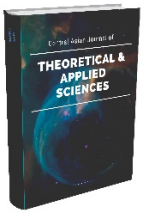

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Adverse Effects of Pesticides on Health of Human Beings

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Abstract: *A pesticide is any substance used to kill, repel, or control certain forms of plant or animal life that are considered to be pests. Pesticides include herbicides for destroying weeds and other unwanted vegetation, insecticides for controlling a wide variety of insects, fungicides used to prevent the growth of molds and mildew, disinfectants for preventing the spread of bacteria, and compounds used to control mice and rats. Because of the widespread use of agricultural chemicals in food production, people are exposed to low levels of pesticide residues through their diets. Scientists do not yet have a clear understanding of the health effects of these pesticide residues. The Agricultural Health Study, an ongoing study of pesticide exposures in farm families, also posts results online. Other evidence suggests that children are particularly susceptible to adverse effects from exposure to pesticides, including neurodevelopmental effects. People may also be exposed to pesticides used in a variety of settings including homes, schools, hospitals, and workplaces.*

Keywords: *pesticides, health, human, children, life, herbicides, fungicides, insecticides, people, exposure.*

Introduction

Pesticides can cause short-term adverse health effects, called acute effects, as well as chronic adverse effects that can occur months or years after exposure. Examples of acute health effects include stinging eyes, rashes, blisters, blindness, nausea, dizziness, diarrhea and death. Examples of known chronic effects are cancers, birth defects, reproductive harm, immunotoxicity, neurological and developmental toxicity, and disruption of the endocrine system.

Some people are more vulnerable than others to pesticide impacts. For example, infants and young children are known to be more susceptible than adults to the toxic effects of pesticides. Farm workers and pesticide applicators are also more vulnerable because they receive greater exposures. Immediate health effects from pesticide exposure includes irritation of the nose, throat, and skin causing burning, stinging and itching as well as rashes and blisters. Nausea, dizziness and diarrhea are also common. People with asthma may have very severe reactions to some pesticides, particularly pyrethrin/pyrethroid, organophosphate and carbamate pesticides. In many cases, symptoms of pesticide poisoning mimic symptoms of colds or the flu. Since pesticide-related illnesses appear similar or identical to other illnesses, pesticide poisonings are often misdiagnosed and under-reported. Immediate symptoms may not

be severe enough to prompt an individual to seek medical attention, or a doctor might not even think to ask about pesticide exposure. [1]

Chronic health effects include cancer and other tumors; brain and nervous system damage; birth defects; infertility and other reproductive problems; and damage to the liver, kidneys, lungs and other body organs. Chronic effects may not appear for weeks, months or even years after exposure, making it difficult to link health impacts to pesticides.

Pesticides have been implicated in human studies of leukemia, lymphoma and cancers of the brain, breasts, prostate, testes and ovaries. Reproductive harm from pesticides includes birth defects, still birth, spontaneous abortion, sterility and infertility.

Endocrine disruptors are chemicals that — often at extremely low doses — interfere with important bodily functions by mimicking or blocking hormones (the chemical messengers that circulate in blood and regulate many body processes including metabolism, brain development, the sleep cycle and stress response). Some pesticides act as endocrine disruptors and have been shown to cause serious harm to animals, including cancer, sterility and developmental problems. Similar impacts have been associated with human exposure to these chemicals.

Children are not simply “little adults.” Children are more vulnerable to pesticide exposure because their organs, nervous systems and immune systems are still developing. Children are also less able to detoxify and excrete pesticides. Exposure during certain early development periods can cause permanent damage.

In addition to being more vulnerable to pesticide toxicity, children’s behavior and physiology make them more likely to receive greater pesticide exposure than adults. Most pesticide exposure occurs through the skin and children have more skin surface for their size than adults. Children have a higher respiratory rate and so inhale airborne pesticides at a faster rate than adults. Children also consume proportionately more food and water — and pesticide residues — than adults. With their increased contact with floors, lawns and playgrounds, children’s behavior also increases their exposure to pesticides.[2]

Organophosphates & Carbamates: These pesticides are like nerve gas: they attack the brain and nervous system, interfering with nerve signal transmission. Symptoms include headaches, nausea, dizziness, vomiting, chest pain, diarrhea, muscle pain and confusion. In severe poisoning incidents, symptoms can include convulsions, difficulty breathing, involuntary urination, coma and death. Acute poisoning of the nervous system by these pesticides affects hundreds of thousands of people around the world each year.

Soil Fumigants: These pesticides are applied to soil, forming a gas that is toxic to nematodes, fungi, bacteria, insects, and plants in the soil. Because they are gases, they move from the soil into the air and expose people living or working nearby. Commonly used soil fumigants in California include 1,3-dichloropropene, chlorpicrin, metam sodium, and metam potassium. Symptoms of fumigant exposure include irritation of skin, eyes, and lungs (dichloropropene and chloropicrin), and extremely irritating to eyes and lungs (metam sodium and metam potassium). Dichloropropene, metam sodium, and metam potassium are all cancer causing chemicals and metam sodium causes reproductive harm. In counties where fumigant use is high, premature birth is more common than in counties with low fumigant use.

Pyrethroids: These insecticides are synthetic chemicals that are structurally similar to botanical compounds but have been designed to be more persistent. They are toxic to the nervous system, and there is concern that during pregnancy a fetus is not able to efficiently break down these chemicals. Symptoms of pyrethroid poisoning include tremors, salivation, headache, fatigue, vomiting, stinging and itching skin, and involuntary twitching.[3]

Many pyrethroids also cause long term health problems. For example, resmethrin causes both cancer and reproductive harm. Cypermethrin, fenvalerate, and deltamethrin all cause genetic damage and

reproductive harm. Data from the Center for Disease Control and Prevention's national biomonitoring program links pyrethroid exposure to heart disease.

Discussion

The most widely known organochlorine pesticide is dichlorodiphenyltrichloroethane, i.e., the insecticide DDT, the uncontrolled use of which raised many environmental and human health issues .Dieldrin, endosulfan, heptachlor, dicofol, and methoxychlor are some other organochlorines used as pesticides.There are a few countries that still use DDT or plan to reintroduce it for public health purposes .Furthermore, DDT is also used as a solution in certain solvents .It is a ubiquitous chemical substance, and it is believed that every living organism on Earth has a DDT body burden, mainly stored in the fat There is also evidence that DDT and its metabolite p,p-dichlorodiphenyldichloroethylene (DDE) may have endocrine-disrupting potential and carcinogenic action . In utero exposure to both DDT and DDE has been associated with neurodevelopmental effects in children . Moreover, a recent study related DDE to hepatic lipid dysfunction in rats The general class of organochlorine pesticides has been associated with health effects, such as endocrine disorders effects on embryonic development lipid metabolism and hematological and hepatic alterations .Their carcinogenic potential is questioned, but concerns about possible carcinogenic action should not be underestimated .

Organophosphates, which were promoted as a more ecological alternative to organochlorines include a great variety of pesticides, the most common of which is glyphosate. This class also includes other known pesticides, such as malathion, parathion, and dimethoate; some are known for their endocrine-disrupting potential .This class of pesticides has been associated with effects on the function of cholinesterase enzymes decrease in insulin secretion, disruption of normal cellular metabolism of proteins, carbohydrates and fats and also with genotoxic effects and effects on mitochondrial function, causing cellular oxidative stress and problems to the nervous and endocrine systems .Population-based studies have revealed possible relations between the exposure to organophosphorus pesticides and serious health effects including cardiovascular diseases negative effects on the male reproductive system and on the nervous system dementia and also a possible increased risk for non-Hodgkin's lymphoma .Furthermore, prenatal exposure to organophosphates has been correlated with decreased gestational duration and neurological problems occurring in children .Regarding glyphosate, the safety of which is the subject of an ongoing scientific controversy it is the most widely used herbicide in current agriculture especially since the introduction of glyphosate-tolerant genetically modified crops, such as certain types of soybean and maize .Its extensive use in genetically modified soybean cultivation has raised concerns about possible synergistic estrogenic effects due to the simultaneous exposure to glyphosate and to the phytoestrogen "genistein," which is a common isoflavone present in soybeans and soybean products .[4]

Glyphosate can display endocrine-disrupting activity affect human erythrocytes in vitro and promote carcinogenicity in mouse skin . Furthermore, it is considered to cause extreme disruption in shikimate pathway, which is a pathway found in plants and bacteria as well as in human gut bacteria. This disruption may affect the supply of human organism with essential amino acids . Commercial glyphosate formulations are considered to be more toxic than the active substance alone . Glyphosate-based herbicides, such as the well-known "Roundup," can cause DNA damages and act as endocrine disruptors in human cell lines , and in rat testicular cells ,cause damages to cultured human cutaneous cells ,and promote cell death in the testicular cells of experimental animals .There is evidence also for their possible ability to affect cytoskeleton and intracellular transport .A recent study examined the possible relation between glyphosate, genetically modified crops, and health deterioration in the USA. Correlation analyses raised concerns about possible connections between glyphosate use and various health effects and diseases, such as hypertension, diabetes, strokes, autism, kidney failure, Parkinson's and Alzheimer's diseases, and cancer .Furthermore, there are concerns about the possible ability of glyphosate to cause

gluten intolerance, a health problem associated with deficiencies in essential trace metals, reproductive issues, and increased risk to develop non-Hodgkin's lymphoma .

Carbamate pesticides, such as aldicarb, carbofuran, and ziram, are another class of chemical pesticides that have been associated with endocrine-disrupting activity possible reproductive disorders and effects on cellular metabolic mechanisms and mitochondrial function .Moreover, in vitro studies have revealed the ability of carbamate pesticides to cause cytotoxic and genotoxic effects in hamster ovarian cells and to induce apoptosis and necrosis in human immune cells natural killer cells and also apoptosis in T lymphocytes .Furthermore, it has been confirmed that carbaryl, which belongs to the category of carbamate pesticides, can act as a ligand for the hepatic aryl hydrocarbon receptor, a transcription factor involved in the mechanism of dioxin toxicity There is also evidence for the ability of carbamate pesticides to cause neurobehavioral effects increased risk for dementia and non-Hodgkin's lymphoma .[5]

Results

The major types of pesticides used in agriculture, forestry, landscape, medical and veterinary sectors are listed in Table 1.

Type of pesticide	Active ingredient	Target pests
Insecticides	Natural and synthetic	Insect (6-legged) pests of agricultural, forestry, landscape, medical and veterinary importance
Miticides/acaricides	Natural and synthetic	Mites (8-legged) pests of agricultural, forest, landscape, medical and veterinary importance
Fungicides	Natural and synthetic	Fungal diseases (molds, mildews, rust) of agricultural, forestry and landscape importance
Herbicides	Natural and synthetic	Unwanted plants (weeds) of agricultural and landscape importance
Insect growth regulators	Synthetic	Disrupt the growth and reproduction of insect pests. IGR are species or genus specific.
Pheromones	Natural and synthetic	Attract and trap male insects and are often species-specific.
Plant growth regulators	Synthetic	Alter plants growth, e.g., induce or delay flowering
Algaecides	Natural and synthetic	Algae growing on different surfaces, e.g., patios
Molluscicides	Natural and synthetic	Slugs and snails of agricultural, forestry and landscape importance
Biopesticides	Natural	Can be insecticides, fungicides or herbicides
Antimicrobials	Synthetic	Microbes (mostly bacteria) of medical and veterinary importance
Rodenticides	Natural and synthetic	Rodents (mice, rats) in agriculture, landscape, building, storages and hospitals
Treated seeds	Synthetic	Seeds coated with an insecticide or fungicide or both to prevent damage from soil insect pests and fungus diseases
Wood preservatives	Synthetic	Pesticides to protect wood from insect pests, fungus and other diseases
Minimum risk pesticides	Natural and synthetic	Any pesticides which have been proven safe for human and are exempt from registration by any regulatory authorities

The long-term chronic adverse effects of pesticides exposure are cancers, birth defects, reproductive harm, neurological and developmental toxicity, immunotoxicity, and disruption of the endocrine system. The chronic effects of pesticides on human can be categorized into three major groups; neurotoxic effects, genotoxic and carcinogenic effects, and reproductive effects. Neurotoxicity can be defined as any adverse effect on the central or peripheral nervous system caused by chemical, biological or physical agents. A developing nervous system in children (during replication, migration, differentiation, myelination of neurons, and synapse formation) is more susceptible to neurotoxic chemicals including pesticides. Chemicals (pesticides) can cause neuronal cell death by disruption of the cytoskeleton, induction of oxidative stress, calcium overload, or by damaging mitochondria. Most of the synthetic insecticides, some fungicides and herbicides, currently in use are neurotoxicants.

Pesticide molecules are small and lipophilic in nature, and can enter from blood to brain and then in neurons, glial cells and brain micro vessels. Pesticides can disrupt blood-brain barrier receptors in the central nervous system which enhance chronic toxicity and affect the receptor-mediated transcytosis. Neuronal cells are more susceptible to oxidative stress due to their high polyunsaturated fat content in the myelin sheaths, low anti-oxidative capabilities, enzymatic systems with transient metals that aid in the production of free radicals, and demand for high oxygen and glucose metabolism rate.

OPs and carbamates bind to and phosphorylate/carbamalate the AChE which causes accumulation of acetylcholine at cholinergic synapses causing overstimulation of muscarinic and nicotinic cholinergic receptors. Neuropsychiatric disorders, such as anxiety and depression, are observed in patients with acute and long-term poisoning from OPs. OPs may also cause an intermediate syndrome and OP-induced delayed polyneuropathy (OPIDP) 1-3 weeks after a single exposure. In carbamates, the AChE inhibition is reversible and acute intoxication is generally resolved within a few hours.

The OP insecticides can disturb the function of mitochondria by inducing oxidative stress in central nervous system through critical depletion of mitochondrial energy, the activation of proteolytic enzymes, and DNA fragmentation leading to apoptosis. The dysfunction of mitochondria and oxidative stress is responsible for several neurological diseases, including Parkinson's disease, seizure, cognitive dysfunction, attention and memory deficits, dementia, depression, and Alzheimer's disease. OP triggered induction of a xanthine oxidase may play a role in cognitive impairment.[6]

In a study, increased inhibition of cholinesterase enzyme with increased exposure to OP insecticides was confirmed in both occupationally exposed (OE) and environmentally exposed (EE) groups of people. The OP exposure, mainly in the EE group, was associated with a diminished neuropsychological performance; general mental status, language, memory, attention, executive function, praxis and psychomotricity.

Acute poisoning due to exposure to OP (particularly chlorpyrifos) was reported with higher prevalence of peripheral polyneuropathy, and deterioration of cognitive functions (verbal fluency, and visual and auditory memory) was observed in agricultural workers and in inhabitants of rural agricultural areas. Exposure to OP insecticides in rural schoolchildren was associated with a lower processing speed in children and an IQ lower than expected for their age.

Exposure to type I pyrethroids cause tremor syndrome (behavioral arousal, aggressive sparring, increased startle response, and fine body tremor progressing to whole-body tremor, and prostration) while type II pyrethroids exposure cause salivation syndrome (profuse salivation, coarse tremor progressing to choreoatetosis, and clonic seizure). The poisoned cerebral cortex affect learning, memory, emotions, and movement. Pyrethroids exposure has been positively associated with hearing loss in U.S. adolescents. Pyrethroids exposure induced Tau protein malfunction which may be the mechanism underlying cognitive impairment. Paraquat, triazine and pyrazole (herbicides) through oxidative stress, raised influx of calcium

and the stimulation of nitrogen oxide species, and aggravated Aβ amyloidogenesis cause cognitive impairment.

Exposure to endocrine disrupting chemicals (EDCs) including many pesticides can disrupt maternal thyroid imbalance which can result in permanent and lifelong neurodevelopmental consequences for their children, including attention-deficit disorder, autism spectrum disorder, and cognitive and behavioral dysfunction. Workers of fruit and seed export companies in a rural area of Santiago exposed to methyl bromide (CH3Br, a fumigant) had increased concentration of CH3Br in blood after application which resulted in a higher frequency of insomnia, headaches, paresthesias, mood swings, memory loss, and decreased concentration [7].

Parkinson's disease (PD) is characterized by progressive degeneration of dopaminergic neurons of the nigrostriatal pathway and the formation of alpha-synuclein (α-syn)-containing Lewy bodies. Dieldrin (OC) is selectively toxic to dopaminergic cells, disrupts striatal dopamine activity, and may promote α-syn aggregation while ziram (dithiocarbamate fungicide) increases the probability of synaptic vesicle release by dysregulation of the ubiquitin signaling system and increases excitability in both aminergic and glutamatergic neurons leading to PD.

Implications

A genotoxic agent can be a physical, chemical or biological agent that can interact with the genetic material (DNA) causing alterations, damage or ruptures, and those that interfere with enzymatic processes of repair, genesis or polymerization of proteins involved in chromosome segregation. These alterations could lead to impaired embryonic development or be the initial steps in the development of cancer. Pesticides exposure can cause genomic damage. Genetic damage caused by pesticides is broadly classified into three classes; (i) Pre-mutagenic damage like DNA strand breaks and DNA adducts (ii) gene mutations like insertion, deletion, inversion and translocation (iii) chromosomal aberrations, including loss or gain of whole chromosome (aneuploidy), deletion or breaks (clastogenicity), and chromosomal rearrangements.Farmers exposed to pesticide mixtures in Greece had possible clastogenic (chromosome breakage cause mutation) and aneugenic (abnormal number of chromosomes) effect of pesticides on the genetic material. DNA methylation changes in the placenta were significantly associated with the maternal plasma concentrations of OCs in early pregnancy causing prenatal toxicity. OPs affect DNA methylation, induce the AChE gene expression and activate the NMDA glutamate receptors resulting in calcium influx in the post-synaptic neurons leading to degeneration.

Genetic damage has been reported from exposure to malathion (OP), carbofuran (carbamate), triflumuron (Insect growth regulator), imidacloprid, acetamiprid and thiamethoxam (neonicotinoid insecticides), pentachlorophenol (OC), Emamectin benzoate (used in agriculture, household, and veterinary medicine), and tembotrione (novel post-emergence herbicide) [8]

(Table 2). Pesticide hazard classification by the FAO

WHO Hazard Class	Band color	Signal word	Dermal LD_{50} (mg/Kg)	
			Solid formulation	Liquid formulation
Class Ia Extremely Hazardous	Red	VERY TOXIC	<10	<40
Class Ib Highly Hazardous	Red	TOXIC	10–100	40–400
Class II Moderately Hazardous	Yellow	HARMFUL	100-1000	400-4000
Class III Slightly Hazardous	Blue	CAUTION	>1000	>4000
Class U **Products unlikely to present a hazard**	Green			

Conclusions

Pesticides are used in managing pests of agricultural and public health importance, and their use will continue in future because of food security and vector control. Additionally, pesticides are used at home in fumigation for structural pests and to mitigate household pest using aerosols or sprays. It is difficult to eliminate pesticides in the near future, but they should be used with care and caution. Most pesticides are potentially toxic to human beings resulting in severe health consequences including cancers.

Epidemiological evidence suggests that there is an increased incidence of different diseases including leukemia, lymphoma, and several other types of cancers in farmers, and those who are associated with application of pesticides. There is also evidence that parental exposure, as well as, exposure in early life or adolescence could increase the longer-term risks.

Since animal studies are problematic, expensive and often generate ethical problems, cell cultures are increasingly used as a model of research. Correctly conducted and properly selected, the cell culture is an excellent experimental model reflecting human exposure to different xenobiotics through all relevant routes. The cell cultures are also becoming more widely used to study the effect of pesticides on the human body at a molecular level, which is necessary to understand the hazards and determine the level of exposure. [9]

Some pesticides (OCs) are no longer used worldwide due to their persistence and toxicity. However, their residues or metabolites are still found in food and water samples. The use of OPs and carbamate insecticides has been reduced since the arrival of newer chemistries in different parts of the world but most of them are still use around the world.

The workplace safety standards and proper pesticide management and storage must be implemented to reduce the risks posed to human health. Pesticide users should be aware of their risks and proper handling, as well as must use personal protective equipment which are effective in reducing damage to human health. To ensure healthy childhood growth, efforts should be made to develop comprehensive pesticides risk mitigation strategies and interventions to reduce children's exposure.

It is critical to achieve sustainable development in agricultural systems. Newer approaches in pest management have been developed which should be encouraged. For example, RNA interference- (RNAi-) based pesticides are emerging as a promising new biorational control strategy [61] and steam treatment at temperature of 150.56°C can kill 93.99% of nematode 97.49% of bacteria [8].

Future research need in the context of minimizing the impact on human health due to exposure to pesticides include an urgent need to eliminate the use of carcinogenic pesticides and to develop environmentally sound integrated pest management (IPM) strategies that use the minimum amount of pesticides. Such IPM strategies should aim at reducing the pesticides residues on food products and pesticides-free water and air.[10]

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