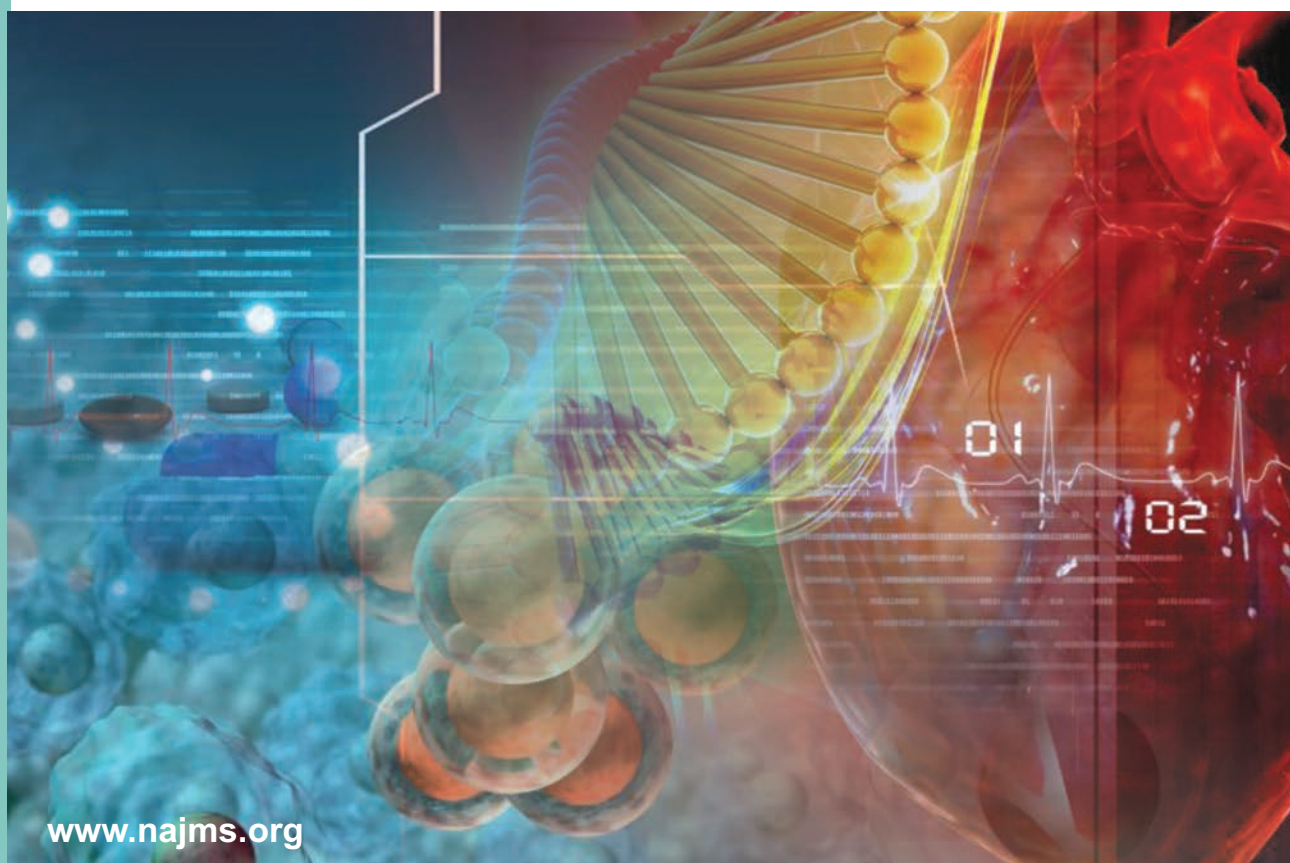


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# The Environment and Amyotrophic Lateral Sclerosis: Converging Clues from Epidemiologic Studies Worldwide

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The etiology of one of the most severe human neurological diseases, amyotrophic lateral sclerosis (ALS), remains obscure nearly 150 years after its original description by Charcot, despite substantial advancements in the biomedical research on this disease. The possibility that one or more environmental risk factors may trigger or contribute to the degenerative process of motor neurons characterizing this devastating disease remains appealing, and it is supported by a number of epidemiologic studies,<sup>[1]</sup> though specific causative factors are yet to be confirmed. Among these, pesticides,<sup>[2]</sup> the metalloid selenium and heavy metals,<sup>[3]</sup> trauma, electrical shocks, magnetic fields, and several other environmental factors, including infectious agents, have been associated with an excess risk of the disease, and geographical analyses appear to add support for an environmental etiology of the disease.<sup>[4]</sup>

Converging indications from different epidemiologic studies and contexts represent an important clue to the validity of etiological hypotheses. Therefore, the results of the study by Das *et al.* published in this issue of the North American Journal of Medical Sciences appear to be particularly interesting as they have added further indications of an etiologic role in ALS of some putative environmental risk factors from a setting entirely

different from those subject of epidemiologic studies in Western countries, and apparently never previously investigated with regard to the study hypotheses.<sup>[5]</sup> In particular, this study, carried out in eastern India using a sound methodological approach provides evidence of an etiologic role of pesticides (not farming per se), smoking, and electrical shock, though these results must be weighed against studies that have reported conflicting results, duly mentioned by the authors. This discrepancy underscores the need to address these etiological hypotheses in large epidemiologic studies in different geographic areas, seeking better concordance. Such effort would greatly help to confirm or refute previously identified risk factors and make them more specific, e.g., to identify the specific toxin in tobacco smoke, or single drinking water chemicals and neurotoxic pesticides to which the neurodegenerative process may be at least in part ascribed. Furthermore, this evidence should be further investigated in light of the results of genetic studies, whose contribution may be to identify factors that make some people more susceptible to environmental factors, in line with the environment-gene interplay that is currently considered to underlie most chronic disease. Although researchers have been so far unable to confirm in an unequivocal manner an environmental etiology of ALS or to identify any of its singular causes, valuable contributions, studies such as the present one by Das *et al.*<sup>[5]</sup> are important to elucidate this still elusive and disturbing issue, which should be considered a primary research priority in biomedical research.

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