

Special Article - Pesticides and Human Health

Pesticides: Undisputed Hazards for Environmental Health

Caldas LQA*

Department of Pathology, Faculty of Medicine, Federal Fluminense University, Niteroi, Rio de Janeiro, Brazil

***Corresponding author:** Caldas LQA, Professor of Clinical Toxicology (Former), Department of Pathology, Faculty of Medicine, Federal Fluminense University, Niteroi, Rio de Janeiro, Brazil**Received:** May 07, 2021; **Accepted:** June 03, 2021;**Published:** June 10, 2021**Abstract**

Airborne pesticides are now disseminated over vast regions of the planet even where they were not spilled, remotely from its preceding source. Their deleterious effects have been sensed overwhelmingly increasing all along with the shifts provoked in the nature, fauna, and flora derangements', regardless from where they come from either disseminated by air or water sources. They will insidiously, gently, or harshly impact the living beings (target and non-target organisms). Their effects will certainly be massive for those exposed and, consequently, at danger of death, extinction, or damage (grow retardation, physiological or behavioural shortages), the most vulnerable and susceptible individuals or species being quenched. The endocrine deleterious responses to adults as compared to the embryonic/fetal/neonatal responses have been described. Changes in the hormonal system development are often irreversible, in contrast to reversible changes induced by the exposure to transient hormones in adults. The toxic effects start as the pesticides get into the lungs or in the equivalent blood-water/air exchanging system. In mammals, birds and reptiles breathed air entering through the noses touch the sinus cavities, it irritates their fragile membranes as, in response, may lead to an inflammation as it also can occur topically. In the pesticides risk assessment, hormesis can have significant practical impact, because this concept assumes the existence of limits for doses higher than the hormetic ones; and its acceptance would therefore erroneously lead to modification in the current practice of cancer risk assessment. Thus, long run health advance may succeed by replacing hazardous pesticides by sustainable biopesticides and along with other non-poisoning methods.

Keywords: Lung damage; Hormesis; Vertebrates Effects

Introduction

Biota damages - Overview

In the last two centuries, the most has been done to avoid industrial pollutants although the least has been achieved to prevent exposure to pesticides in rural areas both in its farm borders, far-off and away from it. Airborne pesticides are now disseminated over vast regions of the planet even though where they were not spilled, i.e., remotely from its preceding source. Their deleterious effects have been sensed dramatically and overwhelmingly increasing all along with the shifts provoked in the nature, fauna, and flora derangements'. The potential degradation and accumulation in the atmosphere of newly formed compounds within the environment are still quite unknown because of a vast complex pattern of possibilities generated by climate deviations and anthropic actions around the globe [1].

When an air pollutant gets into intimate contact with live beings it sticks to the cellular arsenal either to be used or eliminated by it. Their properties - size, type, and concentration of the particles - will determine the kind of interaction to be established with cell system. For instance, in humans and animals, they can be attached to the skin and hair, adsorbed by the upper and lower respiratory system, or slightly ingested by the oral tract. The deposition pattern will vary widely according to the time, superficies extension, and volume of exposure. The detrimental damages will all depend on how the particle properties will be absorbed, adsorved, degraded and/or

biotransformed or readily eliminated by the organism, degree of photochemical activation may also influence them.

As regarding the environment, recurrent internal damages are hard to predict when the nature is affected; changes in this tender balance take ages, in general, decades to recover. Modifications in the metabolic system of plants and pollinator insects are bound to occur as well as it happens in phytobacteria, fungi and lichen which normally belongs to the life cycle of these microorganisms. Crops might be irremediably affected although some of the pesticides can be detoxified by microbial reactions such as dealkylation, esters and amides hydrolysis, dehalogenation, and cleavage after ring oxidation. Cooperative metabolism amongst microbe strains is not unusual as it may result in complete degradation of the pesticide. If this is not the case, the microbial population will be thoroughly affected as happens with pesticides that blocks nitrification system of some vital bacteria.

Thus, the lessons to be learned are that regardless from where the airborne pesticide residues burden come from, either disseminated by wind drift, airplanes, or chemical knapsacks, they will insidiously, gently, or harshly impact the living beings (target and non-target organisms). This will certainly be massive, both for those chronically or acutely exposed and, consequently, at danger of death or damage (grow retardation, physiological or behavioural shortages), the most vulnerable and sensitive individuals or species being quenched. Consequently, in the environment, the structure predator-prey

relationship due to the massive and persistent exposure to airborne pesticides will be surely and severely be affected by it, oversizing deep ecological changes in the local biota.

Much study has been accomplished lately; the movement and transformation of pesticide residues ensuing mitigating processes have also been pursued and still showing detrimental interactions between soil, water, air, plant, and animals, shallowly pondered. For instance, industrial and agricultural management procedures are responsible for more than a few contamination-related diseases such as endocrine disruption, heart and brain illnesses, breast and lungs cancer, and asthma in both adults and children.

This is the case of uncontrollable pesticide residues overwhelmingly distributed in nature, as what happens with all vertebrates such as mammals (including humans), fishes, amphibians, birds and reptiles. Special attention should be paid to the action of pesticides in two hormonal structures: gonadal and thyroid glands, particularly because during their normal embryonic development, these organs are especially sensitive and, therefore, affected by exposure even to low concentrations of such compounds, sex steroids and thyroid hormones production altered. Although, it is recognized that there is a difference in the endocrine response to adults as compared to the embryonic/fetal/neonatal responses. Changes induced by exposure to these hormones during development are often irreversible, in contrast to reversible changes induced by exposure to transient hormones in adults [2]. Hayes and his coworkers [3-5], have studied, a decade ago, the impact of the pesticide's actions in the environment, as an endocrine interfering factor. They considered the isolated (Atrazine 0.1ppb) and combined effect of 9 pesticides (4 herbicides, 2 fungicides and 3 insecticides) used in corn plantations in the Middle West of the North American. By examining larvae growth and development, sexual differentiation, and immune function in leopard frogs. It was found hormonal changes in sexual differentiation, body development and damage to the thymus resulting in immunosuppression. They concluded that the evaluation of each pesticide alone is inadequate to estimate the adverse impact on amphibian development or to link pesticides to the decline in the number of amphibians, as blends of pesticides provoked more effects than the isolated components.

Major effects in humans

In humans, apart from the bare skin exposure effects explained further on, the lungs of those occupationally exposed, remain usually the major cause of ailments just as the deaths amongst this workforce (rural mostly) although the effects in the endocrine system shall not be disdained.

Inhalation of various volatile forms of aerosols, vapours, dust, or mist can be the source of respiratory diseases in these works, particularly in those without proper personal protective equipment or when they work in confined spaces. Agricultural occupations accounts for about 10% of cases of respiratory hazards as compared with the general population in rural areas [6]. The main outcomes usually observed are Bronchial Asthma (BA), Chronic Obstructive Pulmonary Disease (COPD) (emphysema) and lung cancer. As explained forward, the etiopathogenetic agent varies, each one with their distinctive mechanism of action, some of them affecting the lung clearance by the mucocilliary tracheobronchial cells system, some affecting the bronchiolar smooth muscles physiology, others

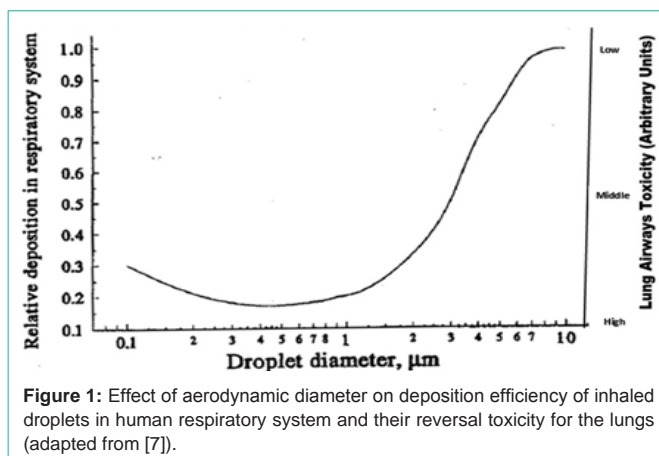


Figure 1: Effect of aerodynamic diameter on deposition efficiency of inhaled droplets in human respiratory system and their reversal toxicity for the lungs (adapted from [7]).

destroying alveolar wall and burdening pneumocytes and the last but not the least some pesticides molecules may deeply affect the oxygen supply and to get rid of the body exchange byproduct, carbon dioxide. This, ultimately and decisively, will interfere in the metabolic turnover entirely, not rarely leading to death.

At body rest, in an average-sized person, the ratio O_2 : CO_2 is 1.25 (250ml: 200ml/min) whereas incrementing the metabolic activity (e.g., exercise), the oxygen demand as well as its byproduct CO_2 increases to preserve the body homeostasis. The bronchial ducts and alveolar sacs serve to conduct fresh air into the lungs (inhalation), this active gas exchange occurs between the environment and blood whereby O_2 molecules migrate from alveoli into a continuous capillary blood sheet by diffusion to combine with haemoglobin. Pressure gradients also determine the gas exchange from the opposite direction, breathing out the body byproducts. The lungs transport 8 liters of clean fresh air or polluted air per minute, therefore, each day a huge amount (11.500 l) is breathed as compared to the daily intake of food (1.5l or 1.5kg) or water (2l or 2kg) which make obvious that inhalation is the foremost cause of exposure of environmental chemicals, pesticides included, particularly, when workers are in close contact fully exercising their duties. In the latter situation, the pulmonary ventilation rate may increase 20% as a result from nasal to mouth breathing shifting. In such cases, particles deposition and airborne substance doses will be concomitantly incremented compromising the worker's health since the intimate contact with the vast alveolar-surface ($70m^2$) area will be potentially damaged by the toxic material (sometimes causing an irreversible damage in wall lining - septum - that separates the alveolar sacs).

Deposition of airborne particulates in the human respiratory system is dependent on the aerodynamic diameter of the inhaled material. The relationship between deposition efficiency of inhaled droplets and the droplet diameter is shown in Figure 1. Basically, all droplets larger than $10\mu m$ are deposited in the upper respiratory tract (nose and mouth). This sort of deposition is of toxicological concern as it is swallowed. In the tracheobronchial region, droplets between 3 to $10\mu m$ are deposited with 50 to 90% of the inhaled droplets deposited. Only 20 to 30% of the inhaled droplets in the range of 0.1 to $3\mu m$ are deposited, primarily in the alveolar region [7].

When coarse particles ($>5\mu m$) reach the upper respiratory tract they are usually trapped into the conducting airways while fine ($<0.2-$

5 μm) particles (such as pesticides) are deposited by impaction and sedimentation others are adsorbed (or not) so that material dissolved in solvents or water vapour (hygroscopic) may get into contact with the airways ducts or alveolar septum a 80-120 ml monolayer of blood, their fate differ, the deposited particles will be expelled by the mucocilliary escalator mechanism within 24-48 h on healthy individuals, a pseudostratified columnar epithelium shed with goblet responsible for a continuous coating of thin mucous secretion through the cilia projection into the lumen of the bronchus.

The pesticide-containing particles (mostly small molecules $<0.001\mu\text{m}$) may be engulfed by local macrophage where proteolytic enzymes play a role. If they are in the end destroyed, the immune reaction perpetrated by a cascade of cytokines and other chemotactic substance are released which on the other hand can modulate the inflammation and/or provoking an extensive damage in the lining layer that separate the alveolar sacs which leads to formation of scar tissue [8]. In this case, lung function and gas exchange abnormalities will be deemed to occur but not before the tissue damages trying to eliminate the injury locally, repairing the bronchial walls to become them again functional. Instead, when a massive cytokines release (or their deficiency) occurs, chronic, repetitive disabling inflammatory response leading to a tentative of respiratory remodeling, excessive of matrix accumulation with fibronectin and collagen flooding the alveolar sacs, pulmonary fibrosis overcoming.

The toxic effects of pesticides start as the breathed air entering through the noses touch the sinus cavities, it irritates their fragile membranes as, in response, may lead to an inflammatory reaction with glands secretion with significant mucous production which, ultimately, may become infected. Supposedly, cleansed air, free from foreign substances, humidified and regulated to the body temperature must reach the alveoli nevertheless, potentially injurious substance such as the airborne pesticides turn out to be in close contact in the alveolar system.

Local spasms can then take place with asthma or asthma-like symptoms followed vertigo, wheezing, cough, dyspnoea, nausea, and vomiting. Organophosphates and carbamates pesticides may be the culprits of such episodes since they inhibit cholinesterase activity therefore increasing acetylcholine in the neuromuscular terminals initiating a succession of muscle contractions that driving to extreme muscle weakness and diaphragm paralysis. In the tracheobronchial tree, smooth muscles spasms will resemble an asthmatic response. This storm of clinical symptoms results in a profound change in the acid-basic homeostatic mechanisms that leads to acidaemia, obnubilation culminating with convulsions and death. Pyrethroids compounds are also allergenic, causing bronchospasm, dyspnoea, i.e., asthma-like episodes even in those who have no disease previously.

The squamous pneumocytes I and secretory pneumocytes II play a role linking pulmonary hyper-reactivity of the bronchiolar tree in allergic patients and exposure to pesticides (Figure 2). According to this assumption, it can be explained by the close contact of these cells with surface antigens of T lymphocytes of which, therefore, have been related to exacerbated risk of contracting allergic asthma [9-11]. Also, the smaller particles ($<0.001\mu\text{m}$) of low-molecular weight (including pesticides) can act as haptens both in the lungs and skin [12], forming complete antigens with native proteins that may be additionally

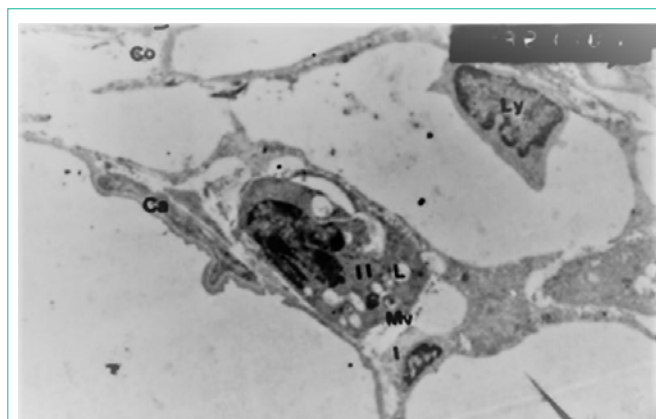


Figure 2: Alveoli bearing particles showing an active type II pneumocyte (II) with multilamellar bodies (L) and microvilli (Mv) bearing particles. Additionally, collagen fibres (Co) are seen in longitudinal, and transverse loosed lined on the alveoli surface. A type I pneumocyte (I) and a lymphocyte (Ly) area also seen. A collapsed capillary (Ca) is displayed as well (x9000) [9].

involved in exacerbation of Type I and IV hypersensitivity of atopic patients [13] with release of inflammatory mediators of early and/or early responses, asthma included. Allergic rhinitis may be seen recurrently in workers or in the community of non-agricultural areas in the boundaries exposed to glyphosate, chlorpyrifos, diazinon, dichlorvos, carbaryl and permethrin, in fact, these pesticides can be predictors of these episodes [14].

Alarming effects elsewhere

The cutaneous hypersensitivity overcomes by the intimate contact of the pesticides with the skin and/or the eyes as many spray adsorbent formulas can be seized and absorbed through the tissues, some other ubiquitous factors also interfering (humidity, temperature, skin damage). In such case, type I (immediate) or type IV (late) hypersensitivity may appear leading to contact dermatitis, asthma, urticaria-like symptoms, rhinitis amongst other effects.

Oxidative stress can be involved in many pathological the conditions into the lungs and in the skin. It may alter irreversibly cell damages that evoke changes in proteins or DNA structures as well as mitochondrial disorders that lead to antioxidant enzymes suppression [13]. This oxidative stress, in turn, will render pathogenic processes such as COPD, emphysema that causes mucous hypersecretion, vascular barriers disfunctions resulting in bronchial oedema, bronchoconstriction and acute or chronic inflammation (chronic pulmonary obstructive disease). This is the case of bipyridyl herbicides (paraquat and diquat) where the enzymatic or spontaneous dismutation of superoxide anions yields hydrogen peroxide, a key mediator of cytotoxicity of activated macrophages, and an intracellular cell amplifier threat, exaggerating the restorative-reparative processes, severe fibrogenic responses supersedes. That is, when these compounds provoke repeatedly cycle oxidation/reduction reactions generating toxic amounts of reactive oxygen species it can lead to diffuse pulmonary alveolitis culminating in a rampant acute or chronic fibrosis and, possibly, death [15].

Controversial Issues

A final consideration goes to the role played by incremental decimal log dose-effect relationship of pesticides as concerning

to their environmental or health outcomes, both in plants and in animals, including humans. The concept of hormesis (see footnote 3) will certainly have an impact on the view of which pesticides could harm these organisms. Its definition is of descriptive nature, evokes several biological mechanisms, regulating molecular processes and cellular strategies to harmonize the metabolic turnovers involved. To accomplish these tasks in the allocation of regulatory resources, no isolated hormetic mechanism is expected, but it is the existence of homeostasis in the maintenance of regulatory strategies [16]. Recognition of the hormetic response to carcinogenic agents (including pesticides) may have enormous impact on the assessment of cancer risk, if it could challenge the assumption of low-dose linearity [17]. Thus, in the assessment of the risk of carcinogens, hormesis can have an incredibly significant practical impact, because this concept assumes the existence of limits for doses higher than the hormetic ones; and the acceptance of hormesis would therefore erroneously lead to modification in the current practice of cancer risk assessment [17].

Alternative use of traditional pesticides has been recently revealed in robust progress on non-hazardous biopesticides, very efficient for controlling insects, fungus, nematodes but not so much for herbicides. New devices and some in development, use sensors to discriminate herbs from the culture reducing the applied herbicides amount. Herbs can also be eliminated with laser beams. Nevertheless, the introduction of biopesticide into use has shown difficulties, the challenge being to identify how to overcome these problems including cost-effective public policies.

Thus, long run health improvement may be succeeded by replacing hazardous pesticides by sustainable biopesticides and along with other non-poisoning methodologies whereas these social and environmental problems may also not be alleviated by embracing renewable energy practices and green sources replacement effectively, also, taking into account that economic development compromises and influences social and environmental performance of developing countries, eco-friendly policies must be law-enforced targeting unconcealed thoughts.

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