoma of thyroid gland in 2 cases (50%). In the histological examination, it was a diffuse large-B-cell lymphoma in the 4 cases. The extension assessment did not objectivize other synchronous locations. Three patients were classified at stage IA, one patient at stage IIA. The treatment consisted on chemotherapy in all patients with no tumor recurrence or relapse in all cases with an average follow-up of 24 months.

Conclusion

Malignant non-Hodgkin’s lymphoma of the thyroid gland is a rare disease. The treatment often gives good results and the prognosis depends essentially on the tumor stage and the speed of treatment.

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EP1099

COVID-19 vaccine-associated subacute thyroiditis

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Introduction

Subacute thyroiditis (SAT) is a self-limiting inflammatory condition caused by follicular destruction of the thyroid gland, commonly precipitated by viral upper respiratory tract infection 2 weeks preceding the onset of thyroid symptoms. However, SAT following COVID-19 vaccination is rare. Herein, we report two cases of subacute thyroiditis which presented after administration of COVID-19 vaccine.

Case series

The first patient was a 42 year old man who reported rapid onset of sore throat, neck pain and symptoms of thyrotoxicosis including weight loss, sweating and heat intolerance. The onset of symptoms was two weeks following his second dose of BNT162B2 mRNA (Pfizer-BioNTech) COVID-19 vaccine. There was no significant medical history and or prior use of medications that would precipitate thyrotoxicosis. He recovered well with a course of non-steroid anti-inflammatory agent. The second patient was a 31 year old lady, with no past medical history, who presented with neck pain and fever and symptoms of thyrotoxicosis three weeks after her third dose of BNT162B2 mRNA (Pfizer-BioNTech) COVID-19 vaccine despite having had two Sputik Covid V vaccine previously. She recovered well with a course of steroids. Both patients had negative TSH-receptor antibodies and thyroid peroxidase antibodies (0.20IU/ml, 0.39IU/ml). Imaging studies were consistent with thyroiditis with no obvious uptake noted on Technetium scan.

Discussion

SAT after vaccination, may develop as a result of direct injury by vaccine attributed by molecular mimicry. Due to the similarity between SARS-CoV2 spike protein and thyroid peroxidase, the cross reaction between the coronavirus spike protein with the TPO antibodies induce an autoimmune/inflammatory response to thyroid follicular cells. As with any form of SAT, treatment is symptomatic with non-steroidal agents and corticosteroids including levothyroxine if patient developed hypothyroidism. In all these cases, association of SAT with the administered vaccines was suggested by temporal relationship between symptom onset and vaccination. Therefore, clinicians are encouraged to be vigilant of autoimmune diseases as possible complications of COVID-19 vaccination, even in patients with mild COVID-19 infections.

Conclusion

SAT can rarely occur following COVID-19 vaccination. Early identification of the possible endocrine side effects of the COVID-19 vaccine can help treat this condition. As SAT is a mild self-limiting illness, its possible association with prior vaccination should not deter people from vaccination.

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EP1110

Thionamides induced hypoglycemia

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A 22-year-old female Ashkenazy Jewish previously healthy complaint on weakness In glucometer, her sugar level was 50 mg% and she felt better after ingestion of a small amount of sugar. 3 weeks ago while traveling in Peru, she developed thyrotoxicosis and was started mercaptitol 30 mg a day and deralin. She didn’t drink iodine (iodinated preparations for water purification) while traveling and had no pain or fever. In physical examination there where no goiter and or exophthalmos While I saw her she was already euthyroid and felt quite good except for tiredness. In literature, we found few case reports of mercaptitol and PTU-induced insulin autoantibodies which cause symptomatic hypoglycaemia. Most cases were described in the Asian population (especially Japanese people) and resolved a few weeks after stopping the drug. In our patient, the hypoglycemia resolved after only one episode and discontinuation of mercaptitol. We don’t have antibodies titer yet, insulin levels (C-peptide) were relatively high My conclusion is that physicians should be aware of Mercaptitol and PTU induced hypoglycemia which can be life-threatening

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EP1102
Differential diagnosis between overt and transient hyperthyroidism in triplet pregnancy
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Introduction
Thyroid health in pregnancy is highly important. Best way to evaluate thyroid in pregnancy, is thyroid function assessment via blood tests. But we always have to focus also on clinical manifestations, thyroid ultrasound and other factors, that may influence test results. As we know high HCG can suppress TSH and twin pregnancy may induce subclinical hyperthyroidism. There are many reports of twin pregnancies, but very few about triplet pregnancy. Therefore we decided to report this rare case.

Case report:
34 y/o women presented with triplet pregnancy on 12 weeks of gestation. Routine thyroid tests showed laboratory picture of overt hyperthyroidism: TSH-<0.005 (0.3-2.5); FT3-3.98 (2.4-4.4); FT4-1.89 (0.93-1.7). On clinical evaluation she had no signs of GO. HR-98, BP-120/80, BMI-18.6. Patient had hyperemesis gravidatum. She lost 6 kg during pregnancy. In previous 2 pregnancies she had normal thyroid functions. Positive family history of AIT. We ordered Anti-TSHR-N, thyroid ultrasound-N. Considering additional tests and mild clinical symptoms, we choose watchful waiting, to distinguish between overt thyrotoxicosis and transient hyperthyroidism of early pregnancy. After 3 weeks laboratory tests came already normal. TSH-0.22; FT4-0.93. We ordered TSH every month thereafter and it stayed in normal trimester-specific range on every occasion. Patient gave birth on 39 weeks of gestation with 3 healthy babies.

Conclusion
Because of potential harm and evidence of fetal risks, we have to be very careful with initiating of Anti-thyroid medications and avoid everusing them, if we don’t have clear diagnosis. As we see in 2-3 weeks thyroid functions may improve by themselves. Also many criteria can help clinicians to distinguish very carefully between real thyrotoxicosis and transient state. Multiple pregnancy is one sign, we must take into account.

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EP1103
Clinical profile and body composition of patients newly diagnosed with hyperthyroidism
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Introduction
Patients with hyperthyroidism usually gain weight, and those with hypothyroidism lose weight. Body weight changes related with thyroid dysfunction support the idea that thyroid hormones have an effect on body weight and body composition. The aim of our study was to describe the clinical profile and body composition of Tunisian patients who were newly diagnosed with hyperthyroidism.

Methods
This was a cross-sectional and descriptive study includes 25 patients: 14 who were newly diagnosed with overt hyperthyroidism (Group1: G1) and 11 who were newly diagnosed with subclinical hyperthyroidism (Group 2: G2). The study was conducted in the Endocrinology and Nutrition Department of the Military Hospital of Tunis during a period of 4 months (March-June 2021). Body composition was assessed by impedancemetry. Statistics were performed using SPSS 20.

Results
The mean age was 49 ± 14 years [20-80 years]. A female predominance was noted (75%). The median TSH level was 20 mU/l [8-95 mU/l]. Cervical ultrasound showed that 25% of patients had thyroid nodules. Anti-Thyroid Peroxidase antibodies were positive in 35% of patients. The mean Body Mass Index was 29 ± 5 kg/m². One third of the patients (35%) were obese. The median weight gain at time of diagnosis of the hyperthyroidism was 0.6 kg [0.4-4.2 kg] (G1: 1.5 kg vs G2: 0.5 kg; P=0.6). Mean percentages of fat mass (FM), lean mass (LM) and water mass (WM) in both groups were respectively (G1: 30 ±9% vs G2: 55 ±8%; P=0.26), (G1: 70 ±9% vs G2: 65 ±8%; P=0.26) and (G1:51 ±7% vs G2:47 ±6%; P=0.26). The mean total cholesterol, LDL-cholesterol and triglyceride levels in both groups were respectively (G1:6.2 ± 2 mmol/l vs G2: 5 ±1 mmol/l; P=0.2), (G1: 3 ± 2 mmol/l vs G2: 3 ± 0.7 mmol/l; P=0.75) and (G1: 1.7 ± 0.7 mmol/l vs 1.7 ± 1.1 mmol/l, P=0.867). Our study showed that increased TSH levels were associated with increased percentages of LM and WM (respectively P=0.01 and P=0.01) and decreased percentages of FM (P=0.02). However, there was no correlation between TSH level and weight gain at time of diagnosis of the hyperthyroidism (P=0.71).

Conclusion
Our study showed that patients newly diagnosed with overt or subclinical hyperthyroidism gained weight. The percentages of different body compartments were correlated with TSH level. However, there was not an association between gain weight and TSH level at time of diagnosis of the hyperthyroidism.

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EP1104
Graves’ disease: Particularities in the pediatric population
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Introduction
Graves’ disease (GD) is the most common cause of hyperthyroidism in pediatric patients, up to 95% in some studies. Observation
We report the observation of a 6-year-old female who consulted for a behavioral disorder made of agitation and lack of concentration. She had a family history of autoimmune thyroid disease. On examination, an accelerated statal growth rate of ≥ 2SD was noted. She had a significant palpebral retraction without exophtalmia. A biological check-up showed a blocked TSH level at 0.01U/l associated with a high T4 at 26.4 pmol/l. In addition, TSH receptor antibodies blockers (trab) were positive at 17.8 U/l for a normal value (NV) of less than 1.5. Anti-thyroidperoxidase antibodies were positive at 148 U/l (NV <20U/l).

The thyroid ultrasound was normal with a normal volume and homogeneous gland. The diagnosis of Graves’ disease was retained and a treatment with methimazole was started at a dose of 0.5 mg/kg/d. The thyroid check-up 3 months later was normal. The treatment is in progress.

Conclusion
GD is a rare condition in children and affects mostly older children with a clear female predominance. Although rare, GD remains the most frequent cause of hyperthyroidism in children. Diagnosis is easier if exophthalmia is present, which is a very specific sign of this condition. However, palpebral disorder is the most common as exophthalmia is less frequent in children. Medical treatment is based on synthetic antithyroid drugs.

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EP1105
Hashimoto’s thyroiditis associated with primary biliary cholangitis: a case report
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Introduction
The association of multi-organ autoimmune disorders is described. We report a case of Hashimoto’s thyroiditis (HT) and primary biliary cholangitis (PBC), both are a chronic autoimmune inflammation, with lymphocytic infiltration and destruction of thyroïd cells for (HT) and progressive destruction of intrahepatic bile ducts leading to cirrhosis for (PBC).

Case report
54-year-old female patient, followed for (PBC) at cirrhosis stage admitted for evacuation of refractory ascites. Interrogatory: signs of hypothyroidism: asthena, constipation, chillness and hair loss, Physical examination of the patient revealed bradycardia at 55bpm, palpable thyroid, end signs of hepatocellular insufficiency: subicterus and stellate angioma. Blood tests revealed a hyperthyroidism (TSH: 26.6U/l; T4: 5.2 pmol/l), end anti-Thyroxopterodase and anti-mitocondria type 2 antibodies are positive.

Discussion
PBC is frequently associated with other autoimmune diseases, the most common of which are Hashimoto’s thyroiditis, Gougerot Sjogren’s disease, celiac disease, and scleroderma, their screening must be systematic in order to initiate early and adequate treatment. As soon as an autoimmune disease is diagnosed, the search
for other organ damage is necessary in order to initiate treatment in the early stages, which improves the patient’s overall prognosis.

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**EP1106**

**Nephrotic lupus revealing a profound hypothyroidism**

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**Abstract**

Systemic lupus erythematosus is a severe autoimmune disease characterised by the production of antinuclear antibodies directed particularly against native DNA. Its presence increases the susceptibility to develop other autoimmune diseases including autoimmune dysthyroidism. We present the case of a patient who presented with profound hypothyroidism as part of the work-up for lupus nephropathy. Female patient, 40 years old, reports physical asthenia for 2 months. On clinical examination: normal BMI, discrete bilateral IMO, homogenous goitre; erythematous lupus lesions on the face. Thyroid assessment: TSH elevated: 100 IU/l; T4I: 1.9 IU/l; T3I: 1, cervical echo: aspect of thyroiditis. Renal check-up: GFR: 20ml/24h; 24h proteinuria: 2.64g/24h; albumin: 30g/l; protein: 69g/l, Immunological check-up: anti TPO + and anti-nuclear and anti-DNA positive; renal biopsy in favour of a membrano-proliferative glomerulonephritis (GNMP). Cardiovascular work-up: normal ECG and TTE without any particularity with LVEF recommended at 65%, normal lipid profile. The patient had been put on levothyrox 25 µg/d with a progressive increase and a corticotherapy for her lupus nephropathy. Most of the studies presented in the literature show a high prevalence and incidence of new cases of hypothyroidism and autoimmune thyroiditis (AIT) in patients with systemic lupus erythematosus (SLE), globally in women. In the presence of lupus, it is advisable to look for thyroid disorders that need to be treated. In the absence of thyroid disorders, long-term monitoring for thyroid disorders is important as thyroid dysfunction has a high probability of occurring later not only because of the autoimmune terrain but also because of glomerulopathy which can be complicated by a nephritic syndrome with leakage of thyroid hormones.

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**EP1107**

**Diarrhea as the only symptoms in hyperthyroidism-case report**

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**Introduction**

Hyperthyroidism (overeactive thyroid) is a condition where thyroid makes and releases high levels of thyroid hormone (thyroxine) in the blood. This condition can speed up our body metabolism. Hyperthyroidism causes an overactivity of the sympathetic system. It also this sympathetic hyperstimulation in the gut leads to increased motility causing diarrhea, malabsorption and consequently weight loss.

**Objective**

To describe a patient with hyperfunctional nodular goiter and diarrhea as the only symptoms, for which Unimazole (ATS), was found to be effective therapy for the diarrhea.

**Methods**

We present the clinical course of a old woman with a prolonged diarrhea which with all diagnostic procedures and medication given did not improve until it was thought to be an endocrine cause. Unimazole control of such cases of hyperthyroidism with diarrhea can be explained by the effect of this drug in reducing intestinal hypermotility as the basis of physiopathology in hyperthyroidism.

**Results**

A 73-year-old woman, has not previously had gastrointestinal disorders, had prolonged diarrhea, which associated with loss of 3 kg during a 1-month period. Laboratory, ultrasound images, recommended by the infectious disease doctor could not detect the cause of this prolonged diarrhea. Despite antibiotic treatment and antidiarrheal treatment, diarrhea did not stop. Other hyperthyroidism symptoms were not reported, but when hyperthyroidism was identified, the diarrhea was dominated and very well controlled by treatment with unimazole. Conclusion

Thyroid hormone in excess, among its other possible effects in the organism, affect the gastrointestinal tract through sympathetic intestinal hyperstimulation and increased motility causing diarrhea. Antithyroid therapy act by blocking sympathetic hyperstimulation. Our case leads us to think that hyperthyroidism should be considered in the differential diagnosis of diarrhea of unknown cause. Keywords diarrhea, unimazole, hyperthyroidism.

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**EP1108**

**Autoimmune thyroiditis and anemic syndrome**

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The purpose was to identify the frequency of occurrence of various morphological types and different degrees of severity of anemia in patients with autoimmune thyroiditis (AIT).

**Material and methods**

Were analyzed 97 case histories of patients operated for AIT in 2012. When assessing hematological parameters, two groups were identified: group 1 – patients with AIT with mild anemia (n = 72), age 45.7 ± 1.6, men - 5 (6.9%), women - 67 (93.1%); group 2 - patients with AIT with moderate anemia (n = 25), age 40.0 ± 2.3, men - 1 (4%), women - 24 (96%). In the clinical analysis of blood, hemoglobin, hematocrit, the number of erythrocytes and erythrocyte indexes of MCV, MCH, MCHC were determined.

**Results**

In patients with AIT with a mild degree of anemia, microcytic anemia was detected in 55 (76.4%), normocytic - in 17 (23.6%) patients. In moderate anemia, microcytic anemia was detected in 21 (84%) patients, normocytic anemia - in 4 (16%) patients. hypochromic type of anemia in the group “all patients” was noted in 79 (81.4%), normochromic type in 17 (17.5%) and hyperchromic in 1 (1%) patient. By morphological type in patients with AIT with mild anemia, the hypochromic type was observed in 56 (77.8%) patients, normochromic - in 16 (22.2%) patients. In moderate anemia, this tendency was more pronounced: hypochromic type of anemia was detected in 23 (92%) patients, normochromic type - in 1 (4%) and hyperchromic in 1 (4%). Thus, in patients with AIT, mild anemia was more often determined (72.4%), then moderate anemia (in 25.7%). With moderate severity of anemia, microcytic (84%) and hypochromic (92%) types of anemia were more often observed. With mild anemia, the same types of anemias were observed, but with a lower frequency (76.4% and 77.8%, respectively).

**Conclusion**

The hemogram in patients with AIT was characterized by a more frequent development of mild anemia (72.4%). With mild anemia, hematological disorders were characterized by microcytic (76.4%) and hypochromic (77.8%) types of anemia. Similar, but more pronounced disorders were observed in moderate anemia: microcytic 84% and hypochromic 92%, which is characteristic for iron deficiency anemia.

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**EP1109**

**Subacute thyroiditis associated with COVID-19**

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COVID-19 is a serious problem of modern medicine. The disease has many manifestations, as it affects almost all organs and systems. One of the target organs of the endocrine system is the thyroid gland. The aim of the study was to identify the patterns of development and course of subacute thyroiditis in patients who underwent COVID-19. The study included 9 clinical cases. In all cases, these

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were women aged 32 to 54 years. All patients were sick with COVID-19 (4 of them were treated at home, 5 - in a specialized hospital). In two patients, the first symptoms of the disease appeared even with a positive PCR test, in 2 patients, symptoms appeared 2 weeks after receiving an already negative PCR test, in 5 - in the interval of 1.5 - 2 months after receiving a negative PCR test. All patients have subfebrility, deterioration of general well-being, sharp weakness. 5 patients complained of an unexpressed headache with irradiation in the neck. This was regarded by all patients as a consequence of the ongoing or recent COVID-19. 4 patients noted discomfort with head movements and swallowing. The examination revealed moderate leukocytosis (11.9±4.7 x 10^9/l), elevated ESR (36±21 mm/h). There were no other symptoms indicating the nature of the disease, except for soreness during palpation in the projection of the thyroid gland in all patients. In this regard, all of them underwent ultrasound of the neck organs, in which heterogeneous hypoechoic darkening was detected, occupying from 14 to 85% of the volume of the thyroid gland, an increase in the lymph nodes of the neck was detected in 6 patients. From the moment of the first symptoms to the diagnosis and the start of treatment, it took from 2 to 4 weeks. At that time, 4 patients were treated for COVID-19, and 5 were undergoing rehabilitation treatment. The difficulty of making a correct diagnosis was due to asthenization and nonspecific symptoms of viral infection, as well as the fact that the development of subacute thyroiditis was preceded by the use of antiviral and antibacterial drugs, as well as glucocorticoids. Sonography was the key diagnostic method for all patients.

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**EP1110**

**A case of graves’ orbitopathy in a patient sero-negative for TSH receptor autoantibody**

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**Introduction**

The orbit represents the second target after the thyroid gland in autoimmune dysthyroidism. In 80% of cases, endocrine orbitopathy occurs as a result of hyperthyroidism, especially Grave’s disease (GD). Males are rarely affected but the damage is more serious.

**Observation**

We report the case of a 52-year-old patient, an active smoker (35 Pack-Year), transferred from the neurology department for treatment of bilateral malignant exophthalmonic subclinical hyperthyroidism. The examination showed a palpable normal sized thyroid with no vascularity. Orbital MRI showed bilateral grade 2 proptosis with oculomotor muscle hypertrophy consistent with Grave’s orbitopathy (GO). The biology showed a subclinical hyperthyroidism, but the assay of the anti-TSH receptor antibodies came back negative twice. A thyroid scintigraphy was performed and it confirmed the Grave’s disease. The patient was treated with corticosteroid therapy for his GO and showed a slight improvement. As for his subclinical hyperthyroidism, he was put on a low dose of an anti-thyroid drug, and developed euthyroidism.

**Discussion**

GO concerns 50% of patients with GD, among them only 3-5% develop severe forms. The responsible pathophysiological mechanism is linked to the presence of TRAKs. But these antibodies are only present in 95% of cases; suggesting are there other mechanisms to this GO?

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**EP1111**

**Graves’ disease refractory to a cumulative dose of 72 mci of iodine 131**

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**Introduction**

Graves’ disease is the most common cause of hyperthyroidism. There are three main therapeutic weapons: synthetic antithyroid drugs, surgery and radioactive iodine. The latter represents an effective treatment without noticeable side effects. We report a case of Graves’ disease refractory to iratherapy.

**Observation**

This is a 38-year-old patient, with no notable history, who consulted for Graves’ disease diagnosed with clinical signs of thyrotoxicosis and a biological profile of primary hyperthyroidism (TSH = 0.00 mU/ml; T3 = 4.23 pg/ml; T4 = 22.13 pg/ml) with positive TRAKs. The morphological assessment objectified a goiter hyper fixing to the thyroid scintigraphy. Iodine-131 treatment is given at an initial dose of 25 mci. The course is marked by a persistence of a suppressed TSH (0.05 mU/ml) after 6 months leading to the administration of an additional dose of 25 mci. Laboratory evaluation after 6 months objected to hyperthyroidism with TSH low at 0.08 mU/ml. The patient received an additional 25 mci dose with the onset of hypothyroidism for which the patient was put on hormone replacement therapy with LT4 with good clinical and biological progress.

Discussion and conclusion

Graves’ disease is a frequent endocrinopathy with potentially serious complications which can sometimes pose a difficulty in choosing a treatment. Iodine-131 iratherapy is a low-cost, simple treatment that is currently considered the treatment of choice for Graves’ disease. However, the course can sometimes be marred by an absence of response to the radioactive treatment requiring a repeat of the doses in order to obtain a clinical and biological resolution as is the case for our patient.

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**EP1112**

**Thyroid tuberculosis: a case report**

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**Introduction**

Thyroid tuberculosis is a rare localization that can pose problems of differential diagnosis with thyroid nodules. Its rarity is explained by the good oxygenation of the thyroid parenchyma and the bacteriostatic role of thyroid hormones. The definitive diagnosis is based on the pathological examination of the surgical specimen or after cytopathology or bacteriological examination of the transparietal puncture in complicated cases of collection.

**Observation**

This is a 30-year-old patient with no notable history who presents with multiheteronodal goiter with the presence of satellite lymphadenopathy confirmed by cervical ultrasound without associated general signs. The thyroid workup is normal. A total thyroidectomy is performed with simple operative consequences. Pathological examination revealed a hyperplastic thyroid parenchyma with the presence of epitheliogigantocellular granulomas with local caseous necrosis. Anti-tuberculosis treatment is started for six months as well as LT4 supplementation with a favorable clinical course and normal TSH.

**Discussion and conclusion**

Thyroid tuberculosis remains a rare condition. It poses a diagnostic problem and sometimes induces inappropriate treatment. Fine-needle aspiration makes it possible to make the diagnosis by looking for an epithelio-gigantocellular granuloma with caseous necrosis and/or a Koch’s bacillus and to initiate the anti-tuberculosis treatment which consists of multiple antibiotic therapy. Excisions are exceptional except in cases of diagnostic doubt as is the case for our patient. The prognosis is very favorable.

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**EP1113**

**Coexistence of two different thyroid malignancies: an exceptional phenomenon**

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**Introduction**

Simultaneous papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) of the same thyroid lobe is a very rare pathology.

**Objective of the presentation**

The objective of this work is to determine the clinical, histological and therapeutic aspects of an association of papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) on the same thyroid lobe.

**Methodology**

We report 2 cases of PTC and FTC on the same thyroid lobe, treated in the ENT department of Fattouma Bourguiba hospital in Monastir over a period of 21 years (2000-2020).

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Case 1
A 22-year-old woman was referred to our department due to nodules in the right thyroid lobe detected on ultrasonography during a routine health check-up. The thyroid function tests were normal. Ultrasound showed multiple nodules in the right lobe, the biggest one was 20mm and classified as EUTIRADS IV. The patient underwent a right lobe-isthmectomy with an extemporaneous examination that suggested the benignity. Postoperative pathology revealed that the nodule with a size of about 18 mm in the right lobe was a follicular thyroid carcinoma with angio-invasion associated with another nodule in the same lobe that was a micro papillary carcinoma (6mm) developed on a lymphocytic thyroiditis. The patient underwent a totalisation with central ipsilateral lymph-node dissection 1 month later. She was initiated with thyroid hormone replacement therapy and a radioactive iodine treatment. The evolution was judged good, no recurrence or metastasis, with a follow-up of 20 months.

Case 2
A 54-year-old women was evaluated at our hospital for a quick installation of a paraplegia. X-ray-imaging revealed a spinal compression. Vertebral biopsy was suggestive of a bone metastasis of a follicular thyroid carcinoma. Cervical ultrasonography showed a 29mm nodule in the right lobe that was suspected of malignancy. The patient underwent a total thyroidectomy with bilateral central lymph node dissection. There were no postoperative complications. Final histological examination revealed the coexistence of a large invasive follicular carcinoma associated with a micro papillary carcinoma in the right lobe of the thyroid. She was initiated on suppressive doses of thyroid hormone replacement therapy, a radioactive iodine treatment and vertebral radiotherapy. During its monitoring, the patient developed skull, femoral and spinal dorsal metastases with the indication of external radiotherapy.

Conclusion
Pathologists and surgeons should be aware of the possibility of the simultaneous presence of PTC and FTC tumours to avoid possible misdiagnoses.

EP1114
Differentiated thyroid carcinoma in Basedow disease: a series of five cases
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Introduction
The occurrence of thyroid cancer in Basedow disease is rare. We report a series of five cases of patients with Basedow disease who were operated on and whose pathological examination showed an association with differentiated thyroid cancer.

Clinical cases
We report a series of five patients with a mean age of 39 years. The diagnosis of Basedow disease was made on the basis of clinical, biological and scintigraphic evidence. Cervical ultrasonography was normal. Multiheteronodular goitre was present in four patients, while thyroiditis with a nodule classified as EU-TIRADS V was present in one patient. All patients underwent a total thyroidectomy after medical monitoring, the patient developed skull, femoral and spinal dorsal metastases with the indication of external radiotherapy.

Conclusion
Pathologists and surgeons should be aware of the possibility of the simultaneous presence of PTC and FTC tumours to avoid possible misdiagnoses.

EP1115
Coexistence of chronic lymphocytic thyroiditis with papillary thyroid carcinoma: about 13 cases
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Introduction
The association between chronic lymphocytic thyroiditis (CLT) and papillary thyroid carcinoma (PTC) has been investigated for several years from different perspectives. In spite of that, there were only few attempts to design a common frame of references to understand the complex mutual interactions between the various pathways of inflammatory response and of thyroid tumor induction and progression. The aim of this study is to investigate the clinical characteristics and outcome of the association between chronic lymphocytic thyroiditis and papillary thyroid carcinoma.

Materials and Methods
Our study was retrospective, realized on 13 cases of simultaneous chronic lymphocytic thyroiditis and papillary thyroid carcinoma collected in ENT department of Fattouma Bourguiba Hospital of Monastir a 20-year period (2000-2020).

Results
Among the 13 patients, there were 2 men and 11 women. Mean age was 41 years (20-56). 4 patients were under hormone replacement therapy for hypothyroidism. Patients presented to our consultation for management of anterior neck swelling in 10 cases, associated to compression symptoms in one case. We noted 2 cases of an incidental finding of thyroid nodule during an ultrasound (US) examination of neck. Thyroid nodules were highly suspicious for malignancy on US in 4 cases. The mean size of nodule was 4 cm. We noted the presence of antithyroidal antibodies in 2 cases. All of patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection in 10 cases. Histologic examination confirmed the diagnosis of papillary carcinoma in all cases. Surgical treatment was followed by radioactive iodine therapy except in one case which was a papillary micrometastasis measuring 4 mm. In all cases, Thyroglobulin level was not detectable after withdrawal of T4 treatment with an average follow-up of 3 years.

Conclusion
The association between chronic lymphocytic thyroiditis and papillary thyroid carcinoma is not a rare entity. Patients with CLT were younger and predominantly female. The presence of CLT in patients with PTC has been associated with better prognostic outcome, lower recurrence rate and less aggressive disease, which are the most important and well-known prognostic variables for thyroid cancer mortality.

EP1116
Distant metastases from thyroid cancers: About 4 cases
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Introduction
Metastases of thyroid tumors are rare. Metastatic sites are in order of frequency: pulmonary, bone and brain. Facial bones metastases are exceptional. These metastases are more frequent in vesicular than papillary carcinoma histological.
The aim of our work is to describe the clinical and radiological aspects as well as the therapeutic modalities.

**Observation 1 and 2:**
A 38-year-old woman and 13-year-old boy consulted for a chronic cough with thyroid nodules on examination. The chest X-ray showed a micronodular mililiary.
The diagnosis of distant metastases was confirmed on an adenectomy specimen for the boy and on a lung biopsy for the woman. A total thyroidectomy with bilateral central and functional lymph node dissection was undertaken and radio-iodine ablation for both cases.

**Observation 3:**
A 55-year-old woman consulted for low back pain with neurological deficit due to lumbo-sacral osteosynthesis. A bone biopsy showed a metastases of a vesicular carcinoma of the thyroid. Further imaging showed 2 left nodules. The patient underwent decompressive radiotherapy followed by a total thyroidectomy and bilateral central lymph node dissection.

**Observation 4:**
A 43-year-old woman consulted for chronic nasal obstruction and decreased visual acuity. Clinical examination showed a median basivascular swelling that measured 9 cm and a tumoral mass filling the right nasal cavity that bleeded on contact. The ophthalmological examination showed the presence of a compressive optic neuropathy. Imaging showed a large tissue mass in the right pterygopalatine fossa extending to the right nasal cavity, the right maxillary sinus, the sphenoid sinus, the sella turcica and the endocranial mass associated with a right thyroid mass with endothoracic extension and secondary pulmonary lesions. Biopsy of these lesions confirmed a poorly differentiated thyroid carcinoma. The therapeutic decision was taken in a multidisciplinary consultation meeting and was palliative chemotherapy. The evolution was marked by death.

**Conclusion:**
Distant metastases of thyroid cancer have no clinical or radiological specificity. The metastatic potential remains independent of the size of the thyroid nodule. These metastases are more common with the vesicular histological type and have more reserved prognosis.

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**EP1117**
**Managing thyroid storm in acute setting: a single centre experience case series**
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**Background:**
Thyrotoxicosis is one of the commonest endocrine disorders and its severe form can manifest as thyroid storm in acute setting leading to organ dysfunctions including heart failure.

**Cases:**
1: A 58-year-old female with a significant past medical history of MI, paroxysmal AF, atrial flutter, and hyperthyroidism presented with a one-week history of palpitations, plethora, diaphoresis, heat intolerance, loose stools, and a TSH < 0.01; Free T4-33. On physical exam, patient was warm and well perfused, minimal pedal edema. She was in fast AF. She was medically managed on Carbimazol 125μg, halted for 3 months, admitted for hyperthyroidism. The patient was then put on Carbimazol 90 mg/day + corticotherapy for 1 month. As the hyperthyroidism persisted and did not improve, he was given radioactive iodine therapy at a rate of 100mCi. All this evolved in a context of weight loss of 24 kg in 4 months. The clinical examination found a patient in general good condition, BMI: 17 kg/m², Burch Wartofsky score at 10, free thyroid hormones during his hospitalization with clinical improvement of the patient and hormones during his hospitalization with clinical improvement of the patient.

2: A 55-year-old patient, followed for papillary thyroid microcarcinoma under L-Thyroxin 125μg, halted for 3 months, admitted for hyperthyroidism. The diagnosis of distant metastases was confirmed on an adenectomy specimen and scores between 25 and 44 suggest thyroid storm as a likely diagnosis. Scores below 25 points make a diagnosis of thyroid storm unlikely.

**Conclusion:**
Thyrotoxicosis is one of the commonest endocrine disorders and its severe form can manifest as thyroid storm in acute setting leading to organ dysfunctions including heart failure. A score greater than or equal to 45 aligns with a clinical diagnosis of thyroid storm, and scores between 25 and 44 suggest thyroid storm as a likely diagnosis. Scores below 25 points make a diagnosis of thyroid storm unlikely.

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**EP1118**
**Factitious thyrotoxicosis: A case report**
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**Introduction:**
Although the most common cause of thyrotoxicosis is Graves’ disease, identification of other causes is important to establish appropriate management. The diagnosis of factitious thyrotoxicosis often presents a difficult challenge but should not be overlooked. We report a case of a patient with treated thyroid carcinoma who presented with factitious hyperthyroidism.

**Observation 50-year-old patient:**
followed for papillary thyroid microcarcinoma under L-Thyroxin 125μg, halted for 3 months, admitted for hyperthyroidism. The patient was then put on Carbimazol 90 mg/day + corticotherapy for 1 month. As the hyperthyroidism persisted and did not improve, he was given radioactive iodine therapy at a rate of 100mCi. All this evolved in a context of weight loss of 24 kg in 4 months. The clinical examination found a patient in general good condition, BMI: 17 kg/m². Burch Wartofsky score at 10, free thyroid compartment, no gynecomastia, testicles in place, not swollen, normal size. On biological test T4L: 3051 pmol/l vs 50 pmol/l (8.5-34.90), T3L: 30.43 ng/l vs 6.22 ng/ml (8.5-34.90), TSH<0.01, TSHs<0.05 μIU/ml, Tgus: 0.1 ng/ml, BHCg<5 IU/l (<5), CEA: 0.99 ng/ml (<4.30), AFP:5.5 ng/ml (<8.80), LDH: 144 IU/l (125-220), cervical-thoracic-abdominal-pelvic CT scan objectified an anterosuperior mediastinal mass of thymic appearance with adenolymphitis of the ileo-coecal region, F-FDG PET-CT did not show a hypermetabolic processes at the thyroidectomy lodge, locoregional lymph node, or distant suspicious processes for dedifferentiated recurrence of papillary microcarcinoma. The diagnosis of factitious thyrotoxicosis was retained in view of the depression of thyroid hormones during his hospitalization with clinical improvement of the patient during the hospitalization: depression of symptoms, and weight gain of 3 kg. The diagnosis was confirmed after a psychiatric evaluation.

**Conclusion:**
Thyrotoxicosis has a wide spectrum of etiologies. Patients with factitious thyrotoxicosis are extremely difficult to identify because they do not appear to be different from patients with thyrotoxicosis of other causes.

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**EP1119**
**Simultaneous occurrence of medullary and papillary thyroid carcinomas: a report of 2 cases**
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**Introduction:**
Papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC) are two different types of thyroid carcinoma with significant different clinical and histological findings. Synchronous occurrence of these two carcinomas is uncommon. The aim of the study is to determine the clinical, histological and therapeutic aspects of the coexistence of medullary and papillary thyroid carcinomas.

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Materials and Methods
We report two rare cases of simultaneous medullary thyroid carcinoma and papillary thyroid carcinoma collected in ENL departament of Fattouma Bourguiba Hospital of Monastir over a period of 20 years.

Results
Case one was a 46-year-old woman, with no personal history of radiation exposure and family history of thyroid cancer, presented to our consultation for management of a left thyroid nodule discovered by ultrasound examination of neck. The patient underwent a total thyroidectomy with node dissection. The histology disclosed a medullary carcinoma in left lobe and a micropapillary carcinoma in the right lobe. Three months post-surgery, the patient’s calcitonin levels were less than three ng/l and there was no distant metastasis. The second case was a 49-year-old man, with no apparent family history of endocrine disorders or any previous external radiation therapy, hospitalised in our ENL department for multinodular goiter with compression symptoms. A cervical computed tomography objectified a laryngo-tracheal invasion by an endoluminal tissue lump. Fine needle aspiration cytology from the thyroid nodule was performed showing a medullary carcinoma. A total thyroidectomy and total laryngectomy with node dissection were performed. The histology results showed a medullary carcinoma occupying the majority of the thyroid associated to a papillary carcinoma in the right lobe. Surgical treatment was followed by I-131 100 mCi therapy and external radiotherapy. The extension assessment revealed synchronous renal cell carcinoma associated to bone and lymph node metastases due to MTC.

Conclusion
PTC and MTC are two different types of thyroid carcinoma with significant different histology. Synchronous occurrence of these two carcinomas is uncommon and rare. The prognosis depends essentially on MTC.

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EP1121
Metastatic medullary carcinoma of the thyroid
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Introduction
Medullary thyroid carcinoma (MTC) is a rare and silent endocrine tumor representing 5-10% of thyroid cancers. It is the most aggressive form of thyroid carcinoma, usually diagnosed at advanced stages.

Purpose of study
Study the phenotypic and genotypic profiles as well as the anatomical-histological characteristics related to the recurrence of the disease.

Materials and methods
Descriptive cross-sectional study including patients followed for CMT in the Endocrinology and Diabetology Department of the Ibn Rochd University Hospital of Casablanca from 2007 to 2021. The statistical analysis was performed by the software SPSS version 25.0.

Results
The study included 24 patients followed up for CMT, the mean age was 47.6 ± 14.35 years, the majority were women (70.8%), a family history of thyroid carcinoma was found in two patients, clinically the thyroid nodule was the reason for consultation in thirteen patients (54.2%), all patients underwent total thyroidectomy, lymph node dissection was performed in eighteen patients, CMT was in the context of MEN2 in six patients (25%), the genetic study of RET proto-oncogene mutations was positive in three patients. Fourteen patients had metastatic disease (58.3%). Lymph nodes were the most frequent metastatic site. Calcitonin levels at diagnosis were > 500 pg/ml in 57.1% of patients. Most of them had undergone an incomplete first thyroid surgery. In addition, the tumors were larger, multifocal (P < 0.05) and with capsular invasion (P < 0.02). Of these patients three received chemotherapy, radiotherapy was performed in two patients, and two patients were scheduled for treatment with Sorafenib.

Conclusion
The prognosis of CMT is more pejorative than papillary thyroid carcinoma, several factors were correlated with the development of metastasis, which requires adequate management with close monitoring of the disease.

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EP1122
Papillary thyroid carcinoma revealed by hyperthyroidism
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Introduction
Papillary thyroid carcinoma is the most common histological type of differentiated thyroid malignancy. This type of tumor is rarely associated with thyroid hormone hypersecretion. We report the case of a patient with papillary thyroid carcinoma revealed by hyperthyroidism.

Case report
A 35 years old patient was admitted for the management of malignant hypercalcemia discovered incidentally on the biological workup performed preoperatively for a humerus fracture. The biological and radiological assessment revealed a primary hyperparathyroidism secondary to a parathyroid adenoma and hyperthyroidism secondary to a nodular goiter. TSH anti-receptor antibodies and calcitonin were negative. After obtaining normocalcemia and normalisation of the thyroid assessment, the patient underwent a total thyroidectomy with a left parathyroid adenectomy. The anatopopathological study confirmed the presence a parathyroid adenoma without signs of malignancy, as for the thyroidectomy specimen, the histological study revealed a vesicular carcinoma with presence of a capsular effraction and vascular emboli, classified pT3aNMX.

Conclusion
The association of thyroid cancer and hyperthyroidism is a rare event. Its pathogenesis remains poorly elucidated. Hyperthyroidism in these cases may be
secondary to the primary carcinoma, as well as due to metastases, hence the importance of a complete extensive evaluation.

EP1123

Two types of thyroid cancer in one patient

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A 65-year-old male was referred to endocrinologist due to significantly elevated calcitonin level of 3662 pg/ml. Previously, almost 3 decades before, the patient underwent right thyroid lobectomy for papillary carcinoma. Then, 9 years afterwards, he was reoperated and total thyroidectomy with neck exploration was performed. In pathologist finding, metastatic papillary carcinoma was proved. Radioactive iodine ablation was used as a post-surgical treatment. After completing a proposed therapeutic course, a patient has not been motivated for a regular follow-up. During the hospital examination, CT scan of the neck region revealed a solitary pathological node in front of the trachea, 18 mm in diameter which was surgically removed. Pathologist finding was suggestive for metastatic medullary thyroid carcinoma. A bone scan and nuclear magnetic resonance demonstrated a 32 mm extramuralbullary intraspinal solid mass in Th10 region. In further course, a Gallium PET/CT scan showed an increased update in right cervical level lymph node, measuring 12x8 mm in diameter, and in left side of the spinal canal at the level of Th9-Th10, consistent with metastasis, without pathological uptake on brain images, thorax, abdomen or pelvis. One month afterwards, a solid mass in spinal region and neck dissection were removed, followed with calcitonin level normalization.

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EP1124

Branchial cyst into the thyroid gland: an usual presentation

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Introduction

Fourth branchial cleft cyst are commonly reported as recurrent low-neck abscesses, acute suppurative thyroiditis, and neck masses. We report an accidental finding of a fourth branchial cleft as a suspected thyroid nodule.

Case presentation

We present a case of a 47-year-old woman who consulted the Ear, Nose, and Throat department of our hospital with a 4-year history of thyroid nodule. The thyroid nodule was discovered incidentally on ultrasonography. She reported no cervical swelling, pain, dysphagia or dysphonia. She did not report any recent infections, neck trauma, or surgery. The patient had no palpable neck mass or fistulous orifices, with a strictly normal ENT examination. Several ultrasonographic examinations revealed the thyroid nodule. Its size was a 14x8.7 mm, with a suspicious nodule in the right lobe and 3.3x.2 cm in the left lobe. Several infections episodes were recurrent.

Conclusion

Fourth branchial anomalies are very rare and can remain asymptomatic for a long time. Its localization and mode of discovery may be unusual. Clinical presentation and imagery can’t always help to diagnosis. In our case, it was considered as a suspicious thyroid nodule, but the anatomo-pathological examination rectified the diagnosis.

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EP1125

Thyroid nodule: an exceptional mode of revelation of extrapulmonary Tuberculosis

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Introduction

The incidence of extrapulmonary forms of tuberculosis has increased. Thyroid tuberculosis is an uncommon condition even in developing countries where tuberculosis is endemic. Herein we report an original case of a 62-year-old woman in whom tuberculosis was revealed by thyroid nodule.

Observation

Our patient is a 62-year-old woman with a history of mild asthma for 7 years. She presented with a slight neck swelling and a loss of weight and appetite for three months, with no discomfort on swallowing nor tenderness. There were no specific signs suggestive of dysthyroidism. She denied any history of tuberculosis, night sweats, fever, dyspnea or cough. At examination, she had a slight thyromegaly without tenderness nor bruising. Other systemic and regional examinations did not show any abnormality. The blood routine tests were normal. The thyroid function tests disclosed normal levels of serum thyroid stimulating hormone (TSH) and free thyroxin (FT4). Blood and urine calcium levels were normal. Cervical ultrasonod revealed multiple nodules of various sizes in the right lobe associated to lymph nodes in the lower internal jugular chain. Ultrasound (US)-guided fine needle aspiration biopsy of lymphadenopathies demonstrated non-caseating granulomatous lymphadenitis. A CT scan was performed and revealed apical ground glass opacities, symmetric hilar, mediastinal and abdominal adenopathies. Quantiferon test was positive. Tuberculin skin test was positive with an 18 mm-diameter reaction. Sputum smear microscopy was negative. Bronchoalveolar lavage was normal: there was no alveolitis, CD4/CD8 ratio was normal, mycobacterium tuberculosis PCR was negative. The angiotensin-converting enzyme and beta2-microglobulina were not elevated. The patient was diagnosed with ganglionar and thyroid tuberculosis. The patient is now put on anti-tuberculosis drugs: combination of Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for 2 months, which will be followed by Rifampicin and Isoniazid for 4 months. Now the patient is remaining euthyroid, neck swelling is not progressing and her appetite improved significantly. Follow-up sonography is scheduled in one month.

Conclusion

Thyroid tuberculosis is a scarce condition which should be considered in front of thyroid nodule. Fine-needle aspiration cytology may avoid unnecessary surgical intervention. Treatment options for thyroid tuberculosis are antituberculous drugs and/or surgery.

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EP1126

Multinodular goiters: management

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Background

We report a retrospective study of 120 patients operated on for multinodular goiter over a period of 5 years between January 2017 and December 2021.

Results

In our study a female predominance was noted with a sex ratio F/H of 8:1. The average age of the patients was 44 years with extremes from 15 to 74 years. A familial thyroid pathology was reported by 42 patients in our study (35%). On clinical examination 82 patients had a single nodule; the consistency of the GMN was firm in 88%, soft in 3% and hard in 9% of cases. 44% of the dominant nodules within the MNG were smaller than 4 cm. Cervical adenopathies were palpated in 13 patients (11%). Clinical signs of tracheobronchial axis compression were present in 45 patients or 37.5%. Recurrent paralysis was found at the IL in 3 patients (2.5%). A thyroid workup was performed in all patients. 96.6 of patients were euthyroid, the rest were hypothyroid. Ultrasound was performed in all patients. It revealed nodules larger than 1 cm in all patients. Cytopuncture was performed in 23 patients (19%). It concluded to a benign nodule in 19 cases (76%), a suspicious nodule in 3 cases (12%) and was non-contributory in 3 cases (12%). In 52 patients, surgical treatment consisted of total
thyroidectomy (44%) and lobectomy in 68 patients (56%). The surgical treatment was complicated by 4 unilateral recurrent paralysis of which two were definitive and 5 definitive hypoparathyroidism.

Conclusion

Thyroid goiter is the most frequent endocrine disorder. Clinical testing, thyroid function testing, and imaging studies are all part of the diagnostic process. Additional FNAC testing may be necessary. Depending on the results of the diagnostic examination and related consequences, treatment options include medications, surgery, and radionuclide (1-131).

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**EP1127**

Graves' disease: surgical management

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The goal of this study is to examine the role of surgery in the treatment of Graves’ disease and to assess the surgical outcomes.

Methods

We present the results of a retrospective analysis of 31 Graves’ disease cases operated on in the ENT and cervico-facial surgery departments of Farhat Hached Sousse Hospital during a six-year period [2015-2021]. Our group consisted of 05 males and 26 women. The average age ranged from 12 to 70 years. Between diagnosis and operation, the average period was 35.6 months [06-120 months]. A homogenous goiter (93.5%) and a thyroid of normal volume were discovered during a cervical examination (6.5 percent). TSH and FT4 levels were 14.42 pmol/l and 1.12 mU/l, respectively, at the median. When faced with: resistance to medical therapy (77.4%), existence of compression signals (9.7%), presence of thyroid nodules (6.5%), severe ophthalmopathy (3.2%), and patient desire, surgery was recommended (3.2 percent). In all of the patients, a complete thyroidectomy was performed. Following surgery, one patient experienced brief recurring paralysis. Hypoparathyroidism was discovered in 38.7% of the patients. In any event, it was only temporary. After surgery, no patient experienced an acute thyrotoxic crisis. A histological investigation revealed Graves’ disease, but no evidence of cancer. The average period of follow-up was three years.

Conclusion

Graves’ disease is a thyroid autoimmune illness. Because of the disease’s evolutionary vagaries, treating it is tough. Medical therapy has been related to repeated recurrences and a variety of side effects, all of which have a negative impact on these patients’ quality of life. Surgery based on total thyroidectomy represents a safe alternative with a low rate of complications.

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**EP1128**

Hypoparathyroidism Post-total thyroidectomy: pathophysiology and management

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Thyroid surgery is a frequent procedure that has certain risks. After a complete thyroidectomy, hypocalcemia is the most prevalent consequence. It has a variety of causes, with hypoparathyroidism being the most frequent and dangerous.

Materials and procedures

A retrospective analysis collected 27 cases of patients who had a total thyroidectomy complicated by hypocalcemia among 320 patients who underwent a total thyroidectomy throughout the study period, which spanned nine years (2010-2020). The goal of our research is to identify the characteristics that predict post-total thyroidectomy hypocalcemia, as well as the consequences and various therapy options.

Results

The average age of the participants was 40.5 years [17–78 years]. Females made up 92.6 percent of the patients. On D3, postoperatively, a systematic assessment of serum calcium was performed. In terms of clinical symptoms, 48% of individuals were asymptomatic. On D1 surgical day, 3 patients had symptomatic hypocalcemia, and on D2 postoperative day, 11 patients had symptomatic hypocalcemia. In addition, all of the patients’ preoperative serum calcium levels were normal. Apart from surgical devascularization of the parathyroid glands, 23 individuals had postoperative hypocalcemia. The primary symptom in symptomatic individuals was paresthesia of the extremities (85.7 percent). In two of the patients, muscle cramps were noted. There were no cardiac arrhythmias or tachyarrhythmias in any of the individuals. The mean serum calcium concentration was 1.67 mmol/l (range: 1.4 to 1.9 mmol/l). In 18 individuals, intra-hospital parental correction with calcium gluconate was required. On discharge, all patients were given calcium supplements along with vitamin D. The average treatment time was 3.7 months [1–9 months]. In 25 cases, the result was positive (correction of hypocalcaemia). Two patients were misplaced.

Conclusion

Hypocalcemia following thyroid surgery can be severe, but it is usually reversible. The first step in prevention is to carefully dissect the parathyroid glands and preserve their circulation. Despite this, a low preoperative vitamin D level predicts the development of postoperative hypoparathyroidism, which might be asymptomatic prior to surgery. Other prospective trials are needed to clarify the interest in a possible preoperative vitamin D supplementation as well as the mode of supplementation.

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**EP1129**

Management of refractory Graves' disease

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The goal of this paper is to analyze the factors that cause people to flee medical treatment and to put forth management guidelines. Materials and methods: This is a retrospective analysis of 27 instances with Graves’ disease that were resistant to medical treatment after escaping from well-conducted medical treatment in the ENT and cervico-facial surgery departments at Farhat Hached Sousse Hospital over a six-year period [2015-2021]. Results: All of the patients were put on a synthetic antithyroid medication as a first line of treatment (ATS). Carbimazole (thyrotoxol) was the most commonly used compound in 81.5 percent of instances, followed by propylthiouracil (basdene) in 18.5 percent. In 74 percent of instances, a beta-blocker was used as an adjuvant treatment. Medical treatment lasted an average of 33.7 months. Following an escape from medical treatment, surgical treatment was advised in all of the patients: resistance to medical treatment in 24 patients, 2 of whom had tried IRACIB therapy cures but were ineffectual, and the presence of a gigantic goiter with compressive indicators in 3 patients. In all patients who achieved euthyroidism, a total thyroidectomy was performed (mean follow-up of 18 months).

Conclusion

Graves’ illness is the most prevalent cause of thyrotoxicosis, which has life-threatening effects. Iodine and surgery are the alternatives to euthyroidism, which must be achieved first.

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**EP1130**

Graves’ disease revealing primary biliary cirrhosis (a case report)

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Introduction

Liver function abnormalities in hyperthyroidism are common, several abnormalities have been reported: hepatic cytolyysis, cholestasis, insufficiency or even non-specific abnormalities. The pathophysiology of hepatic dysfunction secondary to hyperthyroidism is not yet well established. Graves' disease can be associated with various autoimmune diseases. However, association with Primary biliary cirrhosis has been described in few cases in literature. We report a case of Graves’ disease revealing primary biliary cirrhosis

Case report

F, I, 47-year-old female patient, with no pathological history, consulted for a syndrome of thyrotoxicosis. Physical examination showed: Bulging eyes, homogeneous diffuse goiter, with vascular thrill. Thyroid function tests revealed: low serum TSH <0.05 UI, and high serum free T4: 41.46 pmol/l and free T3: 19.6 pmol/l. An ultrasound exam showed an enlarged thyroid with increased vascularity.
compatible with thyroiditis. Meanwhile, the patient presented a cholestatic and
cytolysis syndrome, serology tests for hepatitis were negative; high level of total
IGGs, anti-mitochondrial antibodies not made. The abdominal ultrasound:
dysmorphic liver. On fibroscann: Elasticity estimated at 114.4 (F3). The patient
was put on prednisone and beta blocker, with a normalization of liver and thyroid
tests. Then a total thyroidectomy was performed. The anatopathological study
confirmed the diagnosis of Graves’ disease.

Discussion

Hepatic involvement in Graves’ disease is uncommon, however, abnormal liver
function tests are relatively common. Clinical and biological cholestasis syndromes
are less common. The pathophysiology of hepatic dysfunction in hyperthyroidism is
multifactorial, it may be secondary to hyperthyroidism, to antithyroid drugs, or
associated with autoimmune liver disease. Various theories attempt to explain
cholestasis in hyperthyroidism. Its association with hyper metabolism, increases
hepatic oxygen consumption, without an increase in hepatic blood flow, and
therefore a decrease in oxygen in the centrilobular areas. Our patient had a clinical
and biological cholestasis syndrome, the etiological assessment was negative, the
fibroscann confirmed hepatic cirrhosis. The normalization of liver tests under
corticosteroids is in favor of diagnosis of primary biliary cirrhosis.

Conclusion

Primary biliary cirrhosis is another autoimmune disease that should be considered as
an association with Grave’s disease when other causes of cholestasis syndrome are
ruled out. Early identification could help plan disease management and prognosis
improvement.

Bibliography

Grave’s Disease and Primary Biliary Cirrhosis—An Unusual and Challenging
Association Shiran Shetty*, Senthilkumar Rajasekaran, Leela Venkatakrishnan*

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EP1131

Coronary insufficiency during hyperthyroidism: Report of six cases

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Introduction

Cardiothyrois is the consequence of the effects of excess free thyroid hormones on
cardiovascular wall and myocardium. This complication is the most serious
aspect of hyperthyroidism. Rhythm disorders and heart failure are the most
frequently noted. The prevalence of coronary insufficiency is lower. The aim of
this study is to evaluate the characteristics of coronary insufficiency in patients with
hyperthyroidism.

Method

This is a retrospective descriptive study including six patients among a hundred
patients who were followed for hyperthyroidism and cardiothyrosis, during a period
of 20 years, in the Endocrinology department of Hedi Chaker Hospital in
Sfax. These six patients had coronary insufficiency related to cardiothyrosis.

Results

The prevalence of coronary insufficiency in cardiothyrosis was 6%. All six
patients were male, with a mean age of 44.16 years [extremes: 25-61]. The
majority were aged ≤ 35 years (4 cases). They had no personal history of
musculoskeletal pathology except hypertension for one patient. The etiology of
hyperthyroidism was Graves’ disease in 2 cases, Hashimoto’s thyroiditis in 2
cases, toxic multinodular goiter and iodine overload. The mean TSH level was
0.054 μIU/ml [extremes: 0.01 -0.19 μIU/ml]. FT4 was 54.36 pmol/l [extremes:
31.3 - 71.43 pmol/l]. No cases of subclinical hyperthyroidism were reported. The
diagnosis of hyperthyroidism was concomitant with the diagnosis of cardiothyrosis
in 5 patients and delayed in one patient. Tachycardia was present in all patients with
a mean heart rate of 101.2 bpm. The different forms of coronary insufficiency were
objectified, ranging from unstable angina to myocardial infarction with
or without necrosis Q wave. Coronary angiography reports of 4 patients were
obtained: they showed arterial occlusion in 2 cases and a healthy coronary
network in the other 2 cases. Coronary insufficiency was always associated with
one or more of the other types of cardiothyrosis. Rhythm disorders were present in
5 cases (atrial fibrillation in 4 cases and atrialextrasystoles in one case).
Systolic ejecction fraction was low in all patients with a mean of 35.83%
[extremes: 20-55%]. 2 patients had died in major heart failure. The others had
not developed new coronary events after obtaining euthyroidism.

Conclusion

The risk of coronary insufficiency during hyperthyroidism is well established.
Less common than rhythm disorders and heart failure, it is usually associated with
them. Early diagnosis and adequate treatment of hyperthyroidism would prevent this
complication.

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EP1132

Long-term disease recurrence in the adipose tissue and striated muscle of
a mininally invasive papillary thyroid carcinoma

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Introduction

Differenziated thyroid carcinomas (DTC), particularly papillary thyroid
 carcinomas (PTCs), usually have an indolent behavior, however 10-20% of
the patients develop recurrences, following surgery: There are several histological
features associated with more frequent recurrences as the histopathological
variants of PTCs, the presence of vascular invasion or lymph node metastases and
the presence of extrathyroidal extension (ETE). Case history: a 56yrs old male
patient previously treated for PTC, with excellent response to the first treatment,
presented twelve years after a gradual increase of thyroglobulin (Tg) (from 0.3 to
0.76 ng/ml in 6 months) and a neck lump in the left cervical region at ultrasound
imaging. Fine needle aspiration cytology of the mass and Tg measurement in the
wash out liquid of the needle was 472 mg/l. Cytology revealed polymorphous
epithelial cells with atypical nuclei suggesting metastasis of PTC. Surgery was
then performed and pathology showed a massive metastasis in the local adipose
tissue and striated muscles of the neck. Genetic analysis of the primary tumor and
metastatic tissue revealed a BRAF p. V600E in both primary tumor and in
metastatic tissue (37% and 48% respectively). Conclusions: Our patient’s history
suggests the need of a continuous and prolonged follow-up in patients with
multiple features that increase the recurrence risk (minimal ETE, size > 2 cm,
BRAF V600E mutation as in our case).

References

association management guidelines for adult patients with thyroid nodules and
differentiated thyroid cancer: The American thyroid association guidelines task
force on thyroid nodules and differentiated thyroid cancer: Thyroid 26(1):133
differentiated thyroid cancer patients using the eighth TNM/AJCC classification
system: a comparative study. Thyroid 28(2), 201-209.
difference between minimal and gross extension into the strap muscles for the risk
of recurrence in papillary thyroid carcinomas. Thyroid 30(7), 1008-1016.
extrathyroid extension in differentiated thyroid cancer : systematic review and
5 T. P. de Castro, R. C. C. Penha et al. (2020) Molecular predictors for advanced

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EP1133

Epidemiological, clinic-pathological, evolutionary profile of noninvasive
follicular thyroid neoplasm: About 27 cases

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Introduction

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features
(NIFTP) is a newly defined entity accepted as a tumor precursor. Objective of the study
To describe the epidemiological, clinical characteristics, and the evolutionary
profile.

Methods

Retrospective study including 27 patients followed for noninvasive follicular
thyroid neoplasm collected at the Endocrinology and Diabetology department of
Ibn Rochd Casablanca University Hospital, spread from 2017 to 2021.

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Results
The mean age of our patients was 51.3 years, with a clear predominance of women (88.8% of cases). The most frequent symptomatology was cervical swelling in 88.36%, the discovery was fortuitous in 11.63%. In our series 92% patients had multinodular goiter, 14.8% followed for dysthyroidism, 26.7% had no personal history and 2 patient had a familial history of thyroid carcinoma. All patients had clinical and biological euthyroidism except 3 patients who had hyperthyroidism. All patients underwent total thyroidectomy with noninvasive follicular thyroid neoplasm, the average size of 1.07 cm. Multifocality was objectified in 5 patients, without associated malignancy. Their was no indication for lymph node dissection and fatherythroidectomy (P = 0.000), with no distant metastasis (P = 0.000). The remission rate was objectified in 100%.

Conclusion
The diagnosis of NIFTP can only be made after complete resection of the lesion.Patients diagnosed with NIFTP without associated malignancy and without nodules detected can be spared from additional treatment and from the traditional follow-up recommended for differentiated thyroid cancer.

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EP1134
Severe hyperthyrosis
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A 72-year-old male patient presented to the ER because of general weakness, malaise, frequent paroxysms of rapid atrial fibrillation, shortness of breath, and hoarseness. The symptoms persisted for two months, gradually worsening and causing him to lose weight. At some point, he noticed redness of the sclera and soreness of the eyeballs. Paroxysms of rapid atrial fibrillation have been known for more than 15 years, so he had amiodarone in therapy. His initial laboratory findings showed markedly elevated fT4 > 100 pmol/l, fT3 36 pmol/l, and suppressed TSH < 0.01 mU/l. Thyroid antibodies were normal. Ultrasound showed a diffusely altered thyroid with normal blood flow, and no nodular changes. Therapy was started with thiamazole 30 mg daily, propranolol 80 mg daily, and methylprednisolone 32 mg daily. Amiodarone was excluded from therapy. Two weeks later, fT4 was still significantly elevated, above 100 pmol/l. The thiamazole dose was increased to 60 mg per day, and two weeks after that, fT4 began to decrease, so the thiamazole dose was reduced to 30 mg per day. Two weeks after the dose reduction, he came to ER due to rapid atrial fibrillation. The fT4 level was again greater than 100 pmol/l, so the thiamazole dose was increased to 60 mg per day and lithium carbonate was added to the therapy, while the dose of methylprednisolone was gradually reduced in the meantime. Because the fT4 level was still extremely high 400 pmol/l after 1 week despite therapy, the patient was hospitalized and therapy was continued with thiamazole at a dose of 90 mg daily, lithium carbonate, parenteral corticosteroid, and supportive therapy. After 7 days, a decrease in fT4 level to 64 pmol/l is observed. As the gradual decline in thyroid hormones continued, the dose of lithium carbonate and parenteral corticosteroids was gradually reduced but continued with high doses of thiamazole of 90 mg per day. As the patients recovery was monitored by continued reduction of corticosteroids, lithium, and thiamazole, it was planned to perform thyroidectomy after complete physical recovery and achievement of euthyroidism. The patient was discharged for home treatment. Lithium carbonate was discontinued after 1 week, corticosteroid after 3 weeks, and thiamazole after 6 months of gradual reduction with achievement of euthyroidism. The patient recovered completely, so he refused thyroidectomy.

Conclusion
Thyroid storm due to amiodarone therapy.

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EP1135
When unilateral exophthalmos is the only manifestation of graves' disease: diagnostic and therapeutic issues
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Introduction
Basedowian exophthalmos is an inflammatory disease of the orbit of autoimmune origin, potentially threatening with severe functional and psychosocial effects. It is usually accompanied by hyperthyroidism. It constitutes a real diagnostic challenge in patients with euthyroidism, as is the case with our patient.

Observation
A 34-year-old young woman with no particular pathological personal or family history. Who initially consults, a year ago, in ophthalmology for a unilateral, right, non-painful, hardly retractive exophthalmos, estimated at 27mm, and associated with ipsilateral palpebral retraction, without other signs, in particular inflammatory. The clinical activity score was 1. Faced with the unilateral character, an orbito-cerebral CT scan was performed, ruling out a tumor cause and confirming unilateral proptosis with slight infiltration of the periorbital muscles. It is oriented at our level for further exploration. The clinical examination does not find any clinical signs of hyperthyroidism or goiter. The thyroid balance was normal, namely TSH: 0.981 mu/ml, FT4: 15.67 pg/ml, TPOAb/TgAb negative, only positive TSH anti-receptors at 3.74. Thyroid ultrasound shows the appearance of lymphocytic thyroiditis. The patient received oral corticosteroid therapy which did not allow the regression of this proptosis, a cure of silicon was prescribed.

Discussion
Unilateral exophthalmos may be the only clinical manifestation of Graves' disease in euthyroidism, thus posing a diagnostic challenge. And although the management of Basedowian exophthalmos is well codified, it still remains problematic in some patients.

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EP1136
Correlation between plasmatic long pentraxin PTX3 and nodular thyroid disease: a preliminary report
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Introduction
The long pentraxin-3 (PTX3) is a key component of humoral innate immunity that is expressed in various cell types during stress and tissue injury. PTX3 also acts like an oncosuppressor regulating tumor-promoting inflammation and it is implicated in tissue repair and autoimmunity. Autoimmune disease, tissue remodelling and oncogenesis often coexist in the thyroid. PTX3 role in thyroid disease is still unknown. Aim of the study is to evaluate if plasmatic levels of PTX3 in patients submitted to thyroidectomy for benign or malignant nodular disease are higher than normal.

Materials and methods
After informed consent, patients over 18 years old with nodular disease of the thyroid who were eligible for thyroid surgery were enrolled in this study. All patients underwent total or hemi-thyroidectomy at Humanitas Mater Domini Clinical Institute in Castellanza (VA). A blood sample was taken on the day of surgery and another one was taken 45 days after surgery to evaluate plasmatic PTX3 level. Blood samples were centrifuged and PTX3 levels were evaluated with ELISA test. In this preliminary report, we evaluated the data of the first 53 consecutive patients enrolled in the study.

Results
We found that preoperative plasmatic PTX3 levels were significantly higher than normal in patients with thyroid disease (P < 0.05). Plasmatic PTX3 mean value was 4.54 ng/ml (range 1.06 – 8.63 ng/ml), when normal value is considered 2 ng/ml with 1 ng/ml of standard deviation. At 45 days follow-up PTX3 mean value was reduce to 3.40 ng/ml (range 0.89 – 9.21 ng/ml); this reduction was statistically significant (P < 0.05).

Conclusions
For the first time, at the best of our knowledge, we observed a correlation between elevated PTX3 plasmatic levels and nodular disease of the thyroid. We hope to identify if plasmatic PTX3 could be used as a marker for nodular thyroid disease.

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EP1137
Graves' orbitopathy: clinical evaluation and therapeutic aspects
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Introduction
Graves' orbitopathy is a common complication of Graves' disease, characterized by various degrees of ocular inflammatory manifestations, ranging from mild proptosis to severe exophthalmos, eyelid retraction, and extraocular muscle dysfunction. Although the pathogenesis of Graves' orbitopathy is not well understood, it is believed to involve a complex interplay between immune and non-immune factors.

Materials and methods
We conducted a retrospective study of 72 patients with Graves' orbitopathy who were treated at our institution over a 5-year period. Patients were divided into two groups: Group A (n = 36) received systemic corticosteroids alone, and Group B (n = 36) received systemic corticosteroids plus orbital radiotherapy. The primary outcome was the change in ocular symptoms and signs.

Results
Patients in Group B had a significantly greater reduction in ocular symptoms and signs compared to Group A. Furthermore, Group B showed a higher rate of complete remission and a lower rate of relapse compared to Group A.

Discussion
The results of our study suggest that orbital radiotherapy in addition to systemic corticosteroids may be an effective therapeutic option for patients with Graves' orbitopathy. Further studies are needed to confirm these findings and to investigate the mechanisms underlying the observed clinical improvements.

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Introduction

Graves' disease is a common autoimmune disease that can be complicated by orbital damage sometimes threatening the visual prognosis. We report the case of a patient with Graves' orbitopathy and we discuss the difficulties of clinical evaluation and therapeutic management.

Case report

A 68-year-old woman presented to our department complaining of eye protrusion and progressive vision reduction in both eyes. She has had a history of Graves' disease treated with synthetic antithyroid drugs for 1 year, then thyroideectomy. The ophthalmological examination revealed in the right eye a visual acuity at 1/10, a proptosis, intraocular pressure (IOP) at 20 mmHg, a limitation of abduction, a dense cataract with a pale optic disc at the fundus. In the left eye, visual acuity was at 3/10; there was a proptosis, IOP at 22 mmHg, a mild cataract with optic disc hyperaemia at the fundus. We completed with an orbital MRI and a thyroid assessment. The patient was put on hypotonic eye drops and received bolus of intravenous corticosteroids. The evaluation was marked by an improvement in oculomotricity and a partial regression of proptosis and IOP. Given the persistence of the threat to the visual prognosis, orbital decompression surgery was indicated.

Discussion

The diagnosis of dysthyroid orbitopathy is often obvious. The clinical evaluation must specify the evolutionary stage (clinical activity score) and the gravity or severity according to the classification of the European group EUGOGO. It is important to recognize the 3 major stages of the disease: diagnosis with an ophthalmological and thyroid evaluation, the activity phase which may or not require specific treatment, and the sequelae phase after 6 months of stability and inactivity. Initially, rapid restoration of euthyroidism, smoking cessation and simple ophthalmological symptomatic treatment are proposed. In the event of advanced and active dysthyroid orbitopathy, oral or intravenous corticosteroid therapy associated or not with orbital radiotherapy. The place of emergency decompressive surgery in cases of optic neuropathy is controversial.

Conclusion

Dysthyroid orbitopathy is a complex pathology whose management is often difficult. A multidisciplinary management is recommended in order to allow an adequate biological, clinical and radiological evaluation and to propose an adequate treatment.

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EP1138

Autoimmune thyroiditis and hypothyroidism: a personalized medical approach

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Autoimmune thyroid diseases (AITD) are organ specific autoimmune disorders with a T-cell-mediated immune attack directed against the thyroid. Hashimoto’s thyroiditis and Graves’ disease are the two principal AITD clinical presentations, which are characterized by hypothyroidism and thyrotoxicosis, respectively. We review the available data in literature about personalized medicine in patients which are characterized by hypothyroidism and thyrotoxicosis, respectively. We review the available data in literature about personalized medicine in patients which are characterized by hypothyroidism and thyrotoxicosis, respectively.

We divided according to the degree of the thyroid-stimulating hormone (TSH) of the atypical appearances often makes it difficult to exclude a mitotic lesion. We have set forward few recommendations and clinical perspectives to overcome some of these challenges and minimise misdiagnosis.

Case 1

30 yrs F with established Hashimoto’s on Levothyroxine and under the care of Rheumatology for suspected mixed connective tissue disease. Thyroid USG was reported to be in keeping with THY5 and the patient underwent total thyroidectomy. The biopsy was then

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Hepatocellular Carcinoma of the Thyroid Gland: Diagnostic, Therapeutic and Prognostic Features

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Introduction
Oncocytic tumors of the thyroid gland are rare (3-10%). They are usually benign. Hepatocellular (oncocytic) carcinoma is uncommon: 5% of thyroid carcinomas. Our aim is to describe the diagnostic, therapeutic and prognostic features of Hepatocellular carcinomas.

Materials and Methods
We report 3 cases of Hepatocellular carcinoma treated in our department between 1988 and 2021.

Results
Our series included 35 cases of oncocytic tumors. Hepatocellular carcinoma was noted in 3 cases. The mean age was 50 years (35 – 67 years). All patients consulted for anterior neck mass with compressive symptoms. Ultrasonography showed a unique thyroid nodule in all cases: EUTIRADS 5 in 2 cases and EUTIRADS 4 in 1 case. The mean size was 4.2 cm. Thyroid-stimulating hormone (TSH) serum level was normal in all cases. Fine needle aspiration (FNA) result was “nondiagnostic” in all cases. Surgical treatment consisted of a thyroid lobectomy in all cases. The intraoperative examination was benign in all cases. The postoperative histological examination confirmed the diagnosis of Hepatocellular carcinoma; it was associated with papillary microcarcinoma in 1 case. All patients underwent totalization of the thyroidectomy with unilateral central neck dissection. No lymph node or distant metastases were noted. A complement by radioactive iodine was indicated in all cases. The evolution was favorable in all cases after a mean follow-up of 6.5 years.

Conclusion
The benignity or malignancy of oncocytic tumors cannot be confirmed by cytology. The diagnosis of malignant oncocytic tumor is usually made on postoperative histological examination. Surgery is the mainstay of treatment of Hepatocellular carcinomas. Responses to treatment with radioactive iodine are much lower when compared to other types of thyroid carcinomas. Hepatocellular carcinomas are more aggressive.

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**EP1144**

**Thyroid cancer arising from thyroglossal duct cyst: What are the therapeutic strategies?**

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**Introduction**

Thyroglossal duct cysts are the most common congenital cervical anomaly. Malignant transformation is very uncommon: 1-1.5%. However, therapeutic strategy is still not codified. Our aim is to describe the therapeutic features of thyroid cancer arising from thyroglossal duct cyst.

**Materials and Methods**

We report 3 cases of thyroid cancer arising from thyroglossal duct cyst, treated in our department between 1996 and 2021.

**Results**

Two men and one woman were included. The mean age was 17 years. The mean size of the cervical swelling was 36 mm. The treatment consisted of excision of the thyroglossal duct according to the Sistrunk procedure in the 3 cases. The diagnosis of malignancy was made on intraoperative examination in one case and on postoperative histologic exam in 2 cases. The histologic type was papillary carcinoma in all cases. Total thyroidectomy and radioactive Iodine were performed in all cases and bilateral central neck dissection was associated in two cases. The evolution was favorable in all 3 cases after a mean follow-up of 30 months.

**Conclusion**

The therapeutic management of thyroid cancer arising from thyroglossal duct cyst remains a subject of debate regarding the need for thyroidectomy and radioactive iodine. According to several authors, carcinoma can develop de novo within the thyroglossal duct, while others believe that the thyroglossal duct may be a natural route for the spread of carcinoma from the thyroid gland.

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**EP1145**

**Thyroid ultrasound characteristics in malignancy prediction**

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**Objective**

To evaluate the diagnostic accuracy of thyroid ultrasound characteristics of nodules in prediction of malignancy.

**Material and methods**

Respectively were analyzed 102 patients who underwent for FNA biopsy of thyroid nodule. All patients were examined by one ultrasound examiner. Size, taller than wide, echogenicity, borders, halo, calcification, and internal vascularity were recorded in all examined nodules. The Bethesda System for Reporting Thyroid Cytology was used in all ultrasonographic diagnoses.

**Results**

Out of the 102 patients, 88 (86.3%) were females. The mean age was 58.7 ± 14 years. The study included 14 malignant and 88 benign nodules. Size, microcalcification and internal vascularity showed statistically significant positive associations with thyroid malignancy (P < 0.05). The highest OR was found for the microcalcification (22.5 95% CI 4.48-112.78). The sensitivity and specificity of ultrasound characteristics in predicting malignancy were: size 66.76% (95% CI 34.89 – 90.08%) and 70.45% (95% CI 59.78 – 79.71%); microcalcification 83.33% (95% CI 51.59 – 97.91%) and 81.82 (95% CI 72.16 – 89.24%); and internal vascularity 66.67% (95% CI 34.89 – 90.08%) and 68.18% (95% CI 57.39 – 77.71%), respectively. Each ultrasound characteristic had negative predictive value from 93 - 97% in malignant nodules.

**Conclusion**

The presence of microcalcification was found the most important criteria in prediction of thyroid malignancy.

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**EP1146**

**Papillary carcinoma of the thyroid associated with Marine-Lenarth syndrome: about a case**

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**Introduction**

The Marine-Lenhart syndrome (MLS) is commonly defined as a combination of Graves’ disease and autonomous functioning thyroid nodule (s). The risk of malignancy of these nodules is less than 1%. We report a case.

**Observation**

27-year-old patient, hospitalized for treatment of a basal disease, cervical ultrasound found a 1.5 cm lower left lobe thyroid nodule classified eutirads 4. The sintigraphy found an aspect of diffuse hypercaptive goiter, TSI rate at 18 ui/l, confirming the SML. Fine needle aspiration of the nodule is suspected of malignancy, a total thyroidectomy is performed after preparation with Iodol. Anatomo-pathological examination found a papillary carcinoma of the thyroid of 1.5 cm classified PT1bNxMx supplemented by ietherapy of 30mci.

**Discussion**

MLS can affect up to 4% of Graves’ disease cases. Since the reported incidence of malignancy in all cold nodules is about 1%, it’s recommend to practice ultrasound and FNAC before treatments.

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**EP1147**

**Papillary thyroid carcinoma in its cystic form: a case report**

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**Introduction**

The cystic nodule is an unusual presentation of papillary thyroid carcinoma (PTC), seen in less than 10% of cases. Ultrasound discovery of a thyroid cyst represents less than 5% risk of malignancy. We report the case of a patient followed for papillary thyroid carcinoma in its cystic form.

**Observation**

A 42-year-old patient with no specific history. The patient underwent a right isthmolobectomy for a thyroid nodule. Anatomopathological exam found a papillary carcinoma of the thyroid of less than 5% risk of recurrence. The patient benefited from TSH-suppressive Levothyroxine therapy, with good clinical and biological evolution.

**Discussion**

The malignant potential of cystic thyroid nodules should never be neglected, even if it carries a low risk of malignancy. The diagnosis of PTC in its cystic form relies primarily on typical nuclear features, however, in case of histologic uncertainty, immunohistochemical stains such as HBME-1 can be used to help classify unusual presentations of PTC. Treatment and monitoring of cystic PTC follows the conventional guideline for solid PTC.

**Conclusion**

Papillary thyroid carcinoma in its cystic form is rare. Our case illustrates the importance of the management of cystic thyroid nodules with an adapted follow-up in order not to ignore a malignant etiology such as papillary thyroid carcinoma.

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EP1148
Metastasis of breast cancer in the thyroid gland: Report of two cases
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Introduction
Breast cancer is the most frequently diagnosed cancer in women. Common sites of metastatic spread are bone, lungs and liver. Metastases to the thyroid gland are exceptional.

Objectives
The aim of the study is to document two rare cases of thyroid metastasis from breast carcinoma and to specify their clinical, radiological and therapeutic particularities.

Methods
Review of 2 clinical cases of thyroid gland metastasis identified in women with no known breast carcinoma.

Case 1
A 33-year-old female patient reported extensive neck swelling that had progressed over several months. The physical examination showed a lower anterior cervical swelling. Cervical ultrasound showed a 3 cm calcified left thyroid nodule. The patient underwent a left lobe subtotalectomy. The final pathology with immunohistochemical studies revealed an intrathyroidal metastasis of a papillary thyroid cancer and background autoimmune thyroiditis.

Case 2
The second case was a 70-year-old woman with no pathologic history, admitted for the management of high dyspnea and progressive dysphonia for 2 months. On examination, she presented a hard lower cervical swelling with a non-palpable lower border, without cervical adenopathy. Laryngoscopy showed a fixity of the left vocal cord. Cervical ultrasound and scan confirmed the thyroid origin of this mass by showing a plunging calcified lower left nodule. Fine needle aspiration, suggested a follicular thyroid carcinoma. The treatment was surgical. The patient was then referred to her gynaecologist and the primary breast origin was confirmed. The evolution was good with a follow-up of 24 months.

Conclusions
Intra thyroid metastases, although rare, should be considered in any patient, especially females. Rarely observed in clinical practice, they often pose a diagnostic and therapeutic challenge.

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EP1149
A female patient with diffuse sclerosing variant of papillary thyroid cancer and background autoimmune thyroiditis
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Introduction
Diffuse sclerosing variant of papillary thyroid carcinoma (DSPC) represents a rare but rather more aggressive subtype of PTC.

Case description
A 33-year-old female patient reported extensive neck swelling that had progressed over several months. The patient had been diagnosed with hypothyroidism attributed to autoimmune thyroiditis, 3 years before. At that time, goiter was also found with a reported predominant nodule in the right lobe. On examination, the patient was euthyroid, with a palpable enlargement of the right lobe and isthmus, with particularly hard texture. Ultrasound imaging revealed diffuse enlargement of the thyroid gland particularly of the right lobe, where a formation of a suspicious mass was noted. Linear hyperechogenic foci were dispersed throughout the entire thyroid surface. Hypoechoic areas with ill-defined borders were noted centrally, possibly representing lymph nodes. A fine-needle aspiration biopsy of the right lobe was positive for papillary thyroid cancer and the patient underwent total thyroidectomy. Histopathology showed a 2.4 cm papillary carcinoma of the right lobe, with psammommatous bodies, squamous metaplasia, and background sclerosis. Vascular infiltration by the tumor cells was present. The remaining thyroid parenchyma exhibited extensive lymphocytic and plasmacytic infiltrates with abundant lymphohistiocytic elements. Dispersed foci of the neoplasm were observed in all sections of the entire gland. Metastases were recognized in 3 excised central lymph nodes. A few weeks later the patient underwent a completion surgery with central and right lateral compartment exploration, with metastases found in 13/24 and 4/30 lymph nodes, respectively.

Conclusions
The imaging characteristics and the overlapping presence of Hashimoto’s thyroiditis can lead to a delayed diagnosis of DSPC. Considering the more aggressive nature of this variant, raising awareness for early recognition of its particular ultrasonographic characteristics is of paramount importance for effective treatment and improved prognosis.

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EP1150
Ectopic cushing’s syndrome : a rare cause
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Introduction
Medullary thyroid carcinoma (MTC) accounts for 1-5% of all thyroid cancers. It is a neuroendocrine tumor arising from the calcitonin-secreting parafollicular cells of the thyroid. In rare cases, the neoplastic cells additionally secrete other substances, such as histamine, serotonin, ACTH, CRF etc, leading to paraneoplastic syndromes.

Case report
An 80 year old male presented to our Department with an already diagnosed metastatic MTC. Three years ago he had undergone a total thyroidectomy together with a right cervical lymph node dissection. His pre- and post-thyroidectomy calcitonin measurements were 2900 and 400pg/ml, respectively. Past medical history
Rheumatoid arthritis At his present visit, he was in good clinical condition. Calcitonin and CEA were measured 3640pg/ml and 123ng/ml, respectively.

Whole body imaging revealed metastatic lymph nodes on the right cervical and the upper mediastinum, as well as multiple secondary liver lesions, larger than those shown in last imaging. Because of disease progression, the patient was commenced on Vandetanib (Tyrosine Kinase Inhibitor, TKI) 300 mg/d. One month later, he presented with an itchy maculopapular, exanthema, starting from face and upper extremities and extending rapidly to almost the whole body, with local exfoliation and inflammation and was barely tolerated by the patient. Antibiotics, antihistamines and local and systemic corticosteroids were administered, with almost no improvement. Vandetanib had to be discontinued for four months, during which the exanthema subsided to a great extent, while, concomitantly, melachronosis appeared on the upper extremities and then almost everywhere on the body. In addition, the patient complained about proximal weakness and had oedema on lower extremities. Imaging and blood tests showed disease progression. There was suspicion of hypercortisolism which was confirmed by relevant tests and led to diagnosis of ECS. The patient was then administered Metopyrone 250 mg bid and Cabozatinib 40 mg, which is a different TKI. Six months later, the patient is in good clinical condition.

Conclusion
At most 0,7% of patients with MTC are reported to develop ECS. MTC represents 2-2-7.5% of all causes of ECS. ECS rises morbidity and mortality of MTC, due to consequences of hypercortisolism. TKIs are considered as the first-line therapy for ECS in the setting of unresectable or progressive MTC.

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EP1151
Papillary thyroglossal duct carcinoma: report of two cases

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Introduction
The thyroglossal duct cyst is frequently diagnosed in front of an anterior cervical swelling. Its degeneration is possible and observed in 1% to 2% of cases. The clinical feature is not specific, and the diagnosis of malignancy is most often established on final histological examination.

Purpose of review
The purpose of this paper is to review the presentation of thyroglossal duct carcinoma and discuss the clinical and therapeutic particularities.

Methods
Two cases of papillary carcinoma developed on a thyroglossal duct were identified over a period of 12 years (2010-2021).

Results
A man and a woman with no pathological history, aged 44 and 27 years old, consulted for upper cervical swelling evolving for 5 months and 3 years. The physical examination found an add-hyoid swelling of four cm and two cm, mobile on the protraction of the tongue. Cervical ultrasound suggested the degeneration in one case. The Sistrunk operation was performed associated with total thyroidectomy at the same time in a single case where the extemporaneous examination suggested malignancy. The histological study confirmed a papillary carcinoma developed on a thyroglossal duct in both cases. The other patient therefore underwent a thyroidectomy in a second time. Both patients were put on freenetic hormone therapy. Additional iodine radiation therapy was indicated in both cases. With a follow-up of 12 months no one showed recurrence.

Conclusion
Malignancy on thyroglossal duct cyst is a rare situation. Papillary carcinoma is the most common cancer. The treatment remains a subject of debate, even if, currently, most authors recommend associating a total thyroidectomy with the Sistrunk procedure.

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EP1152
Cholestatic jaundice: think of thyrotoxic hepatitis

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Introduction
Liver dysfunction during hyperthyroidism may be secondary to thyrotoxicosis, to an associated liver pathology, or to the medical treatment of hyperthyroidism posing a problem of etiological diagnosis. In this context, we report a demonstrative observation.

Case presentation
We report the observation of a 23-year-old female patient, followed for Basedow disease under carbimazole since 1 year, not controlled under medical treatment. During her follow-up, she presented cholestatic jaundice, associated with significant cytolsis and biological cholestasis, which persisted despite the discontinuation of synthetic antithyroid drugs. Biliary tract obstruction, viral or autoimmune hepatitis, and primary biliary cirrhosis were excluded. Liver biopsy showed lymphocytic infiltrate with discrete hepatic steatosis without stigma of autoimmune or toxic hepatitis. Our patient was treated only with liodine 131. The post-therapy evolution was marked by the achievement of clinical and biological euthyroidism with normalization of the hepatic balance. This constitutes a major argument in favor of the thyrotoxic origin of this hepatitis.

Discussion
Jaundice, during uncomplicated thyrotoxicosis, is rare and moderate (5-11%). Its exact etiopathogenesis remains poorly elucidated. An increased hepatic oxygen consumption due to hypermetabolic state not compensated by an increase in hepatic blood flow has been suggested. This imbalance leads to a decrease in oxygen tension in the centrilobular areas, which may lead to hepatocyte dysfunction with cholestasis. On anatomopathological examination, lymphocytic infiltrate in portal spaces, vacuolation and more rarely hepatic steatosis and intrahepatic cholestasis are often described, which was found in our patient.

Conclusion
Hyperthyroidism is an unusual cause of cholestatic jaundice that should be evoked in the absence of underlying liver disease.

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EP1153
Role of plasmapheresis in the management of severe amiodarone-induced hyperthyroidism refractory to conventional medical treatment

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Introduction
Amiodarone is an antiarrhythmic drug whose high iodine content may influence thyroid function. The first line treatment of amiodarone-induced hyperthyroidism (AIH) is mainly medical. Plasmapheresis has been used in cases of antithyroid intolerance or refractory hyperthyroidism, although clinical experience is poor.

Clinical case
We present a case of a patient with structural heart disease and severe AIH refractory to medical treatment who required a high number of plasmapheresis cycles to achieve adequate control of thyroid function before definitive treatment. A 53-year-old man, with atrial fibrillation treated with amiodarone (200 mg/day) for 3 years until 2 months prior to admission, was hospitalized due to chest pain. Echocardiography showed an atrial septal defect, with indication for non-urgent surgical closure. During admission, severe hyperthyroidism was discovered (TSH <0.01 μU/mL, normal range (NR): 0.35-5.0; free T4 (FT4) 10.03 ng/dl, NR: 0.7-1.98; and free T3 (FT3) 9.3 pg/ml, NR: 2.3-4.2). A grade 2 diffuse goiter was palpable. Thyroid autonoumous study was negative. Suspecting AIH, medical treatment with antithyroid drugs and corticosteroids was started. The difficulty in controlling thyroid function led to an increase in treatment up to 45 mg/day of methimazole, prednisone (90 mg/day), cholestyramine (16 g/day) and of potassium perchlorate (800 mg/day). After 3 weeks, hyperthyroidism persisted (TSH <0.01 μU/mL, FT4 11.92 ng/dl and FT3 9.76 pg/ml), establishing the diagnosis of severe AIH refractory to medical treatment; therefore, total thyroidectomy was considered. In order to reduce the perioperative cardiovascular risk, treatment with plasmapheresis was started. As complications, he presented several episodes of skin rash, a slight tendency to anemization (hemoglobin nadir 11.2 g/dl, NR: 12.0-17.0) and asymptomatic hypocalcemia with a minimum value of 7.6 mg/dl (NR: 8.7-10.3 mg/dl). After 17 sessions of plasmapheresis, a reduction in circulating levels of thyroid hormones was achieved (TSH 0.01 μU/mL, FT4 4.33 ng/ml and FT3 4.95 pg/ml), which allowed definitive treatment with surgery 40 days after diagnosis.

Conclusion
Plasmapheresis in association with medical treatment is a useful tool in the management of severe AIH refractory to conventional therapy with maximal doses in preparation for definitive treatment with thyroid surgery.

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EP1154
Stop oral therapy and start later: This is a new perspective for hypothyroid patients who need lifelong intravenous levothyroxine

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Introduction
Although the replacement route is oral in most hypothyroid patients, euthyroidism cannot be achieved with oral therapy in some patients rarely (1). Although oral levotiroxine is used above the standard dose (1.6-1.9 mg/kg/day), there is resistance to oral therapy if there are laboratory and clinical signs of hypothyroidism (2). Crushing the drug and using it with vitamin C increases absorption of levotiroxine (3). Rarely, some patients require lifelong intravenous levotiroxine.

Case report
Total thyroidectomy was performed in a 60-year-old female patient in 2014, after thyroid nodule FNAB result was found to have AUS. Its pathology was reported as medullary thyroid cancer. Despite increasing oral doses of levotiroxine after surgery, the patient with severe hypothyroidism had a negative pseudomalabsorption test, a negative celiac panel, and a negative Helicobacter pylori antigen.

Although the patient was given high doses of levothyroxine and lioiodotroin, his hypothyroidism did not improve. Combining levothyroxine with vitamin C/acid
drinks and crushing the levothyroxine tablet did not ameliorate hypothyroidism. Euthyroidism was achieved with intravenous levothyroxine 200 mg/session three times a week (Table 1). Due to a change in our healthcare system, the patient could not receive intravenous treatment for about two months. The patient drank 450 micrograms of levothyroxine to overcome this problem by dissolving it in tap water. The patient’s thyroid function tests, who came to the outpatient clinic in the first month of this treatment, were euthyroid. Euthyroidism was observed again in the patient who used the treatment he received for one more month (Table 2).

Table 1 Patient's history summary

<table>
<thead>
<tr>
<th>Age (year), Gender</th>
<th>60, Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism etiology</td>
<td>Medullary Thyroid Cancer</td>
</tr>
<tr>
<td>Duration of hypothyroidism (year)</td>
<td>7</td>
</tr>
<tr>
<td>Levothyroxine dose (mg/day)</td>
<td>600</td>
</tr>
<tr>
<td>Pseudomalousorption</td>
<td>Negative</td>
</tr>
<tr>
<td>Celiac panel</td>
<td>Negative</td>
</tr>
<tr>
<td>Helicobacter pylori antigen</td>
<td>Negative</td>
</tr>
<tr>
<td>LT4 + LT3</td>
<td>No-response</td>
</tr>
<tr>
<td>LT4 intake with vitamin C/sodas</td>
<td>No-response</td>
</tr>
</tbody>
</table>

Comment and new perspective:
The patient, who needed a total of 600 mg intravenous per week for seven years, switched to oral therapy because intravenous therapy could not be performed. Clinical response was obtained from the patient. In patients who do not respond to oral therapy in the first period, oral therapy can be tried later. This may indicate that intestinal levothyroxine absorption may increase after oral levothyroxine absorption is not taken for a while.

Keywords refractory hypothyroidism, switching, levothyroxine

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Table 2 Oral levothyroxine only (450 mcg/day)

<table>
<thead>
<tr>
<th>Treatment Phase</th>
<th>1st month</th>
<th>2nd month</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mIU/L)</td>
<td>(0.27-4.2)</td>
<td>0.7</td>
</tr>
<tr>
<td>Free T3 (ng/dL)</td>
<td>(0.33-1.7)</td>
<td>0.8</td>
</tr>
<tr>
<td>Free T4 (pg/mL)</td>
<td>(2.0-4.4)</td>
<td>1.8</td>
</tr>
</tbody>
</table>

EP1155

Refractory hypothyroidism and chronic gastritis
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Introduction
Refractory hypothyroidism is a fairly common situation in the practice of any endocrinologist, being defined by the persistence of hypothyroidism despite adequate doses of replacement therapy with Levothyroxine, generally supraphysiological. We report the case of refractory hypothyroidism under high doses of Levothyroxine.

Observation
The patient was a 54-year-old woman, diabetic Type 2, followed for 6 years for papillary carcinoma of the thyroid gland, for which it was operated and irradiated, currently in clinical, biological and morphological remission. She was also under 325 micrograms of levothyroxine taken orally, or 4 micrograms/day, for a target of TSH between 0.1 and 0.5 micrograms/L. The patient has a TSH suppressant treatment. The patient recognizes having a regular pace of taking his medicine with omission or errors related to the schedule of her medication. On examination, she shows symptoms of hypothyroidism, asthenia and pallor, with alteration of the face and integuments. Biology revealed a TSH = 30 mIU/L, and FT4 at 0.8 ng/dL (usual values between 0.7 and 1.5). An oral thyroid hormone absorption test was performed, at a dose of 1000 micrograms in a single dose on an empty stomach, under strict medical supervision. The FT4 assay was performed at times 0, 1h, 2h, 3h, and at 24h after intake. The results showed the absence of elevation of FT4, which is in favor of malabsorption. After elimination of the obvious causes, a malabsorption assessment was requested and returned without anomalies: the total cholesterol level at 1.8 g/l, ferritinemia at 77 mg/l, calcium phosphorus and vitamins B9 and B12 normal. A serology of celiac disease, anti-parietal antibodies, and digestive fibroscopy were requested. This finally led to the diagnosis of autoimmune gastritis, considered the cause of the malabsorption of levothyroxine. The patient was put under levothyroxine in the form of soft capsules and has marked a good evolution.

Conclusion
Our observation illustrates the interest of the thyroid hormone absorption test, a key examination to distinguish between true malabsorption and pseudo-malabsorption. This load test must lead to an etiological assessment in search of an organic cause for the malabsorption.

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EP1156

Low testosterone: An unexpected journey
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A 68 year old gentleman referred to endocrinology clinic with a few years history of erectile dysfunction (ED), which manifested as reduced libido and partial erections. Investigations revealed primary hypogonadism with a low morning serum Testosterone of 4.8 Ref: 7.9-31 nmol/L, raised PSH at 47 Ref:1.5-12.4 IU/L) LH at 36.8 Ref: 1.7-8.6 IU/L) and normal thyroid function tests (TFTs). The patient declined testosterone replacement therapy following a discussion of pros and cons of the risk vs benefit. Clinical examination revealed a deep seated right thyroid lobe and also a possible right thyroid nodule. Ultrasound (US) thyroid showed a right U3 nodule of 6.3x4.1 mm. Subsequent cytology following US guided Fine Needle aspiration (FNA) of the right U3 nodule revealed Thy3f. According to the Royal College of Pathologists Thy3f suggest follicular neoplasms whose characteristics are difficult to distinguish between benign or malignant nature. The Royal college of pathologists also states that the malignant potential of Thy3 nodules is approximately 15-30% [2].

The options of surgery vs monitoring by means of US guided FNA of the thyroid nodule were discussed. Patient opted for the latter option, repeat Cytology showed Thy1 (non-diagnostic). In view of all of the above and the recommendation from the British Thyroid Association guidelines, patient elected for right hemithyroidectomy [2].

The histology revealed the presence of variable size thyroid follicles containing colloid material and no evidence of malignancy. Patient had an uneventful post-operative recovery, and subsequent examination showed a well healed post thyroidectomy scar.

Conclusion
While modern clinical practice tends to lean towards investigations and imaging to guide clinical management, a good history, thorough examination and patient engagement should always be at the cornerstone of every consultation. This in turn can lead to improved patient care and outcome.

References

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who presented with a 3-year history of lethargy, tiredness, poor concentration and hair loss. She had a history of iron deficiency anemia previously requiring iron transfusions. On clinical examination and neck palpation rather tender and prominent thyroid nodules were noted. She was biochemically euthyroid with TSH 3.65 mU/l (range 0.27-4.2 mU/l), free T4 13.15 pmol/l (range 12-22 pmol/l) and free T3 4.7 pmol/l (range 3.1-6.8 pmol/l). Other blood tests showed vitamin D deficiency and an iron deficiency anaemia. Thyroid ultrasound (US) identified a large heterogeneous exophytic left paracervical thyroid nodule measuring 2.1 x 1.1 cm with moderate vascularity within the nodule, classified as U3. Fine needle aspiration cytology (FNAC) described a colloid nodule (Thy2) with no malignant features seen. The management options were jointly discussed with the patient; do nothing, surveillance with repeat US and FNAC or referral for surgery. The patient opted for repeat US performed four months later which showed the nodule had slightly increased in size to 2.4 x 1 cm with significant heterogeneity within the solid and cystic components and moderate vascularity, classified again as a U3 nodule. Repeat FNAC was Thy2 with no malignant cells seen. The options of doing nothing, repeated radiological surveillance or surgery were discussed further with the patient and she opted to undergo a left hemithyroidectomy. Histology revealed a 1.1mm focus of papillary thyroid carcinoma (pT1a) within the nodule. She recovered well post-operatively and the patient is currently being treated with L-thyroxine.

Conclusion

UK guidelines recommend an ultrasound (U) graded radiological examination in patients with thyroid nodules which then determines the patients who require fine needle aspiration cytology to aid diagnosis. This case highlights that thyroid nodule size, particularly if there has been an increase, may correlate with malignant potential. This has been emphasised in the American Thyroid Association management guidelines, but does not feature within UK guidelines.

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EP1158

The combination of multi-nodular goiter and Thevenard’s disease: about 3 familial cases

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Introduction

Thevenard’s disease is a sensory neuropathy with a type of ulcerative-mutilating course. It has a hereditary character with autosomal dominant inheritance. It is a scarce disease, which usually affects feet but can also affect hands. It causes disorders of thermosensory sensitivity, leading to painless ulcerations at the pressure points and then bone deformities with osteoarticular dystrophy and ‘cubic foot’ appearance. Repeated superinfections, often with multi-resistant germs, are the cause of frequent amputations. Les surinfections à répétition, à des germes souvent multi-résistants, sont à l’origine des amputations fréquentes. We report the case of the three sisters who suffer from Thevenard’s disease with multinodular goiter.

Cases

They are three sisters whose age varies between 30 and 40 years, they are under treatment for Thevenard’s disease since the age of 18, with unilateral trismalateral amputation in the three and deformities of the third phalanges of the hands in the youngest. They had multi-nodular goiter in euthyroidism (Thy 2 and 3 nodules) revealed around the age of 30. The autoimmuneity record was negative. They were operated on for signs of compression (dysphonia +). Anatom examination opathological was benign with signs of thyroiditis among the three sisters. The clinical and biological course was good under L-thyroxyne. Note that there is no notion of goiter in their family or other predisposing factors.

Discussion

Thevenard’s disease begins during adolescence or in adult age. Its diagnosis is made in practice, on bundles of clinical, electrophysiological and family arguments. Neuromuscular biopsy has only a differential diagnostic interest, discardine other polyneuropathies responsible for impaired thermosensory sensitivity, such as diabetic, amyloid, para-amyloid and leprosy neuropathies. The diagnosis of certainty requires the detection of a mutation in the SPTLC1 gene. Preventive treatment of skin lesions is the mainstay of the care of these patients because no curative treatment is available. Its association with multinodular goiter has not been reported in the literature. Moreover, this association among three sisters suggests a link between Thevenard’s disease and multinodular goiter which remains to be defined.

Conclusion

Goiter is most commonly caused by iodine deficiency, autoimmune or nodular diseases. Nevertheless, its appearance outside these circumstances and in association with serious diseases such as Thevenard’s disease opens up a perspective for clinical and genetic research.

References

Ngheuand. Thevenard’s disease: about a new observation, dermatology department, CHU Farhat Hached, Sousse, Tunisia, the journal of internal medicine, volume 40 supplement June 1, 2019, Pages A215-A214.

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EP1159

Role of iatraphy in the treatment of Graves’ disease in children: a case report

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Introduction

Graves’ disease is a rare and severe disease in children with a marked female predominance. The diagnosis is made in front of a very suggestive clinical picture most often grouping together a goiter, an exopthalmos and a picture of thyrotoxicosis, confirmed biologically by the presence of hyperthyroidism with positive anti-TSH receptor antibodies and radiologically by diffuse, homogeneous, hypervascular goiter. There are three essential therapeutic weapons: synthetic antithyroid drugs, radioactive iodine or surgery. We report the observation of an adolescent girl in whom Graves’ disease posed management difficulties.

Observation

We report the case of a 12-year-old patient, followed for Graves’ disease for 4 years on 40 mg per day of carbimazole with poor adherence to therapy. She currently has a thyrotoxicosis syndrome made up of palpitations and thermophoria. Cervical examination revealed a diffuse and homogeneous goiter. Biological hyperthyroidism is confirmed by suppressed TSH. The thyroid scintigraphy showed hyperfixing goiter. The patient underwent iatraphy treatment at a dose of 20 mci with a good clinical course and obtaining biological hypothyroidism after 6 months. LT4 treatment was started.

Discussion and conclusion

Graves’ disease is rare in children. It occurs in 0.02% of children. Its positive diagnosis is often easy, but its disease management remains a subject of controversy in pediatric endocrinology. Medical treatment with synthetic antithyroid drugs is always attempted as a first-line treatment. Other treatment alternatives are surgery and iatrotherapy which allows rapid healing while avoiding complications from surgery.

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EP1160

Surgical treatment of Graves’ disease

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Introduction

Graves’ disease is an autoimmune disease of the thyroid gland, which represents the most common cause of hyperthyroidism, accounting for 50 - 80% of all cases. Three treatment options are available for Graves’ disease: anti-thyroid drugs, radioactive iodine and thyroidecmy. But therapeutic management is still controversial. The aim of our study is to discuss, after a review of the literature, the role of surgery in the treatment of Graves’ disease.

Patients and methods

We conducted a retrospective study of medical records of 40 patients who underwent surgery for Graves’ disease in our department between 1996 and 2019.

Results

Our series included 30 women and 10 men, aged between 11 years and 63 years. All our patients had hyperthyroidism. Thirty-eight patients had a diffuse goiter whereas the gland was not palpable in 2 patients. A vascular thrill was perceived in 4 patients. Twelve patients had Graves’ ophthalmopathy. All our patients were treated with anti-thyroid drugs and β blockers. The average duration of medical treatment was 18 months. No patient in our series was treated with radioactive iodine. Indications for surgery were: failed medical therapy after 2 years of treatment (29 cases), a compressive goiter (4 cases), concomitant suspicious thyroid nodules (4 cases), second effect of antithyroid drugs (2 cases) and pregnancy (1 case). All our patients had a total thyroidecmy. Seven patients...
Hypothyroidism: the interest of thyroid hormone test
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Introduction
Hypothyroidism is a common endocrine disease with reduced systemic metabolism and its treatment consists on hormonal supplementation. However, despite concurrent replacement therapy with high doses of L-thyroxin, some patients might be seen with clinical and biochemical evidence of hypothyroidism. We report a case of persistent hypothyroidism on high dose of levothyroxine.

Case presentation
It was a 41-year-old female, with a history of recurrent chronic Helicobacter pylori gastritis and total thyroidectomy for a multinodular goitre in 2017, treated with 900 m/day of L-thyroxin with good compliance and regular intake. She had signs of hypothyroidism: asthenia, puffy face, pudgy fingers and macroglossia. Blood revealed a TSH = 55.32 µIU/ml and a FT4 < 0.42 ng/dL. A levothyroxin absorption test under medical supervision was performed with 600µg of L-thyroxin. TSH and FT4 were measured before the test and at 2h, 4h, 6h and 24h after the test. The FT4 remained low with a peak at 0.48 ng/dl (2h after the start of the test). The test concluded that there was malabsorption of thyroid hormones. Serological markers for celiac disease and a new digestive fibroscopy were requested.

Conclusion
This case illustrates the interest of the thyroid hormone test which allows to distinguish between malabsorption and pseudomalabsorption, non compliance to the treatment. If the diagnosis of malabsorption is retained, further investigations for etiological purposes should be carried out.
A 50-year-old peri-menopausal lady has had a background history of hypertension on single-agent antihypertensive medication (ACEI), chronic headache, recurrent collapses, and panic attacks for the past 14 years. She has been visited by her GP frequently and performed countless blood tests including FSH, LH, and TSH which confirmed that her symptoms were neither related to menopause nor hyperthyroidism. She also presented to the Emergency Department a dozen times and called paramedics 8 times for similar symptoms. She was diagnosed with panic attacks or investigated for meningitis. Her symptoms have never been resolved or getting better after discharge from the hospital. Unfortunately, her chronic catecholamines symptoms were controlled with anxiolytics and anxiolytics. She was the main patient to a slightly anxious disposition. Her BP was 150/90 with a pulse rate of 100 beats/min. Hypertensive retinopathy grade 1 was detected in fundoscopy. There was no postural drop and no thyroid nodules. MRI adrenals showed 39 mm high intensity right adrenal lesion. Alpha blockade with Phenoxylbenzamine was used before surgery. She underwent laparoscopic right adrenalectomy in January 2015 and the histology reported encapsulated tumour without lymphovascular invasion and low risk for malignancy. The adrenergic symptoms were entirely resolved postoperatively. She became normotensive and Urinary catecholamines were dramatically normalized although she required hydrocortisone replacement for a few months due to the suboptimal short synacthen test. It was stopped subsequently as her adrenal response has recovered fully thereafter. She has been followed up in endocrine outpatient clinic from 2015 to 2020 with 6-monthly urinary catecholamine but there is no biochemical as well as clinical features of pheochromocytoma relapse.

**Discussion**

The diagnosis of a very rare and potentially life-threatening endocrine tumour was made by a General Practitioner instead of an endocrinologist. This case also highlighted that the definitive treatment is not only curative and reducing cardiovascular risks, but also improving her quality of life.

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**EP1165**

Prevalence of endocrine autoimmune pathology in adult patients with vitiligo

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**Introduction**

In Russia, full-scale studies aimed at assessing the incidence of endocrine autoimmune diseases (eAID) in adult patients with vitiligo have not been conducted.

**Objectives**

- analysis of occurrence of eAID in patients with vitiligo.
- Methods
  1) The first part of the study included 39 patients aged 19-73 years with endocrine pathology and vitiligo, who were initially examined in Endocrinology Research Centre.
  2) The second part of the study included 26 patients aged 19-71 years with vitiligo who were initially examined in Moscow Scientific and Practical Center of Dermatovenerology and Cosmetology.

**Results**

1) eAID were diagnosed in 85% of cases (n = 33): 38.5% of patients (n = 15) had one eAID, 46.1% of patients (n = 18) had multiple eAID, other participants (n = 6, 15.4%) had antibodies to thyroid or insulin apparatus of pancreas without disruption of their functions. Autoimmune leison of thyroid (ALT) was diagnosed in 69% of cases (n = 27, of these n = 19 (70%) – primary hyperthyroidism and n = 8 (30%) – Graves’ disease (GD)), Addison’s disease was diagnosed in 28% of cases (n = 11), type 1 diabetes mellitus was diagnosed in 21% of cases (n = 8), hyperparathyroidism was diagnosed in 13% of cases (n = 5), hypergonadotropic hypogonadism was diagnosed in 10% of cases (n = 4). Multiple eAID were presented by autoimmune polyglandular syndrome (APS)-2 in 61% of cases (n = 11) and APS-1 in 22% of cases (n = 4), 3 patients (17%) had GD in combination with endocrine ophthalmopathy. Vitiligo preceded the manifestation of eAID in 30% of cases (n = 10) and developed simultaneously with eAID in 12% of cases (n = 4). 97% of patients (n = 38) had the non-segmental vitiligo. One patient (3%) with APS-2 (Addison’s disease, primary hyperthyroidism, autonomic gastritis) had universal vitiligo. 2) ALT was found in 15% of patients (n = 4, of these n = 3 (75%) – primary hyperthyroidism and n = 1 (25%) – GD), other eAID were not detected. Carriage of antibodies to thyroid or insular apparatus of pancreas without disruption of their functions was detected in 19% of patients (n = 5).

Vitiligo preceded the manifestation of eAID in 50% of cases (n = 2) and developed simultaneously with eAID in 25% of cases (n = 1). 96% of patients (n = 25) had the non-segmental vitiligo. One patient (4%) without manifest eAID and antibodies carriage had segmental vitiligo.

**Conclusion**

The non-segmental vitiligo is most often associated with the development of eAID, especially ALT. The development of vitiligo precedes the manifestation of eAID in 30-50% of cases, which necessitates a regular screening examination of these patients.

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**EP1166**

Does Autonomic cortisol secretion really affect metabolic parameters? preliminary results

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**Aim**

Autonomic cortisol secretion (ACS) is a clinical picture without overt signs of Cushing’s Syndrome despite adrenal adenoma and ACTH-independent cortisol secretion. These patients, who currently do not have a standard treatment, are followed up, especially for known comorbidities of hypercortisolism such as obesity, diabetes mellitus, hypertension, osteoporosis, and hyperlipidaemia. However, it remains unclear how long the patients will be followed and when the treatment should be begun. This study aimed to evaluate the parameters to be examined in the clinical follow-up by comparing the metabolic and hormonal parameters of ACS patients with the control group with non-functional adenoma (NFA).

**Material and methods**

Our study included 54 female patients diagnosed with ACS (n = 30) and age-matched NFA (n = 24) as the control group. 1 mg overnight dexamethasone suppression test cut-off point was accepted as ≥ 1.8 mg/dL in ACS diagnosis. Age, body mass index, waist circumference, fasting blood glucose, HbA1c, AST, ALT, lipid profile, thyroid function tests, basal cortisol, ACTH, DHEAS, maximum mass size of adrenal adenoma, 24-hydroxyvitamin D, HOMA-IR measured, and visceral adiposity index (VAI) were calculated for both groups.

**Results**

The mean age of ACS was 52.13 ± 8.8 years, while the mean age of NFA was 49.1 ± 6.8 years (P < 0.05). The prevalence of hypertension and diabetes mellitus was similar (P > 0.05). There were significant differences between the two groups in terms of maximum adenoma size (P = 0.007), DHEAS levels (P = 0.013), and TSH levels (P = 0.01). No significant difference was found in other comparisons (P > 0.05). Maximum adenoma size showed a significant positive correlation with waist circumference (r = 0.331, P = 0.018), and significant negative correlations with DHEAS and ACTH (r = -0.519, P < 0.001, r = -0.289, P = 0.049, respectively). There was no significant difference in VAI scores between the two groups (P > 0.05).

**Conclusion**

In our study, no significant difference was found between ACS and NFA patients in terms of metabolic disease frequency. While the maximum adenoma size was found to be significantly higher in ACS patients than in NFA patients, DHEAS and TSH levels were shown to be lower in those patients. These results were consistent with the possible effects of mild hypercortisolism. Our study showed that DHEAS and TSH levels might play a role in patient follow-up, and it was emphasized that the diagnosis of ACS should be considered, especially in patients with larger adenoma sizes. Further studies are needed to eliminate the uncertainties in the diagnosis and follow-up of ACS.

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Silent giant pheochromocytoma: about a rare entity

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Introduction
Phaeochromocytomas are catecholamine producing tumors which arise from chromaffin cells within the adrenal medulla. Silent pheochromocytomas are rare entities that do not present with the classical symptoms commonly seen in catecholamine-secreting tumors.

Case report
We report a case of 70-year-old woman patient who presented with left sided abdominal pain and discomfort for 6 months. A preoperative Computed tomography (CT) scan showed a huge left suprarenal tumor 99x112x153mm in size. The right adrenal gland was normal and there were no finding of distant metastatic. The urinary catecholamines were very elevated. The patient underwent a laparoscopic surgical resection without untoward intraoperative and postoperative events. In the pathological evaluation, the mass weighed 1157 g and showed a pheochromocytoma with a PASS score of 8. The patient is on long term follow up. She was well and completely asymptomatic at last review six months after surgery.

Conclusion
This case brings to the attention of clinicians the need to have a high index of suspicion of a giant pheochromocytoma in a patient presenting with vague abdominal symptoms whose CT scan shows a large retroperitoneal tumor, even in the absence of clinical symptoms. Key-words : Pheochromocytoma-silent-giant tumor-surgery

EP1169
Silent primary adrenal insufficiency: a case of treatment-resistant hyponatremia

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64 year old male with known hypertension presented with fatigue and mild vertigo to the emergency department. Blood pressure was 110/65 mmHg. Physical examination revealed bilateral inspiratory crackles with bilateral pedal oedema. There was not any skin discolourisation or bruises. Patient history indicated a suspected lung malignancy but pathological diagnosis was yet to be concluded. Laboratory test showed that sodium level was 117 mEq/l, potassium level was 5.2 mEq/l, venous blood gas pH was 7.37, HCO$_3$ level was 22 mEq/l, PaCO$_2$ was 44 mmHg. Spot urine sodium mEq/l, serum osmolarity was 271 mOsm, urine osmolarity was 425 mOsm/l. Other renal, liver, thyroid function tests and lipid levels were within normal laboratory values. He had no obvious hyponatremia symptoms other than fatigue and mild nausea without vomiting. Previous medical center initiated hypertonic saline for two days, yet sodium level did not improve. He was transferred with the suspicion of inappropriate ADH syndrome. Lung imaging showed a right mid-zone opacity with bilateral basal pleural effusion. Further investigations revealed no head injury or cranial pathology, morning serum cortisol level was 26 µg/dL. Patient admitted and started on furosemid and water restriction to 1.5 L for hyponatremia. Due to two days without improvement, PET-CT imaging was requested for evaluation. A 85x60 mm heterogeneous, hypodens mass at left adrenal gland with metabolic activity (suv maks 6.93) was reported. Despite patient’s lack of metabolic acidosis, hyponatremia or confusion, it is suspected to be adrenal function disorder and insufficiency. Serum ACTH, cortisol, renin, aldosterone levels were sent and short synachten test was performed before corticosteroid treatment with 100 mg hydrocortison four times daily started. Second cortisol level was 11 µg/dL and later Synachten test was consisted with primary adrenal insufficiency. Patients' sodium level was improved after two days of steroid treatment and increased to 128 mEq/l. Later on, patient was diagnosed with squamous cell lung cancer with adrenal and lymph node metastasis. This case was complicated with mild nonexpansive symptoms with initial high basal cortisol levels and absence of hyperpigmentation. It is suggested that patients with low plasma sodium should be carefully evaluated for laboratory errors, differential diagnosis; and adrenal functions should not be overlooked.

EP1170
Post-thyroidecmy hypocalemia: a single-center retrospective study

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We report a case of 39-year-old woman presenting with sudden severe abdominal pain and vomiting. She had a past medical history of anti-phospholipid antibody syndrome (APLS) diagnosed in the United States (US) 20 years ago. She had multiple episodes of vomiting over the last 10 years and was diagnosed with cyclical vomiting as investigations including CT abdomen and endoscopy did not reveal a structural cause. She was taking warfarin for APLS. She was haemodynamically stable and clinical examination was unremarkable. Investigations showed normal electrolytes, subtherapeutic international normalised ratio (INR), raised carciollpms antibody and raised activated partial thromboplastin time (APTT). CT abdomen showed enlarged bilateral adrenal glands with heterogeneous parenchyma suggestive of adrenal haemorrhage and warfarin was stopped. A morning cortisol level was 171 nmol/l and short synachten test showed inadequate cortisol response rising from 166 nmol/l only to 179 nmol/l at 30 minutes confirming the diagnosis of primary adrenal insufficiency. She was commenced on oral hydrocortisone. Subsequent MRI adrenals confirmed bilateral adrenal haemorrhage with cystic area of peripheral methaemoglobin and central haemosiderin. As the adrenal haemorrhage was non-progressive, anticoagulation was restarted due to high risk of thrombosis in the future. She is being followed up in the endocrine clinic with full adrenal work up including renin and aldosterone awaited. Adrenal infarction or haemorrhage is a rare complication of APLS, and hypercoagulable state may lead to adrenal vein thrombosis with haemorrhagic transformation of adrenal glands. The presenting features of adrenal thrombosis and haemorrhage include localised pain and/or adrenal insufficiency but often such patients do not have any symptoms. Patients with APLS and adrenal insufficiency may not present with hypotension as patients with APLS are commonly hypertensive, therefore masking hypotension. Unless promptly treated with intravenous glucocorticoids, complete adrenal insufficiency associated with vascular phenomenon of APLS can potentially be fatal. Therefore, physicians should have a high index of suspicion in such cases. Anticoagulation should be individualised but most patients need anticoagulation as they remain at high risk of thrombotic phenomenon elsewhere.

Background
Post surgery hypocalcemia is the most common sequel of thyroidectomy. An accurate prediction of hypocalcemia in the immediate postoperative period would enable the selection of patients for appropriate treatment and facilitate early discharge.

Objective
This study aims to investigate the prevalence of hypocalcemia after thyroidectomy and to identify potential risk factors.

Methods
This is a retrospective cohort study of 91 patients who underwent total thyroidectomy in a tertiary center between 2017 and 2019. Data were extracted from patient medical records. Hypocalcemia was evaluated in relation to risk factors (age, sex, body mass index and type of thyroid disease). Serum parathyroid hormone (iPTH) was measured 24 h (h) after surgery. Serum ionized calcium (Ca2+) was analysed 8h, 24h and 48h post-surgery.

Results
Hypocalcemia was noted in 28 (30%) of 91 patients who underwent thyroidectomy. There was no significant relationship between the occurrence of hypocalcemia and age, sex, body mass index and type of thyroid disease. The best cut-off values of serum iPTH to predict hypocalcemia was found to be 19 pg/ml at 24h post total thyroidectomy with a sensitivity and specificity of 92.45% and 100%, respectively.

Conclusion
Clinical factors are not reliable predictive markers of immediate post-thyroidectomy hypocalcemia. Prediction of hypocalcemia using serum iPTH

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seems to be a promising approach. In our cohort, a cut-off value of 19 pg/mL at 24h after surgery showed a good sensitivity and specificity. Serum vitamin D levels were not performed preoperatively. This can be considered a limitation of our study.

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EP1171
A case of postgravid osteoporosis
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Introduction
Of interest are cases of osteoporosis of unknown etiology after a recent delivery. Material and methods
A 33-year-old woman complained of frequent fractures of the bones of both feet (four times in the last year) after the birth of her third child. For the woman, this was the fourth pregnancy, according to her, after the birth of her second child, she had pain in the lower back, which aggravated with physical exertion (at 24 years old).

Results
The patient’s calcium level was 2.37 mmol/l, phosphorus 1.25 mmol/l, vitamin D - 20.07 ng/mL, parathyroid hormone - 50.04 ng/ml, NTX - 79.74 nM BCE (normal 17-94 nM BCE), osteocalcin - 5.28 ng/mL (normal 6-43 ng/mL), alkaline phosphatase - 60.0 U/L. Dual-energy x-ray absorptiometry (DEXA) showed that the Z-score of 1-4 lumbar vertebrae was -3.3, the left hip was -2.2, the neck of the left femur -2.3, the right hip -2.8, the neck right thigh -2.0. The analysis of the obtained results showed that the resorption markers were within the normal range, and the formation markers were below the norm, therefore it was advisable to prescribe teriparatide, but due to the lack of access to teriparatide in our country, the patient was recommended to continue therapy with teriparatide. The patient is being monitored.

Discussion
In our country, the incidence of post-gravid osteoporosis is not yet known. The patient was diagnosed with osteoporosis at the age of 33 years. The duration of the disease was 4 months. The patient was planning to have another child. Taking into account all the above factors, the patient was recommended to receive further therapy.

Conclusion
In conclusion, the diagnosis of post-gravid osteoporosis is confirmed. The patient was advised to use phytoestrogens, vitamin D, and calcium supplements. Further study is needed to establish the prevalence and risk factors of post-gravid osteoporosis in our country.

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EP1172
Osteoporosis after menopause: interaction between genes related to iron metabolism and estradiol
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Introduction
Osteoporosis is a common metabolic bone disease characterized by reduced bone mass and increased risk of fragility fractures. The pathogenesis of this disease is complex and influenced by multiple risk factors, where genetic factors play an important role. Menopause predisposes women to osteoporosis due to declining estrogen levels. Osteoporosis and iron metabolism have an important relationship. Iron overload suppresses osteoblast formation and stimulates osteoclast resorption of bone, suggesting that polymorphisms in genes affecting iron homeostasis can increase the susceptibility for the development of osteoporosis.

Objectives
This study aimed to investigate the potential implication of genetic polymorphisms in genes related to iron metabolism and their interaction with estradiol in the development of osteoporosis in a sample of postmenopausal women.

Material and methods
A case-control study was carried out for a sample of 169 Portuguese postmenopausal women, of which 78 had osteoporosis and 91 had normal bone mass. Polymorphic analyzes on the HFE gene (H63D and C282Y) were performed by PCR-RFLP. The haptoglobin (Hp) phenotype was determined by polyclarimide gel electrophoresis. Plasma 17β-estradiol concentration was determined by ELISA. All statistical analyzes were performed using SPSS software, version 24.0.

Results
An association was found between lower levels of 17β-estradiol and osteoporosis [OR (95% CI) = 5.946 (2.199-16.079); P<0.001]. When the genes were analyzed separately, no significant differences were found between the two populations in relation to the polymorphisms under study. However, women with the presence of the H allele of the H63D polymorphism of the HFE gene and lower levels of estradiol had an increased risk of developing osteoporosis [OR (95% CI) = 22.750 (2.492-207.731); P=0.001], as well as the presence of the CC genotype of the C282Y polymorphism of the HFE gene and lower levels of estradiol [OR (95% CI) = 11.667 (2.139-63.038); P=0.002]. Also women who had the Hp 2 allele and lower levels of estradiol had an increased risk of developing osteoporosis [OR (95% CI) = 7.023 (1.813-27.200); P=0.005].

Conclusion
Since these genes are related to iron metabolism, the results of this study suggest an action of this metabolism in interaction with estradiol levels in the development of osteoporosis in postmenopausal women.

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EP1173
Primary hyperparathyroidism-induced osteoporosis: lessons from the DENOCINA trial
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An 89 years old caucasian female patient with antecedents of hemihydratodectomy in 2016 due to benign nodular disease, and actually supplemented with 0.1 mg/day of levothyroxine, was referred to the Endocrinology consultation because of a primary hyperparathyroidism diagnosed in the sequence of the study of an episodic of nephrolithiasis that happened in 2012 and a diagnosis of osteoporosis that was established in 2017. A 99mTc-Sestamibi revealed an augmented right parathyroid gland. Although the patient had surgical indication for paratidectomy (symptomatic hyperparathyroidism), it was decided to treat the patient medically, because of her age and functional dependence, with the agreement of the patient and her family. She was initially treated with alendronic acid 70 mg once week during 5 years, but without significant response in terms of bone mineral density, hypercalcemia and osseous pain. The treatment was then switched to denosumab 60 mg twice year in 2020, and, in 2021, because the hypercalcemia didn't ameliorate, inspired by the results of the DENOCINA trial, we decided to introduce, in add-on, cinacalcet, initially in the dose of 30 mg/day. The calcium was 11.5 mg/dL and the PTH was 147 pg/mL (with adequate levels of vitamin D) before the initiation of cinalcalcet. Actually, 4 months after the initiation of cinacalcet, with a dose that was titrated to 60 mg/day, the calcium is in the upper limit of the normality (10.5 mg/dL) and the PTH has fallen to 85 pg/mL. But most important, the patient tolerated well both drugs, did experience an improvement in the osseous pain and gained more autonomy in the accomplishment of her daily activities.

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EP1174
miR-15b mediates the obesity-induced adipocyte insulin resistance by targeting insulin receptor
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Background
In recent years, the morbidity of obesity has been increasing rapidly worldwide, which is a major risk factor for type 2 diabetes mellitus (T2DM). Obesity, mainly characterized by abnormal and excessive white adipose tissue accumulation, is the most common cause of insulin resistance (IR), where the insulin target tissues fail to respond normally to circulating insulin. However, the precise mechanism by which obesity affects insulin resistance in the major insulin sensitive tissues remains unclear. Adipose glucose uptake plays a significant role in systemic insulin sensitivity, therefore clarifying the regulatory factors of adipose insulin sensitivity is of great significance to find effective therapeutic targets of obesity. Obesity causes the increase of hepatic miR-15b, which provokes hepatocyte insulin resistance, but has no effect in skeletal muscle. The upregulation of miR-15b induced by obesity causally resulted in an impairment of hepatocyte insulin signaling and the decrease of the insulin receptor (INSR) expression. However, no studies have explored whether miR-15b is involved in adipose tissue insulin resistance induced by obesity so far.

Aim
To study the role of miR-15b in the adipose tissue of DIO mice and IR 3T3-L1 adipocytes

Method
We fed mice with high-fat diet (HFD) for 10 weeks to construct obesity and insulin-resistant (IR) mice models, and treated 3T3-L1 adipocytes with chronic hyperinsulinemia to establish IR adipocyte models. Cell transfection was performed using riboFECTTM CPC or Lipofectamine2000. Insulin stimulated fluorescence labeled 2-NBDG uptake assay was used to detect the capacity of glucose uptake in adipocytes. The expression levels of miR-15b, the insulin receptor (INSR) and its downstream insulin signaling molecules were detected by real-time PCR and Western blot respectively.

Results
We found that expression of miR-15b was increased, while INSR expression was downregulated in adipose tissue of diet-induced-obese (DIO) mice. In IR 3T3-L1 adipocytes, the expression of miR-15b also ascended, accompanied by the decrease of INSR expression. Bioinformatics analysis and luciferase reporter analysis suggested that INSR was a potential target of miR-15b. Overexpression of miR-15b led to decreased INSR expression and impaired insulin signal transduction in adipocytes, and inhibition of endogenous miR-15b can reverse the downregulation of INSR and insulin resistance induced by high insulin. In addition, when miR-15b was overexpressed, the simultaneous overexpression of INSR partially alleviated the insulin resistance in adipocytes.

Conclusion
These results suggested that the impaired insulin signaling in adipocytes caused by obesity was at least partially mediated by the downregulation of INSR induced by elevated miR-15b.

EP1175
Greece: Study of people’s mobility in parks vis-à-vis internet searches for diet or obesity in the Covid-19 era
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Introduction
In the Covid-19 era mass media present people worldwide, including in Greece, to transiently flock to green spaces and parks. A study from the Western United States in 2020, indicated that indeed, park visitation may have increased by 20% compared to baseline (the immediate pre-Covid-19 period). The Google mobility index (GMI) is based on location data/visits - from smartphone users - to various places, among areas of mobility the GMI can focus specifically on visits to parks. Studies have shown that internet searches honed on diets may have fluctuated during the Covid-19 era, while obesity may have increased.

Aim
To assess whether the GMI for parks, as a surrogate of physical activity, is related to Google Trends (GT) searches for diet and obesity.

Methods
We extracted the GMI data for Greece, regarding people’s mobility in parks, from March 2020 to February 2022; the data were analyzed by two-way analysis of variance (ANOVA) vis-à-vis season and non-lockdown (NLD)/lockdown (LD) time. For the same time period we also extracted the GT data for internet searches in Greece regarding ‘diet’ and ‘obesity’ (in English and Greek). We assessed the autocorrelation of the parameters, to search for periodicity/seasonality, and we performed cross-correlation analysis of the GMI vis-à-vis GT searches. Separate cross-correlation analyses were done for NLD and LD time periods also.

Results
Park visitations’ GMI vs baseline had a markedly dimorphic aspect during NLD/LD time periods; in winter, NLD: +16%, LD: -11%, in spring, NLD: +38%, LD: +4%, in summer, NLD only: +150%, in autumn, NLD: +76%, LD: -5% (p were 0.067 for comparisons by season and <0.001 for comparisons by NLD/LD status). The autocorrelations for periodicity/seasonality of the parameters did not reach statistical significance. Mostly negative cross-correlation coefficients for GMI against GT, lagging mainly from to +2 to +11 weeks (with GT trailing GMI) were noted, ranging from -0.22 to -0.56 (P<0.05). Analyses done separately for NLD and LD periods yielded analogous results.

Discussion
Surprisingly, during LD periods, when stay-at-home mandates were in effect, whereas walking in parks was allowed for exercise, park visitations mostly declined. Moreover, periods of increased mobility in parks during the Covid-19 era were coupled, with a time delay, to a drop in internet searches for ‘diet’ and ‘obesity’. Whether this represents a counterintuitive perception in the community, in Greece, that physical activity in parks renders dieting superfluous remains to be evaluated.

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Diagnostic significance in the light of early detection and enable preventive intervention in terms of prevention.

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**EP1177**

Prolonged oral glucose tolerance test in the diagnosis of postprandial non-diabetic hypoglycemia

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Introduction

Tests alternative to the fasting test are necessary for the diagnosis of numerous causes of non-diabetic hypoglycemia (NDH), that not provoked by starvation (postprandial hypoglycemia), such as insulin autoimmune syndrome (IAS) and noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS). However, there is no consensus on the most optimal test (prolonged oral glucose tolerance test (pOGTT) or mixed meal test (MMT)) in this cohort of patients.

Objectives

1) To determine the accuracy of pOGTT and MMT in the diagnosis of postprandial NDH. 2) To compare the glycemic curves during pOGTT in patients with IAS and NIPHS.

Methods

We included 152 patients aged 18-74 years: with IAS (n = 14), NIPHS (n = 9), fasting NDH (n = 108) and without NDH (n = 21). All patients underwent pOGTT and MMT. During pOGTT the analysis of venous blood for glucose was performed at baseline, 120 minutes after a 75 g oral dextrose load, and then every 30 minutes until reaching 6 h, if hypoglycemia in venous blood has not been previously recorded. During the MMT the analysis of venous blood for glucose was performed at baseline, and then every 30 minutes after a mixed meal (containing 36.8 g of carbohydrates, 12 g of proteins, 11.6 g of fats (calorie content - 300 kcal)) oral load until reaching 5 h, if hypoglycemia in venous blood has not been previously recorded. During both pOGTT and MMT, analysis of insulin and C-peptide levels was performed once in a blood sample with diagnosed hypoglycemia.

Results

1) Sensitivity, specificity, AUC of the pOGTT were: 100.0% [82.7%; 100.0%]; 61.1% [44.8%; 75.2%]; 80.6% [72.5%; 88.6%], respectively. Sensitivity, specificity, AUC of the MMT were: 22.2% [5.7%; 55.9%]; 77.4% [67.2%; 85.0%]; 49.8% [34.7%; 64.9%], respectively. When comparing the AUCs of pOGTT and MMT the significant difference was found, P < 0.001. 2) The minimal level of glycemia in patients with IAS and true positive result of pOGTT (2.84 [2.60; 2.93] mmol/l) and in patients with NIPHS and true positive result of pOGTT (2.52 [2.15; 2.63] mmol/l) didn’t differ significantly, p = 0.130. Patients with IAS developed hypoglycemia at the 180-300 minutes after beginning of the pOGTT, and patients with NIPHS developed hypoglycemia at the 120-180 minutes after beginning of the pOGTT.

Conclusion

1) Patients with suspected NDH should undergo 5-hour pOGTT for the purpose of postprandial hypoglycemia excluding. 2) Patients with NIPHS develop postprandial hypoglycemia earlier, than patients with IAS.

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**EP1178**

Dietary education for patients with type 2 diabetes : state of art

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Introduction

Dietary practices are essential in diabetes control and acquiring HbA1c target. The aim of our work is to evaluate the prevalence of dietary education practice in a type 2 diabetes population and its associated factors.

Methods

Cross-sectional study enrolling 84 type 2 diabetes patients followed up in the outpatient endocrinology department. The data was collected through a questionnaire in face-to-face interviews with patients. Age, body mass index (BMI), diabetes duration, glycosylated hemoglobin (HbA1c) and serum lipid profile were assessed.

Results

The mean age was 59 ± 12 years. Of the study population, 42 % were females. The mean diabetes duration was 9.4 ± 6.4 years. The mean HbA1c was 9.9% ± 2.4. The mean BMI was 27.7 ± 4.7 kg/m². More than two-third (71%) of the patients were overweight/obese. Less than the half of the participants (45%) were measuring their blood glucose level at their home. Only 33% got nutrition education on diabetes diet from a health professional. The rest of respondents reported getting dietary information from media in 30% and from friends and family in 37%. Receiving nutrition education from a health care professional was associated with following dietary recommendations (P = 10⁻¹), self monitoring of blood glucose (P = 0.04) and a better glycemic control (P = 10⁻³). Patients who got a dietary education had lower BMI (26.6 ± 3.1 kg/m² vs 28.3 ± 5.2 kg/m² P = 0.06) and better serum lipid profile including a lower triglycerides levels (1.09 ± 0.36 mmol/l vs 1.52 ± 1.1 mmol/l; P = 0.009). Getting nutrition education was significantly associated with good dietary practices including : getting meals meals based on a diet plan (P < 10⁻²), knowing different food groups (P = 0.003) and reducing sweets and sugary consumption (P < 10⁻³). Patients who received a nutrition education insisted more on the importance of having a physician nutrition specialist (P = 0.002)

Conclusion

Among the patients, diabetic dietary awareness and management are still a major challenges faced by healthcare professionals. This study highlights the importance of reinforcement of an active dietary education through health-care providers (physician nutrition specialist, dietitian…) to encourage patient to make changes in their nutritional habits and improve their dietary knowledge and practices.

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**EP1179**

Differential effect of vitamin D therapy on insulin resistance in vitamin D deficient women

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Forty-one vitamin D deficient women (aged 26-75 years, mean 56.2, median 57) were treated with Vitamin D3 (50000 IU/week for 1.5 month and 25000 IU/week for another 1.5 month). Before treatment their serum 25(OH)D was 17.3 ± 6.1 ng/ml (mean ± SD) and after treatment 37.0 ± 7.5 (P < 0.0001). Their HOMA-IR was 2.2 ± 1.1 before and 2.3 ± 1.1 after (P = NS), serum insulin 9.0 ± 4.2 mIU/l before and 9.6 ± 4.5 after (NS), glucose 96.2 ± 8.2 mg/dl before and 97.0 ± 10.0 after (NS), calcium 9.4 ± 0.4 mg/dl before and 9.2 ± 0.5 after (NS), parathyroid hormone (PTH) 82.5 ± 34.2 mg/ml before and 61.4 ± 29.4 after (P < 0.0001), and BMI 26.2 ± 3.8 before and 26.3 ± 3.8 (NS) after treatment. The changes in HOMA-IR and Insulin after therapy was not uniform in all the women. In 24 women (group I) HOMA-IR increased significantly: from 1.7 ± 0.7 before to 2.4 ± 1.2 after treatment (P < 0.0001), and Insulin from 7.2 ± 2.7 to 9.5 ± 5.0 (P = 0.0003). In 17 women (group D) HOMA-IR decreased significantly: from 2.9 ± 1.2 to 2.2 ± 1.0 (P < 0.0001), and Insulin from 11.7 ± 4.5 to 9.2 ± 3.9 (P < 0.0001). HOMA-IR and Insulin were significantly different before treatment (P = 0.0002 and P = 0.0003) between the two groups I and D, but they were not significantly different after treatment. PTH was not significantly different between the two groups either before or after treatment. The values of some parameters before and after treatment were combined and thus for group I the number of cases became n = 48 and for group D n = 34. There was a negative significant correlation between the combined values of PTH and 25(OH)D in group D but not in group I. The values of 25(OH)D were not significantly correlated with those of HOMA-IR in both groups. However, there was a significant negative correlation between HOMA-IR and PTH in group I (P = 0.04), but a significant positive correlation between HOMA-IR and PTH in group D (P = 0.04). Similar were the correlations between 25(OH)D or PTH with Insulin in both groups. Our conclusion is that during vitamin D therapy of vitamin D deficient women there is no direct effect of the serum 25(OH)D level on HOMA-IR or Insulin. The effect of the treatment is mediated by the level of PTH which is significantly correlated with HOMA-IR or Insulin. This conclusion is in keeping with the known from the literature direct effect of PTH on the beta cells of pancreatic islets affecting the secretion of insulin. It seems that the treatment increases the HOMA-IR in women with relatively low baseline values, but it decreases it in those with relatively high baseline HOMA-IR values.

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**EP1180**

**The Global Threat of non-communicable Diseases**

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**Background**

Since the last decade, the disease pattern has significantly changed around the world. Non-communicable diseases, most commonly diabetes mellitus, have become the main threat to global health. The incidence of diabetes mellitus type 2 (DM2) is rising steadily, accounting for about two-thirds of deaths in Germany. Based on a prevalence of 9 million diabetic patients per year, DM2 constitutes a considerable medical and economic burden in Germany. However, the healthcare spending and its cost drivers are not yet sufficiently known.

**Aims of the study**

The primary objective of this study was to describe healthcare resource use and cost development of DM2 treatment in Germany, focusing on the most significant cost drivers and opportunities for cost-savings. The secondary objective was to analyse the impact of technical progress on diabetes care.

**Methods**

A systematic literature search was conducted in PubMed and Embase. Additionally, publications of the national health authorities (Robert Koch Institute RKI), Federal Joint Committee (Gemeinsamer Bundesausschuss G-BA) and the German Diabetes Society (Deutsche Diabetes Gesellschaft DDG) were included. Following the PRISMA guidance, the review identified the study design, epidemiological approach, analytical perspective, and data collection approach in each of the included studies.

**Results**

From 1.965 records, the final sample was composed of 41 articles. Most of the studies addressed direct costs and were based on calculations by extrapolations. The annual diabetes-specific direct costs of DM2 were between 542 and 6,323 € per patient. The most used method is the incremental or excess cost approach (1.8-fold higher costs compared to individuals without DM2). Confirmed risk factors included physical inactivity, obesity, genetic predispositions, and tobacco use. People with low social and income status had a significantly increased risk of developing DM2. The major cost drivers are demographic change with aging, exponentially increasing obesity, the availability of medications and therapies and the increased use of medical services by patients due to available treatment options of diabetic complications. Increasing prevalence, especially in childhood, is a major cost driver on its own. The preventive measures taken so far have not yet paid off. The potential financial savings from medical-technological progress are eroded by increasing age and use of medical services.

**Conclusion**

DM2, based on the results of this study, constitutes a considerable medical and economic burden in Germany and has a serious impact on the government health expenditures. To successfully combat diabetes and reduce healthcare expenditures, preventive efforts must be intensified.

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**EP1182**

**Association between lipid profile and diabetic nephropathy in type 1 diabetes mellitus**

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**Introduction**

Diabetic nephropathy (DN) is a severe complication of type 1 diabetes mellitus (T1DM) and has become common primary disease leading to end-stage renal disease worldwide. Abnormalities in lipid metabolism is very important in the progression of renal damage in patients with T1DM.

**Aim**

To assess the relationship between lipid abnormalities and diabetic nephropathy in type 1 diabetes mellitus patients.

**Methods**

We performed a retrospective analysis of clinical data from Liti Diane database from 2013 to 2016. 18-67-year-old 100 patients with type 1 diabetes were enrolled in the study. Participants filled questionnaires about T1DM, disease duration, complications and treatment. Anthropometric parameters height and weight were measured. Laboratory tests including total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, glycated hemoglobin (HbA1c), creatinine, albumin in 24 urine sample were performed. Study included group of 50 T1DM patients with DN and group 2 of 50 T1DM patients without DN. Patients taking statins and patients with eGFR < 30 mL/min were excluded from the trial.

**Results**

62 females and 38 males participated in the study. Mean age in DN group was 38±11.2 years and in group without DN 30.4±10.3 years. Mean duration of diabetes was 17.7±11.1 years, average body mass index (BMI) was 24.2±3.9 kg/m². HbA1c 9±2.2 %, eGFR 92±30.9 mL/min/1.73m². Patients with macroalbuminuria (26%) and microalbuminuria (40%) had significantly increased serum cholesterol (<0.05). LDL cholesterol was significantly higher (3.3±0.9) in DN group (P<0.005). Cases of hypertension were significantly more frequent between males than females (39.5% vs 9.7% P<0.001). Statistically significant relationship was verified between higher serum cholesterol (5.8±1.5) and DN group (P=0.001).

**Conclusion**

Lipid metabolism is significantly impaired among patients with diabetic nephropathy. Early monitoring, regular screening and appropriate lipid-lowering drug therapy may delay further renal complications in type 1 diabetes mellitus patients.

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EP1183
Weight loss induced by bariatric surgery may improve systemic inflammation: Preliminary results
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Background
Obesity is a widespread disease that causes chronic low-grade inflammation and related chronic diseases such as steatohepatitis, metabolic syndrome, diabetes mellitus (DM), and cancer. It is known that weight loss positively affects life expectancy by reducing obesity-related complications. Therefore, effective management of particularly morbidly obese patients is getting prominent in clinical practice. Bariatric surgery (BS) is the main effective treatment option and weight loss method for morbid obesity. This study aimed to investigate the impact of bariatric surgery on systemic inflammation and metabolic parameters.

Methods
Morbid obesity patients who underwent BS between December 2014 and June 2020 were screened retrospectively. Patients with inadequate data or diagnosed acute or chronic inflammatory disease were excluded. A total of 693 patients between 18 and 65 years were included in the study. The preoperative and postoperative 12th-month data were analyzed. A novel hematologic and immune biomarker systemic inflammation response index (SIRI) was calculated to evaluate inflammation. ∆SIRI computed as the preoperative SIRI (SIRI1) minus the postoperative 12th-month SIRI (SIRI2). The percent of total weight loss (%TWL) was also calculated to classify participants. The patients with %TWL < 40 were defined as Group 1, and patients with %TWL ≥ 40 were defined as Group 2. All parameters were compared between the groups.

Results
The mean age of 693 patients (152 female/541 male) was 39.9 ± 10.3 years. The mean body mass index was 47.7 ± 6 preoperatively and 30.2 ± 5 postoperatively at the 12th month. The mean SIRI1 (1.14 ± 0.54) was significantly higher than the mean SIRI2 (0.77 ± 0.45) for all patients (P < 0.001). Group 2 had significantly higher ∆SIRI and lower age than Group 1 (P < 0.001, P < 0.001, respectively). In addition, the frequency of both diabetes and hypertension increased in group 1 (P < 0.001 for both). After controlling for age, gender, hypertension, and DM covariates, only ∆SIRI levels sustained the significant difference status (P = 0.007). All metabolic parameters significantly improved after bariatric surgery (P < 0.05).

Conclusion
The present study showed that regardless of age, DM, and hypertension, increased inflammation recovery is significantly associated with effective weight loss. In the light of this finding, we suggest BS may give an independent contribution to the improvement of chronic inflammation induced by obesity. Further prospective studies in larger populations may improve the management of morbidly obese patients by clarifying the inflammation mechanism and process.

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EP1184
The relevance of managing ketoacidosis in otologic mucormycosis
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Background
Uncontrolled diabetes mellitus in ketoacidosis, as well as other kinds of metabolic acidosis, are major risk factors for mucormycosis. As the frequency of diabetes mellitus increase, so does the number of individuals at risk for this lethal infection. However, a lack of symptoms could lead to a delay in diagnosis. The aim of this paper is to study the clinical features of otologic mucormycosis and to analyse the impact ketoacidosis the disease’s course.

Materials and methods
The zygomycete infection was confirmed by either or both histologically and mycological examination of specimens. The underlying diseases were kidney failure in one patient, cell-mediated immunity defect in another one and diabetes mellitus was noted in one case. No underlying condition was registered in one case. Auricular mucormycosis involved otocerebral (2 patients), chronic otitis media (1 patient) and malignant otitis externa (1 patient). Diagnosis was obtained by positive histology, positive direct microscopy and fungal culture in all patients. The species identified were Lichtemia corymbifere in two cases, Rhizopus arrhizus in one case, and Rhizopodium form in the latter case. The great majority of antifungal-treated patients (3/4 cases) received an amphotericin B formulation (amphotericin B deoxycholate in two cases and liposomal amphotericin B (L-AmB) in one case). Two (2/3) of these patients received amphotericin B in combination with other antifungals (fluconazole in one case and itraconazole in the other case). Mucormycosis was considered responsible for death in one patient.

Conclusion
Ketoacidosis is a significant factor in the development and in the control of this lethal infection; thereby it is important to optimize information for clinicians in charge of diabetic patients.

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EP1185
The role of preoperative thyroid function tests in weight loss after bariatric surgery in morbidly obese patients
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Background
Obesity is one of the most critical problems nowadays, its frequency and consequences. Since the risk of morbidity and mortality increases in obese individuals, lifestyle changes, pharmacotherapy, and bariatric surgery (BS) methods are used for treatment. BS is generally considered the most effective method to treat morbid obesity. However, it is known that thyroid function has a role in weight regulation, the effect of preoperative thyroid function on weight loss after BS is not fully understood. Therefore, we aim to evaluate the impact of thyroid function tests and metabolic variables on weight loss after BS.

Methods
The patients who underwent bariatric surgery between 01.12.2014 and 01.06.2020 in our hospital were retrospectively screened. Patients with a history of thyroid disease treated with thyroid hormone or antithyroid drugs were excluded from the study. A total of 635 patients between 18 and 65 years were included, preoperative and postop 1st-year data were recorded, and the percent of total weight loss (%TWL) was calculated, in our study. Patients were divided into two groups in terms of %TWL: Those with %TWL < 35 were defined as Group 1, and those with %TWL < 35 were defined as Group 2. All parameters were compared between the groups. Regression analysis was applied to evaluate which factors affected postoperative weight loss contributed more to the outcome.

Results
The mean age of 635 patients (154 male/481 female) was 39.3 ± 10.6 years. Age, pre-and postop fasting plasma glucose (FPG), postop ALT levels were significantly higher in Group 1 than Group 2 (P < 0.001, P < 0.001, P < 0.001, respectively). FT3 level was significantly higher in Group 2 than Group 1 (P < 0.005). While there was no significant difference between the two groups regarding gender, DM and HT patients were significantly more frequent in Group 1 (P = 0.003, P = 0.005, respectively). The regression analysis determined that increasing FT3 levels raised the probability of being in %TWL ≥ 35 group by 1.6-fold (OR = 1.577, P = 0.027).

Conclusion
Weight loss after BS varies according to individuals. Therefore, predicting who will respond better to surgery is essential for the clinical management and follow-up of patients with obesity. In this regard, the present study showed that increasing FT3 levels raised the probability of being in %TWL < 35 significantly higher in Group 1 than Group 2 (P < 0.001, P < 0.001, P < 0.005, respectively). While there was no significant difference between the two groups regarding gender, DM and HT patients were significantly more frequent in Group 1 (P < 0.005). While there was no significant difference between the two groups regarding gender, DM and HT patients were significantly more frequent in Group 1 (P = 0.003, P = 0.005, respectively). The regression analysis determined that increasing FT3 levels raised the probability of being in %TWL ≥ 35 group by 1.6-fold (OR = 1.577, P = 0.027).

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EP1186

Hypobetalipoproteinemia: case report and literature review

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Introduction

Primary hypobetalipoproteinemia corresponds to a series of congenital disorders that have a variable incidence from 3.2% to less than 1 in 1 million, depending on the type of genetic mutation. The diseases that comprise it occur due to different types of mutations in genes that will encode important proteins at different stages of lipid metabolism. Individuals with determinant mutations of severe phenotypes, such as Bassen-Kornzweig syndrome, as known as Abetalipoproteinemia (ABL), chylomicon retention disease (CRMD), homozygous familial hypobetalipoproteinemia (FHBL), may present manifestations even during childhood with a picture of malabsorption of fats with vomiting, steatorrhea and weight-height deficit, and later on, they progress with progressive affections resulting from deficiency of fat-soluble vitamins, such as retinal degenerations and neuropathies. Heterozygous individuals are often asymptomatic although they may develop fatty liver disease and eventually some vitamin deficiencies.

Case report

A 20-years-old male patient was referred to endocrinology service due to a lipogram alteration. Asymptomatic, reported having a balanced diet, without being submitted to any type of diet. Maintained a preserved intestinal habit, with no significant history of diarrheal conditions. Laboratory tests showed total cholesterol 61 mg/dl, HDL 30.4 mg/dl, LDL 17.4 mg/dl, VLDL 10.6 mg/dl and triglycerides 53 mg/dl are associated with a deficiency of fat-soluble vitamins (vitamin D, E, and K). Apolipoprotein B dosage was 24 mg/dl (RV: 55 to 155 mg/dl) and also had an abdominal ultrasound with evidence of mild hepatic steatosis.

Conclusion

Hypobetalipoproteinemia corresponds to a heterogeneous group of diseases. Most of them do not cause serious manifestations and go unnoticed. However, even of these can lead to late repercussions such as liver disease and hypovitaminosis. Therefore, it is important to be attentive to patients with low levels of LDL and total cholesterol, avoiding dismissing these findings as "benign" changes. Despite this, it must be recognized that, possibly, these patients have some cardiovascular protection due to low LDL titer. The severe forms, despite being very rare, lead to evident clinical manifestations in the first years of life, showing the importance of lipids for humans.

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EP1187

Endocrinological and inflammatory markers in individuals with spinal cord injury: A systematic review and meta-analysis

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Introduction

The prevalence of diabetes mellitus (DM) continues to increase worldwide. Diabetic retinopathy (DRP) is one of the most common complications of Type 2 DM. Currently, the effect of thyroid hormones on diabetic microvascular complications has gained much attention. This relationship is explained by the important effects of thyroid hormones on endothelial function. There are studies investigating the relationship between TSH and diabetic nephropathy and DRP. There are very few studies evaluating free thyroid hormone levels. In this study, it was aimed to investigate the relationship between free thyroid hormone levels and DRP in euthyroid patients with type 2 DM.

Method

In this study, the biochemical records of patients with Type 2 DM who had euthyroid status and evaluated for retinopathy, applied to the endocrinology and ophthalmology clinics of our hospital between January 2018 and August 2018. Demographic data of the patients and characteristics that may be associated with diabetic retinopathy were evaluated. Whether the patients had DRP and, if any, retinopathy levels were recorded. It was evaluated whether there was a difference in free thyroid hormone levels between the groups with and without DRP.

Results

A total of 171 patients, 106 men and 65 women, were included in the study. Mean age was 57.19 ± 10.81 years. DRP was not present in 127 patients (74.2%), nevertheless 36 patients (21%) had nonproliferative DRP and 8 patients (4.6%) had proliferative DRP. There was no difference between the groups in terms of age, gender, hypertension, cardiovascular disease, fasting plasma glucose, serum creatinine, lipid levels and microalbuminuria. The duration of diabetes was longer in the nonproliferative DRP group (P = 0.026). HbA1c levels were higher in the proliferative DRP group (P = 0.035). No significant difference was found in terms of TSH levels and free thyroid hormone levels in all three groups.

Conclusion

In our study, the relationship between free thyroid hormone levels and DRP in euthyroid type 2 DM patients was investigated. Diabetes duration and HbA1c levels were found to be risk factors in DRP similar to the literature. When the
groups with and without DRP were compared, no difference was found in TSH and free T4 and free T3 levels.

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**EP1189**

Diabetes mellitus in the Tashkent region of Uzbekistan

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Objective

Studying the prevalence of diabetes mellitus is necessary to assess the epidemiological situation in the region.

Aim

To study the prevalence of diabetes mellitus in the Tashkent region.

Methods

The source of information was the data of the statistics office of the endocrine dispensary of the Tashkent region for the period 2018-2020. For the statistical processing of the data, the Microsoft Excel 2010 program was used.

Results

The largest number of patients is observed in Zangiata district of Tashkent region, which is 2.29% of the adult population of the district, the lowest prevalence of diabetes is observed in Bekabad and Bustanlik districts (1.11%); the number of diagnosed patients with diabetes in 2020 in the Tashkent region was 3461 people (0.17%); the highest percentage of type 1 diabetes mellitus type 2 diabetes is observed in the Angren region 26.3% to 73.7%.

Conclusion

Analysis of the situation with diabetes mellitus in the Tashkent region showed that, like throughout the Republic of Uzbekistan, there is late diagnosis of type 2 diabetes mellitus, and not all patients are registered.

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**EP1190**

NanoLuc® Binary Technology to explore the mechanism of action of a Magmas inhibitor

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Introduction

Magmas encodes for an integral constituent of the TIM23 translocase complex located in the mitochondrial inner membrane that drives proteins from the intermembrane space into the mitochondrial matrix by functionally interacting with Tim14. We previously demonstrated that Magmas silencing is able to sensitize ACTH-secreting mouse pituitary adenoma cells to pro-apoptotic stimuli, reduce DNA synthesis, accumulate cells in G0/G1 phase with concomitant decrease in S phase, supporting the hypothesis that Magmas may play a role in tumor development by protecting neoplastic cells from apoptosis and by promoting cell proliferation. We then synthesized a protein Magmas inhibitor, reported herein as “Compound 5”, which does not affect viability of cancer cells, but sensitizes them to the pro-apoptotic effects of chemotherapeutic agents such as Staurosporine, Doxorubicin and Cisplain. These studies provide evidence for a role of Magmas in chemoresistance and indicate that Compound 5 may be useful to restore sensitivity of chemoresistant cancers cells, possibly allowing for a reduction in chemotherapy-agent effective dose, with consequent decrease in side effects.

Aim

The purpose of this research is to understand whether the mechanism of action of Compound 5 is to disrupt Tim16-Tim14 interaction. This issue is important to explore the key features of Magmas inhibitors, providing information as to the better chemical structure of these compounds which might increase their chemosensitizing effects.

Methods

Tim16 and Tim14 were amplified from pCMV6-Entry vectors and cloned into NanoBiT® Expression Constructs using unique restriction enzyme sites present in the MCS of each vector. The resulting vectors containing Tim16 or Tim14 genes were transformed into One Shot® TOP10 Chemically Competent E. coli and the resulting ligation DNA was miniprepped. For each gene of interest, 4 possible ligation combinations may exist considering both -C and -N terminal tags. These constructs were transfected into chemoresistant cells 2 by 2 (Tim16:Tim14). After 48 h Compound 5 was added at a final concentration of 5mM and after 3 h luminescence from living cells was detected by use of furimazine for up to 2 h.

Results

Tim16 and Tim14 interaction was confirmed by measuring luminescence, developing when Tim16 and Tim14 were -C terminal tagged. The addition of Compound 5, on the other hand, decreased by >65% luciferase emission (P<0.0001).

Discussion

Compound 5 could be further developed to aid the treatment of chemoresistant cancer. Not only it is devoid of toxic activity, but enhances the pro-apoptotic stimuli of chemotherapy, by specifically targeting Tim16-Tim14 interaction.

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**EP1191**

Hypoglycemia due to non islet cell tumor hypoglycemia (NICTH) is a rare but severe complication of malignancy. NICTH has been related to the production of IGF II by tumours of mesenchymal or epithelial origin. It gives rise to frequent episodes of severe hypoglycemia and can have negative impact on quality of life. This case report describes a case of Non Islet cell tumor hypoglycemia due to hepatocellular carcinoma with hypoglycemia as the first presentation.

Clinical presentation

34 years old male patient brought to the ER by ambulance as patient was found unresponsive with blood sugars of 30 mg/dl. Patient was started on dextrose infusion and regained consciousness. On history patient has been having episodes of headache and increased hunger and abdominal discomfort for the past 1 month duration. These episodes occurred thrice a week. He had noticed increase in size of abdomen, fullness and loss of appetite. Patient denied history of Alcohol or Drug use. He had no positive past medical/surgical/family history. On examination patient was cachexic, Abdomen non tender hepatomegaly and ascites. Cardiovascular and Respiratory system examinations were normal. Laboratory investigation of the patient revealed Hb 10.9 mg/dl, WBC 5.8(n- 67.6, 1-19.7), PLT-363, LFT- AST-83, ALT-39, GGT-399, Alk phosphatase 278, Insulin-0.20 mU/mL, C-peptide 0.68 ng/mL, creatinine 0.78, Hba1c-4.5, Insulin antibodies negative, Hepatitis B +ve. USG Abdomen revealed large heterogenous predominantly hyperechoic lesion of right lobe of liver with the possible thombotic occlusion of right portal vein seen likely suggestive of neoplastic aetiology, ascites present. CT abdomen and pelvis reported hepatomegaly and large mass lesion involving right lobe of liver measuring 18.2 x 14.8 x 13.5 cm in size. The mass had invaded portal vein confluence and right branch of portal vein. Patient was subsequently evaluated for AFP-181500 IU/mL, IGF-1-36.74 mg/ml, CEA-0.50 ng/mL. The diagnosis of Hepatocellular carcinoma was made, Multidisciplinary team was formed, patient was treated for hypoglycemia with dextrose infusion and prednisolone 60 mg/day , planned for PET scan to check for metastasis, debulkling/palliative care for relief from hypoglycemia.

Conclusion

NICTH is a rare condition and its incidence is unknown. It is more likely to develop in those with large tumor burden. The diagnosis can be confirmed by a combination of suppressed serum insulin levels and suppressed C peptide and growth hormone concentrations in the setting of hypoglycemia, along with elevated IGF-II levels. Initial treatment aims at maintaining euglycemia, managed with parenteral dextrose infusion. Identification of NICTH and complete tumor resection represents ideal management.

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**EP1192**

Insulin autoimmune syndrome (hirata’s disease) -a case report

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Insulin-0.20 mIU/ml, C-peptide 0.68 ng/ml, creatinine 0.78, Hba1c-4.5, Insulin antibodies negative, Hepatitis B +ve. USG Abdomen revealed large heterogenous predominantly hyperechoic lesion of right lobe of liver with the possible thrombotic occlusion of right portal vein seen likely suggestive of neoplastic aetiology, ascites present. CT abdomen and pelvis reported hepatomegaly and large mass lesion involving right lobe of liver measuring 18.2 x 14.8 x 13.5 cm in size. The mass had invaded portal vein confluence and right branch of portal vein. Patient was subsequently evaluated for AFP-181500 IU/mL, IGF-1-36.74 mg/ml, CEA-0.50 ng/mL. The diagnosis of Hepatocellular carcinoma was made, Multidisciplinary team was formed, patient was treated for hypoglycemia with dextrose infusion and prednisolone 60 mg/day , planned for PET scan to check for metastasis, debulkling/palliative care for relief from hypoglycemia.

Conclusion

NICTH is a rare condition and its incidence is unknown. It is more likely to develop in those with large tumor burden. The diagnosis can be confirmed by a combination of suppressed serum insulin levels and suppressed C peptide and growth hormone concentrations in the setting of hypoglycemia, along with elevated IGF-II levels. Initial treatment aims at maintaining euglycemia, managed with parenteral dextrose infusion. Identification of NICTH and complete tumor resection represents ideal management.

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**Background**

Insulin autoimmune syndrome (IAS) or Hirata disease, is a rare cause of hyperinsulinemic hypoglycemia characterized by autoantibodies to endogenous insulin in individuals without previous exposure to exogenous insulin. IAS has been described as a form of type VII hypersensitivity, characterized by the presence of autoantibodies against a circulating antigen. The cornerstone of the IAS is the appearance of circulating insulin autoantibodies (IAA), which have a pathogenic role in the development of the syndrome. Occasionally it develops when a triggering factor that is a medication or a viral infection acts on an underlying predisposing genetic background. Here, we report a case of Insulin Autoimmune Syndrome.

**Clinical presentation**

43 years old Asian woman presenting to the ER with diaphoresis and tremors for the past 10 days duration. She had 3-4 episodes/day and were triggered by fasting and exercise. Her blood glucose when checked was noted to be 45 mg/dl. Patient was administered dextrose infusion and evaluated for hypoglycemia. She is non diabetic, no other comorbidities and was not on any medications. General physical examination revealed an obese, alert and healthy female. Her blood pressure 130/82 mmHg and pulse rate was 84/min. She was admitted for 72 hours fast test, patient was kept NPO and closely monitored for symptomatic hypoglycemia. Patient developed diaphoresis and tremors, blood glucose of 50 mg/dl, Samples for insulin, C-peptide, Pro Insulin, serum Beta hydroxy butyrate, and urine ketones were collected, fast terminated and patient was given oral carbohydrates and her condition improved confirming presence of Whipples triad. Her laboratory investigations revealed renal function, liver function tests, thyroid profile and hemogram to be normal. Her 8 am cortisol 12, Hba1c 5.5, Insulin > 1000.0 mU/ml, Pro insulin 6.70 pmol/l (<11), Beta butyric acid <60 umol/l,C-peptide 6.29 ng/ml (0.78-5.19), Insulin antibody >100 U/ml (>10 positive). Usg Abdomen was normal. Contrast enhanced CT abdomen was performed to look for pancreatic pathology and was normal. Diagnosis of Insulin autoimmune syndrome is made. She was advised frequent small meals and also treated with antidiabetic therapy (metformin, dapagliflozin, gliclazide, and sitagliptin) for one year. She had suffered from type 2 diabetes for ten years. She had been unable to control the blood glucose level adequately, 1 year history of amenorrhea, generalized fatigue and weight loss for the last one year. She had been on oral antidiabetic therapy (metformin, dapagliflozin, gliclazide, and sitagliptin) for one year with bad glucose values. On examination, her vital signs were within normal. Physical examination revealed acromegalic coarsened facial features but she had no clear-cut cushingoid features and acral enlargement. Anthropometry and laboratory tests were as follows: Height, 150 cm; body weight 55 kg; body mass index (BMI), 24.84 kg/m² basal and postprandial glycemia 202, and 280 mg/dL respectively. Ali level of 11.6%. Serum investigations revealed GH levels of 15-735 mg/l (101–267 mg/l) and growth hormone nadir (1 hour after a 75-g oral glucose load) was 30 mg/l (<1 ng/mL). Complete pituitary hormonal profile revealed prolactin 28.29 ng/ml (4–25 ng/mL), thyroid-stimulating hormone 1.02 mU/ml (0.35–4.94 mU/mL), FT3 2.81 pg/ml (2.3–4.2 pg/mL), FT4 1.25 ng/dl (0.89–1.76 ng/dl), follicle-stimulating hormone 57.78 mU/mL (3.35–21.63 mU/mL), luteinizing hormone 15.94 mU/mL (2.39–6.6 mU/mL), adrenocorticotropic hormone 26.7 pg/ml (7.2-63.3 pg/mL) and cortisol 22.71 mg/l (5.27-22.45 mg/dL). Magnetic resonance imaging of the sella demonstrated a 17x14 mm pituitary adenoma. The patient was diagnosed with acromegaly, and acromegaly-associated exacerbation of diabetes mellitus. Trans-sphenoidal resection was performed and histopathological and immunochemical findings indicated GH and PRL producing pituitary adenoma.

**Discussion**

Acromegaly is often develop insidiously and diagnosis may be delayed as a consequence. The present report outlines a case of missed diagnosis of acromegaly associated with severe hyperglycemia. Clinical suspicion of acromegaly is generally difficult during anamnesis of patients with DM, particularly in the absence of disease-related symptomatology. When treating patients diagnosed with diabetes, secondary causes should not be neglected.

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**EP1194**

**Acrornagaly presenting with type 2 diabetes: a case report**

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**Introduction**

Alterations in glucose homeostasis and diabetes mellitus (DM) are the most common metabolic comorbidities in acromegaly. DM has been reported in 16–56% of patients with acromegaly. It is estimated that 20% of patients with acromegaly have developed DM before the formal diagnosis of acromegaly. We report a case of a patient with acromegaly secondary to a pituitary macroadenoma who presented with diabetes.

**Case report**

A 47-year-old female patient was admitted to our internal medicine clinic for control and assessment of diabetes before tooth extraction due to dental caries. She had suffered from type 2 diabetes for ten years. She had been unable to control the blood glucose level adequately. 1-year history of amenorrhea, generalized fatigue and weight loss for the last one year. She had been on oral antidiabetic therapy (metformin, dapagliflozin, gliclazide, and sitagliptin) for one year with bad glucose values. On examination, her vital signs were within normal. Physical examination revealed acromegalic coarsened facial features but she had no clear-cut cushingoid features and acral enlargement. Anthropometry and laboratory tests were as follows: Height, 150 cm; body weight 55 kg; body mass index (BMI), 24.84 kg/m² basal and postprandial glycemia 202, and 280 mg/dL respectively. Ali level of 11.6%. Serum investigations revealed GH levels of 15–735 mg/l (101–267 mg/l) and growth hormone nadir (1 hour after a 75-g oral glucose load) was 30 mg/l (<1 ng/mL). Complete pituitary hormonal profile revealed prolactin 28.29 ng/ml (4–25 ng/mL), thyroid-stimulating hormone 1.02 mU/ml (0.35–4.94 mU/mL), FT3 2.81 pg/ml (2.3–4.2 pg/mL), FT4 1.25 ng/dl (0.89–1.76 ng/dl), follicle-stimulating hormone 57.78 mU/mL (3.35–21.63 mU/mL), luteinizing hormone 15.94 mU/mL (2.39–6.6 mU/mL), adrenocorticotropic hormone 26.7 pg/ml (7.2-63.3 pg/mL) and cortisol 22.71 mg/l (5.27-22.45 mg/dL). Magnetic resonance imaging of the sella demonstrated a 17x14 mm pituitary adenoma. The patient was diagnosed with acromegaly, and acromegaly-associated exacerbation of diabetes mellitus. Trans-sphenoidal resection was performed and histopathological and immunochemical findings indicated GH and PRL producing pituitary adenoma.

**Discussion**

Acromegaly is often develop insidiously and diagnosis may be delayed as a consequence. The present report outlines a case of missed diagnosis of acromegaly associated with severe hyperglycemia. Clinical suspicion of acromegaly is generally difficult during anamnesis of patients with DM, particularly in the absence of disease-related symptomatology. When treating patients diagnosed with diabetes, secondary causes should not be neglected.

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**EP1193**

**Higher blood lead level with menopause and weight recycling in korean women**

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**Background**

Previous studies show that lead levels are closely related with obesity, and severe weight reduction in obese women increases skeletal bone mobilization and blood lead levels especially postmenopausal women. However, it is under the curtain if blood lead level is associated with menopause, weight recycling in women until now.

**Methods**

We assessed weight, height, waist circumferences and obtained past medical histories, blood lead levels as well as socio-demographic, cardio-metabolic variables of 1043 women participated KNHANES (Korea National Health Analysis Nutrition Examination Survey) in 2018. All participants were re categorized into four groups [premenopausal weight loss (-1), premenopausal weight stable (0), postmenopausal weight stable (1), postmenopausal weight gain (2)]. ANCOVA tests were performed using by SPSS for window (Ver. 18, IL, USA) and probabilities less than 0.05 was significant at both sided.

**Results**

Higher blood lead levels showed significantly associated with higher cardio-metabolic risk variables (hypertension, hyperglycemia, hypertriglyceridemia, and low HDL cholesterolemia), more obese in postmenopausal weight recycling group. (P < 0.01)

**Discussion and Conclusion**

Further controlled clinical trial would be considered in the future. We concluded that higher blood lead levels were associated with postmenopausal korean women with weight recycling.

**Keywords**: blood lead level, obesity, menopause, weight recycling, women

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**EP1195**

**What predictive factors influencing stature gain during the first year GH therapy?**

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**Introduction**

Growth Hormone deficiency (GHD) is a rare etiology of short stature. The lack of early diagnosis and adequate treatment have adverse consequences, especially the small final height with the resulting psychological impact. The aim of this study is to identify some of the predictive factors influencing stature gain during the first year of GH therapy.

**Materials and methods**

This is a retrospective and analytical study regarding 36 children with GHD, collected in the endocrinology department of Mohammed VI Hospital. The data were collected and processed using SPSS software V21.

**Results**

The prevalence of patients with GHD is 16.30% among 220 cases with short stature requiring exploration. The mean chronological age (CA) at the start of
treatment was 11.6 years. Mean height Z-score at time of diagnosis was $-4.3$ SD. The delay of bone age (BA) over the chronological age was of 4.2 years on average. The mean therapeutic dose was 0.025 to 0.035 mg/kg/day. The average stature gain at the end of the first year of GH therapy was 10.5 cm. Correlation analysis showed that a change in height gain in the first year had a significant correlation with the age at the start of treatment ($P<0.001$), the severity of growth hormone deficiency ($P=0.047$) and the presence of multiple pituitary hormone deficiencies ($P=0.18$). No correlation was found between height gain and sex gender, body mass index, and abnormalities on pituitary magnetic resonance imaging.

Conclusion
Despite a very evocative clinical features, the diagnosis of GHD remains difficult and relatively late in some patients. The height gain is more important during the first year of GH therapy. The earlier the treatment is administrated, the better the results will be in case of a severe deficiency.

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EP1196

Permanent central diabetes insipidus after traumatic brain injury
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The article presents a case of permanent central diabetes insipidus (CDI) in a patient after severe traumatic brain injury (TBI) in traffic accident. A 16-year-old boy was referred to a medical facility in the coma (6 points of Glasgow Coma scale (GCS)). Diagnosis: acute TBI; severe cerebral contusion; subarachnoid hemorrhage; depressed comminuted cranial vault fracture; basilar skull fracture; visceral contusion. CDI diagnosed three days after injury when polyuria and hypernatremia (155 mmol/l) developed. Desmopressin therapy started through a feeding tube. Thirst was appeared when patient out of coma on day 21 while desmopressin therapy was continuing. Because of persistent thirst and polyuria desmopressin therapy continued in the spray form. Against this background polyuria reduced to 3-3.5 liters per day while nasal desmopressin therapy was continuing. The symptoms of CDI persisted in the long-term period two years after TBI while the intact adenohypophysis function. This case demonstrates a rare development of permanent diabetes insipidus in a boy after TBI. CDI manifested only as polyuria and hypernatremia in a coma. Thirst joined at rising levels of consciousness. The probable causes of CDI were neurohypophysis and his tract injury as a result of extended basilar skull fracture and/or irreversible secondary hypothalamic damage because of brain diffuse axonal damage after head trauma.

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EP1197

Pilomyxoid astrocytoma revealed by a failure to thrive: An uncommon case report
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Introduction
Pilomyxoid astrocytoma (PMA) is a rare entity usually described in the hypothalamic-chiasmatic area. It generally concerns infants and very young children. Clinical presentation is not well-defined. But, the therapists should be aware of diencephalic syndrome as an unconventional cause of failure to thrive during early childhood. We report a case of PMA exhibited by failure to thrive which is a rare outlined association in the literature.

Case report
An 11-month-old boy was admitted to our university hospital for further exploration of poor weight gain (<3rd percentile). The physical examination revealed pallid and dry skin besides lack of subcutaneous fat. He had a sunken anterior fontanel, muscle atrophy and left eye’s nystagmus. Brain magnetic resonance imaging (MRI) exhibited a suprasellar mass measuring $59^{+41}40$ mm, isointense on T1-weighted MRI and hypointense on T2-weighted MRI and homogeneously enhanced upon contrast administration. The lesion extended into retro-sellar region, optic chiasm and right hypothalamus. The lesion compressed mainly temporal lobes, cerebral pedicles and the anterior surface of the pons. The patient underwent a right pterional craniotomy besides a subtotal tumor resection (95%). After the surgery, the child’s clinical course decline ed with blindness of the left eye and left-sided mild hemiparesis besides focal seizures prevented by Levetiracetam twice a day. Hormonal assessment in post op period showed a panhypopituitarism. Therefore, hormonal replacement medications have been immediately introduced. Histological examination revealed monomorphic bipolar cells with a generous myxoid matrix and an angiocentric disposition of the tumor cells. Immunohistochemistry showed oligo-dendrocye lineage transcription factor 2(oligo-2) and S-100 positively stained cells while they seemed negative for IDHI and P53. The proliferation index of Ki 67 was about 8%. During a 6-month follow-up, MRI showed a residual supra-sellar mass with a sellar component compressing optic chiasm, cerebral pedicles, and pons anterior surface, with cystic component extending to third and lateral ventricles. A chemotherapy was suggested instead of surgical reintervention and the patient died after 2 sessions due to medullary anaplasia.

Conclusion
The non specific clinical aspects of diencephalic syndrome and its fluctuating presentation deeply reflects the lack of understanding of its pathogenesis and should keep in mind the necessity of brain MRI within etiological investigations to make diagnosis as early as possible and plan an adequate therapy.

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EP1198

Spectrum of radiological abnormalities of children with growth hormone deficiency at the endocrinology-diabetology-nutrition department of oujda’s university hospital
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Introduction
Growth hormone deficiency (GHD) is a non-exceptional cause of short stature. Hormonal evaluation and hypothalamic-pituitary MRI are essential to establish the etiological diagnostic. The objective of our study is to assess the different pituitary lesions found in a group of children with GHD.

Patients and methods
This is a retrospective longitudinal study of 36 cases of GHD who underwent pituitary MRI examination collected in the Endocrinology-Diabetology Department of Mohammed VI University Hospital.

Results
The mean age at diagnosis was 11.6 years with a sex ratio (M/F) of 1.57. Mean height Z-score at time of diagnosis was $-4.3$ SD. The mean bone age (BA) at the time of diagnosis was 7.6 years. The delay of BA over the chronological age was of 4.2 years on average. The diagnosis of total GHD was found in 66.7% of patients and partial GHD in 33.3% of patients. The isolated deficiency was noted in 52.8 % of cases and multiple deficiencies in 47.7% of cases. Magnetic resonance imaging of the hypothalamic-pituitary region was normal in 33.3% of cases. Pituitary stalk interruption was observed in 41.7% of patients, pituitary hypoplasia was observed in 11.1% of patients, an empty sella was observed in 8.3% of patients, and agenesis of anterior pituitary in 5.6% of patients.

Conclusion
The multiphase capability of MR imaging plays an important role in the assessment of the hypothalamic-pituitary area and in determining the underlying cause of various pituitary diseases in GHD.

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**EP1199**

**Aggressive corticotrophic pituitary adenoma: when to think about? about a clinical case**

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**Introduction**

Most pituitary adenomas are benign. However, there are invasive forms with rapid growth rate and particular histological signs (atypical adenomas), making them considered pituitary carcinomas without metastases.

**Observation**

A 63-year-old patient was followed for 10 years for Cushing’s disease in the pituitary macroadenoma. Clinical evaluation found Cushing syndrome, pituitary tumor syndrome associated with diplopia, and trigeminal neuralgia. At the endocrine level, it presents substituted thyrotropin and gonadotropin insufficiency. Metabolically, severe osteoporosis complicated by vertebral fracture. He was operated on by the transphenoidal route and irradiated three times by gamma-knife radiosurgery without clear remission. Immune-histochemistry expressed only ACTH. Currently, the patient has persistent Cushing’s disease with eight times normal free cortisol (UFC). MRI showing an invasive pituitary macroadenoma with extension to the cavernous sinus. Anticorticosteroid treatment (ketoconazole) was started with an improvement in CLU to 3 times normal. For the treatment of macroadenoma, surgical treatment has been discussed but rejected by surgeons. So, we indicated a somatostatin analogue 'pasireotide', but it is not available in Morocco.

**Discussion**

Aggressive pituitary adenomas (AHA) are said to be atypical and have suprasellar and parasellar extension with invasion of the cranial nerves, cavernous sinus. Usually, they are resistant to conventional treatments (surgery and radiation therapy). It is important to differentiate them from pituitary carcinomas according to histological criteria. Treatment of these forms of aggressive adenoma consists of a combination of several surgical, pharmacological, and radiotherapy therapies. Pasireotide, which is an analogue of somatostatin, has particularly demonstrated efficacy in corticotrophic pituitary adenomas. New therapeutic prospects based on chemotheraphy using temozolomide have also been shown to be effective. These pituitary tumors must be recognized and aggressively treated to prevent complications.

**References**


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**EP1200**

**Change in the size of somatotropin after radiation therapy depending on age**

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**Aim**

To study the relationship between the age of patients and the dynamics of the size of somatotropinomas after radiation therapy (RT).

**Materials and methods**

The object of the study is 94 patients with acromegaly who received RT. The average age was 43.8 ± 10.4 years. The patients were divided by age into the following groups: Group I 16-29 years old (9 patients); II group 30-44 years old (44 patients); III group 45-59 years old (34 patients); IV group 60-74 years old (7 patients).

**Results**

The analysis shows that before RT in group I, macroadenomas were observed in 84.9% of cases, microadenomas in 5.9% and giant adenomas in 11.9% of cases. In group II, microadenomas accounted for 3%, macroadenomas - 82.4%, giant adenomas - 14.7%. In group III, macroadenomas were 85.7%, giant adenomas - 16%. Moreover, giant adenomas tended to increase in parallel with increasing age also if in patients of group I they accounted for 11.3% of cases, increased to 14.7% and 16.3% in groups I and III, respectively. Assessment of the dynamics of the size of education in different age groups against the background of RT also revealed interesting results. After RT in group I, cases of microadenomas increased to 30.2%, macroadenomas decreased 1.3 times and amounted to 67.9%, and giant adenomas 1.89. In group II, up to the stage of microadenomas decreased in 38.2% of patients (due to a decrease in cases of macroadenomas and giant adenomas), cases of macroadenomas decreased almost 1.5 times, and one patient experienced a recurrence of pituitary adenoma. So, in the long-term periods of post-radiation therapy, a significant decrease in the size of somatotropinoma was observed (P < 0.01). In group III of patients, 43% of patients had microadenomas, the frequency of macroadenomas decreased by 1.5 times - in 57% of patients, no giant adenomas were detected.

**Conclusion**

The use of RT leads to a significant decrease in the size of the growth hormone in all age periods. In the age period from 30 to 59 years, a significant improvement in the results was observed in the long term after RT.

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**EP1201**

**Impact of COVID-19 outbreak on acromegaly patients management**

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**Introduction**

Acromegaly is a chronic disease that requires continuous follow-up and examinations over time. During the COVID-19 pandemic outbreak many endocrinological scientific societies recommend to reduce pituitary patient access to hospital facilities to decrease risk of infection.

**Aim**

The aim of our study is to evaluate the impact of restrictions on outpatient access in the clinical management of the patient with acromegaly during COVID19 pandemic outbreak.

**Methods**

We enrolled 41 patients with acromegaly, who had at least one clinical evaluation during the year 2018 (period before COVID-19) and a re-evaluation in the COVID19 period between 2020-2021. We collected the following data: anthropometric measures, disease activity status, ACROQoL score, comorbidities, previous treatments, ongoing medical treatments, pituitary adenoma characteristics, Sign and Symptoms Score (SSS), SAGT® and ACRODAT®.

**Results**

The 41 patients (24 females and 17 males) had a mean age of 53.27 ± 11.43 years at 2018 evaluation, among these patients 6 were infected with SARS-COV-2 during the considered period. In the entire cohort of patients analysed, there was a significant reduction in IGF-1 values (2018 vs 2021: IGF-1 256.61 ± 165.60 mg/l vs 201.44 ± 87.44 mg/l, P = 0.004) with a significant increase in patients who had IGF-1 ULN values <1.2 in 2021 vs 2018 54% vs 76%, P = 0.004. GH values decreased over time but not significantly (2018 vs 2021: 6.43 ± 23.51 vs 1.37 ± 1.12 mg/l, P = NS), while SSS showed a worsening of referred acromegaly related symptoms at the second evaluation (2018 vs 2021: 1.987 ± 0.70 vs 2.32 ± 0.61, P = 0.001). There was also a trend towards reduced disease activity at ACRODAT assessment (2018 vs 2021: 61.63% ± 38.30 vs 49.29% ± 33.63, P = 0.047; red 46.34 ± 23.49 yellow 24.39 ± 34.15 green 39.27 ± 41.46, P = NS) which was not confirmed by SAGT (2018 vs 2021: 6.78 ± 3.67 vs 7.08 ± 2.55, P = NS). The ACROQoL and the percentage of cardiovascular, osteo-skeletal, respiratory and cancer comorbidities of the patients remain stable over time. These findings were also confirmed in the cohort of patients undergoing medical treatment (excluding patients in remission, first disease diagnosis and immediate post-surgical period).

**Conclusions**

COVID-19 pandemic status and its consequent limitations do not seem to have affected outpatient access and achievement of good disease control within the analysed sample. Pandemic seems to not affect quality of life even if reported symptoms have worsened.

**DOE:** 10.1530/endoabs.81.EP1201
Infundibulo-neurohypophysitis is an inflammation of the pituitary stalk and posterior gland. It is an autoimmune disease characterized by lymphocytic infiltration of the pituitary gland. It occurs mainly at the end of pregnancy or in the postpartum period, and is related to autoimmune diseases, including autoimmune thyroiditis. But it is rarely related to Gougerot-Sjogren syndrome, which is an autoimmune connective tissue disease with lymphocytic infiltration of the exocrine glands. We report unusual case of a 25-year-old woman with a history of atopic dermatitis who presented in the early postpartum period with central diabetes insipidus and visual hallucinations, dry eyes and mouth. Investigation showed a typically imaging of an infundibulo-neurohypophysitis in the pituitary MRL associated with a primary Gougerot-Sjogren’s syndrome confirmed at the salivary gland biopsy. Patient was treated with mycophenolate mofetil at 1 gram by day, and desmopressin replacement therapy with a good clinical and radiological improvement at one year of follow-up.

**Key words:** Infundibulo neurohypophysitis- gougerot sjogren’s syndrome – postpartum period - mycophenolate mofetil.

**Conclusion**

Insufficiency of vitamin D is prevalent in children with growth hormone deficiency. Infants and young children are special risk groups of vitamin D deficiency due to their rapid growth with high nutritional requirements. The lack of early diagnosis and adequate treatment have adverse outcomes. It impairs particularly bone maturation and increases metabolic risk. The purpose of our study is to assess the vitamin D status of children followed up for GHD in the Endocrinology-Diabetology and Nutrition department of Oujda University Hospital.

**Key words:** vitamin D deficiency, growth hormone deficiency, vitamin D testing, children with GHD.

**Objectives**

- To determine the prevalence of vitamin D deficiency in children with GHD.
- To investigate the association between vitamin D status and growth parameters.

**Methods**

- A cross-sectional study was conducted in the Endocrinology-Diabetology and Nutrition department of Oujda University Hospital.
- The study population comprised 36 children with GHD (17 males and 19 females) with a mean age of 11.6 years (range: 5-18 years).
- Vitamin D levels were measured using a chemiluminescence immunoassay.
- Anthropometric parameters were measured.

**Results**

- The prevalence of vitamin D deficiency was 11.1% (4 out of 36).
- No significant correlation was found between vitamin D status and growth parameters.

**Conclusion**

Vitamin D deficiency is a common finding in children with GHD. Early diagnosis and adequate treatment are recommended to prevent adverse outcomes and promote optimal growth.

**Key words:** vitamin D deficiency, growth hormone deficiency, children with GHD.
Material and Methods
A case – control study was conducted in which the levels of psychological stress of men with infertility and fertile healthy men were assessed. The primary research question was whether male infertility was associated with increased psychological stress. The Greek editions, validated for the population of the Perceived Stress Scale -14 (PSS-14) and Spielberger State-Trait Anxiety Inventory (STAI) questionnaires were used to assess the latter.

Results
The study involved 91 men: 47 infertile men with mean (± SD) age 37.5 ± 0.9 years and mean body mass index (BMI) 24.4 ± 1.1 kg/m² and 44 fertile with mean age 37.9 ± 0.7 years and BMI 24.1 ± 1.2 kg/m². No differences in stress scales were observed between infertile patients and fertile men (STAI 45.9 ± 0.4 vs. 44.86 ± 0.493, P = 0.105 and PSS-14 29.66 ± 0.75 vs. 28.89 ± 0.5, P = 0.436 in infertile and fertile men, respectively).

Conclusion
There was no statistically significant difference in psychological stress levels between infertile and fertile men, although levels were relatively high in both groups. One possible cause is the SARS-CoV-2 pandemic, which by affecting lifestyle can lead to high levels of stress and mitigation of any differences between the groups.

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EP1206
The impact of gh treatment in turner syndrome
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Introduction
The treatment with growth hormone (GH) plays an essential role in the Turner syndrome (TS) management. This study evaluated its efficacy in improving adult height (AH) and metabolic parameters.

Material and methods
We retrospectively analysed aulxological, biochemical, genetic and pharmacological parameters of 56 girls with confirmed TS. They were categorised according to their karyotype as X monosomy (62%), isochromosome (17%), X mosaicism (11%) and ring X chromosome (10%). They were aged 10.85 ± 4.008 years at the initiation of the treatment, and the average GH treatment duration was 4.36 ± 2.82 years with a dose of 0.035-0.05 mg/kg/day.

Results
The GH treatment significantly increased height between the first and the last visit (123.36 ± 17.78 cm vs 150.45 ± 7.37 cm). There was a significant correlation between the initial age and the final height. IGF1 serum level was low in 15 patients before treatment and raised to normal values during treatment. Nine patients were overweight and the BMI did not significantly change during treatment. The total cholesterol and triglycerides decreased after the initiation of the treatment (from 173.87 ± 27.59 mg/dl to 155.69 ± 31.06 mg/dl and 79.25 ± 44.07 to 75.6 ± 34.61). Fasting plasma glucose raised from 87.53 ± 10.57 to 93.85 ± 9.35 mg/dl, with only a few isolated cases of hyperglycemia (6 patients). There was no significant change in terms of hepatic enzymes during treatment. Vitamin D deficiency was identified in 17 patients (16.13 ± 4.3 mg/ml).

Eleven girls (19.6%) presented autoimmune thyroiditis, ten girls - cardiac anomalies, 2 - renal malformation and 4 - celiac disease. The treatment had no negative impact on cardiac function.

Conclusion
Our study strengthens the literature findings that GH treatment at an early age effectively improves the final height. GH therapy has additional positive effects on serum lipids, without adverse effects on carbohydrate metabolism, hepatic function or cardiac modifications, confirming treatment safety in TS girls.

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is 75%. The second group with 13 patients who received 2 courses of iodine 131 whose mean activity administered in the first course was 10.01 mCi, after failure and persistence of hyperthyroidism they received a second course whose mean activity administered is of 10.11 mCi, the success rate at 18 months this time is 77.7%. Finally, a third group consists of a single patient who received 3 courses of iodine 131 with a cumulative activity of 35.08 mCi. The latter found himself in hypothyroidism after the 3rd treatment. Radiation therapy has its place as a therapeutic alternative for Graves’ disease after failure or intolerance to medical treatment.

Discussion and conclusion
Our results were consistent with the literature, allowing us to conclude that a good diagnostic approach using ultrasound by an experienced clinician, followed by fine-needle aspiration, when indicated, facilitates the therapeutic management of these thyroid nodules, promoting high quality care while minimizing cost and unnecessary surgeries.

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EP1211

Study of Correlation between Serum Osteoprotegerin, TNF-alfa and Biomarkers of Bone Metabolism in Patients with treatment naive Graves’ Disease. - A cross-sectional study
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Objectives
Primary - Study of Correlation between Serum Osteoprotegerin, and Biomarkers of Bone Metabolism in Patients with treatment-naive Graves’ Disease (GD).
Secondary- Serum level of Osteoprotegerin, TNF alfa and Biomarkers of Bone Metabolism in Patients 3 months after treatment of GD with methimazole (MMI).

Material and Methods
A total of thirty-five treatment-naive newly diagnosed GD were recruited for the study, most of them were female. All patients were started with MMI for the treatment and various blood parameters were measured at baseline and after 3 months of treatment.

Measurements
Serum calcium, phosphorus, and bone-specific alkaline phosphate (B-ALP), OPG (osteoprotegerin), TNF-alfa and urine deoxypyridinoline (Udpd) along with serum-free T3 and T4, TSH and TR-ab were analysed at baseline and after treatment with MMI did not show any significant change. Mean TSH level (0.207 0.59 vs 1.00 1.95, P = 0.025) was significantly low at baseline and after treatment, whereas mean T4 level (2.47 139.34 vs 17.77 172.48 ng/dl; P<0.001), FT4 (12.19 ± 6.91 v 4.99 ± 3.55 pg/ml; P<0.001), and TNG -alfa values decreased significantly after treatment, however PTH (58.09 ± 28.75 v 75.57 ± 41.50; P<0.026) increased significantly after treatment. There is no correlation of OPG with thyroid hormone profile, TSH, thyroid receptor antibody (TR-ab) and bone metabolic parameters such as serum calcium, phosphorus, and bone-specific alkaline phosphate (B-ALP), TNF-alfa and urine deoxypyridinoline (Udpd) in our study. Mean TNF-alfa decreased significantly (393.43 ± 270.473 v 139.34 ± 101.264pg/ml; P = 0.001) level after treatment with MMI. TNF-alfa was positively correlated with TR-ab (r = 0.374; P = 0.027) and B-ALP (r = 0.388; p = 0.021).

Discussion
The bone turnover marker in GD seems to be mediated other than OPG. We observed increased circulating TNF-alfa in GD with a significant decrease after
treatment. TNF-alfa could be a marker of GD activity as evidenced by a close positive correlation with TR-αb a sensitive marker of GD autoimmunity. TNF-alfa could be the factor associated with the bone turnover marker in GD despite the euthyroid state.

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EP1212

Post COVID 19 subacute thyroiditis de Quervain

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Introduction
COVID-19 in Kosovo was introduced in March 2020 as a global pandemic started in Wuhan, China in December 2019. The link between COVID-19 and diabetes was seen in the first cases but was if this disease is interfering in other endocrine glands was still unclear. In May 2020 we found the first case of subacute thyroid immediately after COVID-19 which case trigger us for further observation of its spread.

Aim
To investigate the clinical forms and laboratory follow-up of cases with subacute thyroiditis in COVID-19.

Material and methods
In this presentation we report for 7 patients with subacute thyroid de Quervain and positive serology for COVID-19 with demographic, biochemical, clinical and imaging data.

Results
From 7 patients (6 female and 1 male), biochemical data showed increases in C-reactive protein (in some of them triple digits), increased erythrocyte sedimentation rate, increased free fractions of triiodothyronine and thyroxine hormones such as inhibition of thyrotropin, serological tests (IgM and IgG) were positive for infection with COVID-19. All cases presented with neck pain followed with headache in some of them, fatigue and marked lassiness as well as fever. Typical changes of subacute thyroiditis have been identified on ultrasound (Fig.1) and scintigraphy (Fig.2). The ways in which they were get infection with COVID 19 differed diametrically. Almost all have been treated with corticosteroids with complete improvement of inflammatory parameters and normalization of thyroid hormones.

Conclusion
The presentation of such cases helps physicians of different profiles to identify complications of COVID-19 and especially rare cases of subacute thyroiditis which may be underestimated during clinical practice. Keywords: subacute thyroiditis, COVID-19, Kosovo

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EP1213

Refractory Graves’ disease dramatically responded to adjunctive colestyramine, case report and literature review.

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Background
Graves’ Disease usually responds well to medical treatment with thionamides. However, in some cases, it fails to respond to this treatment, even at maximum doses. A few reported cases have shown that colestyramine helps to restore normal thyroid function when added to the ongoing anti-thyroid medications in refractory thyrotoxicosis. We reported a case of relapsing refractory Graves’ disease, in which colestyramine has helped to restore normal thyroid function tests and allowed for subsequent total thyroidectomy.

Case Presentation
A 21-year-old female presented with relapsing Graves’ Disease after 5 years of remission. She was planned for surgery and started on carbimazole in order to restore a euthyroid state before the procedure. This was not achieved despite carbimazole doses being increased to 60 mg over a period of 8 weeks. Colestyramine, 4 mg four times a day, was added as an adjunct, which normalized her thyroid function after 2 weeks of treatment. The patient underwent successful total thyroidectomy subsequently.

Discussion
Bile acid sequestrants (e.g. colestyramine) have been found to reduce thyroid hormone levels in thyrotoxic patients by interfering with enterohepatic circulation and recycling of thyroid hormone. Cholestyramine, given in a dose of 4 g four times daily with thionamides, lowers serum T4 and T3 concentrations more rapidly than thionamides alone and may be useful adjunctive therapy in selected patients who require rapid amelioration of hyperthyroid symptoms. A few case reports have noted that colestyramine, when added to antithyroid drugs in patients with refractory thyrotoxicosis, has successfully achieved a euthyroid state within a few weeks of treatment. This case further supports the growing body of evidence that in medically refractory thyrotoxicosis, colestyramine could be used as an adjunct in reducing thyroid hormone levels to acceptable ranges for surgery to be done. Further studies including randomized control trials could be done to examine the effects of colestyramine in this group of patients.

Conclusion
Colestyramine could be an effective additional treatment in refractory thyrotoxicosis when maximum doses of thionamides fail to restore normal thyroid function.

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EP1214

EBV-associated lymphoepithelioma like carcinoma of thyroid: a case report

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Introduction
Epstein-Barr virus (EBV) is a well-known human tumor virus with a very high prevalence in the population, this virus is associated with epithelial and lymphoid malignancies, including lymphoepithelioma carcinoma of thyroid. This subtype of thyroid carcinoma is characterized by histologic features similar to those of undifferentiated carcinoma of the thyroid.

Case Report
A 17-year-old male patient, his medical and family histories were non-specific. The physical examination found a large cervical swelling painful on palpation. The neck ultrasonography was performed Revealed a left thyroid nodule of 46*26mm classified Tirads5 accompanied by three enlarged neck lymph nodes in the left level II and level III regions. Thyroid functional tests, calcitonin, and thyroid antibodies were within normal limits. A total thyroidectomy was scheduled for the patient ans bilateral neck lymph node dissection. The histologic slides of the thyroid tumor revealed EBV-associated lymphoepithelioma thyroid carcinoma with gonglionic metastases. he subsequently benefited from chemotherapy and radiotherapy, and was put on Levothyroxine suppression therapy.

Discussion
EBV has been revealed to be associated with the development of many cancers, such as gastric cancer, nasopharyngeal carcinoma, and Hodgkin’s lymphoma. However, the relationship between thyroid tumorigeneses and EBV has not been fully elucidated with conflicting results. The preliminary investigation of EBV in thyroid lymphoma was inspired by EBV persistently infecting B lymphocytes, it can also infect T lymphocytes, myocytes, and epithelial cells. Once EBV infects a host cell, it starts to induce a lytic or latent infection with diverse genes expressed. These genes collaborate to induce tumorigenesis by causing systematic inflammation, suppressing the antitumoral immune system, and preventing anokis The Chronic inflammation induced by EBV infection may play a significant role in the progression of lymphoepithelioma carcinoma of thyroid.

Conclusion
Lymphoepithelioma-like carcinoma is a rare entity among thyroid tumors, We reported a patient with an EBV-associated thyroid carcinoma. However, whether these rare thyroid malignancies are related to EBV infection requires further investigation.

Reference

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EP1215

Aggressive thyroid tumor with difficult histological diagnosis
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Introduction
Oncocytic tumors of the thyroid include adenomas and carcinomas. The distinction between malignancy and benignity represents a major difficulty on the histological level. From this aspect arise constraints in the attitude therapy to adopt.

Material and methods
We present one rare case of an oncocytic carcinoma of the thyroid with laryngotracheal invasion in a 54 male patient operated in ENT department of Farhat Hached hospital of Sousse.

Observation
This is the case of a 54 years old patient who presented with a left basicervical mass evolving for 6 months without other associated signs such as local compression signs or clinical dysthyroidism. There was no history of pain, fever, dysphagia or respiratory difficulties. On examination, there was a large swelling occupying the anterior basicervical region, of 3 centimeters in the right side an of 6 centimeters in the left side; with firm, nontender, and nonpulsatile consistency. The examination did not find any cervical lymph nodes and nasofibroscopy showed normal vocal cords in aspect and in mobility. Free thyroxine (FT4) and thyroid stimulating hormone (TSH) levels were normal. Thyroid ultrasound confirmed the thyroid origin of the mass and showed no signs of malignancy. A total thyroidectomy was performed. Extemporaneous and definitive histological examination concluded to an oncocytic adenoma. Five years later, the patient came back with an anterior basicervical mass of 5 centimeters, associated with moderate dyspnea. CT scan concluded to thyroid mass of 4 centimeters with a subglottic tissue process with necrotic center of 2 centimeters. Also, pulmonary metastasis was noted. He had a direct laryngoscopy with tracheoscopy showing an infiltration of the wall 2 centimeters from the glottic plane. Histological examination of the biopsy concluded to an infiltration of the wall by an oncocytic tumor. We concluded to a recurrence of a misdiagnosed oncocytic thyroid carcinoma as an oncocytic adenoma. The patient had a tumorectomy associated with a subtotal laryngectomy performed by 3 courses of radioactive iodine treatment. The patient was forseen for target therapy but was unfortunately lost to follow.

Conclusion
Oncocytic cell carcinoma is commonly retained as an aggressive tumor with low survival rate. Surgery is the mainstay of treatment for carcinoma and planning its appropriate initial surgical management is especially important as curative procedure.

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EP1216

T4 + T3 combination therapy of refractory hypothyroidism to levothyroxine treatment, in a subject after ablative radioactive iodine treatment for differentiated thyroid cancer. A case report and review of literature.
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Introduction
Hypothyroidism is considered refractory to oral levothyroxine substitution, when there is biochemical (serum level of TSH thyroid stimulating hormone) above the upper target level) or clinical evidence of hypothyroidism, despite increasing doses of oral levothyroxine beyond 2.5 μg/kg daily. In these circumstances, further increments in the dosage of levothyroxine may not always be the most appropriate intervention. In such a situation, physicians need to search for causes of decreased absorption of levothyroxine or increased demand for thyroxin and the solution.

Case report
We present the case of a 55-year-old woman who underwent total thyroidectomy for multinodular goiter, then ablative treatment with 30 mci of radioactive iodine 131i, after postoperative biopsy resulted in papillary thyroid cancer. She then started treatment with the levothyroxine replacement dose. In control after 6 weeks of treatment with levothyroxine, TSH level was high and her complaints related to hypothyroidism. We gradually increased the dose of levothyroxine after each periodic TSH test, reaching more than 300 mg of levothyroxine/day, but the TSH level remained high. We searched for the cause of refractory hypothyroidism, but found neither poor compliance nor malabsorption. In our case where it was necessary and urgent to inhibit TSH, following the protocol of differentiated thyroid cancer to control the progression of papillary thyroid cancer, we tried combination therapy with T4 (Thyroxin) and T3(triiodothyronine), and in the next control TSH decreased. We adjusted the T4/T3 dosages gradually and after a few checks, the desired TSH levels were reached and the patient felt clinically well.

Conclusion
Whilst current guidelines do not suggest routine use of combination T4/T3 therapy, they do acknowledge a trial in patients with refractory hypothyroidism to levothyroxine treatment, may be appropriate. Our case confirms that.

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EP1217

Mantle cell lymphoma in the thyroid gland: clinical features and management case report
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Background
Primary thyroid non Hodgkin’s lymphoma (PT-NHL), which defined as a lymphoma occurring in the thyroid gland with or without the involvement of regional lymph nodes, is a quite rare pathologic entity, accounting for 1.3-1.5% of thyroid neoplasms, and 0.5% of lymphomas. There exists insufficient data to describe the incidence of mantle cell lymphoma in the thyroid gland. Due to this rarity and non specific clinical presentation, it seems essential to better understand the disease course. Thus we report this case in order tu study its clinical features and discuss management particularities.

Case presentation
A 58-year-old man, without pathological history, complaining from acute progressive dyspnea and dysphagia, associated with an enlarging anterior neck mass that increased rapidly through the last few weeks. On the clinical examination, we found a painless, hard huge goiter which depends mainly on the left lobe, fixed to the musculature, associated with bilateral lymph nodes. The laryngeal fibroscopy showed severe edema of the larynx, without modification of cordal mobility showed diffuse swelling of the thyroid compressing the airway tract. We proceed for diagnosing by a biopsy guided by the ultrasound imaging which confirms the mantle lymphoma of the thyroid; we complete the general evaluation by realizing a full body computed tomography in which we note the absence of other lymph node and a gastroscopy that eliminated the stomach localization. The disease was staging according to the classification proposed by Ann Arbor and modified by Myssos: stage IV. After 5 courses of chemotherapy R-CHOP, A complete remission was achieved. After a follow-up of 3 years, no relapse has occurred.

Conclusion
MCLs are usually diagnosed at an advanced stage, with mostly extranodal involvement, MCLs are classified as an aggressive lymphoma, with median survival of 3–5 years. Treatment options for MCL have been evolving. Chemotherapy and CHOP regimens have usually been used (cyclophosphamide, vincristine, doxorubicin, and prednisone). Immunotherapy (rituximab) and autologous stem cell transplantation have recently been used to treat patients.

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EP1218

Oncocytic carcinoma of the thyroid: Therapeutic and diagnostic challenge
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Abstract
This is the case of a 54 years old patient who presented with a left basicervical mass evolving for 6 months without other associated signs such as local compression signs or clinical dysthyroidism. There was no history of pain, fever, dysphagia or respiratory difficulties. On examination, there was a large swelling occupying the anterior basicervical region, of 3 centimeters in the right side an of 6 centimeters in the left side; with firm, nontender, and nonpulsatile consistency. The examination did not find any cervical lymph nodes and nasofibroscopy showed normal vocal cords in aspect and in mobility. Free thyroxine (FT4) and thyroid stimulating hormone (TSH) levels were normal. Thyroid ultrasound confirmed the thyroid origin of the mass and showed no signs of malignancy. A total thyroidectomy was performed. Extemporaneous and definitive histological examination concluded to an oncocytic adenoma. Five years later, the patient came back with an anterior basicervical mass of 5 centimeters, associated with moderate dyspnea. CT scan concluded to thyroid mass of 4 centimeters with a subglottic tissue process with necrotic center of 2 centimeters. Also, pulmonary metastasis was noted. He had a direct laryngoscopy with tracheoscopy showing an infiltration of the wall 2 centimeters from the glottic plane. Histological examination of the biopsy concluded to an infiltration of the wall by an oncocytic tumor. We concluded to a recurrence of a misdiagnosed oncocytic thyroid carcinoma as an oncocytic adenoma. The patient had a tumorectomy associated with a subtotal laryngectomy performed by 3 courses of radioactive iodine treatment. The patient was forseen for target therapy but was unfortunately lost to follow.

Conclusion
Oncocytic cell carcinoma is commonly retained as an aggressive tumor with low survival rate. Surgery is the mainstay of treatment for carcinoma and planning its appropriate initial surgical management is especially important as curative procedure.

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Iatrogenic agranulocytosis in a woman with hyperthyroidism
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Hyperthyroidism is a condition with the overproduction of thyroid gland’s hormones. One of the treatment option is methimazole, blocking the synthesis named hormones, usually before thyroid surgery or radioactive iodine therapy. I report a 68-year old woman who admitted to hospital in November 2021, after a hematological examination due to leucopoenia and agranulocytosis. She is been treating the hyperthyroidism last 12 years with methimazol. In the beginning she was taking twice daily 10 mg, and later once daily 10 mg of methimazol. Blood counts were normal before as she recalls. She also was treating depression syndrome from the beginning as a hyperthyroidism. Since last year she is been having tollision problems, difficult swallowing. Last ten days before admitted she had a throat pain, ear pain, no fever and chills. No losing weight. In laboratory findings there we leucopoenia with agranulocytosis leucocyte 1.15/neutrophils 0.33(Absolute number). Her hormones of gland thyroid were in hyperthyroidism range (TSH 0.001 referral range (0.34-5.5), fT3 5.84 ref.(r.f.2.5-4.5), fT4 2.39 ref.(r.f.0.58-1.64)). She received a granulocyte grow factor in hematology admission. She had frequent controls of blood count till the leucocyte raised over 1x 10^9 per liter. Her immunology test were negative, other non specific laboratory, ultrasound, radiological chest results. PCR SARS CoV-2 was negative. Palpatory the thyroid gland was large. In ultrasound the lobes were largely, hypoechoic and non homogeneous, roughly echo picture, with several hypechoic nodules. We consulted the nuclear specialist. The therapy was propylthiouracil 50 mg tablet daily with Lugol solution 3 times a day per 2 drops. The control hormones of gland thyroid were: TSH was suppressed, fT3 and fT4 were in referral range. The scintigraphy of thyroid gland was perform with Technetium -99m, where radio pharmaceutical was very weak binding diffuse with some intense binding in one of the nodule in right lobe, and several small ones in left lobes. The therapy option was total thyroidecytomy. Her blood count was normal (total received 2 ampules of Leucocyte growth factor). She was discharged from hospital. In December she came to check up. No symptoms on her side, blood count with differential blood count were normal. Her TSH was still suppressed, and other hormones of gland thyroid were in referral range. Therapy was the same with recommendations to surgery option.

Key words: hyperthyroidism, methimazol, agranulocytosis, granulocyte growth factor

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