Monaldi Arch Chest Dis
2001; 56: 4, 364–368

First report of the Italian register for diffuse infiltrative lung disorders (RIPID) (*)

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ABSTRACT: ***First report of the italian register for diffuse infiltrative lung disorders (RIPID). The RIPID Scientific Committee: C. Agostini, C. Albera, F. Bariffi, M. De Palma, S. Harari, M. Lusuardi, A. Pesci, V. Poletti, L. Richeldi, G. Rizzato, A. Rossi, M. Schiavina, G. Semenzato, C. Tinelli.***

RIPID was established in 1998 as a joint project of the major Italian scientific societies for Respiratory Medicine, with the aim to create an Italian Register on diffuse infiltrative lung disorders that can provide the basis for epidemiological and clinical studies of adequate sample size.

In the period from May 1998 to December 2000, 1,382 cases were submitted from 54 Centers in 15 regions of Italy, 54.2% males (mean age ± SD 50.5 ± 16.8 years) and 45.8% females (50.2 ± 15.3 years). A current smoking habit emerges in 18% of subjects; former smokers and never-smokers represent 26% and 56% of the total case series, respectively. The most frequent disease registered is idiopathic pulmonary fibrosis (37.6%), followed in decreasing order by sarcoidosis (29.2%), and Langherans' cell hystiocytosis (6.6%). High resolution computed tomography (HRCT) was considered as the most important tool for final diagnosis in the majority of cases (74.4%); 39.4% of patients underwent transbronchial biopsies, 39.2% bronchoalveolar lavage (BAL). A surgical biopsy was performed in 20.5% of patients.

A web site has been activated from December 2000 (www.pneumonet.it/ripid), allowing prompt access to all information and scientific material concerning the project and to an electronic form for data collection that can be completed on-line.

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(*) RIPID = REGISTRO ITALIANO DELLE PNEUMOPATIE INFILTRATIVE DIFFUSE.

Keywords: Diffuse infiltrative lung disorders, rare lung disorders, registers, epidemiology, idiopathic pulmonary fibrosis, sarcoidosis, Langerhans' cell histiocytosis.

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The RIPID project

RIPID (Registro Italiano Pneumopatie Infiltrative Diffuse, or the Italian Register for Diffuse Infiltrative Lung Disorders) was effectively established in 1998 as a joint project of the three major Italian scientific societies for Respiratory Medicine, AIPO (Associazione Italiana Pneumologi Ospedalieri, or the Italian Association of Hospital Specialists in Respiratory Medicine), SIMeR (Società Italiana di Medicina Respiratoria, or the Italian Society for Respiratory Medicine), and the Italian Chapter of WASOG (World Association on Sarcoidosis and Other Granulomatous Disorders), who agreed on the need to have a common project and a single Italian Register, following parallel projects in other European countries [1–4].

The aim of the RIPID project is tocollect cases of diffuse infiltrative lung disorders (also known as interstitial lung disease), diagnosed in different settings (both in-hospital and out-patient), complete with the information requested in the data collection form published in the main national journals of Respiratory Medicine (Medicina Toracica and Rassegna di Patologia dell'Apparato Respiratorio) and now available also on-line.

The intention of its promoters and contributors is to exploit RIPID for research studies, not only in the epidemiological but also in the clinical and therapeutic fields. In the meantime a series of educational activities (courses, seminars, articles) has been planned to improve knowledge on diffuse infiltrative lung disorders and advertise the project in order that new Centers may become involved in the collection of data.

To this end, a new internet web site on RIPID was activated in December 2000 (www.pneumonet.it/ripid), allowing prompt access to all information concerning the project (aim, programmes, meetings), to scientific material on diffuse infiltrative lung disorders and to an electronic, updated

form for data collection that can be completed online. The scientific societies involved in the project have also undertaken a campaign to diffuse the initiative at grass-roots level, by circulating letters among their own members, publishing information material in their scientific journals and organizing symposia at national meetings.

The present report refers to the period of RIPID's activity from May 1998 to December 2000. Data are those limited to the cases submitted by fax, using the first version of the data collection form. The collection of cases was in this period both retrospective and prospective; since January 2001, inclusion has been exclusively prospective and will be the object of a second report.

Data collection

The recruitment of cases has followed a regular linear trend since it started in May 1998. Up to December 31, 2000, submission of forms was exclusively via fax, with 1,382 cases included in the registry. Fifty-four Centers in 15 regions of Italy participated (figure 1). Most cases (787, 57%) were submitted from the region of Lombardia, followed by Emilia Romagna with 186 patients (13%). The most frequent disease registered is idiopathic pulmonary fibrosis (IPF), followed in decreasing order by sarcoidosis, and Langherans' cell hystiocytosis (LCH) (table 1); these three disorders account for more than two-thirds of the total number of cases. Also represented are a number of very infrequent lung disorders, that individual specialists rarely have the occasion to encounter more than once in their career. For these rare diseases, a national register can represent an extremely important tool for a systematic study and deeper knowledge.

Socio-demographic characteristics

Male sex is slightly more represented than female (54.2% vs 45.8%); mean age (± SD) is 50.5 years (± 16.8) for males and 50.2 years (± 15.3) for females. A current smoking habit emerges in 18% of subjects; former smokers and never-smokers represent 26% and 56% of the total case series, respectively. The analysis of smoking habits corrected by disease and sex demonstrates, as expected, that most smoker/ex-smoker patients, in both sexes, belong to the LCH group.

Fig. 1. – Case series divided according to the Region where patients were recruited (only cases registered up to December 2000 with the first version of the data form).

Table 1. – Cases enrolled according to type of pathology*

	%	No
Idiopathic pulmonary fibrosis	37,6	520
Sarcoidosis	29,2	403
Langerhans' cell Hystiocytosis	6,6	91
BOOP	5,0	69
Extrinsic allergic alveolitis	3,7	51
Lymphangioleiomyomatosis	2,5	35
Eosinophilic pneumonia	1,9	26
Drug-induced lung disease	1,7	23
Wegener syndrome	1,3	18
Alveolar proteinosis	1,1	15
Constrictive bronchiolitis	0,8	11
Hamman-Rich syndrome	0,8	11
MALT pulmonary lymphoma	0,6	8
Diffuse alveolar haemorrhage	0,5	7
Lymphomatoid granulomatosis	0,5	7
Other diagnosis	6,2	85

* Data here reported are limited to the cases submitted up to December 31 2000, by fax, using the first version of the data collection form.

BOOP = bronchiolitis obliterans organizing pneumonia; MALT = mucosa associated lymphoid tissue.

Clinical features

The number of symptoms at the onset of the disease was 1 in 39.4%, 2 in 37.8% and 3 in 15.6% of cases; in 7.3% of subjects no symptoms were reported. Eighty percent of asymptomatic cases with occasional diagnosis were represented by pulmonary sarcoidosis. Symptom prevalence is reported in figure 2; "other" refers to several different symptoms, mainly extrapulmonary. In 33 patients presentation of the disease was pneumothorax; of these, 45% were affected by histiocytosis X and 48% by lymphangioleiomyomatosis. Percent distribution of symptoms at onset for the main disorders is shown in table 2; dyspnea is the most frequent symptom at onset for numerous diseases, such as pulmonary fibrosis, extrinsic allergic alveolitis (hypersensitivity pneumonitis), and drug-induced lung disorders. It is interesting to note that extra-pulmonary symptoms were common at the onset of sarcoidosis (mainly erythema nodosum), histiocytosis X and lymphangioleiomyomathosis.

Respiratory function data were in the normal range in 39.9% of cases; a restriction pattern was found in 43.4%, an obstruction pattern in 9.7% and a mixed pattern in 7.1% of patients. At the time of inclusion in the Register respiratory function was normal in most cases of sarcoidosis, Wegener's syndrome, and pulmonary lymphoma; an obstructive pattern was found to be quite characteristic for lymphangioleiomyomatosis and obstructive bronchiolitis. Restriction was typical for pulmonary fibrosis, alveolar proteinosis and drug-induced lung disease.

Diagnostic procedures

An analysis of the individual diagnostic procedures shows that chest high resolution computed tomography (HRCT) was considered as the most important tool for final diagnosis in the majority of cases (74.4%); 39.4% of patients underwent transbronchial biopsies, 39.2% bronchoalveolar lavage (BAL). A surgical biopsy was performed in 20.5% of patients, of whom 62.8% by thoracotomy, 31.7% by videothoracoscopy (VATS) and 5.5% by thoracoscopy. Interestingly, the use of VATS

Ist SYMPTOM	N°	%
DYSPNEA	619	48.3
COUGH	285	22.2
FEVER	99	7.7
OTHER	278	21.7
Total	**1281**	100.0
Missing data (101)		

IInd SYMPTOM	N°	%
COUGH	269	36.4
DYSPNEA	226	30.6
FEVER	71	9.6
OTHER	172	23.3
Total	**738**	100.0

IIIrd SYMPTOM	N°	%
DYSPNEA	40	18.7
COUGH	29	13.6
FEVER	37	17.3
OTHER	108	50.5
Total	**174**	81.3

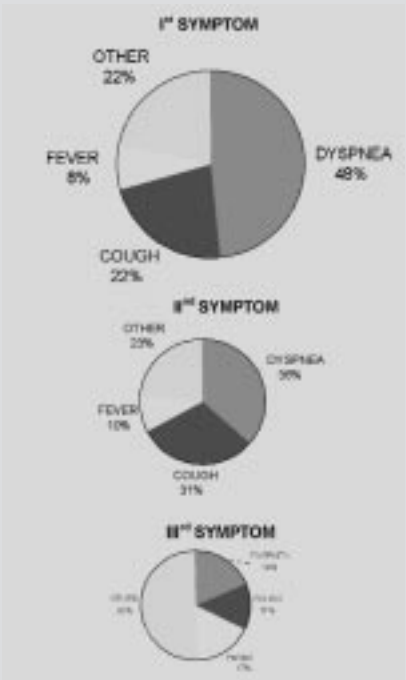

Fig. 2. – Symptoms at onset in order of frequency.

Table 2. – First symptom at presentation in the individual disorders

	cases no.	DYSPNEA %	COUGH %	FEVER %	OTHER %	MD* %
Idiopathic Pulmonary Fibrosis	520	63.5	22.5	3.5	6.9	3.7
Sarcoidosis	403	29.5	18.6	4.2	35.5	12.2
Langerhans' cell Hystiocytosis	91	26.4	26.4	5.5	34.1	7.7
Other Disorders	85	54.1	16.5	7.1	17.6	4.7
BOOP	69	30.4	14.5	37.7	10.1	7.2
Extrinsic Allergic Alveolitis	51	39.2	33.3	13.7	3.9	9.8
Lymphangioleiomyomatosis	35	31.4	8.6	0.0	51.4	8.6
Eosinophilic Pneumonia	26	26.9	30.8	30.8	11.5	0.0
Drug Induced Lung Disease	23	39.1	21.7	13.0	8.7	17.4
Wegener Syndrome	18	22.2	0.0	22.2	55.6	0.0

* = Missing data.

showed a significant increase during the year 2000 (17%), as compared to an average use in 6% of cases in the six years prior. On the contrary, over the same period the use of HRCT (in 72% of cases on average) remained fairly constant.

Table 3 shows the number and percentage of cases in whom diagnosis was supported by a combination of investigative tools; the first ten account for 80% of all combinations employed. Reporting data for the individual disorders (see table 4), the most represented diagnostic combination in almost all cases (excepting only obliterative bronchiolitis and extrinsic allergic alveolitis) involves only radiological investigations.

Conclusions

This preliminary report on RIPID activities makes the point that it is a joint project of the major Italian scientific societies for Respiratory Medicine in the field of diffuse infiltrative lung disorders, with the aim to create an Italian Register(following the example of scientific societies in other European countries) that can provide the basis for designing epidemiological and clinical studies of adequate sample size. Collateral activities have been implemented in the course of the project, such as joint seminars with pathologists and radiologists in accordance with the respective national scientific societies. These joint seminars represent a very profitable forum for the interdisciplinary discussion of case reports. Other important activities are represented by the different sections of the RIPID website, i.e. the possibility for debate, education, newsgroups, on-line consultation, on-line publication of scientific material and general information, and real time update of statistics following on-line input of new cases.

The Scientific Committee and the promoting scientific societies are confident that the RIPID Register can represent a "lab" to test new forms of scientific research based on cooperation among specialists with a common interest in a field of Respiratory Medicine, i.e. diffuse infiltrative lung disorders, that, without such joint collaboration, could risk neglect with, as the inevitable consequence, inadequate standards of patient management.

Table 3. – Combination of diagnostic procedures used

	No.	%
Clinical examination + standard chest X-ray + HRCT	282	20.4
Clinical examination + standard chest X-ray + HRCT + BAL + transbronchial biopsy	176	12.7
Clinical examination + standard chest X-ray + HRCT + transbronchial biopsy	147	10.6
Clinical examination + standard chest X-ray	100	7.2
Clinical examination + standard chest X-ray + HRCT + BAL	139	10.1
Clinical examination + standard chest X-ray + HRCT + thoracotomy	59	4.3
Clinical examination + standard chest X-ray + transbronchial biopsy	56	4.1
Missing data	47	3.4
Clinical examination + standard chest X-ray + transbronchial biopsy + BAL	55	4.0
Clinical examination + standard chest X-ray + BAL	56	4.1
Other combinations	265	19.2

HRCT = high resolution computed tomography; BAL = bronchoalveolar lavage.

Table 4. – Combination of the diagnostic investigations for the individual disorders

	A	B	C	N°
Idiopathic Pulmonary Fibrosis	130	61	61	520
Sarcoidosis	68	33	49	403
Other disorders	23	7	12	85
Langerhans' cell Hystiocytosis	19	3	14	91
BOOP	8	16	10	69
Extrinsic Allergic Alveolitis	4	8	9	51
Lymphangioleiomyomatosis	9	3	4	35
Eosinophilic Pneumonia	4	5	4	26
Drug-induced lung disease	6		3	23
Wegener Syndrome	4	5	4	18
Constrictive Bronchiolitis	1	1	1	15
Alveolar Proteinosis	1			11
MALT Pulmonary Lymphoma	2	1		11
Diffuse Alveolar Haemorrhage	1	2	2	8
Hamman-Rich Syndrome	1	1		7
Lymphomatoid Granulomatosis				7
Missing Data	1	1	3	2
Total	282	147	176	1382

A: Clinical examination + standard chest X-ray + HRCT
B: Clinical examination + standard chest X-ray + HRCT + transbronchial biopsy
C: Clinical examination + standard chest X-ray + HRCT + BAL + transbronchial biopsy.

BOOP = bronchiolitis obliterans organizing pneumonia; MALT = mucosa associated lymphoid tissue; HRCT = high resolution computed tomography; BAL = bronchoalveolar lavage.

Acknowledgements: The following colleagues contributed to the enrolment of patients in RIPID: Harari and De Juli (Milano); Cervio, Ratta and Rossi (Pavia); Luisetti (Pavia); Donazzan, Bonazza, Seebacher and Triani (Bolzano); Poletti and Grosso (Bologna); Albera (Torino); Ledda (Cagliari); Pesci, Capra, Cacciani and Greco (Parma); Cosma, Fugagnoli, Merizzi, Marruchella (Sondalo); Palamidese and Ledda (Padova); Giorgio and Pierucci (Bari); Sinigaglia and Spedini (Brescia); Zaccara and Viola (Rho); Lusuardi and Capelli (Veruno); Rizzato and Montemurro (Milano); Ghio (Crema); Brunetti (Pavia); Moretti (Bari); De Toni (Vicenza); Panizza, Tassi and Tondini (Brescia); Pela (Osimo); Moschini (Orbassano); Anghinolfi (Cremona); Mazzucchelli (Tradate); Trianni and Barozzi (Modena); Durante (Taranto); Giampiccolo (Trento); Zucchi and Roggeri (Reggio Emilia); Klotzner (Bolzano); Celano (Potenza); Franco (Piacenza); Sugamiele (Trapani); Valentino (Napoli); Ortu (Sassari); Vincenzo (Desenzano); Provenzano (Palermo); Ferranti and Tazza (Terni); Azzarone (Reggio Emilia); Bisconti and Scoditti (Lecce); Consalvi (Terni); Valerio (Brindisi); Canessa (La Spezia); Visca (Torino); Marvisi (Fiorenzuola); Faggionato (Bolzano); Ukmar (Trieste); Moceo (Palermo); Nolita Pulerà (Livorno); Pecis (Lodi); Colombo (Varese); Felletti (Genova); Allegri (Milano); Lo Coco and Vitale (Palermo); Salio (Alessandria); Tazza (Terni); Richeldi (Modena); Sciascera (Como); Confalonieri (Trieste); Provenzano (Palermo). Due to problems in the readability of several forms transmitted by fax there might be unwanted errors in the above list: the Authors apologize in advance for any mistake or omission.

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