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## Research Article

# Excessive Pesticide Use Likely to Cause the Onset of Myasthenia Gravis in the Moroccan Agricultural Population

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## Abstract

**Background and Objective:** As pesticides have been and are widely used in agriculture. This work consists of highlighting one of the probable consequences of these xenobiotics. The aim of the study is possible association between the onset of autoimmune disorders and the exposure of rural populations to toxic substances will be discussed. **Materials and Methods:** To carry out this work, the data recorded in the medical records of myasthenic men and women living in the countryside were used. Of all the 117 cases withdrawn from the specialties hospital in Rabat (Morocco), 77% lived in urban areas and 23% in rural areas. **Result:** The result of the analysis of the files of rural inhabitants revealed a male predominance, unlike previous data on the distribution of myasthenia gravis by sex, women were in the lead in terms of quantity for this disease. **Conclusion:** These findings may lead to highlight exposure to pesticides and their accumulation during the time spent by these agricultural workers in the fields and sometimes without appropriate personal protective equipment.

**Key words:** Autoimmune diseases, rural myasthenic, pesticides, male predominance, xenobiotics

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**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

The immune system is the target of xenobiotics of very diverse origins: Drugs, metals, phytosanitary products, air pollutants, cosmetics and food additives, etc., Although, most of the available data have been obtained from animals, several collective poisonings have affected thousands of people<sup>1</sup>. Myasthenia gravis is defined as an autoimmune disease concerning the neuromuscular junction and its impact varies between 1.5 and 10 cases per 1 million inhabitants<sup>2,3</sup>. The objective of this work was to strengthen previous research by adding information through the analysis of diseases encountered in rural farmers, in particular myasthenia gravis. Directly or indirectly, these workers are exposed to pesticides suspected of being triggers of various autoimmune diseases. The realization of this work required the exploitation of 117 files classified at the university hospital of specialties. In the files of confirmed myasthenics, 23% of them came from suburbs. The percentage was low compared to what was wanted, but this amount revealed a male predominance of around 90% of the total.

The majority of studies have confirmed that for most autoimmune diseases, especially myasthenia gravis, women are generally the most commonly affected compared to men<sup>4</sup>. A review of the medical records of this rural cohort revealed a male predominance. This predominance is reflected in the fact that the rural male population is the main labor force in the fields and is subject to higher cumulative exposure and pesticide handling. Some research has reported that exposure to chemicals may increase the incidence of autoimmune diseases in certain populations<sup>5</sup>. Regarding the triggering of autoimmune diseases, many lines of research highlight the effects of environmental factors on genetically sensitive individuals<sup>2</sup>. Indeed the environment is no longer breast and full of pollutants of all kinds including pesticides, in general xenobiotics are made to kill only one type of target organism and must be selective to kill only that organism. However, most of these products do not have these characteristics and their safe use is based solely on the application technique and the quantities used<sup>6</sup>. The lack of these characteristics has prompted researchers to draw attention: Agricultural workers face many occupational risks and exposure to pesticides is one of the most important<sup>7</sup>. In this paper, the possible association between the onset of autoimmune disorders and the exposure of rural populations to toxic substances will be discussed.

## MATERIAL AND METHODS

**Study area:** The study took place at: "Unit of Clinic and Cognitive Neuroscience, Laboratory of Biology and Health, Department of Biology, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco and this from 01.05.18-30.10.19.

**Material:** The study was carried out on the basis of data archives from 117 clinically confirmed myasthenic patients hospitalized in the neurology department of the Hospital of Specialties in Rabat.

**Methods:** Patient records were archived by doctors in the neurology department. Retrospective examination of these archives allowed us to record several key parameters in this sample. However, we focused only on the parameters of myasthenic patients living in the countryside, who represented 23% of the overall sample at the time. The settings chosen were the sex and age of this group.

**Statistical analysis:** The one-sample Kolmogorov-Smirnov test was used to test the normality of the distribution of quantitative variables. Characteristics were compared by means of a chi-square test with Yates correction. All statistical comparisons were made with a defined significance threshold ( $p < 0.05$ ).

## RESULTS

**Distribution by residence:** According to the distribution by residence, as shown in Fig. 1, the prevalence of myasthenia gravis is higher in the urban community than in rural areas. The percentage of the total sample was 77% of the urban environment against 23% of the rural environment and we are interested in this last category. Analysis of the files of these 23% of rural areas revealed a male predominance. This predominance began at the age of 26 and reached its maximum at the age of 56 and over. The total of women affected in this group did not exceed 1/5 of the sample.

**Breakdown by sex and age:** The Table 1 shows from the age of 55, a male trend substantially equal to 4/5 of almost all. For these rural inhabitants the female representation was almost insignificant (Table 1).

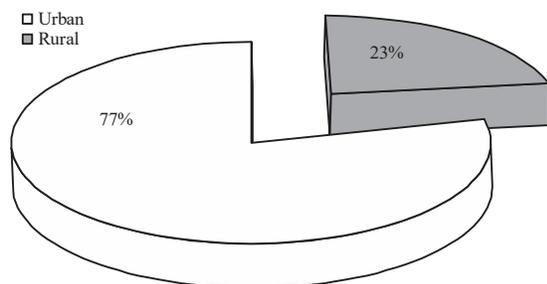


Fig. 1: Distribution by residence

Table 1: Observation of rural myasthenic population

| Age                                | Sex    |      |
|------------------------------------|--------|------|
|                                    | Female | Male |
| <b>Rural myasthenic population</b> |        |      |
| 0 to 25                            | 3      | 0    |
| 26 to 55                           | 2      | 6    |
| >56                                | 1      | 14   |
| Total                              | 6      | 20   |

## DISCUSSION

Autoimmune Myasthenia Gravis (MG) encompasses all immunologically mediated disorders affecting the end plate region of the postsynaptic neuromuscular junction<sup>8</sup>.

The factors involved in the induction and perpetuation of autoimmune diseases and the immunopathogenic role of autoantibodies are poorly understood<sup>9</sup>. Today, pesticides are believed to pose a major risk to human health and the environment. They are frequently implicated in the degradation of biodiversity. In addition, numerous epidemiological studies suggest a correlation between the professional use of pesticides and the appearance of certain pathologies in the populations concerned. In the whole of the same sample analyzed for our previous study, without separating villagers from country people, myasthenia gravis in general was predominantly female (about 2.7 for 1 man)<sup>4</sup>. These data reinforced those of other studies which had traced a bimodal distribution according to age, with a peak of appearance at 20-40 years, mainly female, and at 50-60 years with a clear male tendency<sup>10,11</sup>. In the current survey of rural areas, we found that the first peak for females has become almost negligible. This remarkable decrease has reversed the rule by giving the maximum to the male side. This finding was consistent with Nemet *et al.*,<sup>12</sup> who found an increased prevalence of myasthenia gravis in adult rural male populations. Given that agricultural workers face many occupational risks, exposure to pesticides is the most dangerous, especially those who perform manual work in pesticide-treated areas.

Some research based on evidence from several studies indicates that pesticides can interfere with the immune system and have several immunotoxic effects<sup>13,14</sup>. Another adds that there are data on the relationship between pesticide-induced immune deficiency and the prevalence of diseases associated with alterations in the immune response<sup>15</sup>. Indeed, certain environmental chemicals, including pesticides termed as endocrine disruptors, are known to elicit their adverse effects by mimicking or antagonising natural hormones in the body and it has been postulated that their long-term, low-dose. Exposure to pesticides has been found to cause many abnormalities, including immunosuppression<sup>16,17</sup>. Other studies have reported that exposure to a variety of toxic and irritating substances encountered in the environment may be associated with the development of certain diseases, including those of an autoimmune nature<sup>18</sup>. The following researchers Banerjee *et al.*<sup>19</sup> Flipo *et al.*<sup>20</sup> and Sharma<sup>21</sup> reported that there is ample evidence that certain pesticides affect immune function, but their potential role in inducing human autoantibodies and autoimmune diseases has not been adequately assessed. A few studies have stated that pesticide exposure may play a greater role in suspected immune system fragility and may lead to a change in susceptibility to disease<sup>21</sup>. Previous studies have reported that the real causes of many autoimmune diseases are still unknown, the interaction of many factors, including gender, genetics, infectious agents and exposure to environmental toxicants, seems to be involved<sup>22</sup>. Other research has found that the origin of autoimmune disease is a disturbance in the immune tolerance of autoantigens. This is thought to occur in genetically sensitive individuals after exposure to environmental triggers<sup>23</sup>. Studies have confirmed that there are other potential environmental factors, including chemical compounds that are foreign to a living organism. Examples include drugs, pesticides or other organic molecules that have the potential to alter host proteins and make them more immunogenic<sup>24</sup>. Some authors are convinced that there is ample evidence that pesticides interfere with normal immune function, and preliminary information suggests that, at least in laboratory animals, pesticides can induce [autoimmune] antibodies<sup>25</sup>. Other studies affirm the link between exposure to pesticides and deregulation of the immune system as well as the predisposition to autoimmune diseases<sup>15</sup>. Some studies have reported that agricultural occupation and pesticide use have been associated with a high risk of systemic autoimmune diseases<sup>26-34</sup>.

Animal studies clearly show that some pesticides can modify the immune system morphologically or functionally. However, in several cases, the concentrations or doses tested

did not reflect relevant exposure concentrations for humans, making it difficult to correlate immunotoxic effects in laboratory animals and humans. Autoimmune diseases are a pathophysiological condition in which immune responses are directed against the body's own tissues and damage them<sup>4</sup>. Autoimmune diseases caused by xenobiotics are the consequence of a deregulation of the immune system, consisting of a response directed against the constituents of the "self"<sup>35</sup>. Our results converge and reinforce the precedents in which we find that pesticide exposure is suspected to play a key role in the causes of many autoimmune diseases.

This report about the effects of pesticides on the human immune system makes one thing abundantly clear: We need to know more about these linkages, but we already know more than enough to take preventive action.

### CONCLUSION

The establishment of the causal relationship between pesticides and myasthenia gravis escapes pollutants from our environment which has a mode of operation and often latent effects like persistent pollutants. This analysis requires too long a follow-up, which makes research difficult. In addition, the evaluation of the impact of pesticides on the environment is very complicated since the doses absorbed are often low and must be studied over the long term. Especially, since we do not ingest a single type of pesticide but a different chemical family with distinct toxicological effects. We found an increased prevalence of MG in rural adult men populations. The exposure to agricultural pesticides might be one possible etiology. In conclusion, it is believed that pesticides can contribute to the onset of myasthenia gravis, but this relationship remains difficult to prove and similarly to exclude.

### SIGNIFICANCE STATEMENT

It is known that the extensive use of pesticides in agriculture involves significant risks for the environment and human health. This study revealed that farmers are the main targets of these xenobiotics, which cause the appearance of several autoimmune diseases and a probable link with myasthenia gravis.

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