


# The Importance of Otoneurological Evaluation in Brazilian Workers Exposed to Pesticides: A Preliminary Study

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## Abstract

**Introduction** Agrochemicals, also known as pesticides, are widely used in agriculture and in public health. They are organic and inorganic chemical substances with a high level of toxicity not only for the environment, but also for human health.

**Objective** To verify findings on labyrinthine assessment in endemic disease control agents, and to recommend the inclusion of the vestibular exam in the set of tests for pesticide-exposed populations.

**Methods** Descriptive, prospective, cross-sectional study with a sample comprising 15 endemic disease control agents, males, mean age of 51.6 years old (standard deviation [SD] = 5.9). All of the participants were submitted to anamnesis, otorhinolaryngological screening, and vestibular assessment.

**Results** Regarding the most reported complaints, dizziness (73.4%), headache (60%), and tingling in the extremities (53.4%) were observed. The findings of the vestibular exams were normal in 53.3%, while 46.7% showed peripheral vestibular disorder, of which 26.7% were of deficitary type, and 20% of the irritative type.

**Conclusions:** Alteration in the vestibular system was verified in 50% of the workers, with a greater prevalence in the caloric testing. Several disorders related to pesticides intoxication are scientifically known. Actions promoting knowledge and qualification of this population for the proper handling of chemicals are suggested, in addition to the elaboration and inclusion of protocols of vestibular assessment in hearing health programs for the prevention, diagnosis and treatment of vestibular disorders.

## Keywords

- ▶ occupational risks
- ▶ dizziness
- ▶ pesticides
- ▶ pesticide exposure
- ▶ organophosphate insecticides
- ▶ toxicity

## Introduction

In the past 10 years, the Brazilian market of pesticides has grown 190%, which has made Brazil the largest consumer of these substances since 2008.<sup>1</sup> According to data from the

Brazilian Institute of Geography and Statistics (IBGE, in the Portuguese acronym),<sup>2</sup> during the past years, there has been an annual increase of 6.9Kg/ha in agrochemicals sales in Brazil, with incremented their use in the rural area. Since 2008, Brazil has been the global leader in pesticide consumption.<sup>3</sup> The

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most recent data by the Information System on Diseases of Compulsory Declaration of the Brazilian Ministry of Health (SINAN/MS, in the Portuguese acronym) show that acute intoxications by agrochemicals rank second among the reported exogenous intoxications. According to the World Health Organization and the Pan-American Health Organization (WHO/PAHO),<sup>4</sup> the number of cases increased 67.3% between 2007–2011.

Agrochemicals, known as pesticides, widely used in agriculture and in public health, are organic and inorganic chemical substances with a high level of toxicity, not only for the environment, but also for human health.<sup>5</sup>

Excessive exposure to agrochemicals, associated with the absence of individual protection, has caused severe intoxications, mainly in farmers and in endemic disease control agents.<sup>5</sup> To the WHO/PAHO, in the future, 3 million workers are estimated to present with some sort of agrochemical intoxication, and 220 workers may die a year; 70% of those deaths will occur in the so-called Third World countries.<sup>6</sup>

For decades, aiming at eliminating the agents of plagues and diseases, the health area has been relying on agrochemicals to do away with the vectors of endemic diseases. Recently, supervised by the National Health Foundation (FNS, in the Portuguese acronym), campaigns against endemic vectors, such as Zika, Chikungunya and Dengue, have been using organophosphate and pyrethroid insecticides, being Malathion the most commonly used in these campaigns. Their level of toxicity is publicly known, which features a hazardous condition for the exposure of workers in the programs and campaigns of municipal health secretaries.<sup>7</sup>

Agrochemical intoxication may occur in three ways: inhalation, ingestion and skin absorption. Organophosphate agrochemicals and pyrethroids are known for their anticholinesterase effect, that is, they inhibit the acetylcholine enzyme, which is, according to the literature, an efferent-control neurotransmitter for the vestibular system.<sup>8</sup>

To Morata et al.,<sup>9</sup> agrochemicals may cause severe disorders in the vestibular system, associated with the impairment of the brainstem and of the cerebellum. In the labyrinthine testing, the presence of central positional nystagmus, vestibulo-ocular hyporeflexia or hyperreflexia, and absence of the inhibition effect of visual fixation in the caloric testing can be observed. According to Andrade,<sup>3</sup> agrochemical exposure may cause injuries to the hair cells of the crista ampullaris of the semi-circular canals, and to the macula hair cells of the saccule and utricle, which are responsible for balance. The degree of the lesion caused by those substances will depend on individual predisposition, administered dose, duration, route of administration, age, and family tendency.<sup>10</sup>

Studies on pesticide effects (organophosphates or pyrethroids) over the vestibular system are still very insipient. Research, which investigates vestibulotoxicity and neurotoxicity, enables to refine the knowledge on the direct effect of chemicals on the vestibular system.

Therefore, the present study aims to verify findings on labyrinthine assessment in endemic disease control agents, and recommends the inclusion of the vestibular exam in the set of tests for pesticide-exposed populations.

## Methods

### Participants and Study Design

The present study was approved by the Ethics Board—Brazil Platform—opinion number 1.242.014/2015, and was authorized by the participants after having signed the Free Informed Consent Form.

The present study is a descriptive, prospective, cross-sectional study with the participation of 15 endemic disease control agents, all males, aged between 49 and 67 years old, mean age of 56.1 years old (standard deviation [SD] = 5.9), referred by the Union of Federal Civil Servants on Health, Labor, Social Security and Social Action for evaluation at the Otoneurology Department of a Higher Education Institution. The research included workers > 18 years old, exposed to organophosphate and pyrethroid agrochemicals for > 20 years, with a mean of 32.4 years (standard deviation = 4.3), and excluded workers (endemic disease control agents) < 18 years old, suffering from major neurological, psychological, visual and/or musculoskeletal disorders, in addition to otological disorders, such as presence of cerumen and otorrhea, which could prevent them from undergoing the exam.

### Procedures

**Anamnesis** - the questionnaire was applied, focusing on otoneurological signs and symptoms (→ Fig. 1).

**Otorhinolaryngological Assessment** - this was performed to rule out any alterations that could affect the testing.

### Vestibular Assessment

The workers underwent the following tests that make up the vestibular examination. Initially, we checked vertigo and spontaneous and semispontaneous positional nystagmus.

Thus, we have used digital vector electronystagmography (VENG), which has its own software: VecWin2 (Neurograff Eletromedicina Ltda., São Paulo, São Paulo, Brazil), a Ferrante COD 14200 rotating chair with a rotation of between 0.01 and 0.5Hz, (Ferrante, São Paulo, São Paulo, Brazil), an EV VEC visual stimulator (Neurograff Eletromedicina Ltda., São Paulo, São Paulo, Brazil), and an air NGR 05 caloric stimulator (Neurograff Eletromedicina Ltda., São Paulo, São Paulo, Brazil). The flow rate used was of 5 and 13 L/min.

Next, we conducted the eye and labyrinth VENG tests, according to the criteria proposed by Mangabeira-Albernaz et al.<sup>11</sup>

**Eye movement calibration** - We verified spontaneous and semi-spontaneous nystagmus using pendular tracking, checking for pre- and postrotatory plus pre- and postcaloric optokinetic nystagmus. We recorded the caloric stimulation time in each ear using air at 42°C and 18°C during 80 seconds for each temperature, and responses with closed eyes and then with open eyes to observe the inhibitory effect of eye fixation (IEEF). The criteria used in the air caloric test were: absolute value between 2 and 24 degrees/second, with < 2 degrees/second corresponding to hyporeflexia; and with >24 degrees/second corresponding to hyperreflexia; relative values of labyrinth preponderance (LP) < 41% and nystagmus directional preponderance (NDP) < 36%.<sup>12</sup>

**ANAMNESIS**

**I. IDENTIFICATION**

**DATE:**    /    /

Name: \_\_\_\_\_  
 Age: \_\_\_\_\_ Date of Birth: \_\_\_\_\_  
 Country of Birth: \_\_\_\_\_ Race: \_\_\_\_\_  
 Occupation: \_\_\_\_\_

**II. PROFESSIONAL ACTIVITY**

Previous jobs: \_\_\_\_\_  
 Total time working: in noisy place \_\_\_\_\_ exposed to chemical agents: \_\_\_\_\_  
 Is currently ( ) or has been ( ) exposed to chemical agents: \_\_\_\_\_  
 heavy metals (lead, mercury): \_\_\_\_\_ asphyxiants (CO<sub>2</sub>): \_\_\_\_\_

**III. HISTORY OF MORBIDITY**

Smokes ( ) or has been a smoker ( ) how many packs per day? \_\_\_ How many cigarettes per day? \_\_\_\_\_  
 Regularly consumes alcohol? ( ) no ( ) yes - how much per day: \_\_\_\_\_  
 Consumes caffeine? ( ) no ( ) yes - how much per day: \_\_\_\_\_  
 Dietary errors: \_\_\_\_\_  
 Takes medication? ( ) no    yes ( ) Which ones: \_\_\_\_\_  
 Had surgery? ( ) no    yes ( ) What: \_\_\_\_\_  
 Identify subject's health problems:

<b>SIGNS AND SYMPTOMS</b>	<b>YES</b>	<b>NO</b>	<b>MEDICATION TAKEN</b>
Change in blood flow			
Hypertension			
Sensitivity change			
Incoordination of movement			
Sensation of movement of objects			
Diabetes			
Thyroid dysfunction			
Cranioencephalic Trauma			
Heart disease			
Kidney damage			
Rheumatologic disorders			
Degenerative Diseases			
TMJ disorder			
Dysarthria			
Alteration in smell/ taste			
Pain/difficulty in moving neck			
Tingling in extremities			
Dysphonia			
Dysphagia			

**Fig. 1.** Anamnesis by Otoneurology Department. Abbreviation: TMJ, Temporomandibular Joint disorder.

Double /blurred vision

Fatigue

Anxiety/ fear/depression

Headache/migraine

**IV. HEARING LOSS:**

Onset:\_\_\_\_\_ Locale: ( ) right ear ( ) left ear ( ) both  
 Intensity:\_\_\_\_\_ Occurrence:\_\_\_\_\_ Pain in ear: ( ) yes ( ) no  
 Purging in ear: ( ) yes ( ) no  
 Appears or worsens: \_\_\_\_\_  
 Triggering factors: \_\_\_\_\_  
 Aggravating factors: \_\_\_\_\_  
 Factors for improvement: \_\_\_\_\_  
 Concomitant symptoms: \_\_\_\_\_

**V. DIZZINESS**

Onset:\_\_\_\_\_ Definition:\_\_\_\_\_ Intensity: \_\_\_\_\_  
 Occurrence: \_\_\_\_\_  
 Duration ( ) seconds ( ) minutes ( ) hours ( ) days  
 Appears or worsens: \_\_\_\_\_  
 ( ) nausea ( ) vomiting ( ) sweating ( ) gait imbalance ( ) falling  
 Triggering factors: \_\_\_\_\_  
 Aggravating factors: \_\_\_\_\_  
 Factors for improvement: \_\_\_\_\_  
 Concomitant symptoms: \_\_\_\_\_

**VI. TINNITUS**

Onset:\_\_\_\_\_ Locale: ( ) right ear ( ) left ear ( ) both ( ) close to ear ( )  
 head ( ) type : \_\_\_\_\_ Duration: \_\_\_\_\_  
 Definition:\_\_\_\_\_ Intensity: \_\_\_\_\_  
 Occurrence: \_\_\_\_\_  
 Appears or worsens: \_\_\_\_\_  
 Triggering factors: \_\_\_\_\_  
 Aggravating factors: \_\_\_\_\_  
 Factors for improvement: \_\_\_\_\_  
 Concomitant symptoms: \_\_\_\_\_

**VII. NONOCCUPATIONAL EXPOSURE**

Is exposed for more than four hours: ( ) motorcycle ( ) loud music ( ) tools  
 ( ) farming equipment ( ) firearm shooting  
 What does the subject do in free time?  
 \_\_\_\_\_

Does the subject have hobbies?  
 \_\_\_\_\_

**Fig. 1.** (Continued).

**Statistical Analysis**

For the analysis of the results, methods of descriptive statistics were used (frequency tables), as well as the Fisher exact test, correlating the result of the vestibular testing to the most reported otoneurological symptoms. The rejection level established to the null hypothesis was of 0.05 or 5% with the Statistica 13.1 (StatSoft, Inc., Tulsa, OK, USA) software.

**Results**

The most reported complaints in the anamnesis were dizziness (73.4%), headache, and tingling in extremities (53.4%), as shown in ►Table 1.

In the vestibular function assessment, the check for the spontaneous nystagmus with closed eyes (6.7%) and with caloric stimulation (40%) was altered in the endemic disease control agents.

Regarding the result of the vestibular testing, normoflexia was observed in 53.3% of the subjects, and peripheral vestibular disorder in 46.7%, of which 26.7% were of deficitary type, and 20% of irritative type, as shown in ►Table 2.

The correlation between agrochemicals and the three most evidenced otoneurological symptoms can be observed in ►Table 3.

**Table 1** Symptoms in 15 workers

Symptoms	Workers (n)	Frequency (%)
Dizziness	11	73.4
Headache	9	60.0
Tingling in extremities	8	53.4
Anxiety	4	26.7
Tinnitus	3	20.0
Pain, difficulty in neck movement	3	20.0
Insomnia	3	20.0
Fatigue	2	13.4
Hearing Loss	2	13.4
High pressure	2	13.4
Depression	2	13.4
Pain, irradiated to shoulder, arm	1	6.7
Taste alteration	1	6.7
Double vision	1	6.7

**Table 2** Frequency of the vestibular testing results in 15 workers

Vestibular Testing	Workers	
	n	%
Peripheral vestibular dysfunction	7	46.7
Normal vestibular testing	8	53.3
Total	15	100.0

Abbreviations: n, number of workers; %, frequency.

**Table 3** Correlation between the vestibular testing result and the most evidenced otoneurological symptoms in 15 workers

Vestibular Testing	Dizziness		Tingling in extremities		Headache	
	n	%	n	%	n	%
Normal vestibular testing	7	46.7	4	26.7	4	26.7
Abnormal vestibular testing	4	26.7	4	26.7	5	33.3
Total	11	73.4	8	53.4	9	60.0

Abbreviations: n, number of workers; %, frequency.

By applying the Fisher exact test, no significant difference was verified in the correlation between the result of the vestibular testing and the following symptoms: dizziness, headache, and tingling in extremities ( $p = 0.7170$ ).

**Discussion**

In the analysis of the anamnesis, the occurrence of multiple neurological symptoms was verified, among them: dizziness (73.4%), headache (60%), and tingling in extremities (53.4%). According to the literature, symptoms such as dizziness and headache are commonly reported in agrochemical intoxication.<sup>13-15</sup> In addition to those symptoms, Lakhani et al<sup>16</sup> reported sensorineural hearing loss and tinnitus as part of the prevalent symptomatology in the exposure to organophosphates. To Hoshino et al,<sup>15</sup> dizziness is a major symptom, considered one the most outstanding clinical manifestations to agrochemical exposure.

Delgado et al<sup>17</sup> applied a questionnaire to 55 farmers on the use of agrochemicals, and observed that 92% of those workers did not use any personal protection equipment to handle the products; 62% reported discomfort during their handling, and the referred symptoms were: headache, nausea, vomiting, vertigo, skin rash, and blurred vision.

According to Tuma et al,<sup>18</sup> the central nervous system (CNS) is responsible for processing and organizing sensory information, resulting in proper ocular and spinal reflexes to keep the postural balance in the environment, as well as the static and dynamic spatial orientation, which justifies the complaint of dizziness reported by workers exposed to agrochemicals.

Regarding the vestibular assessment, alteration in the vestibular system in 46% of the workers, higher prevalence in the caloric testing, with predominance of the peripheral vestibular deficitary syndrome, were observed in the present study. These finding are in line with studies by Hoshino et al,<sup>15</sup> who assessed 18 rural workers exposed to organophosphates, and observed peripheral vestibular disorders in 89% of the cases. The reported dysfunctions were observed when they checked for nystagmus, and/or positional vertigo, and hyperreflexia to the caloric testing. In another study,<sup>19</sup> the authors checked 50 rural workers exposed to organophosphate agrochemicals for hearing and vestibular symptoms, and reported that 76% complained about dizziness episodes, 58% reported

daily dizziness, 54% complained about tinnitus, and 46% reported ear fullness. The authors observed that agrochemicals may cause hearing and vestibular systems disorders. A study by de Araújo et al<sup>20</sup> assessed the vestibular system of workers exposed to organophosphates, and evidenced alterations in the caloric testing, unveiling irritative peripheral vestibular dysfunction. The authors showed that these chemicals have neuro-ototoxic potential; however, the safe dosage and exposure time, so that those chemicals are not deleterious to health, cannot be stated. To Werner,<sup>21</sup> organophosphates have, as their main action mechanism, the inhibition of the acetylcholinesterase enzyme, responsible for the degradation of the acetylcholine neurotransmitter, which performs the synapses in the peripheral and CNS.

Körbes et al<sup>22</sup> performed a study with guinea pigs submitted to agrochemical exposure and considered organophosphates an acute lesion agent of the outer hair cells, as there is a correlation between the applied dosage and the amount of alterations observed by means of electronic microscopy. The morphological injuries in the cochlea prevailed in the stereocilia of the outer hair cells, progressing to the basal spiral. The authors reported morphological cochlea alterations in the sacule and utricle of guinea pigs exposed to a daily dosage of organophosphates, evidencing the degrading effect of agrochemicals to the vestibulocochlear system.

Occupational ototoxicity caused by chemicals, including pesticides, has called scarce attention on the part of health professionals. Therefore, its impact on auditory and vestibular systems of exposed workers is a matter of concern. Injuries are known to vary according to innumerable risk factors: type of chemicals, interactions, dosages, method and time of exposure, presence of physical conditions, and individual susceptibility.

Thus, it should be pointed out that the assessment of the vestibular system in workers exposed to agrochemicals should be performed periodically by monitoring any injuries, in addition to the performance of specific clinical anamnesis.

The evaluation of complaints and symptoms associated with hearing disorders must include information on balance as well as questions related to their impact on general health and social life. Balance disorders can be a risk factor for occupational accidents. Due to lack of knowledge and of access to the exam which evaluates the vestibular function in the Brazilian Unified Health System (SUS, in the Portuguese acronym), the authors of the present study suggest the inclusion of the protocol for balance assessment to be applied to workers exposed to pesticides, which can also be extended to other chemicals (– Fig. 1). In addition, the labyrinthine testing can be suggested as part of the assessment routine.

## Conclusion

The most reported otoneurological symptoms were: dizziness (73.4%), headache (60%), and tingling in extremities (53.4%). Moreover, the most reported clinical symptoms were: anxiety (26.7%), tinnitus (20%), and neck cranking (20%).

Disorders in the vestibular system were verified in 50% of the workers, being more prevalent in the caloric testing.

Actions promoting knowledge and qualification of this population for the proper handling of chemicals are suggested, as well as the elaboration and inclusion of protocols to vestibular assessment in programs of hearing health to prevent, diagnose, and treat vestibular dysfunctions.

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## Conflicts of Interest

The authors have no conflicts of interest to declare.

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