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IMPACT OF THE USE OF PESTICIDES BY RURAL WORKERS IN BRAZIL

IMPACTO DO USO DE AGROTÓXICOS POR TRABALHADORES RURAIS NO BRASIL

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ABSTRACT

Brazil is the third largest market and the eighth largest consumer of pesticides per hectare in the world, with herbicides and insecticides accounting for 60% of the products traded in the country. The use of pesticides has increased worldwide in the last decades, which may represent a risk for several diseases in humans, including cancer. Although in Brazil the research on the impact of the use of pesticides on human health has grown in recent years, it is still insufficient to really know the real dimension of health damage caused mainly by occupational and food exposure, due to the intensive use of pesticides. This article aims to review the use of pesticides by rural workers in Brazil, highlighting the importance of preventive measures for their health.

Keywords: health disorders; occupational health; cancer; genotoxicity; oxidative stress; strategies.

RESUMO

O Brasil é o terceiro maior mercado e o oitavo maior consumidor de agrotóxicos por hectare do mundo, com herbicidas e inseticidas correspondendo a 60% dos produtos comercializados no país. O uso de agrotóxicos tem aumentado em todo o mundo nas últimas décadas, o que pode representar um risco para diversas doenças em humanos, incluindo o câncer. Embora, no Brasil, a pesquisa sobre o impacto do uso de agrotóxicos na saúde humana tenha crescido nos últimos anos, ainda é insuficiente para de fato conhecer a real dimensão dos danos à saúde, causados principalmente pela exposição ocupacional e alimentar, em virtude da utilização de agrotóxicos. Esta revisão tem por objetivo destacar o uso de pesticidas por trabalhadores rurais no Brasil, evidenciando a importância de medidas preventivas para a saúde do trabalhador.

Palavras-chave: transtornos de saúde; saúde ocupacional; câncer; genotoxicidade; estresse oxidativo; estratégias.

INTRODUCTION

Pesticides, according to the World Health Organization (WHO, 2008), is any substance capable of controlling a pest that can have consequences for both the population and the environment. Among the countries with agricultural power involving the consumption of herbicides, fungicides and agricultural insecticides, Brazil ranks first in the Latin American and Caribbean Newsletter, dated 23 of April 2011 (STÉDILE, 2012; NEVES, 2017).

In Brazil, the diversity of agrochemicals is big, about 300 active principles in more than 2 thousand commercial formulations (NEVES, 2017). Humans are often their final recipients, and they can be found in the soil, water, air, in animals and vegetables, being thus considered with great capacity of dispersion (NEVES, 2017). Different symptoms are caused by pesticide poisoning, mainly among farmers, and may even make them stop working and having to look for another type of profession. Among the symptoms, we can highlight anemia, headache, dysthymia, decreased immune defenses, sexual impotence, insomnia, changes in arterial depression and behavioral disorders (LEVIGARD; ROZEMBERG, 2001; SOUZA *et al*., 2011).

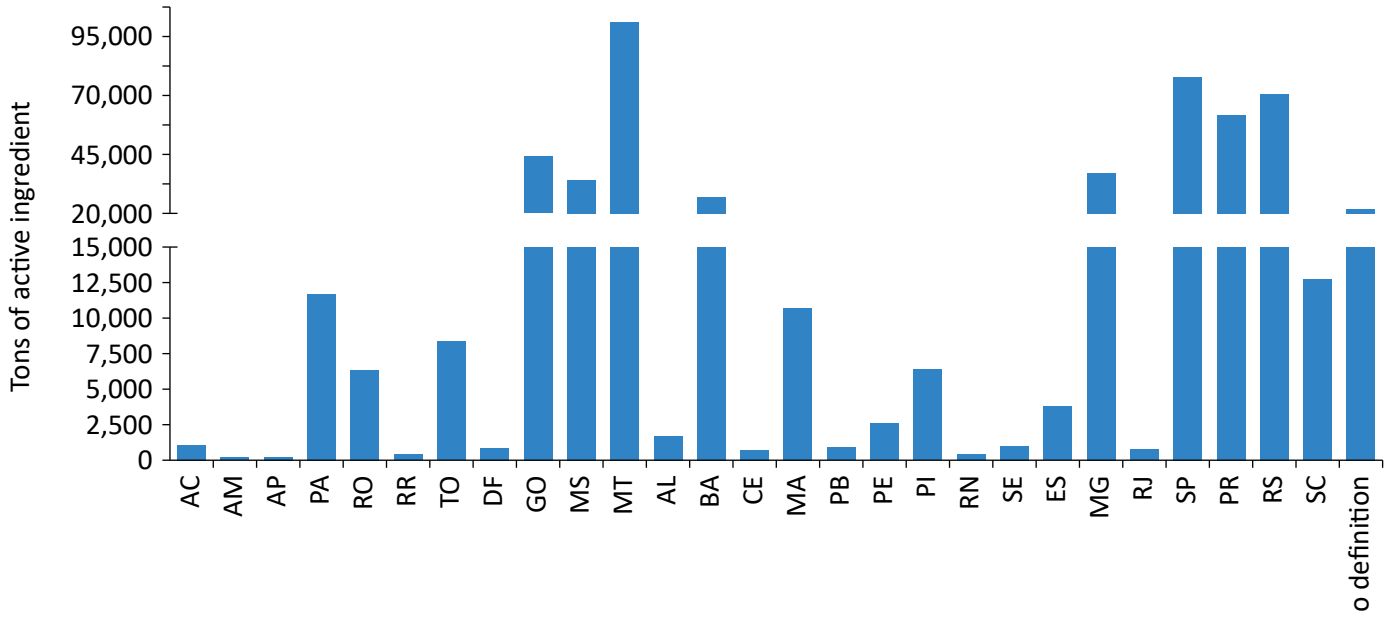
With its effect based on insect neurotoxicity, dichlorodiphenyltrichloroethane (DDT), is a widely known pesticide, mainly because it is sold at a low cost and can act for several years (STOPELLI; MAGALHÃES, 2005). However, it has some limitations: insects have developed resistance to it and experiments with animals showed their carcinogenicity (SMITH; GANGOLLI, 2002; STOPELLI; MAGALHÃES, 2005). Already in humans, high concentrations of Dieldrin in the blood, for example, have a greater amount of thyroid stimulating hormone (TSH), presenting hypothyroidism. Therefore, this pesticide and other organochlorines act as neurotoxicants, as well as in the endocrine function (RATHORE *et al*., 2002; STOPELLI & MAGALHÃES, 2005).

Many studies have presented promising results and made important conclusions beyond the use of pesticides by rural workers, allowing a better understanding of the consequences of its use. Due to the accumulated knowledge, we aimed at conducting a survey on the most important and promising researches on the use of pesticides by rural workers in Brazil until now.

THE BRAZILIAN SITUATION

Because of agricultural practices in the country, around the 1960s the whole scenario underwent modifications leading to a record consumption of agrochemicals and a chemical-dependent context of food production (ABREU; ALONZO, 2014; JACOBSON *et al*., 2009). In the global context, since 2008 Brazil has become the largest consumer of pesticides (CARNEIRO *et al*., 2012; AUGUSTO *et al*., 2012; RIGOTTO *et al*., 2012), standing out as the world's largest agricultural producer. Brazil shows growth rates of 10% per year (AGRONEWS, 2014; BRASIL, 2015; GONÇALVES, 2016) and exports food to 180 countries, being the world's leading exporter of soybeans in grains, sugar, coffee, orange juice, beef and chicken (BRASIL, 2013; GONÇALVES, 2016). According to IBAMA (2002), the states of Mato Grosso, São Paulo, Paraná, Rio Grande do Sul, Goiás, Minas Gerais, Bahia and Mato Grosso do Sul are the main consumer states of agrochemicals (Figure 1).

Especially for the rural worker, along with the evolution of techniques and the use of agricultural inputs, there have been harmful changes in health, mainly related to the loads, ways of working and risks incorporated into these new activities (STOPPELLI & MAGALHÃES, 2005). These risks involve both acute intoxications, with the onset of symptoms fast after excessive exposure, including weakness, vomiting, nausea, seizures, muscle contractions, headaches, difficulty breathing, nasal bleeding and fainting, as well as chronic intoxication. In these, the symptoms are late after months or years, caused by small or moderate exposure to toxic products or multiple products. This type of exposure causes irreversible damage, such as paralysis and neoplasia (PERES, 1999; STOPPELLI & MAGALHÃES, 2005), contact dermatitis, renal and hepatic lesions, delayed neurotoxic effects, chromosomal abnormalities, Parkinson's disease, cancers and teratogens (WILSON; OTSUKI, 2004; STOPPELLI & MAGALHÃES, 2005). Table 1 shows the main studies carried out to date specifically related to the exposure of the rural worker to pesticides in Brazil. Electronic databases were collected from PUBMED and "Portal de Periódicos" from CAPES/MEC (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior/ Ministério



Source: IBAMA, 2018.
*No definition: sum of marketed quantities whose companies are not able to specify the territorial distribution of sales, since it is an activity carried out by third parties.
Figure 1 – Federation sales of agrochemicals by Unit in 2017.

Table 1 – Update of the main publications related to the use of pesticides by rural workers in Brazil.

State	Target	Major findings	Methodology	Reference	Year
HEALTH DISORDERS AND OCCUPATIONAL HEALTH					
SE	High frequency hearing loss; Noise exposure; Quality of life	Pure-tone audiometry, distortion product otoacoustic emissions, and high-frequency audiometry tests were performed. This report is unusual because of the short time of exposure to noise and pesticides and the hearing loss found, indicating a synergy between those agents.	Pure-tone audiometry, distortion product otoacoustic emissions, and high-frequency audiometry tests.	Sena *et al*.	2018
ES	Beck Depression Inventory-II (BDI-II); Depressive Symptoms; Mental Health	Pesticide exposure, tobacco use, poor self-perceived health and the presence of chronic disease contribute as risk factors for the appearance of depressive symptoms at a level above ups and downs considered normal in the BDI-II.	Questionnaire	Conti *et al*.	2018

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
SC	Artificial Targets; Tractor Cabins; Exposure Evaluation; Fenitrothion; Crop Pulverization	Sealed cabin minimized the exposure of the operator to the pesticides, since all samples analyzed showed fenitrothion values below the limit of detection.	Ultrasonic extraction	Barcellos *et al*.	2016
RS	Agrochemicals; Work Environment; Practical Nursing.	Rural workers who apply pesticides present a higher prevalence of dermatological alterations.	Questionnaire	Cezar-Vaz *et al*.	2016
RS	Wheezing; Asthma; Tobacco; Rural Health; Prevalence	Pesticides, dusts exposure, and green tobacco sickness were risk factors for wheezing.	Questionnaire	Fiori *et al*.	2015
Brazilian micro-region	Suicide	Suicide rates have increased in middle age (35–64 years) and younger men (15–34 years). Micro-regions with a higher use of pesticides showed higher rates of suicides. Pesticide poisoning effect on suicide rates was stronger than use of pesticide. Reinforces the hypothesis that pesticide use and pesticide poisoning increase the suicide rates.	Crude suicide rates of a 15-year time series (1996–2010) were examined, followed by an ecological study using age-standardized suicide rates for the period 2006–2010.	Faria *et al*.	2014a
MG	Health and Epidemiological Surveillance; Health Policies	The conclusion is the pressing need to develop a model for sustainable agriculture, healthy, free of pesticides and that organized society and responsible institutions must undertake actions that meet the needs of the people who work in the farms or consume agricultural products harvested there, especially controlling risks and consequences that can and must be avoided.	Questionnaire	Nasrala Neto, Lacaz and Pignati	2014
RS	Poisoning; Mental disorders	Reinforces the evidence of the association between pesticide poisoning and mental health disorders. It also points to increased risk of minor psychiatric disorders from low socioeconomic status, dermal pesticide exposure and exposure to organophosphates. Reveals intense nicotine exposure as a risk for tobacco farmers' mental health.	Characterizing economic indicators of the farms, socio-demographic factors, lifestyle habits and occupational exposures.	Faria *et al*.	2014b

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
SE	Rural Population; Quality of life	Agricultural workers users of pesticides showed the worst levels of quality of life when compared to those who have not handled them. The use of pesticides and their toxicity class interfered in a most striking way in the classification of hearing loss presented by this group.	Audiological evaluation	Sena, Vargas and Oliveira	2013
RJ	Risk Perception; Risk Communication; Defensive Strategies; Community-Based Participatory Research	Risk perceptions and work practices are strongly influenced by local cultural patterns and, therefore, must be taken into account when developing effective intervention strategies, including risk communication initiatives.	Questionnaire	Peres *et al*.	2013
RJ	Small holders; Environment Human health	Do not confirm that the farmers' apparent careless handling of pesticides is linked to an intentional disregard for intoxication risk. The results point to a more complex set of explanatory variables that include: labor scarcity, inadequacy of protective gear, mixing practices and limited educational effectiveness of labeling standards.	Questionnaire	Pedlowskia *et al*.	2012
DF	Knowledge, attitudes, and practices study; Acetylcholinesterase; Butyrylcholinesterase	Although most farmers were aware that pesticides can harm their health, many still use PPDs in an inappropriate manner, or not at all, during pesticide handling. Inhibition of ChE activity during the exposure period for some farmers was higher than the safe, indicating that they might be at risk by the exposure to pesticides during their agricultural activities.	Questionnaire and Blood sample	Pasiani *et al*.	2012
RJ	Hearing; Auditory Perception; Adverse Effects.	Workers exposed to pesticide performed below-average on Temporal Auditory Processing tests. There was association between the index of exposure to pesticides and worse performance in Temporal Auditory Processing tests, suggesting that pesticides may be harmful to central auditory pathways.	Questionnaire, meatoscopy, basic audiological evaluation and temporal auditory processing tests.	Bazilio *et al*.	2012

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
RJ	Health Indicators; Rural Labor; Public Health	The volume of the determinants identified in the DPSEEA Matrix are related to deficiencies in actions for monitoring and surveillance of pesticide use, as well as the lack of technical assistance provided by the Public Sector.	DPSEEA model (WHO) based on analysis of official public documents.	Araújo-Pinto, Peres and Moreira	2012
PR	Poisoning; Economy; Health expenditures	Society, especially the population most affected by agrochemicals, would benefit if the risks of acute intoxication associated with the current model of agricultural production were recognized and eliminated.	Information obtained from Pesquisa de Previsão de Safras from 1998 to 1999.	Soares and Porto	2012
RJ	Mortality rates; Hospitalization rates attributable to suicide attempts; Sales of pesticides	Pesticide exposure may indeed increase the risk of suicide frequency, especially among agricultural workers.	Data on mortality rates, hospitalization rates attributable to suicide attempts, and data on sales of pesticides.	Meyer *et al*.	2010
MG	Rural Settlements; Social Conditions; Family Health; Rural Health; Food Security; Rural Population Health; Landless Worker Movment.	The view held by families from the Landless Rural Workers' Movement was that as they belonged to the Movement and were better organized, their health was better than the temporary rural workers'. The conservative modernization of rural Brazil has led to worse conditions for temporary rural workers, while Agrarian Reform has allowed for a better quality of life and improved health conditions among families in the areas under study.	Questionnaire	Carneiro *et al*.	2008
RJ	Environmental Pollution	Discusses several pesticide-related implications for human health and the environment in the mountainous region of the State of Rio de Janeiro, an important farming center. The article presents the results of the research in the area, identifying possible determinants of the current situation and some of the main challenges in dealing with the problem.	Survey	Peres and Moreira	2007

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
RJ	Intoxication; Multiple Application; Delayed-Neuropathy; Organophosphate Pesticides	These results indicate recurrent multiple overexposures to high concentrations of different chemicals, with serious damage to vital functions, especially considering their young age (average 35 ± 11 years old) and the productive period in their lifetime.	Questionnaire, biological sample collection for toxicology analysis and clinical – general and neurological – assessment.	Araújo *et al*.	2007
RJ	Neurobehavioral	While a few Behavioral Assessment and Research System (BARS) performance measures suggested behavioral impairments for the rural *versus* the urban participants, a stronger and more consistent association between BARS measures (especially impairment of tapping, digit span, and selective attention) and level of exposure to pesticides was noted when the exposure index was input into a multiple linear regression analysis. Exposure seemed to be especially strong for the youngest participants (10-11 years old).	Questionnaire, Behavioral Assessment and Research System (BARS) to assess their performance.	Eckerman *et al*.	2007
MS	Knowledge, Attitude and Practices (KAP) survey	About 92% of the interviewees had worked directly with pesticides and 59.6% reported typical intoxication symptoms. Only 44.3%, however, believe they had been intoxicated. A significant correlation was found between hand washing after pesticide application and reporting symptoms. Less than 20% used masks, impermeable clothes, or gloves during pesticide application.	Questionnaire	Recena *et al*.	2006
RJ	Risk Perception; Risk Communication; Women's Health	Results showed that the inclusion of risk-perception studies in the development of educative and risk-communication campaigns is very important, linking research to action.	Questionnaire	Peres *et al*.	2006

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
RJ	Risk; Rural Population	Results pointed to the importance of risk perception analysis in the process of developing strategies of intervention in rural areas, especially in policies and educational risk communication campaigns.	Questionnaire and assessment of local work processes.	Peres, Rozemberg and De Lucca	2005
MS	Suicide; Poisoning	Poisonings occurred mostly from October to March and the organophosphate insecticides monocrotophos and methamidophos were the main pesticides involved.	Reports from 1992 to 2002, using data from the Integrated Center for Toxicological Surveillance under the State Health Department.	Pires, Caldas and Recena	2005
RJ	Agriculture; Pesticide Exposure	Highlights health professionals' discourse in relation to the association between "nervousness" and pesticides. The authors discuss factors related to this perception and make several suggestions for future research.	Questionnaire	Levigard *e* Rozemberg	2004
RS	Pesticide Exposure; Incidence	Based on Poison regression, applying pesticide, reentering crop fields after spraying and working with pesticides in more than one farm were the types of exposure that presented a positive correlation with pesticide poisoning.	Questionnaire	Faria *et al*.	2004
MG	Risk Factors; Poisoning; Rural Health	The results emphasize the high level of health risk associated to pesticide use among rural workers.	Questionnaire. Data obtained through the Jorge Duprat Figueiredo Foundation for Workers' Safety and Occupational Medicine.	Soares, Almeida and Moro	2003
MG	Economic Assessment	Points to the need for an extensive investigation on the real benefits of pesticide use and its consequences for the environment and health in Brazil.	Data were obtained from the Fundacentro Ministry of Work agency for the years 1991-2000	Soares, Moro and Almeida	2002

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
RJ	Communication; Health Education; Interview; Communication and Health.	This study pointed out to the historical misinformation on pesticides in rural areas.	Questionnaire	Peres *et al*.	2001
RJ	Insecticides; Organophosphate; Poisoning; Socioeconomic Factors; Carbamates; Cholinesterase Inhibitors; Blood.	A result of 3.0 % was found for the BChE values, and 41.8 %, according to AChE. Individuals with at least one positive enzymatic indicator result were considered as "intoxicated". When these data were compared to the social-economic and pesticides use factors, the importance of the educational level in the prevalence of intoxication was highlighted.	AChE and BChE activities	Oliveira-Silva *et al*.	2001
PE	Tomatoes; Environment Impacts; Health Surveillance.	There is a lack of effective policies to protect the health of rural workers who must deal with pesticides and the environment which has already been severely damaged.	Questionnaire	Araújo, Nogueira and Augusto	2000
RS	Pesticide Poisoning; Occupational Accidents; Agriculture	The high prevalence of health problems identified in the study calls attention to the need for measures to promote and protect rural workers' health.	Questionnaire	Faria *et al*.	2000
RS	Mental Health; Poisoning; Educational Status.	The results call attention to the problem's dimension and to the importance of adopting new policies to protect farm workers' mental health.	Questionnaire	Faria *et al*.	1999
RJ	Ddt; Dieldrin; Occupational Exposure	Serum concentrations of organochlorine pesticides found in this study are comparable to the levels reported for the non-occupationally exposed population in Brazil and elsewhere.	Blood samples, Serum levels of organochlorine pesticides measured.	Paumgartten *et al*.	1998
BA	Occupational and Environmental Exposure	Rural workers and public health authorities must become aware of the importance of protective equipment, periodic health examinations and reduced environmental pollution in order to lessen occupational risks of field workers and promote improved conditions of life for the rural population.	Parameters of biochemistry, hematology, and organochlorine insecticide residues in the blood.	Carvalho	1991

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
SP	CNS Magnese Intoxication	Occupational exposure to pesticides containing Mn is a possible source of Mn intoxication of the CNS.	Mn intoxication	Ferraz *et al*.	1988
CANCER, GENOTOXICITY, DNA DAMAGE, OXIDATIVE STRESS					
SP	Machine Learning; Genotoxicity Micronucleus; Smoking; Agriculture	Exposing agricultural workers to pesticides and/or tobacco had genotoxic potential, but concomitant exposure to xenobiotics did not lead to additive or potentiating effects.	Oral mucosa cells, cytogeneticanalysis	Tomiazzi *et al*.	2018
SC	DNA Damage; Oxidative Stress	Exposed individuals, participants of this study, are more subject to suffer genetic damage and, consequently, more susceptible to diseases resulting from such damages	Blood samples, comet assay and the cytokinesis-block micronucleus technique and thiobarbituric acid reactive substance and catalase activity.	Hilgert Jacobsen-Pereira *et al*.	2018
MG	Genotoxicity Test; Bioindicators and Clinical Evaluation	The group exposed to organophosphates presented significant changes in all these parameters compared to the control group and showed significant changes in budding, condensed chromatin and karyolytic cells compared to the group non-exposed to organophosphates. Data from clinical evaluation showed significant changes in the central nervous, respiratory and auditory systems.	Blood, urine and buccal samples, activities of cholinesterases, the levels of urinary dialkyl phosphates, genotoxicity data, from a cytome assay.	Silvério *et al*.	2017
RS	Skin Neoplasms; Occupational Risks; Oncology Nursing; Clinical Competence; Health Communication	This study's results allowed to clarify the combination of clinical knowledge and risk communication regarding skin cancer to rural workers.	Observational-exploratory study	Cezar-Vaz *et al*.	2015
RS	Oxidative stress, TBARS, protein carbonyls.	The results demonstrated a change in the oxidative status of rural workers compared to the control group, mainly by possible inhibition of AChE activity and the occurrence of oxidative stress without showing changes in biochemical parameters.	Questionnaire and blood sample	Murussi *et al*.	2014

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
RJ	Brain Cancer; Age-Period-Cohort; Agriculture; Trend	There is an increasing trend in brain cancer mortality rates in the rural Serrana Region in Brazil. At the ecological level, different environmental factors, especially the use of pesticides, may explain regional disparities in the mortality patterns from brain cancers.	Descriptive study examined brain cancer mortality who died between 1996 and 2010.	Miranda Filho *et al*.	2014
GO	Occupational Exposure; DNA Damage; MN Comet Assay	Occupational exposure to pesticides could cause genome damage in somatic cells, representing a potential health risk to rural workers that constantly deal with agrochemicals without adequate personal protection equipment.	Micronucleus and the comet assay.	Khayat *et al*.	2013
GO	Polymorphism GST; Biomarkers	The authors could not associate a null GSTT1 or null GSTM1 polymorphisms or both to intoxication events caused by pesticides, but instead they presented the importance of using Personal Protection Equipment to prevent such harm.	Blood sample	Godoy *et al*.	2014
CE	Biomonitoring; Human Lymphocytes; Comet Assay; Chromosomal Aberrations	Damages caused by pesticides in our study area were not great enough to induce permanent mutations or to interfere with mitotic apparatus formation; minimal pesticide damages could have undergone cellular repair, explaining the absence of structural and numerical chromosome aberration.	Alkaline comet assay and the chromosome aberration test.	Paiva *et al*.	2011
PE and AL	Carcinogenesis; Analysis of Principal Components	Both endosulfan and its metabolites are electrophilic and have carcinogenic potential.	Electronic paramenters (Electron affinity, dipole moments, electrostatic attaction, formation heat and permeability of the cell membrane).	Bedor *et al*.	2010

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Table 1 – Continuation.

State	Target	Major findings	Methodology	Reference	Year
SP	Cancer; Agriculture;	Cancers of the skin and digestive system were the most prevalent.	Database containing records of Amaral Carvalho Hospital.	De Brito Sá Stopelli and Crestana	2005
RJ	Mortality; Cancer; Ecological analysis	Agricultural workers 30–49 years old showed higher, but not statistically significant, mortality by stomach, esophagus, liver, testis, and prostate cancer, and soft-tissue sarcoma in the period of 1979–1988, and by testis and penis cancer, leukemia, and soft-tissue sarcoma in the period of 1989–1998.	National Mortality Information System between 1979 and 1998	Meyer *et al*.	2003
SP	Chromosome Aberrations; Toxicology; Contamination.	Although workers used protection against the pesticide's fog, the results revealed that they were contaminated with the pesticides.	Toxicological dosages of copper, zinc and manganese, hepatic enzyme dosage and acetylcholinesterase activity	Brega *et al*.	1998
REPRODUCTIVE HORMONES, SPERM QUALITY					
RS	Agricultural Workers; Anogenital Distance; Fungicides; Herbicides; Reproductive Hormones; Sperm Quality	Chronic occupational exposure to modern pesticides, particularly herbicides and fungicides, may adversely affect semen quality in young male farmers, potentially leading to poorer morphology. Also, exposure to agricultural pesticides may acutely increase prolactin and chronically alter sex hormone levels acting at the pituitary level through prolactin and LH suppression, hampering compensatory responses to testicular dysfunction.	Reproductive hormones, semen quality, and genital measures	Cremonese *et al*.	2017
RJ	Endocrine disruptors; Estrogenic compounds; Organochlorines; Testosterone	Seem to support the known capacity of organochlorines pesticides to exert estrogenic and anti-androgenic activity, affecting sex hormone systems through mechanisms of action that may be different for each individual compound.	Interviews and blood sample.	Freire *et al*.	2014

ES: Espírito Santo; SP: São Paulo; RJ: Rio de Janeiro; PR: Paraná; RS: Rio Grande do Sul; MG: Mato Grosso; BA: Bahia; PE: Pernambuco; CE: Ceará; MS: Mato Grosso do Sul; AL: Alagoas; SC: Santa Catarina; BR: Brasília; GO: Goiás; SE: Sergipe; DF: Distrito Federal.

da Educação). The majority of the articles are related to health disorders and occupational health, such as mental disorders, asthma, hearing, suicide, and poisoning.

Reflecting the importance of agriculture to the country's economy, Brazil has a vast legislation specifically designed to regulate the stages of the agrochemicals' life cycle at Federal and State level (GONÇALVES, 2016). All states have a pesticides register and authorization in their territory, but it also left some open controversial points regarding evaluation parameters and the attribution of inspection to the public power (GONÇALVES, 2016). Consequently, according to Pelaez, Terra and Silva (2010) there is a conflict of interests due to the ability of regulators, regulated companies and the companies themselves in adapting to the more stringent criteria for registering toxic substances (PELAEZ; TERRA; SILVA, 2010; GONÇALVES, 2016). There are studies that prove the contamination caused by the indiscriminate use of pesticides in different regions of Brazil (ALBUQUERQUE *et al*., 2016; CALDAS; ZANELLA; PRIMEL, 2011; RISSATO *et al*., 2007; LAABS *et al*., 2002; CALDAS *et al*., 1999; Laabs et al., 2002; ALHO; VIEIRA, 1997); however, this gap between Brazilian and state legislation leads to a panorama of uncertainties about the extent and degree of environmental contamination, as well as the dimension of effects to the human health and to the environment. Since there are no equal control procedures throughout the national territory, there are vulnerabilities associated with the use of agrochemicals. The European Union, one of the world's largest food producers and holding the position of the world's largest wheat producer, is in the process of implementing the world's most rigorous plan to reduce the use of pesticides. It culminated in the adoption of the Directive 2009/128/CE on the sustainable use of pesticides, whose complete implementation is planned for 2020 (GONÇALVES, 2016).

Health disorders and Occupational health

As a result of the analysis of the selected articles, four thematic categories emerged, the first three being linked to the problems that the use or misuse of pesticides generate to the environment and human health and a category linked to the appropriate practices:

- Health disorders and Occupational health;
- Genotoxicity of pesticides;
- Reproductive hormones and Sperm quality;
- Practices to reduce exposure.

Using AChE and BChE analysis, Oliveira-Silva *et al*. (2001), evaluated the exposures of rural workers of Rio de Janeiro State to anticholinesterasic pesticides. According to the authors' results and to the enzymatic indicator used, data were distinct concerning the incidence of excessive exposure. In the studied sample, a result of 3.0% was found for BChE values, and 41.8% according to AChE. Individuals with at least one positive enzymatic indicator result were considered as "intoxicated". Considering these data and comparing them to the social-economic and pesticides use factors, the importance of educational level in the prevalence of intoxication was showed. The other indicators studied did not show any significant and evident correlation (OLIVEIRA-SILVA *et al*., 2001). In the same way, Pasiani *et al*. (2012) conducted a knowledge, attitudes, and practices (KAP)/biomonitoring study in an agricultural setting in Midwestern Brazil. For this purpose, they assessed the knowledge, attitudes, and practices regarding the use of pesticides by farmers in two rural settings and calculated the farmers and residents' levels of exposure to organophosphorous and carbamate pesticides through red cells (AChE) and plasmatic butyrilcholinesterase (BChE) analysis. In relation to these last analyses, for some farmers, the authors found higher activity of cholinesterase inhibition during the exposure period compared to what is considered safe. This may indicate that they might be at risk by the exposure to pesticides during their agricultural activities. AChE activity depletion was also found in family farming settings, and thus may also be at risk from secondary exposure to pesticides (PASIANI *et al*., 2012).

From an epidemiological, clinical and laboratory aspects study of multiple exposure to pesticides in a representative sample of 102 small farmers, Araújo *et al*. (2007), brought some light to moderate episodes of acute intoxication by organophosphorates either described by the farmers or observed during clinical examination. Thirteen cases of delayed neuropathies were diag-

nosed and 29 cases of neural behavioral syndromes and psychiatric disorders associated to the continued use of pesticides. From these results, they found recurrent multiple overexposures to high concentrations of different chemicals that may cause serious damage to vital functions, if considered their young age (average 35 ± 11 years old) and the productive period in their lifetime (ARAÚJO *et al*., 2007).

Genotoxicity of pesticides

The harmful effects on the health of rural workers, who are chronically exposed to mixtures of agrochemicals, are still little elucidated. In Brazil, Antonucci e Syllos (2000) found a positive relationship between genotoxicity and farmers in Parana, and Silva *et al*. (2008) in winery workers in Rio Grande do Sul, being observed chromosomal aberrations as genotoxicity markers (SILVA, 2012).

Among the most serious damage caused by pesticides, genotoxicity or genetic toxicology seeks to identify the action of agents that produce toxic and genotoxic effects on the genetic material. From the interaction between our genetic material and genotoxic agents, the formation of adducts, oxidative alterations or even the breakdown of DNA molecules can happen (SILVA, 2012). The elimination of this cell or its repair by the organism usually occurs, however, if the lesion is fixed it will probably cause mutations, that is, hereditary alterations. Thus, there will be a mutagenic effect, where during the replication process the perpetuation of the mutation in the daughter cells will take place (OBE *et al*., 2002; SILVA, 2012).

The mutagenic potential is common between the pesticides, being extremely toxic to mammals. Because they inhibit the enzyme acetylcholinesterase, Organophosphorus insecticides, for example, cause an accumulation of acetylcholine in nervous tissues, impairing neurotransmission. Therefore, a reaction with DNA molecules occurs, being able to generate substitutions of bases (GRISOLIA, 2005; SILVA, 2012). In 2006, the International Agency for Research on Cancer (IARC) came to consider the organophosphate Dichlorvos as possibly carcinogenic to man (SILVA, 2012).

It is of vital importance to increase studies that seek the detection of cytogenetic damage caused by pesticides, since there is a strong association between occupational exposure to pesticides and different types of cancer (SILVA, 2012). Between them, we can highlight lung cancer (BEANE FREEMAN *et al*., 2005), bladder (VIEL; CHALLIER, 1995), pancreas (ANDREOTTI *et al*., 2009) and leukemias (BONNER *et al*., 2010) (SILVA, 2012). Mechanisms of action between mutagenesis and carcinogenesis may be related. As a consequence of the damage, the mutation may be the initial stage in the process by which most chemical carcinogens initiate tumor formation (RIBEIRO; SALVADORI; MARQUES, 2003; SILVA, 2012). Therefore, genotoxicity and mutagenicity assays for a given pesticide are important for cancer risk assessment. However, they do not have the capacity to predict their carcinogenic potential (SILVA, 2012).

Important and recent articles involving this area are from Tomiazzi *et al*. (2018), Hilgert Jacobsen-Pereira *et al*. (2018) and Silvério *et al*. (2017), performed in SP, SC and MG, respectively. In Tomiazzi *et al*. (2018), the authors study the relationship between the exposure to two xenobiotics with possible carcinogenic potential. In the exposed groups, the total number of cytogenetic abnormalities and MN were higher and the exposure to pesticides proved to be more deleterious than smoking. This finding is consistent with the exposure to a mixture of pesticides in the workplace, including compounds that are potentially carcinogenic in humans, as reported by pesticide group and smoking + pesticide group participants (TOMIAZZY *et al*., 2018).

Results obtained by Hilgert Jacobsen-Pereira *et al*. (2018) indicate the presence of genotoxic and mutagenic effects in the exposed group. Continuous and low dose exposure to complex mixtures of pesticides is associated to single and double strand breaks of DNA, oxidative stress and crosslinks. It is important to highlight that DNA damage, when incorrectly or not repaired, can persist and accumulate, triggering mutagenic processes and causing important cytogenetic changes (BENEDETTI *et al*., 2013; HILGERT JACOBSEN-PEREIRA *et al*., 2018).

From a study in southern Minas Gerais, Silvério *et al*. (2017) showed that workers had a hazardous exposure to organophosphates and afforded valuable data to es-

timate the risk to cancer development. The biomarkers used in this study are useful to assess and distinguish the occupational and environmental exposure to pesticides (SILVÉRIO *et al*., 2017).

Reproductive hormones and Sperm quality

It is interesting to highlight two studies approaching reproductive hormones and sperm quality (CREMONESE *et al*., 2017; FREIRE *et al*., 2014). Cremonese *et al*. (2017) investigated reproductive hormone levels, sperm quality, and genital measures in rural compared to urban young men in the South of Brazil, examining their association with occupational exposure to agricultural pesticides. According to their results, the main findings were:

- the linear dose-response relationship's poorer sperm morphology and life time use of all pesticides, fungicides, insecticides, herbicides, OP insecticides, dithiocarbamates and other chemical lasses, mancozeb, glyphosate, and paraquat;
- the association of lifetime use of pesticides, particularly herbicides and fungicides, with reduced levels of LH and prolactin;
- the association of rural living and maternal farming during pregnancy with larger anogenital distance and testicular volume, but poorer sperm morphology.

The authors suggest that chronic occupational exposure to modern pesticides, particularly herbicides and fungicides, may adversely affect semen quality in young male farmers in the South of Brazil, potentially leading to poorer morphology (CREMONESE *et al*., 2017).

On the other hand, Freire *et al*. (2014) aimed to examine the association between serum concentrations of organochlorine pesticides and levels of sex hormones in adult population in a rural area of Brazil heavily contaminated with these pesticides. The authors found an inverse association between organochlorine pesticide concentrations and testosterone in men and LH and FSH in peri-/postmenopausal women, together with the high proportion of women with elevated prolactina. Based on their findings, the authors suggest that, in this population, these organochlorine compounds may have triggered anti-androgenic effects in men and estrogenic effects in women (FREIRE *et al*., 2014).

Practices to reduce exposure

According to the World Health Organization, accidental poisoning kills about 355,000 people every year. Two thirds of these deaths happen in developing countries and are strongly associated with overexposure and inappropriate use of toxic chemicals, including pesticides (WHO, 2008; GONÇALVES, 2016). The use of pesticides has increased worldwide in the last decades, representing a risk for several diseases in humans, including cancer. As previously mentioned, genotoxicity underscores the importance of increasing studies that seek to detect cytogenetic damage caused by pesticides. It is among the most serious damage caused by pesticides, as there's a strong association between occupational exposure to pesticides and different types of cancer.

The inappropriate use of pesticides is of vital importance and is considered one of the main public health problems, mainly in the interior of Brazil. There are few, however, valuable studies related to the characteristics of their occupational use in order to identify the effects of the agrochemicals' use by rural workers from basic science with enough relevance to give a return to society's health. Therefore, it is necessary to obtain a profile of the rural worker through the study on the use of agrochemicals' impact, as well as the possible genetic and cytological modifications that can be triggered by these treatments.

According to Abreu & Alonzo (2014), the chemical industries encourage the expansion of the use of their products through aggressive marketing and commercialization practices, supported by the Brazilian legislation on agrochemicals (PORTO & SOARES, 2012; MIRANDA *et al*., 2007). They disregard the health impacts on farmers by promoting "safe use" (ABREU & ALONZO, 2014). The safety manuals prepared by the Associação Nacional de Defesa Vegetal (IWAMI *et al*., 2010; ASSOCIAÇÃO NACIONAL DE DEFESA VEGETAL, 2006) credit the hazards and accidents involved in the handling of pesticides to the "incorrect use" by the worker and not to the toxicity of the formulations and to the imposition of the agrochemical model of production in the Country (BREIHL, 2003; ABREU & ALONZO, 2014).

Quite common for rural workers, mainly by poor communication of risks to the population, is mixing active substances with the objective of achieving a potent effect, the so-called cocktail effect (REFFSTRUP; LARSEN; MEYER, 2010; HERNÁNDEZ *et al*., 2013; GONÇALVES, 2016). Individually, these active substances can be approved but mixed imply greater risks. Brazilian legislation does not provide tests on the effects of that, which are frequent and rarely punished. Although already regulated in several States, there is an urgent need to spread the information about the risks of using agrochemicals to the population and gain national dimension (GONÇALVES, 2016).

Stoppelli & Magalhães (2005), cited some strategies to minimize negative impacts to the producer and consumer: greater inspection of manufacturing, import, export and quality, as well as products sales; greater control over use, including correct disposal of empty packaging and waste; application only when necessary, in the correct dose and preferring less toxic formulations; greater control in commercialized foods; restrictions by the responsible organs of those products without full epidemiological and environmental studies; banning, when necessary, classes of pesticides; simplifying labels on packaging; risk communication; changes in the production and labor model; greater adequacy of protective equipment to excessive heat in tropical countries. Also incentive to government policies that incorporate, before crediting these products, an earlier structuring of the system, such as the preparation of labor, certification of Good Agricultural Practices and compliance with laws and improvements in inspection (STOPPELLI & MAGALHÃES, 2005).

As reported by Maroni, Fait and Colosio (1999), in the European Union a set of tests is required and designed to identify a toxicological profile of the substance. This profile includes: acute toxicity (oral, inhalation, dermal), skin and eye irritation, skin sensitization, short-term toxicity (28–90 days), mutagenicity, long-term toxicity (2 years), carcinogenicity, reproductive toxicity and other special effects (MARONI; FAIT; COLOSIO, 1999). According to the same author, developed countries' stringent requirements have to be satisfied before a product is authorized and the costs of meeting these requirements are very high. With the lack of legislation and adequate control's infrastructure to enforce legislation mainly in developing countries, the rural worker, often misinformed, starts to use pesticides that contain dangerous compounds which do not have controlled adverse effects both to humans and to the environment (MARONI; FAIT; COLOSIO, 1999).

The production of organic products through price reduction policies is also worth highlighting as a possible measure to be taken. According to Soares (2010), as it is done with alcohol and cigarettes in Brazil, making the production of pesticides less attractive by charging the products with high toxicity could be done. Having less than 1% of accredited establishments, the organic market in Brazil is considered very shy (IBGE, 2006; SOARES, 2010). Already in Europe, mainly due to the implemented policies encouraged the expansion of this market. About 11% of the land used for agriculture in Austria is occupied by certified organic producers, 7 to 10% in the Czech Republic, Greece, Italy, Sweden and Switzerland, 4 to 6% in Denmark, Estonia, Germany, Finland, Lithuania, Portugal, Slovakia, Slovenia, Spain and the United Kingdom, and less than 3% in other countries (PADEL; RÖCKLINSBERG; SCHMID, 2009; SOARES, 2010).

CONCLUSION

Rural workers and planting care are associated with a variety of occupational health hazards, both by physical factors and extreme weather conditions, and by exposure to hazards arising from the use of toxicological chemicals, such as pesticides and fertilizers. There are also biological and mechanical risks. Farmers are involved in different farming activities, so they are susceptible to numerous work-related health disorders. In many cases, producers do not give adequate attention to preventing and controlling occupational health problems. For the rural environment, comprehensive occupational health programs are adequately developed for this public, involving both preventive, curative and rehabilitation aspects. Studies such as Chaudhuri (2000), Cavalheiro *et al*. (2014) and Rempel, Haetinger and Sehnem (2013) demonstrate that there are health problems related to the occupational health of rural producers and that they demonstrate that specific programs can improve their quality of life.

Several studies report and describe the genotoxic effect of pesticides on farmers who use them, including a study by Doğanlar *et al*. (2018), which shows that populations of areas close to sites that use agrotoxic, even if they are not in contact with them, present an increase in the genotoxicity verified in blood test. These same authors suggest that biological monitoring efforts should be made to control non-occupational exposure to pesticides and thus safeguarding the health of agricultural residents. Despite the possible immediate benefits of using pesticides, it is important to stress that they are toxic substances and that their uncontrolled use causes severe damage to environmental and human health (GONÇALVES, 2016). Many countries encourage sustainable agricultural practices and have restrictions on importing products without proven food security. Therefore, even if the elimination of pesticide use in agriculture is still far away, its use in a rational manner and respecting quantity, application, environmental legislation and with appropriate PPE use, make the genotoxic risks smaller.

Most articles that relate the change in reproductive hormones and sperm quality to the prolonged use of pesticides in agriculture also mention that pregnant women exposed to pesticides accumulate active ingredients and pass them to the fetus. In a study carried out with rural producers in a city in the interior of Rio Grande do Sul, they do not relate the inadequate use of pesticides to their health status, even though they know the problems that pesticides can have on their health (WAHLBRINCK; BICA; REMPEL, 2017).

Many countries, mainly from the European Union, have adopted targets to reduce the use of agrochemicals, but countries that have their agriculture heavily dependent on pesticides must follow the regulations of the US EPA, which is the agency that regulates the amount of pesticide residues considered to be reliable in food. These sustainable environmental measures and practices, such as crop rotation and crop diversity, are necessary to ensure that even using only pesticides, there is less risk of generating health problems. Also, the measures adopted by the EU can be adapted to the Brazilian reality, improving the Brazilian agrochemicals' management system and for the Brazilian products to be certified and accepted in the European market.

This review made it possible to understand the current situation of the association between the exposure to pesticides and their possible effects caused to Brazilian rural workers. Considering the size of the country and although the research on the impact of the use of pesticides on human health has grown in recent years, it is still insufficient to really know the dimension of their damage on human health, caused by occupational exposure and by the intensive use of agrochemicals. It is fundamental to identify the presence of genotoxic and mutagenic effects of the use of pesticides in rural workers, considering the strong relationship between mutagenesis and carcinogenesis in pesticide users, as well as other damages involving health disorders and reproductive hormones.

Brazil has been growing in relation to the consumption of agrochemicals as well as in the production and export of agricultural products. It is up to us, and mainly to the governments, the search for the disciplining of their use, preventive actions and change to an agriculture aware of the environmental health, the consumer and the rural worker (STOPPELLI & MAGALHÃES, 2005).

CONFLICT OF INTERESTS

The authors confirm that this article content has no conflicts of interest.

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