

Deleterious effects of agricultural chemicals on human health
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Abstract

Pesticides and chemical fertilizers are substances that are either naturally occurring or artificially manufactured and used to control a range of pests. These chemical substances are employed in a number of industries, including forestry, agriculture, aquaculture, and food. Since the 1930s, chemical fertilizers have been crucial to the economically efficient cultivation of commercial crops. A plentiful harvest guarantees there is enough food accessible for everyone at reasonable costs in light of the rising population and high expense of living. However, the majority of individuals might not be aware of the hidden risks associated with utilizing chemical fertilizers. Though environmental contamination from pesticides is a primary focus on research, the effects of human contact with pesticides are less clear. Commonly used herbicides for row crops such as corn, sorghum and sugarcane, and even residential lawns have been implicated in negative human health effects. These adverse effects on human health include tumors, breast, ovarian and uterine cancers. Additionally these pesticides have demonstrated heavily impact the nervous system cells as well as muscle cells. Pesticides, herbicides and chemical fertilizers can be harmful to the human body, having underlying molecular impacts. This review will show the influence of specific pesticides and their impacts on the human body. I examine specifically the molecular effects of pesticides on human health through researching available data across several populations. I will also examine outcomes specific to geographic location and government regulation in those areas.

[Pathak VM, Verma VK, Rawat BS, Kaur B, Babu N, Sharma A, Dewali S, Yadav M, Kumari R, Singh S, Mohapatra A, Pandey V, Rana N, Cunill JM. Current status of pesticide effects on environment, human health and it's eco-friendly management as bioremediation: A comprehensive review. *Front Microbiol.* 2022 Aug 17;13:962619. doi: 10.3389/fmicb.2022.962619. PMID: 36060785; PMCID: PMC9428564.]

Introduction

Chemical substances known as pesticides are used to get rid of weeds, fungus, rodents, and insects. It plays important roles in commercial as well as food-based industrial processes, such as aquaculture, agriculture, food processing, and storage, and is typically employed to prevent infections carried by vectors. Pests are any living things—plants or animals—that pose a risk to people or other creatures. Pesticides are chemicals used to eradicate pests or stop them from growing.

Over the past century, pesticide use has increased dramatically, with a sharp rise observed in the first 20 years between 1960 and 2008. From 196 million pounds of pesticide active ingredients in 1960 to 632 million pounds in 1981, the overall amount of pesticides sprayed on 21 chosen crops in the US increased. The creation of novel pesticides and the rise in the proportion of planted acres receiving herbicide treatment for weed management were the main drivers of this trend. In 1960, insecticides made up 58% of all pesticide treatments; by 2008, that percentage had dropped to 6%, while the percentage of herbicide applications had risen from 18% to 76%.

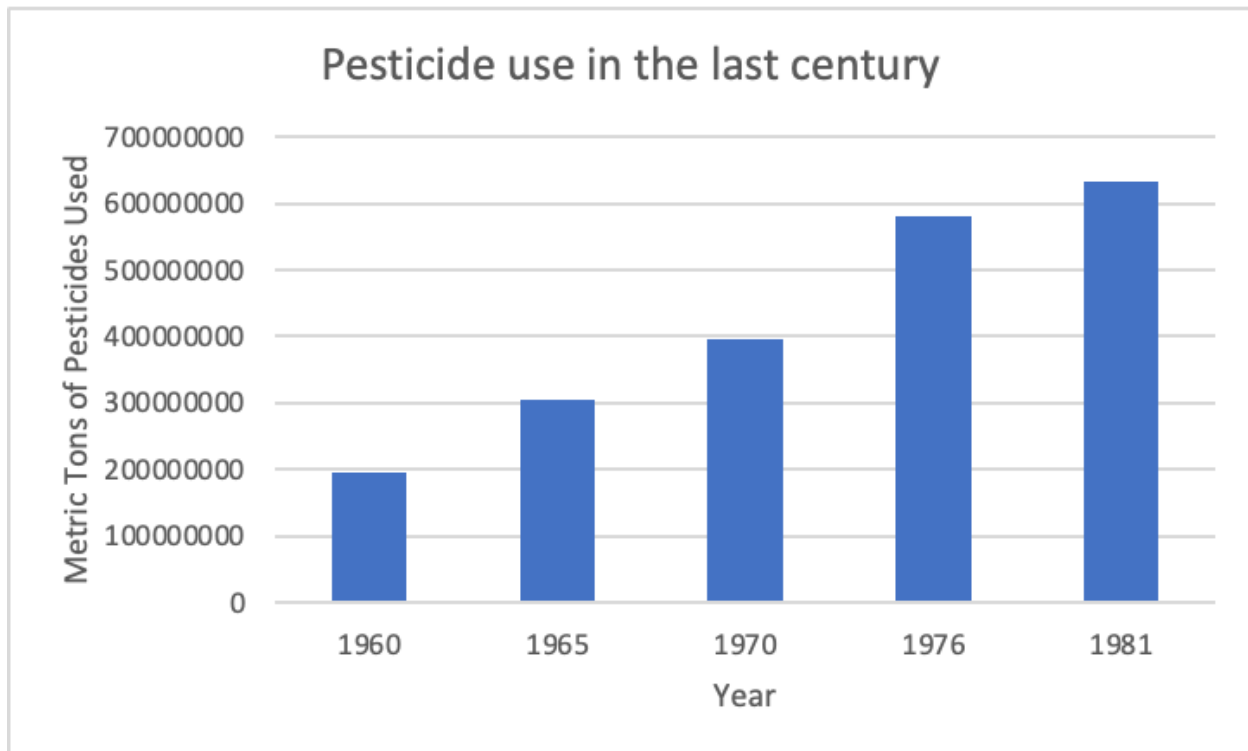


Figure 1: There has been a Global increase in pesticide use since 1960 of over 400 million metric tons.

The global pesticide consumption in 2019 was approximately 4.19 million metric tons. China was by far the largest pesticide-consuming country (1.76 million metric tons), followed by the United States (408 thousand tons), Brazil (377 thousand tons), and Argentina (204 thousand tons). In Southeast Asia, The World Health Organization (WHO) reported increased pesticide use in 20% of the developing countries such as Cambodia, Laos, and Vietnam.

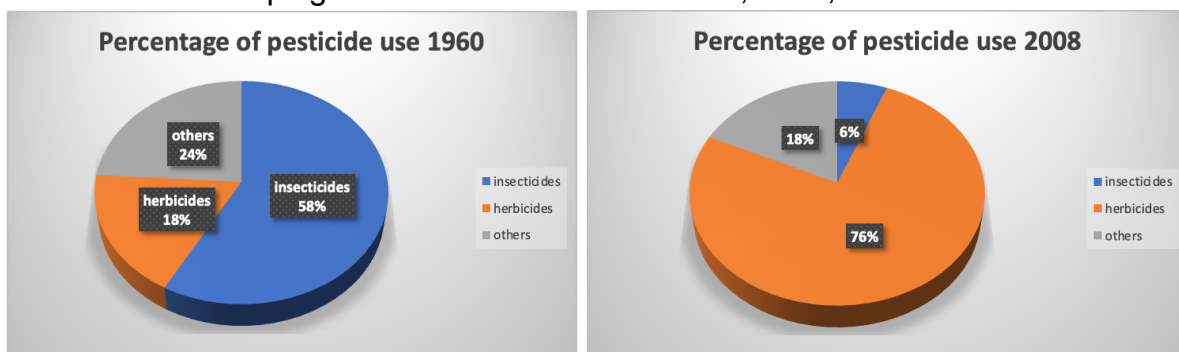
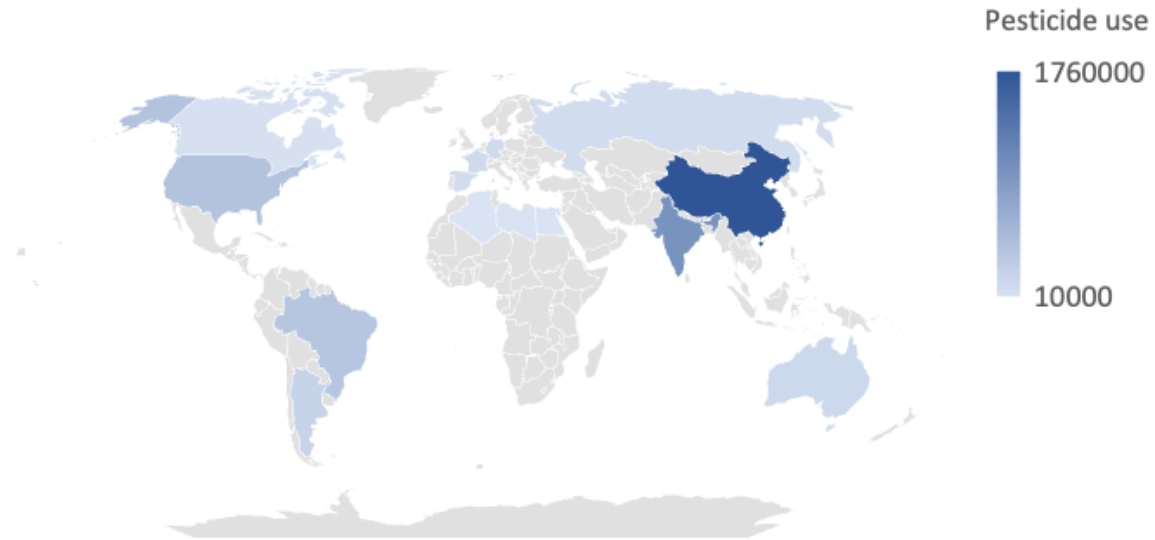


Figure 2: Category of pesticide used in 1960 compared to 2008. This figure demonstrates the shift in use of herbicides in recent years.

PESTICIDE USE AROUND THE WORLD(TONS)



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Figure 3: China is the leading user of pesticides globally as of 2019, with India and the United States also heavily using pesticides.

However, these chemicals can have deleterious effects on human health through increased incidence of neoplasia, reproductive system damage, allergies and immune inflammation, and cellular mutations/DNA damage. The acute health effects of pesticide exposure include irritation of the nose, throat, and skin, which result in symptoms such as burning pain, stinging, pruritus (itching), rashes, and blisters. Additional common symptoms include nausea, dizziness, and diarrhea. In some cases, acute pesticide poisoning can be fatal: there are approximately eleven thousand annual global pesticide-related deaths. These acute health effects are striking, but much rarer than long-term effects of pesticide exposure. Chronic health effects of pesticide exposure include cancer and other tumors, brain and nervous system damage, birth defects, infertility and other reproductive disorders, and damage to critical organs including the liver, kidneys, and lungs. As many as 25 million agricultural workers experience unintentional pesticide poisonings each year. The global distribution of acute unintentional pesticide poisoning is a significant public health problem, with approximately 385 million cases.

Despite mounting evidence of their detrimental impacts on human health and the environment, agrochemical consumption is rising worldwide. Over the past few years, numerous reports of these substances' harmful consequences have emerged. Over the past ten years, the percentage of health problems linked to agrochemicals has sharply climbed and shows no signs of abating. This review will synthesize the literature on the effects of specific pesticides on human health, focusing on the molecular effects of pesticides on human health, using data from various populations. This review additionally highlights region-specific outcomes and evaluates local government regulations for pesticide exposure.

Overview of pesticides

The chemical load on natural ecosystems has increased as a result of the industrialization of the agriculture sector. Agrochemicals, known colloquially as pesticides, are chemicals used to remove pests that are used in urban green spaces, public health initiatives, and agricultural areas to safeguard people and plants against various illnesses. However, their side effects carry significant environmental health risks. Their documented capacity to have numerous detrimental effects on both human health and the environment is striking. There is a pressing need for more ecological and sustainable approaches, including reforms in agriculture and food production that use sustainable practices and eventually lead to food sovereignty. More than ever, it is clear that society needs to adopt a new agricultural concept for food production that is safer for both the environment and humans.

Numerous pesticides have been linked to health and environmental problems, and their agricultural use has been discontinued. Pesticide exposure can occur through ingestion, inhalation, or skin contact. The type of pesticide, the length and mode of exposure, and the individual's health status (such as malnourishment and skin damage) all influence the potential health consequences. Pesticides can be metabolized, eliminated, stored, or bio-accumulated in body fat within the bodies of humans and animals. Chemical pesticides have been linked to a wide range of detrimental health effects, including neurological, respiratory, reproductive, gastrointestinal, dermatological, and endocrine effects. Moreover, prolonged intentional, unintentional, or occupational exposure to pesticides can lead to hospitalization and even death.

The four most well-known pesticides are *insecticides*, *herbicides*, *fungicides* and *rodenticides*.

Insecticides are pesticides used to contain populations of insects and other arthropods. This class of pesticide is the fastest-acting and can cause neurotoxic effects in humans.

Herbicides are pesticides that inhibit or prevent the growth of unwanted plants (weeds). They are more widely used than insecticides and present chronic risks to human health. Ongoing, low-level exposures can increase the risk of diseases or disorders such as cancer, Parkinson's disease, or infertility.

Fungicides are pesticides that are used to control fungal problems like molds, mildew, and rust. They are also used in large amounts; some are more benign than others.

Rodenticides are pesticides that are used to control rodents such as mice. Pesticides can also be grouped according to their mode of action or how they control the target pest. For example, one insecticide may affect an insect's nerves, while another may disrupt the molting process. Other types of pesticides include bactericides, molluscicides, larvicides, desiccants, defoliants, disinfectants, attractants, plant growth regulators, swimming pool treatments, microbial pesticides, and biochemical pesticides.

Pesticides are known to have the biggest impacts on the neurological, respiratory, reproductive, gastrointestinal, dermatological, and endocrine systems. The neurological system includes the brain, spinal cord, and a complex network of nerves. This system sends messages back and forth between the brain and the body. The respiratory system is a biological system consisting of specific organs and structures for gas exchange. The gastrointestinal system's principal functions are to digest and absorb ingested nutrients and to excrete waste products of digestion. In humans, the dermatological system consists of skin, hair, nails, and related glands. Altogether, the dermatological system forms the largest organ in the body. The main function of this system is to protect bones, organs, and other internal structures from harm. A human's endocrine system is a messenger system made up of feedback loops of hormones released into

the circulatory system directly by internal glands and hormones that target and regulate distant organs.

Negative effects of pesticide use

Pesticides are widely used in agriculture to control pests and diseases, ensuring a steady food supply for the global population. However, numerous studies have indicated a potential link between pesticide exposure and the development of solid tumors, particularly brain and prostate cancers. A study published in the *International Journal of Cancer* in 2019 found a significant association between pesticide exposure and glioma, a common type of brain tumor. The study analyzed data from over 1,000 participants and found that those exposed to pesticides had a 1.4 times higher risk of developing glioma than those not exposed. Similarly, a meta-analysis of 31 studies by Van Maele-Fabry et al. (2018) found a positive association between pesticide exposure and brain cancer. The pooled relative risk was 1.45, indicating a 45% increased risk of brain cancer in individuals exposed to pesticides.

There has also been a lot of research done on the connection between pesticide exposure and prostate cancer. In a cohort study conducted by Band et al. (2011) with 55,332 pesticide applicators, individuals exposed to the herbicide *fonofos* had a markedly higher risk of prostate cancer. According to the study, there is a 26% higher chance of prostate cancer with a relative risk of 1.26. Furthermore, people who were exposed to pesticides had a pooled relative risk of 1.14 for prostate cancer, according to a meta-analysis conducted by Van Maele-Fabry et al. (2013) using data from 32 trials. These findings suggest that exposure to pesticides increases the risk of prostate cancer by 14%.

The correlation between pesticide exposure and the diagnosis of multiple myeloma has been the subject of extensive research in recent years. Multiple myeloma, a cancer of plasma cells, has been linked to various environmental factors, including exposure to pesticides. Pesticides, widely used in agriculture and pest control, contain numerous chemicals that can harm human health. Exposure to these chemicals, either through inhalation, ingestion, or skin contact, can lead to various health complications, including cancer. Multiple myeloma is a type of cancer that begins in the plasma cells, a white blood cell in the bone marrow. The exact cause of multiple myeloma is unknown, but several risk factors have been identified, including exposure to certain chemicals, such as pesticides.

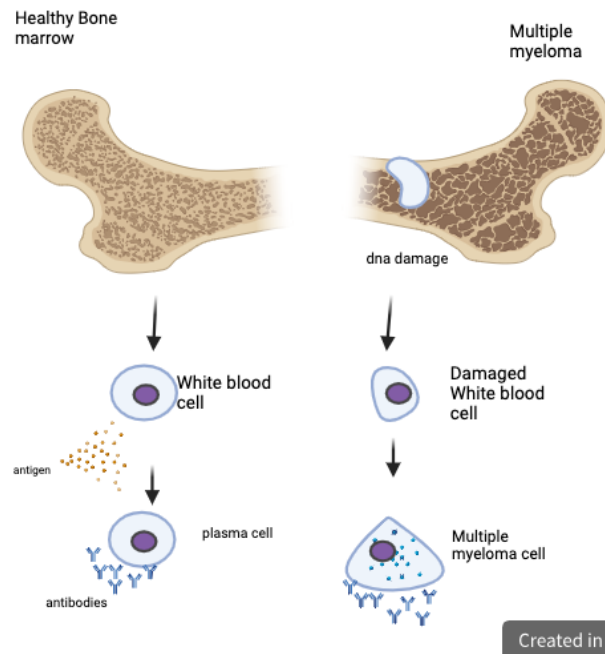
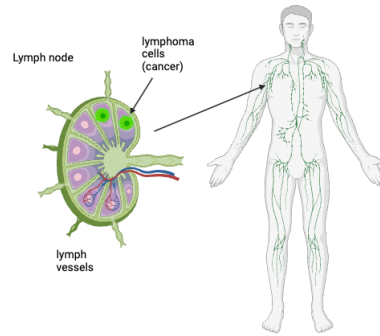


Figure 4: Bone tissue may develop cancer from pesticide exposure. Cancerous bone tissue is unable to produce healthy white blood cells resulting in ineffective immune function. (This figure was generated with BioRender.com)

Several epidemiological studies have shown a positive association between pesticide exposure and the risk of multiple myeloma. For instance, a study published in the International Journal of Cancer in 2012 found that individuals exposed to pesticides had a significantly higher risk of developing multiple myeloma compared to those not exposed.

Another study published in the Journal of Occupational and Environmental Medicine in 2014 found that agricultural workers exposed to certain pesticides had a higher incidence of multiple myeloma. The study suggested that the chemicals in pesticides could damage plasma cell DNA, leading to the development of multiple myeloma.

The development of non-Hodgkin's lymphoma (NHL) is one of the biggest health dangers linked to pesticide exposure. One type of cancer that affects the lymphatic system, which is vital to the body's immunological response, is non-Hodgkin's lymphoma. Several studies have identified a connection between pesticide exposure and a higher chance of acquiring non-Hodgkin's lymphoma (NHL). NHL is a type of blood cancer that affects the lymphatic system, a network of tissues and organs responsible for filtering and carrying fluid throughout the body. Unlike Hodgkin's lymphoma, NHL is characterized by the proliferation of abnormal lymphocytes, a type of white blood cell, in various parts of the lymphatic system. NHL encompasses a diverse group of tumors, with over 30 subtypes identified based on the specific lymphocyte affected and the rate at which the cancer progresses. Prognosis and treatment options vary depending on the subtype, stage of diagnosis, and individual patient factors.



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Figure 5: Repeated exposure to pesticides may result in abnormalities in the lymphatic cells leading to cancer. (This figure was generated with BioRender.com)

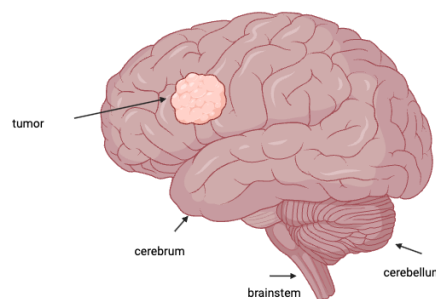
It has long been believed that exposure to pesticides is associated with the emergence of several illnesses, including non-Hodgkin's lymphoma. Several studies have looked at this connection, and while it's still unknown exactly how pesticides affect human health, several mechanisms could make them carcinogenic. Many compounds included in pesticides, including glyphosate and organophosphates, interfere with the endocrine system's regular operation and DNA repair mechanisms. Subsequent genetic alterations resulting from these disturbances may increase an individual's susceptibility to cancer. Long-term pesticide exposure has also been shown to disrupt immune system performance, making it more difficult to stop the spread of cancer cells. Moreover, the vast majority of pesticides used today are designed to be biologically active and are specifically intended to kill pests, making them inherently toxic and posing a significant risk to human health. Consequently, individuals who work directly with pesticides or live near pesticide-treated areas are at an increased risk of developing non-Hodgkin's lymphoma.

Furthermore, several epidemiological studies have been conducted to explore the relationship between pesticide exposure and the development of NHL. These studies have provided valuable insights into the potential association between pesticide exposure and NHL. A case-control study conducted by Alavanja et al. (2004) revealed a positive association between pesticide exposure and NHL incidence. The study compared individuals diagnosed with NHL to a control group and found that those with higher pesticide exposure had an elevated risk of NHL. Similarly, another case-control study by McDuffie et al. (2001) examined the correlation between pesticide exposure and NHL in Canadian agricultural workers. The findings indicated a significant association between the two, with pesticide applicators experiencing a two-fold increase in NHL incidence compared to the control group. These studies highlight the consistent evidence supporting the hypothesis that pesticide exposure is likely linked to the diagnosis of NHL.

Understanding the mechanisms of how pesticides really cause cancers on the molecular level is still an ongoing area of research. One potential mechanism is the ability of certain pesticides to disrupt the balance of hormones in the body. Hormones are critical in regulating various physiological processes, including cell growth and division. Pesticides can interfere with these hormonal pathways, leading to uncontrolled cell growth and, ultimately, the development of cancer. Another mechanism involves the ability of certain pesticides to damage the DNA within our cells. DNA damage can occur directly through the interaction of pesticides with the

DNA molecule or indirectly through the generation of reactive oxygen species that cause DNA damage. Once DNA is damaged, it can lead to genetic mutations that contribute to the initiation and progression of cancer. Furthermore, pesticides can impair the immune system's ability to recognize and eliminate cancer cells, which results in the tumor's ability to grow and spread. Overall, the mechanisms underlying pesticide-induced cancer are multifaceted and involve disruption of hormonal pathways, DNA damage, and impairment of the immune system. By gaining a deeper understanding of these mechanistic pathways, researchers can develop strategies to mitigate the detrimental effects of pesticides on human health.

The link between pesticides and brain tumors has also been a subject of research and discussion in recent years. Numerous studies have indicated a potential correlation between exposure to pesticides and an increased risk of developing brain tumors. One study conducted by the International Agency for Research on Cancer (IARC) found that certain pesticides, such as organophosphates and carbamates, were associated with an elevated risk of brain tumors. These chemicals are commonly used in agriculture and can contaminate soil, water, and food, putting farmworkers and consumers at risk of exposure. Additionally, research has suggested that long-term exposure to pesticides may have cumulative effects on the central nervous system, potentially leading to the development of brain tumors. One of the main mechanisms through which pesticides can lead to the development of brain tumors is by inducing DNA damage. Pesticides contain various chemical compounds that can disrupt the DNA structure, leading to mutations and other genetic alterations. This DNA damage can directly affect the genes responsible for regulating cell growth and division, which are crucial in preventing the formation of tumors. Additionally, pesticides can interfere with the repair mechanisms essential for maintaining the integrity of the DNA. This interference can result in the accumulation of DNA abnormalities, further increasing the risk of tumor formation.



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Figure 6: There is emerging evidence that exposure to pesticides may contribute to the formation of brain cancer. (This figure was generated with BioRender.com)

In examining the epidemiological evidence surrounding the link between pesticides and brain tumors, several noteworthy studies have emerged. One such study by Wigle et al. (1990) examined the relationship between pesticide exposure and brain cancer incidence among Ontario agricultural workers. The results demonstrated a significant increase in brain tumor risk among individuals who worked directly with pesticides, particularly among those working in the manufacturing and formulation sectors. These findings underscore the role of occupational exposure in the development of brain tumors and provide substantive evidence supporting the pesticide-brain tumor connection. Additionally, a population-based case-control study by Lee et

al. (2018) further supports the association between pesticide exposure and brain cancer. Their analysis found a positive correlation between residential proximity to crops treated with pesticides and increased brain tumor risk. These epidemiological studies provide crucial evidence indicating a strong correlation between pesticide exposure and the diagnosis of brain tumors

Benefits of pesticide use

Since their invention in the middle of the 20th century, pesticides have been a fundamental component of modern agriculture. Their revolutionary approach to food cultivation has resulted in higher crop yields, better food quality, and a decrease in the occurrence of diseases. In today's agriculture, pesticides are essential because they protect crops and boost food production. These chemicals are designed to control and eliminate pests such as fungi, bacteria, and insects, which would damage crops. Although pesticides may negatively affect the environment and human health, there are several benefits that should not be disregarded.

An important benefit of pesticides is that they can increase crop productivity. Pesticides prevent or lessen insect, weed, and disease damage by shielding crops from these pests. Because of this protection, plants can use their resources—such as water and nutrients—more effectively, promoting healthier and more vigorous growth. A study by Popp, Pető, and Nagy claims that crop yields have increased by 35-70% due to pesticide use worldwide. Pesticides achieve this by eliminating pests competing with crops for nutrients and water, allowing crops to grow unhindered. For instance, herbicides target weeds that compete with crops, while insecticides eliminate insects that feed on crops. This increased yield is crucial in feeding the growing global population, which is projected to reach 9.7 billion by 2050 (United Nations, 2019).

Pesticides aid in maintaining the nutritional value of crops. Pests can cause significant damage to plants, resulting in reduced nutritional content and compromised quality. By preventing or controlling pest infestations, pesticides help preserve the integrity of crops, ensuring that they retain their essential nutrients and vitamins. This is especially crucial for fruits and vegetables, which are essential parts of a well-balanced diet. Pesticides contribute to the availability of wholesome, high-quality food by shielding crops from pests. According to a 2015 European Crop Protection Association study, crops' vitamin content could drop by as much as 30% in the absence of pesticides. This is so because diseases and pests can harm crops, lowering the amount of nutrients they contain. Furthermore, pesticides can extend the shelf life of food, ensuring that it retains its nutritional value for longer.

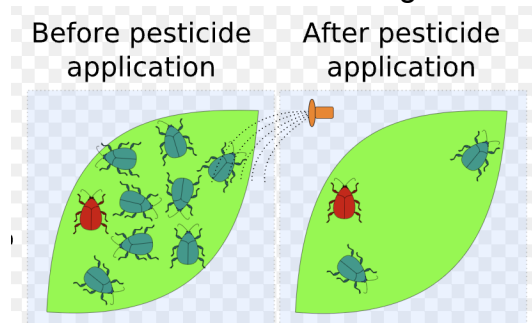


Figure 6: Pesticides can successfully reduce the burden of threat to crops. In this case insecticides can reduce the threat of insects to crop survival by killing the insects. (This figure was generated with BioRender.com)

In agricultural systems, pesticides are essential for reducing the incidence and spread of fungi and diseases. Plant diseases that can destroy entire crops, including rots, molds, and blights, can cause farmers significant financial losses. Pesticides aid in their management through the elimination or suppression of the pathogens that cause these diseases. Pesticides prevent post-harvest spoilage of crops by limiting the growth of fungi, which increases crop shelf life and decreases food waste. In the end, this leads to higher food production and distribution efficiency. Using pesticides helps prevent fungal and disease outbreaks that can destroy crops. The Food and Agriculture Organization (FAO) estimates that illnesses and pests result in a yearly loss of 20–40% crop productivity worldwide. Pesticides, such as fungicides and bactericides, can effectively control these threats, thereby reducing crop losses. For instance, fungicides have been crucial in controlling the spread of Fusarium Wilt, a devastating fungal disease that affects bananas, one of the world's most important staple foods.

The use of pesticides can have positive economic impacts on farmers, particularly in regions where pest pressures are high. By reducing crop losses and increasing yields, pesticides contribute to higher profits for farmers. Protecting crops from pests and diseases helps maintain the stability and sustainability of agricultural operations. With improved economic returns, farmers can invest in better farming practices, technology, and infrastructure, ultimately enhancing the overall efficiency and competitiveness of the agricultural sector. Farmers and growers have altered their agricultural practices over the past 60 years to meet the demands of food processors, retailers, governments, and, more recently, consumers. They have altered their farming practices significantly, using a lot more pesticides. Their main goal in doing this has been to stop or lessen agricultural losses due to pests, which has increased yield and made food more readily available year-round at a fair price. Evidence shows a four-fold return on investments in pest control and an estimated economic return of around \$16 billion from pesticide use in the USA. India, a former country of famine, has quadrupled grain production since 1951 and now feeds itself and exports produce. The use of pesticides can have positive economic impacts on farmers, particularly in regions where pest pressures are high. By reducing crop losses and increasing yields, pesticides contribute to higher profits for farmers. Protecting crops from pests and diseases helps maintain the stability and sustainability of agricultural operations. With improved economic returns, farmers can invest in better farming practices, technology, and infrastructure, ultimately enhancing the overall efficiency and competitiveness of the agricultural sector.

Conclusion

Pesticides, an omnipresent component of modern agriculture, have been instrumental in controlling pests and diseases and thus increasing crop yield and ensuring food security. However, the potential health risks associated with pesticide exposure, including cancers, brain tumors, and other health issues, have raised significant concerns. Pesticides are composed of various chemicals, many of which are carcinogenic. Long-term exposure to these chemicals can lead to the development of different types of cancers. For instance, organophosphates and carbamates, two common types of pesticides, have been linked to leukemia and non-Hodgkin lymphoma. Similarly, exposure to organochlorines, another group of pesticides, has been associated with breast, prostate, and other cancers. The International Agency for Research on Cancer (IARC) has classified several pesticides as "probably carcinogenic to humans," underscoring the potential cancer risk associated with pesticide exposure.

The link between pesticide exposure and brain tumors is also a significant area of concern. Studies have shown that pesticides can cross the blood-brain barrier, leading to neurotoxic effects. Some pesticides, such as organochlorines and organophosphates, have been associated with an increased risk of brain tumors. For instance, a study published in the *International Journal of Cancer* found a positive association between exposure to certain pesticides and the risk of glioma, a common type of brain tumor. Beyond cancers and brain tumors, pesticides can also lead to a host of other health complications. Pesticides can disrupt the endocrine system, leading to hormonal imbalances and reproductive health issues. They can also affect the nervous system, causing neurodegenerative diseases like Parkinson's and Alzheimer's.

While pesticides play a crucial role in modern agriculture, their potential health risks cannot be overlooked. Further research is also needed to understand the mechanisms through which pesticides affect human health fully and to develop effective strategies for mitigating these risks. Currently, we do not have enough evidence and information on specifics on the molecular level on how and why these pesticides are causing deleterious effects on us humans. More research should be conducted for us to understand why pesticides cause these harmful effects. Through more research, we will also be able to understand this field of study fully, improving the safety of pesticides and making the field of pesticides better for human use.

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