

Mini Review

# Effect of Pesticides on Human Health

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## Abstract

The demand for pesticides has increased in today's world of expanding population in order to boost crop productivity and eliminate undesirable plants (weeds) that grow alongside the primary crop. Along with the various benefits, it is also used in animal farms to get rid of pests. This has an impact not only on humans but also on animals and the environment. The usage of pesticides has increased, and occasionally some of them linger in the food products they are applied to, a condition known as pesticide residue. This residue is linked to human health and can result in a variety of diseases and disorders. In the current environment, even pesticides that are marketed as benign have negative long-term effects and exacerbate issues like bioaccumulation and bio-magnification. To avoid food contamination with pesticides, different methods like crop rotation, organic farming, and integrated pest management should be used as alternatives. Today, it is essential for all pesticide users to be aware of the risk and proper handling of these pesticides. New methods of pest management should be fostered in the realm of development.

## Introduction

"Pesticides are any substance or mixture of substances intended for preventing, destroying or controlling any pest, including vectors of human or animal disease, unwanted species of plants or animals causing harm, during or otherwise interfering with the production, processing, storage, transport, or marketing of food, agricultural commodities, wood and wood products, or animal feedstuffs, or substances which may be admixed," according to the Food and Agricultural Organisation (FAO). According to US Environment 2007, pesticides are substances or mixtures of substances used to prevent, eliminate, repel, or mitigate the effects of pests [1].

The public was made aware of the potentially fatal effects of chemical pesticides on people and the environment by Rachel Carson in her book "Silent Spring" in 2002. Masanobu Fukuoka expertly merged spirituality and farming in his 2009 book One Straw Revolution, which offered natural farming methods and emphasized the importance of not adding any external chemicals to the agricultural system [2].

Contrarily, we can say that pesticides are substances that are used to stop the spread of pests (or any micro-organisms) that affect plant growth. In addition to killing pests, pesticides are also used to control plant growth and delay product ripening. According to research, pesticides have both acute and chronic health effects on people, and these effects might manifest months or years after exposure. When we discuss the acute effects, they include mortality, blindness, nausea,

stinging eyes, rashes, dizziness, and diarrhea. The chronic effects include cancer, birth defects, reproductive harm, immune toxicity, neurological damage, and endocrine system destruction.

Any plants, animals, or microorganisms that affect food, health, or comfort are considered pests. The Environmental Protection Agency (EPA) defines pesticides as a class of chemicals used to prevent and control the growth of pests. These are also described as chemical and natural substances that are used to fend off or eradicate noxious pests, organisms that cause plant illnesses, common weeds, and organisms that harm people. It can be summed up as a material used in agriculture to protect crops from pests and insects. For hydration and to boost the crop's yield and output [3].

## Classification of pesticides

According to revised criteria for classification which is in use since the 2009 update, The WHO now utilizes the Acute Toxicity Hazard Categories from GHS8 as the initial basis for classification. This shift aligns with the 1975 World Health Assembly Resolution's intention to evolve the WHO Classification over time in collaboration with nations, global organizations, and regional entities. The Globally Harmonised System (GHS) serves this purpose by being a globally accepted classification system that emerged after extensive international consultation.

## More Information

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It classifies pesticides into five categories:

1. Extremely hazardous
2. Highly hazardous
3. Moderately hazardous
4. Slightly hazardous
5. Unlikely to present an acute hazard.

The categorization differentiates between the more and less risky variations of each pesticide, relying on the toxicity of both the technical compound and its formulations. The classification relies mainly on the toxicity of a substance when ingested or absorbed through the skin in rats, as these assessments are conventional toxicology methods. If a compound's dermal LD-50 value suggests a higher restriction level than its oral LD-50 value, it will always be categorized under the stricter class. There's also a provision to adapt the classification of a substance if there's a difference between the acute danger to humans and what's determined solely based on LD-50 assessments (Table 1).

### Pesticides on the basis of modes of action

**1. Insecticides:** The Insecticide Resistance Action Committee (IRAC) divided insecticides into 32 categories with known modes of action and sites of action as well as 5 additional categories with unknown modes of action or sites of action. Different parts of the nervous system are most frequently affected by insecticides. They also focus on the same nervous system place in humans. Acetylcholine esterase is inhibited by carbamate and organophosphate, which results in overexcitation. Pesticides include, for instance, dichlorvos, Malathion, phorate, etc. Convulsions and hyperexcitability are caused by the blockage of the gamma-aminobutyric acid-activated chloride channel by phenyl pyrazole and cyclodiene organochlorine insecticides. The insecticides endosulfan and fipronil are two examples. Both natural and synthetic pyrethroids maintain the sodium channel open, which leads to hyperexcitation and, in rare cases, nerve blockade. Permethrin and deltamethrin are two examples. Neonicotinoids are insecticides that bind to the nicotine acetylcholine receptor and produce a variety of symptoms, including hyperexcitability, lethargy, and paralysis. Acetamiprid, clothianidin, and imidacloprid are a few examples. Another class of pesticides that affect the neurological system are those that paralyze insects by either allosterically activating nAChRs, glutamate-gated chloride channels, or allosterically inhibiting GABA-activated chloride channels [4].

**Table 1:** Classification of pesticides.

	Class	Oral	Dermal
Ia	Extremely hazardous	<5	<50
Ib	Highly hazardous	5 - 50	50 - 200
II	Moderately hazardous	50 - 2000	200 - 2000
III	Slightly hazardous	Over 2000	Over 2000
U	Unlikely to present acute hazard	5000 or higher	5000 or higher

**2. Fungicides:** Fungicides prevent the growth of fungi by interfering with vital biological functions. Based on the site of action, the Fungicide Resistance Action Committee (FRAC) has divided fungicides and bactericides into 50 groups. They operate on particular target areas that contain particular enzymes to which fungicides bind. Known target sites include respiration, amino acid and protein synthesis, signal transduction, lipid synthesis, transport membrane integrity or function, cell wall biosynthesis, melanin synthesis in cell walls, and host plant defense induction.

Endocrine-disrupting pesticides include several fungicides and herbicides [4].

**3. Herbicides:** These pesticides are used extensively in agriculture, the landscape industry, and non-crop areas for weed control. They prevent normal plant growth and development. Herbicide has been divided into 27 groups by the Herbicide Resistance Action Committee. These include cell membrane disruptors, pigment inhibitors, photosynthetic inhibitors, amino acid synthesis inhibitors, lipid synthesis inhibitors, and growth regulators.

Auxin transport inhibitors and synthetic auxin are the main ingredients in growth regulator herbicides. 2, 4-Dichlorophenoxyacetic acid (2, 4-D), dicamba, quinclorac, dichlorprop, MCPA (2-methyl-4-chlorophenoxyacetic acid), mecoprop, and picloram are examples of synthetic auxins that are often employed. These mimic the auxin (indoleacetic acid) plant growth hormone. The human hormonal system is also disrupted by some synthetic auxin herbicides. Herbicides that limit photosynthetic activity frequently employ atrazine. Tyrosine, tryptophan, and phenylalanine are produced when the enzyme EPSPS, which is a derivative of an amino acid called glyphosate, is inhibited from being produced. When inhaled or swallowed, the electron diverter and respiratory inhibitor paraquat (gramoxone) pose a significant risk to people [4].

### Impact of pesticides use on human health

When used on humans, pesticides have both immediate and long-term negative effects on health. First, let's discuss the short-term acute effects of pesticide exposure on human health. These effects include eye-stinging, blisters, rashes, skin irritation, blindness, nausea, and dizziness. When working in agricultural fields, being exposed to pesticides poses a major risk to the respiratory system, increasing the likelihood of asthma attacks and bronchitis as well as persistent cough, dyspnoea, wheezing, and expectoration. All of these respiratory issues are frequently observed in employees working in Ethiopian flower fields, Brazilian coffee plantations, and Costa Rican banana plantations. The usage of pesticides during banana cultivation in Rio Grande Do Norte, Brazil, results in symptoms such as burning in the throat and lungs, congestion, cramps, skin peeling, diarrhea, headache, chest pain, weakness, and skin irritation [4]. The chronic impacts of pesticides can be fatal and might remain concealed

for years. These long-term effects lead to harm across various organs in the body. Extended exposure to pesticides results in the following outcomes:

- Pesticide contact can trigger neurological issues like coordination loss, memory impairment, reduced vision, and weakened motor signaling [5].
- Prolonged pesticide exposure harms the immune System, possibly causing hypersensitivity, asthma, and allergies [6].
- Pesticide residues have been detected in the bloodstream of cancer patients, with potential links to leukemia, brain cancer, lymphoma, and cancers of the breast, prostate, ovaries, and testes [7].
- The prolonged presence of pesticides in the body also impacts reproductive capabilities by altering male and female reproductive hormone levels, leading to issues like stillbirth, birth defects, spontaneous abortion, and infertility [7].
- Extended exposure to pesticides can also harm the liver, lungs, and kidneys, and may induce blood disorders.

Ingestion of organochlorines leads to heightened sensitivity to light, sound, and touch, accompanied by symptoms like dizziness, tremors, seizures, vomiting, nausea, confusion, and nervousness [5]. Exposure to organophosphates and carbamates generates symptoms akin to those arising from increased neurotransmitter acetylcholine. These pesticides interfere with normal nerve signaling, resulting in headaches, dizziness, confusion, nausea, vomiting, muscle, and chest pain. Severe cases might experience difficulty breathing, convulsions, coma, and even death [7].

Pyrethroids can cause allergic skin reactions, aggressiveness, hyperexcitation, and reproductive or developmental effects, along with tremors and seizures [5]. An association between pesticides and Parkinson's disease as well as Alzheimer's disease has been noted [8].

## Cancer

Numerous studies have reported a connection between pesticides and cancer. A prospective cohort study involving 57,310 pesticide applicators in the USA found that two imidazolinone herbicides (imazethapyr and imazaquin) were linked to bladder cancer [9]. In a separate case-control study conducted in Egypt with 953 cases and 881 controls, male agricultural workers exposed to pesticides showed an elevated risk of bladder cancer (Odds Ratio (OR) = 1.68, 95% Confidence Interval (CI): 1.23 to 2.29), which increased in line with dosage [10]. An additional prospective cohort study involving 57,311 licensed pesticide applicators in Iowa and North Carolina, USA, demonstrated significant correlations between bladder cancer, colon cancer, and imazethapyr, a

heterocyclic aromatic amine herbicide [11]. In a hospital-based case-control study in the USA involving 462 glioma and 195 meningioma patients, Study found that women with occupational exposure to herbicides had notably increased risk for meningioma (OR = 2.4, 95% CI: 1.4 to 4.3) [12]. In a case-control study conducted in France involving 221 newly diagnosed cases of brain tumors and 442 controls matched individually, a noteworthy link was observed between pesticide exposure and brain tumors (Odds Ratio (OR) = 2.16, 95% Confidence Interval (CI): 1.10 to 4.23), as well as gliomas (OR = 3.21, 95% CI: 1.13 to 9.11) [13].

Nonetheless, the International Agency for Research on Cancer (IARC) has categorized many pesticides as unclassifiable in terms of their potential to cause cancer in humans (group 3). However, the U.S. Environmental Protection Agency (US EPA) and the Canadian Pest Management Regulatory Agency (PMRA) have identified evidence of carcinogenicity in animal toxicity studies for pesticides such as alachlor, carbaryl, metolachlor, pendimethalin, permethrin, and trifluralin. This alignment supports the biological plausibility of the observed associations with these pesticides. Extensive mechanistic research has indicated that pesticides are capable of causing mutations in oncogenes while increasing their transcriptional expression *in vitro* [14]. Similarly, studies conducted on human populations have suggested potential links between levels of pesticide exposure and the occurrence of mutations in genes related to cancer.

## Asthma

Numerous clinical and epidemiological studies have indicated a link between pesticide exposure and symptoms of bronchial hyperactivity and asthma. Pesticide exposure might worsen asthma by causing irritation, inflammation, immunosuppression, or disrupting the endocrine system. The study conducted also explored the connection between early-life exposure to Ops and respiratory outcomes among 359 mothers and children in the USA. They concluded that such exposure could lead to respiratory symptoms consistent with childhood asthma [15-17]. In a cross-sectional study involving female farm workers ( $n = 211$ ) in Africa, the prevalence of ocular-nasal symptoms was positively linked to entering a pesticide-sprayed field (odds ratio (OR) = 2.97; 95% confidence interval (CI): 0.93 – 9.50) [18]. In another study conducted in the USA, involving 926 pesticide applicators with active asthma who participated in the Agricultural Health Study (AHS), positive associations were observed between exacerbation and the herbicide pendimethalin (OR = 2.1) as well as the insecticide aldicarb (OR = 10.2) [19]. However, the immunogenicity of most pesticides is weak, limiting their potential to sensitize airways in exposed populations, while only select pesticides possess the potency to harm the bronchial mucosa [20]. A study encompassing 25,814 farm women in the USA found that any use of pesticides on the farm was linked to atopic asthma (OR = 1.46; 95% CI: 1.14 – 1.87) [21].



## Parkinson's disease

Epidemiological investigations suggest that being exposed to pesticides during occupational activities may heighten the risk of Parkinson's Disease (PD). A French case-control study involving 133 cases and 298 controls delved into the quantitative dimensions of pesticide exposure in relation to PD, discovering a connection between pesticide exposure in vineyards and PD (Odds Ratio (OR) = 2.56; 95% confidence interval (CI): 1.31, 4.98) [22]. Similarly, an increase in PD risk by 3% for each 1.0  $\mu\text{g L}^{-1}$  of pesticide in groundwater was noted in the Colorado Medicare Beneficiary Database, USA (OR = 1.03; 95% CI: 1.02 – 1.04) [23].

A Dutch cohort study involving 58,279 men and 62,573 women (aged 55 – 69 years) also indicated a potential link between PD mortality and occupational pesticide exposure [24]. In a study, it is observed a dose-dependent rise in cellular  $\alpha\text{S}$  levels reported an association between PD and the usage of specific pesticides (e.g., paraquat, rotenone, and maneb), insecticides (e.g., organophosphates, and three pyrethroids), and fungicides (e.g., thiophanate-methyl, fenhexamid, and cyprodinil) [25].

Additionally, chronic exposure to metals and pesticides was found to be linked with the development of PD at a younger age compared to patients without a family history of the disease [26]. The duration of exposure played a significant role in influencing the extent of this effect. Meta-analyses combining data from cohort and case-control studies showed an increased risk of PD due to exposure to various types of pesticides, herbicides, and solvents. Specifically, exposure to paraquat or maneb/mancozeb exhibited an approximately two-fold increase in PD risk [27]. In a US population-based case-control study, frequent use of household pesticides elevated the odds of PD by 47% (OR = 1.47, 95% CI: 1.13, 1.92) [28]. Furthermore, the use of Organophosphate (OP) products showed a more substantial increase in PD odds by 71% (OR = 1.71, 95% CI: 1.21, 2.41), while using organothiophosphates nearly doubled the odds of PD. A review study encompassing thirty-nine case-control studies, four cohort studies, and three cross-sectional studies found that exposure to herbicides and insecticides significantly heightened the risk of PD [29].

## Leukaemia

Exposure to pesticides stands as a significant contributor to acute leukemia, particularly in childhood cases. Previous investigations have explored the impact of pesticide exposure on childhood leukemia. In a meta-analysis of 12 case-control studies on childhood leukemia, the author revealed that Odds Ratios (ORs) for Acute Lymphoblastic Leukemia (ALL) linked to pesticide exposure shortly before conception, during pregnancy, and after birth were 1.39, 1.43, and 1.36, respectively [30].

An Iranian case-control study found that occupational

farmers faced a notably elevated risk of developing acute leukemia, especially their children, due to pesticide exposure [31]. Meta-analysis of 40 studies conducted in France indicated a substantial increase in the risk of lymphoma and leukemia in children when their mothers were exposed during the prenatal period (OR = 1.53; 95% CI: 1.22 to 1.91 and OR = 1.48; 95% CI: 1.26 to 1.75) [32]. Exposure during pregnancy to unspecified residential pesticides, insecticides, and herbicides showed positive associations with childhood leukemia. The author in his systematic review and meta-analysis of previous observational epidemiologic studies, found that such exposures during pregnancy were linked to childhood leukemia [33].

Analyzing 13 case-control studies spanning from 1987 to 2009, all the authors identified statistically significant connections between childhood leukemia and pesticide exposure (mRR: 1.74, 95% CI: 1.37 – 2.21). However, the available data weren't comprehensive enough to establish causality, emphasizing the need for further research to validate prior findings based on self-reporting. This also includes exploring potential exposure-response relationships and conducting more in-depth assessments of the toxicological effects of pesticides [34].

## Other effects

The majority of pesticides, including organophosphorus compounds, can impact the male reproductive system through various mechanisms. These mechanisms involve reducing the activities of sperm, such as counts, motility, viability, and density, inhibiting the process of spermatogenesis, diminishing testis weights, causing damage to sperm DNA, and increasing the occurrence of abnormal sperm morphology [35].

Authors found that exposure to organophosphate and organochlorine pesticides might serve as potential risk factors for inducing hypospadias [36].

Moreover, pesticide exposure underscores the significance of genetic polymorphisms in enzymes responsible for metabolizing pesticides. These genetic variations act as biomarkers that can make individuals more susceptible to experiencing adverse health effects [37].

## Preventive measures

Farmers should utilize alternative methods including Integrated Pest Management (IPM), crop rotation, and organic farming to eliminate the harmful effects of pesticides on human health and pesticide contamination of food.

1. The process of education and the provision of protective equipment for personal use to prevent pesticide exposure are two separate techniques to lessen health impact.
2. Teaching farmers how to use less pesticide and protect the environment.

- Reduce the availability of highly dangerous insecticides by taking appropriate action. The concept of organic farming is one of the main solutions to preventing the use of pesticides in agricultural practices. As compared to conventionally grown crops or products produced utilizing integrated pest management techniques, organic produce contains far fewer pesticide residues. According to studies, crops grown organically have a higher nutritious content than crops grown using any other conventional method. When compared to other conventional crops, organically cultivated crops have higher levels of ascorbic acid, lower levels of nitrate, and superior protein quality [1].

## Conclusion

On human health, pesticides have major and alarming effects. Long-term interaction with these substances, ingestion of tainted food, or environmental exposure can all have negative effects on one's health. It is essential to reduce pesticide use by adopting alternative and more sustainable farming practices, such as organic farming and integrated pest management, in order to protect human health. A healthier and safer environment for everyone also depends on raising knowledge among farmers, consumers, and policymakers about the dangers of pesticides and the advantages of eco-friendly farming practices. To lessen the negative impacts and safeguard human well-being, regular monitoring, strict laws, and appropriate pesticide usage are crucial.

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