Chapter 1

Pesticides, Environmental Pollution, and Health

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Additional information is available at the end of the chapter

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Abstract

In recent years, people have been exposed to several types of substances with broad spectrum due to the rapidly evolving technology. One of these chemical substance groups are pesticides. Pesticides have been an essential part of agriculture to protect crops and livestock from pest infestations and yield reduction for many decades. Despite their usefulness, pesticides could pose potential risks to food safety, the environment, and all living things. Concern about the environmental impact of repeated pesticide use has prompted research into the environmental fate of these agents, which can emigrate from treated fields to air, other land, and water bodies. The importance of agricultural pesticides for developing countries is undeniable. However, the issue of human health and environmental risks has emerged as a key problem for these countries in accordance to a number of studies. In the last five decades, pesticide usages increased the quantity and improved the quality of food. However, with the increasing amounts of their usage, concern about their adverse effects on nontarget organisms, including human beings, has also grown. The purpose of this publication is to explain the nature of pesticides and their history, classification, risks, and effects on health and the environment.

Keywords: organic pollution, health concern, environment, pesticides, environmental pollutant

1. Introduction

In the last three decades, there has been an increasing global worry over the public health impacts attributed to environmental pollution. It was the industrial revolution that gave birth to environmental pollution as we realize it today. Populations of developing countries are particularly vulnerable to toxic pollution resulting from industrial processes.

Pollution is the introduction of contaminants into the environments that cause harm or discomfort to other living organisms or damage the environment, which can come in the form of chemical substances or energy, such as heat, light, or noise. Pollutants can be naturally occurring energies or substances but are considered contaminants when in excess of the natural levels. Santos divided environmental pollutants into biodegradable and nonbiodegradable ones. Biodegradable pollutants can be broken down and processed by living organisms, including organic waste products, phosphates, and inorganic salts. Nonbiodegradable pollutants cannot be decomposed by living organisms and therefore persist in the ecosphere for extremely long periods of time. They contain metals, plastics, glass, pesticides, and radioactive isotopes [1].

In recent years, people have been exposed to several types of substances with broad spectrum due to the rapidly evolving technology. Technology has brought us clear conveniences, and thousands of chemicals produced in different areas are up on the market every year. One of these chemical substance groups are pesticides [2,3].

1.1. Pesticides

Through the ages, it seems increasingly that people find a need to minimize the damage of pests with the use of pesticide chemicals and by other means [4]. Of the many examples of how pests have impacted human society, one of the most infamous is the Black Plague in Europe in the 14th century, when millions of people died from mysterious diseases. At that time, the diseases were believed to be because of God's punishment. A number of reports in the literature, art, and public statues certify the fear and destruction of those epidemics. Many years later, scientific data proved that a bacterial disease spread by rat fleas was the cause of the plague, which ruined almost the whole of Europe. Today, this disease, known as bubonic plagues, can be easily treated if it is properly diagnosed. Hence, controlling rodents including rats as well as fleas can reduce the relative frequency of the occurrence of diseases [5].

Ireland's potato crop destruction by a pest in the 19th century is another story. At that time, late blight, a plant disease, wasted potatoes in Ireland. Up to 1 million Europeans starved to death during the Great Irish Famine of 1845 to 1847. Late blight is still one of the major potato pathogens that chemists aim to synthesize new pesticides against [5].

Pesticides are chemical substances used on agricultural land but also in private gardens, along railways, and in other public areas [6]. The use of pesticides for crop protection is expected to increase based on a growing world population and the need for more food supplies. While pesticides increase agricultural production, bioaccumulation through the food chain can eventually become a risk to mammals because pesticides induce certain negative effects [7–10]. Some parts of pesticides sprayed on crops will remain in farmland, but some of them will enter the surrounding soil, water, and air [11,12]. As artificial organic compounds, pesticides can remain in the environment for many years and may be transported over a long distance [13]. Pesticide residues in soil and water are significant environment threats and have been classified as carcinogen pollutants in many countries [14,15]. Hence, the excessive application of these compounds over the past half-century has posed serious risks to human health [16,17].

There have been numerous reports regarding pesticide residues detected in grains [8], milk [18], vegetables [19], and fish [20].

Although the benefits of pesticides have been immense, humans and other living organisms are often exposed to them in the environment [21]. Several epidemiological studies reported in the last two decades suggest harmful effects of pesticides on human health, including a possible relationship between pesticide use and cancers, such as non-Hodgkin's lymphoma, leukemia, and various types of solid tumor [22–24]. Public health concerns regarding the improper use of pesticides and poison have increased in recent years. To date, certain countries, regions, and international organizations have established maximum residue limits (MRLs) for foodstuffs. Additionally, national food monitoring programs for pesticides have been enacted worldwide [7–9] to ensure consumer health, improve the management of agricultural resources, and prevent economic losses [10].

Despite the adoption of the International Code of Conduct on the Distribution and Use of Pesticides (Code of Conduct) [25], the strict control of banned/legacy pesticides has been proven difficult in many developing countries. This could be attributed to weak regulations on importation and use of dangerous substances and the activity or absence of control agencies at international borders [26]. This scenario has led to the proliferation of banned chemicals in local markets located in agricultural areas, making large quantities of pesticides available to rural farmers, which eventually could pose potential threats to the environment and the health of the people [27–29].

The existence of persistent chemical substances in the environment and their effects on the wildlife and mankind has raised a serious global concern. In this case, we need to mention the risks of pesticides.

Pesticides are poisons and can be hazardous. Fortunately, people are becoming more aware of their danger, and even producers are trying to produce safer chemicals and better application methods. Even the awareness is improving for risk-benefit ratio side; the job has not been completed yet. Misuses of pesticides still occur. On the contrary, even if they are used correctly, some pesticides can harm nontargeted living organisms and the environment. Just as the benefits of pesticides are real, so are the risks. The purpose of this publication is to explain the nature of pesticides and their history, classification, risks, and effect on health and the environment [4].

2. Historical perspective

Pesticides are used for a number of decades. People have been fighting with pests for centuries [5]. Chemical experiments during the late 19th and early 20th centuries allowed human beings to develop modern pesticides. Producing new mixtures with a right proportion made it possible to control unwanted organisms. Paris green was one of the first chemical pesticides produced, marking the beginning of chemical insecticide use in the United States in 1867 [30]. By the late 19th century, U.S. farmers were using calcium arsenate, nicotine sulfate, and sulfur to control insect pests in field crops, except Paris green [4]. Since the middle of the 20th century, these chemicals have been widely used to control pests [31,32]. Ancient Romans controlled weeds with salt and killed insect pests by burning sulfur [4]. Sulfur, also known as brimstone, was used by pagan priests 2000 years before the birth of Christ. Additionally, sulfur was used to purify a sick room and cleanse its air of what was believed to be evil. In the 1600s, ants were controlled with mixtures of honey and arsenic. Early plant-derived insecticides included nicotine to control aphids, hellebore to control body lice, and pyrethrins to control a wide variety of insects [5].

The availability of dichlorodiphenyltrichloroethane (DDT), starting in 1945 for civilian/ agricultural usage, opened a new era of pest control, leading to not only its extensive usage but also the development of numerous other synthetic organic insecticides. DDT was especially favored for its broad-spectrum activity against insect pests of agriculture [4]. Unfortunately, its properties of persistence, along with its broad-spectrum biological activity against pests and beneficial insects alike, made it a poor choice for use in agriculture after World War II [33]. Except DDT, aldrin, BHC, endrin, dieldrin, and 2,4-D began to be used after World War II. These new chemicals were effective, inexpensive, and enormously popular [34]. However, with continuous usage of pesticides, some pests developed resistance to them. As a result, nontarget plants and animals were damaged; surprisingly, pesticide residues were observed to be present in unexpected places. Rachel Carson's book, *Silent Spring* in 1962, shook public confidence in pesticide usage. Carson presented a harsh picture of environmental consequences of careless pesticide employment. Although her report has been strictly criticized, Carson pointed out the risks of pesticides more than anyone [4].

As chemical controls became more and more common in agricultural, public health, and nuisance applications throughout the first half of the 20th century, a myriad of problems were being discovered. Chemically reliant methods had quickly resulted in pesticide resistance within the target species, harm to nontarget species, food contamination, water contamination, overall ecological degradation, and public health problems [30].

3. Classification of pesticides

The word "pesticide" is an umbrella term for all insecticides, fungicides, herbicides, rodenticides, garden chemicals, wood preservatives, and household disinfectants that may be used to kill some pests. Pesticides have different identities and physical and chemical properties. Synthetic pesticides are classified based on various ways. In general, there are three main ways to classify them: classification based on the (i) mode of action, (ii) targeted pest species, and (iii) chemical composition of pesticides [35].

3.1. Classification based on the mode of action

Pesticides are classified based on the way they act to bring about the desired effect in this classification. Under this type of classification, pesticides are classified as nonsystemic and systemic pesticides. Nonsystemic pesticides are those that do not appreciably penetrate plant tissues and consequently not transported within the plant vascular system. On the contrary, systemic pesticides are those that effectively penetrate plant tissues and transported within the plant vascular system to bring about the desired effect [36].

3.2. Classification based on the targeted pest species

Classification by target pest is perhaps the most familiar. For example, insecticides are pesticides that target insects, and herbicides target plants. The others are rodenticides, fungicides, acaricides and miticides, molluscicides, bactericides, avicides, and virucides.

3.3. Classification based on the chemical composition

In this type of classification, pesticides are characterized regarding their chemical nature and active ingredients. This is the most useful one for researchers studying the field of pesticides and the environment, because it is this kind of classification that gives the clue of the efficacy and physical and chemical properties of the respective pesticides and precautions that need to be taken during application and the application rates, the knowledge of which is important in the mode of application [37].

According to chemical properties, pesticides can be generally divided into about seven types, including organochlorines, organophosphorus, carbamates, pyrethroids, amides, anilins, and azotic heterocyclic compounds. Organochlorine chemicals are organic compounds with five or more chlorine atoms. Organochlorines were the first synthetic organic pesticides to be used in public health and in agriculture. These pesticides generally have a steady chemical structure and often accumulate and persist in the environment. Most of them are widely used as insecticides for the control of a wide range of insects. Organochlorine insecticides act as nervous system disruptors leading to convulsions and paralysis of the insect and its eventual death. They can cause serious endocrine disorders in mammals, fish, and birds, so most of them have been banned in agriculture worldwide [36,38]. Organophosphates are another type of highly toxic pesticides that contain a phosphate group and occupied up to 48.6% of all pesticides in 1997 [39]. The importance of synthetic organophosphates increased considerably during World War II with their use as warfare materials. Since then, these pesticides have been used in agriculture, industry, cosmetics, medicine, and many other areas [40,41]. These chemical compounds inhibit the acetylcholinesterase enzyme, which hydrolyses acetylcholine in the nervous system of a number of species, including humans [42]. Although they are easier to be degraded than organochlorines, organophosphate pesticide residues is one of the biggest threats to the ecosystem and food industry because their acute toxicities are irreversible [43].

Many people are exposed to pesticides occupationally, and pesticide self-poisoning is a major public health problem [44]. Annually, 3 million cases of acute poisoning have been reported from pesticide exposure, resulting in the deaths of 250 to 370,000 people every year [45,46]. Therefore, the usage of organophosphates has been restricted or banned all over the world [43].

Carbamates are organic pesticides, reversibly inactivating the enzyme acetylcholinesterase; these pesticides are derived from carbamic acid. The cholinesterase inhibition of carbamates differs from that of organophosphates in that it is species specific and is reversible [35,47]. Organochlorines, organophosphates, and carbamates are three generations of traditional highly toxic pesticides, and the later developed pyrethroids, anilines, amides, and azotic heterocyclic compounds are generally less toxic [48].

Pyrethroids are synthetic analogues of the naturally occurring pyrethrins, a product of flowers from pyrethrum plant (*Chrysanthemum cinerariaefolium*), and were detected in the 1980s to mimic the insecticidal activity of the natural pyrethrum. Pyrethroids are acknowledged for their fast knocking down effect against insect pests, facile biodegradation, and low mammalian toxicity [37]. These pesticides are nonpersistent sodium channel modulators and are much less toxic than carbamates and organophosphates to mammals. Therefore, the usage of pyrethroids has been increased greatly in the last 30 years. Unfortunately, pyrethroids are highly toxic to aquatic organisms such as mollusks, fish, and arthropods [49,50].

Amide herbicides, such as acetochlor, butachlor, and metolachlor, are widely used in recent years. However, butachlor can persist in the environment for up to 10 weeks, and what's even worse is that butachlor and metolachlor have been identified as mutagens. Another type of pesticides is aniline and dinitroaniline. Trifluralin and pendimethalin are widely used in this group of pesticides. These pesticides show high toxicity to aquatic organisms and they can impair the thyroid gland and liver. Hence, these two aniline herbicides have been banned in many European countries. Nitrogen-containing heterocyclic compounds, especially for imidazole and triazole heterocyclic chemicals, have become the hotspot for new pesticide development. In the last 10 years, they occupied no less than 70% of all the newly developed chemical pesticides [48].

Except for these classifications, pesticides are classified according to the mode of formulation, activity spectrum, and toxicity level. According to the mode of formulation, pesticides are classified into six groups as wettable powders, emulsifiable concentrates, baits, granules, dusts, and fumigants. In active spectrum, pesticides are classified into two groups as broad-spectrum pesticides and selective pesticides. Broad-spectrum pesticides are designed to kill a wide range of pests and other nontarget organisms. On the contrary, selective pesticides are designed to kill only specific pests. In toxicity level, the World Health Organization (WHO) has developed a classification system that group pesticides according to the potential risks to human health and they are grouped into the following classes: class Ia=extremely hazardous, class Ib=highly hazardous, class II=moderately hazardous, class III=slightly hazardous, and class IV=products unlikely to present acute hazards in normal use [37].

4. Pesticide pollution

Since the middle of the 19th century, pesticides have been commonly used to control pests [31,32] causing a widespread release of these xenobiotics into the environment [51]. The intensive use of pesticide leads to an increased risk of contamination of the environment and harmful effects on biodiversity, food security, and water resources [52,53].

Pests, such as insects, weeds, and plant diseases, are an ongoing challenge to agricultural producers. Oerke [54] reported that, globally, an average of 35% of potential crop yield is lost to preharvest pests. With the expected 30% increase of world population to 9.2 billion by 2050, there is a projected demand to increase food production by 70% according to Popp et al. [55]. Although nonpesticidal tools have a vital role, there will be a continuing need for pesticide-based solutions to pest control and food security in the future [55,56]. **Figure 1** shows the average pesticide use intensity (kg ha^{-1} yr^{-1}) on the cultivable and permanent cropland worldwide. High use intensity countries above 10 kg ha^{-1} yr^{-1} include Surinam, Malta, Columbia, Palestinian, Japan, Korea, Chile, and China [57]. **Figure 2** presents that pesticide sales are increasing in Europe, Asia, and Latin America [58,59].

Figure 1. Average annual pesticide use intensity (kg ha^{-1} yr^{-1}) on arable and permanent cropland from 2005 to 2009. Data are from FAO [57].

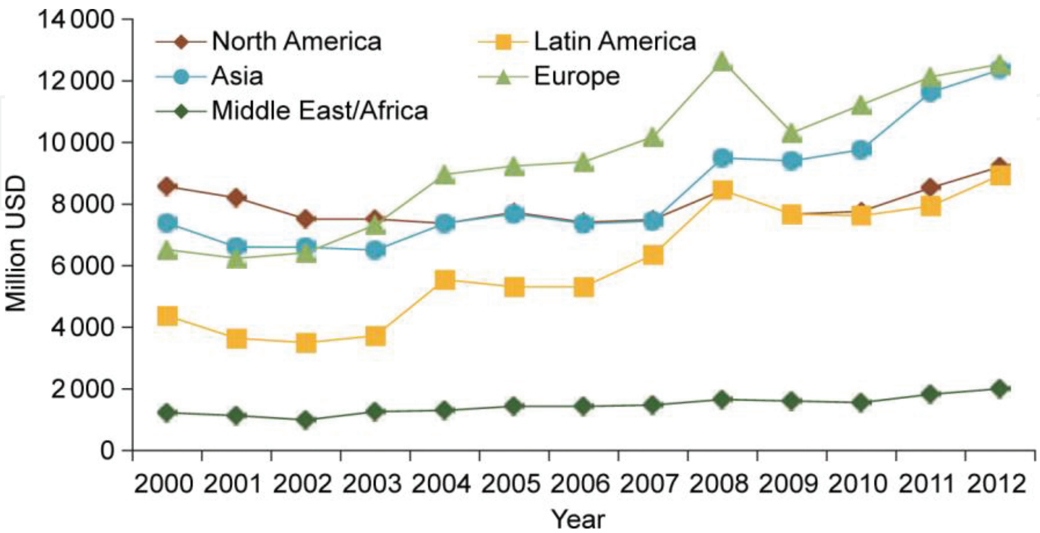

Figure 2. Annual pesticide sales by geographic regions. Data are from FAO [58].

More than 500 different pesticide formulations are being used in our environment, mostly in agriculture [60]. In the past five decades, pesticide usages increased the quantity and improved the quality of food. However, due to their usage with increasing amounts, the concern about their harmful effects on nontarget organisms, including human beings, has also been growing. Nontarget pesticide poisoning has been reported from fish, birds, and humans [61]. Although it is estimated that less than 0.1% of pesticide applied to crops actually reaches the target, the rest of it enters the environment [62]. Additionally, many pesticides can persist for long periods in an ecosystem; organochlorine insecticides, for instance, are still detectable in surface waters 30 years after their use and had been banned [63]. In the food chain, they meet with nontarget organisms, including mankind. They accumulate in the body tissues of organisms and cause a number of health problems [64,65].

Pesticides and herbicides are heterogeneous chemicals used widely in agriculture. Their design as bioactive molecules to exterminate different animal, vegetal, or fungal species implies that they are toxic by definition. Due to this toxicity, their use is regulated in the European Union. Depending on the water solubility and polarity of each specific pesticide, they can follow different pathways to reach water bodies once applied in the crop fields. In the case of surface waters, the most common entry pathway for these pollutants is runoff from agriculture lands after precipitation or irrigation [66]. Pesticides could influence biological communities in lakes, forcing changes from a clear-water, macrophyte-dominated state to a turbid state due to their effect on zooplankton or macrophytes [67,68].

As explained above, both point and diffuse pollution sources of pesticides, herbicides, and polycyclic aromatic hydrocarbons (PAHs) are usually anthropogenic. Therefore, it is expected that the concentration of some of these compounds in surface water is related to human activities that take place in the surroundings. The proportion of cultivated lands around the lake and the agricultural pressure and intensity are especially relevant, as certain substances such as herbicides and pesticides have a close relationship with agriculture. In fact, it has been observed that land uses are strongly related to nutrient concentrations in surface waters [69] and PAH concentrations in wetland sediments [70]. On the contrary, the distance between lakes and point or diffuse pollution sources such as urban areas, thermal power plants, industries and roads could also be related to the amount of these chemical compounds detected in aquatic ecosystems [68].

Pesticide fate in the environment is characterized by a number of complex processes occurring in different environmental compartments, such as air [71], soil [72], plant [73], and surface and groundwater [53,74].

Pollution due to the uncontrolled use of pesticides has become one of the most alarming challenges when pursuing sustainable development. Although pesticides are directly applied in soils and plants, only 1% of pesticide sprayed is delivered to the intended target. An accidental release of pesticides due to leaking pipes, spills, waste dumps, underground storage tanks, and groundwater may lead to their persistence in the environment for a long time (due to long half-lives). For proper management of pesticides, one needs to accurately assess the status of their contamination in soil, water, and air [75,76].

Soil is a major reservoir for a variety of pollutants [77] and is a secondary emission source of contaminants to surface water, groundwater, and air [78]. Multiclass environmental endocrine disruptor compounds (EDCs), such as organochlorine pesticides (OCPs) phthalate esters (PAEs), and polybrominated diphenyl ethers (PBDEs) may coexist in soils and accumulate in crops and human bodies through food chains, posing risks to human health and the ecosystem [79]. In addition, soil plays an important role in pesticide residue in plants. There are two pathways for pesticide transfer between the plants and their planted soils. First, most of pesticides could shift or fall onto the soil when pesticide is applied onto plants. Next, most of the deposited pesticides on the plant could be washed off by rainfall to the soil. Second, the residues of adsorbed pesticides in soil, especially for organochlorine pollutants, remain as contaminants in the environment because of their long-term persistence and mobility, and they could enter into food again via the plant uptake effect [10,80,81].

Persistent organic pollutants (POPs), such as OCPs, are ubiquitous contaminants in different compartments of the environment [82,83]. Although a number of countries have been removed from the circulation of the usage of POPs for nearly 30 years, these synthetic chemicals are found in nature at considerable levels worldwide due to their persistence. These substances are mainly generated by anthropogenic processes and can be introduced into the environment through various routes. These pesticides are toxic, carcinogenic, and mutagenic features. They are extremely hazardous for the both biota and environment [84]. Hence, the investigation of POPs in aquatic environments is needed to provide relevant information on the anthropogenic impact on the environment, and concentrations serve as an indicator of contaminant load [85, 86].

Pesticides are major components of the modern agricultural production because of their reliability and high capability for crop protection against pests [87]. Approximately 5 billion kilograms of pesticides are applied worldwide per year, which can have serious effects on biodiversity, nontarget organisms, and the food chain, posing high risks to the environment and human health [88]. In rural areas of developing countries, 3 million farmers suffer annually from serious pesticide poisoning and 25 million farmers suffer from mild poisoning, resulting in approximately 180,000 fatalities among agricultural workers annually [89] because of incorrect perceptions, lack of knowledge, regulation, and education among farmers [90,91].

Unsafe pesticide use or misuse in developing countries includes the use of pesticides banned by the local government [92], lack of self-protection [93], incorrect pesticide storage [94], overspraying [95], improper handling of pesticide containers [96], and, in extreme cases, reuse of washed pesticide containers as containers for food and drinking water (as reported by 35.4% and 77.2% of farmers in Nigeria and Ethiopia, respectively) [97]. The local authorities, the WHO, the Food and Agriculture Organization (FAO), and various nongovernment organizations that focus on low- and middle-income countries (e.g. China, India, Vietnam, and African countries) have taken initiatives to improve the protective behaviors of farmers in pesticide use, including personal and environmental protection through education [98] and legislation and community intervention [99], although the results were often unsatisfactory [100]. The factors that affect farmers' behavior in pesticide use are far more complex than expected.

Pesticide use can be influenced by age [101], gender [102], perceptions [90,91], level of knowledge, pesticide retailers [103], and even cultural or planting differences [92].

The chemical pesticide provides a necessary guarantee for the output increase, but pesticide abuse has led to daily worsening of the ecosystem of agricultural lands [104,105]. The use of large amount of pesticide is the main reason for agricultural pollution [106].

5. Effect of pesticides on health and the environment

The importance of agricultural pesticides for developing countries is undeniable. However, the issue of human health and environmental risks has emerged as a key problem for these countries in a number of studies [107–112]. Attention to the impacts of pesticide use on the environment and ecosystems has grown since the book *Silent Spring* was published in 1962. Extensive published literature has well documented the impacts of pesticide use to the ecosystem and human health [55]. Pesticides can move off-site to contaminate surface water and leach to groundwater. Damage to nontarget organisms and pollution to the soil and air are well documented [59].

The released pesticides into the environment and their impacts on many species have been known for a long time. The senseless and widespread use of OCPs between the 1960s and the 1970s caused a striking decrease in wildlife populations nearly all over the world [113]. DDT, dieldrin, and other toxic OCPs affected birds and other wild species during that time and have been finally banned from agricultural use. Since then, however, decline in birds, wild bees, and aquatic organism populations have been continuing [114]. This could be linked to usages of newly synthesized pesticides that are present in every kind of habitat on the world. Pesticides are still being discovered in marine, freshwater, and terrestrial communities [115].

Insecticides may kill not only the target species but also other invertebrates on which birds rely on for their food. In addition, herbicides are designed to control weed species and they can also kill many other plant species in fields, including the essentially beneficial species, which give both shelter and food for the members of wildlife. Amphibians are now considered the most threatened and rapidly decreasing species on Earth. Brühl et al. [116] suggested that frogs are sensitive to the toxicity of pesticides that are currently used in agriculture.

In addition, pesticide factory workers and agricultural farm workers have high risk to pesticide direct exposures [88]. In recent years, pesticide residues in food have become a focus for food safety and trade. Quarantine regulations sometimes require pesticide treatment of food shipments to prevent the establishment of exotic pests. Nonetheless, local consumers and international trading partners increasingly demand food that is free from unsafe pesticide residues. Therefore, many countries have initiated programs to monitor pesticide residues in food. In addition, many countries are implementing programs to reduce the use of pesticides and thereby minimize pesticide impacts [59].

Intensively used pesticides, despite their ability to protect crops, threaten the environment and human health [88,117]. Besides, the use of pesticides also results in residue problems. Pesticide residue is defined by the WHO as any substance or mixture of substances in the food of either humans or animals that is caused by the use of pesticides and any specified derivatives, such as degradation and conversion products, reaction products, metabolites, and impurities that are considered toxic [118].

5.1. How are we exposed to pesticides?

People who live in agricultural areas have a high disclosure to pesticides by inhalation of pesticide spray blow in urban areas and parks or in the houses after breathing contaminated air. Farmers and their families can have a higher exposure to pesticides than the general population. Besides, when nursing mothers and pregnant women are exposed to pesticides, their children may also be exposed. Some pesticides can pass through the placenta to the developing fetus in the womb and through breast milk to the nursing infant [119].

These "poisons by design" are prevalent and serious occupational hazards faced by farmers and agricultural workers [117]. The high levels of occupational exposure to pesticides are correlated with low educational levels, which would preclude the ability of farmers to follow the hazard warnings developed by the chemical industries and agencies [120]. Tragedies, such as acute and chronic intoxication and, in some extreme cases, suicide, have frequently been reported, especially in rural regions [117,121]. The lack of a legislative framework regulating the use of pesticides also contributes to the high incidence of poisoning in developing countries [117].

The present data seem to be too limited to analyze the full health effects of pesticide referable chronic exposures. On the contrary, suicide commitments in 2002 using pesticides resulted in 258,000 deaths [122]. In 2002, intentional poisoning from pesticides accounted for approximately one third of the world's suicides, and in 2004, 71% of the unintentional poisonings were considered preventable by improving chemical safety methods [45]. The groups most at risk from unintentional pesticide poisoning are children, especially those between ages 0 and 4 years [123]. Human deaths induced by insecticides were mainly because of ingestion of OPPs. OPP poisoning is evident for "cholinergic syndrome". The symptoms in this syndrome are headache, slurred speech, coma, blurred vision, convulsions, blockage of the respiratory center, and delayed neuropathy [124]. In this sense, survivors of acute OPP poisoning may suffer long-term adverse effects to the nervous system [119].

Data show that there is a positive relationship between high pesticide exposures and occurrence of several types of cancer (e.g. prostate and lung) as well as the increase of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. There are also evidences that pesticides may impair endocrine function and the immune system. Although the mechanisms of such failures are not completely comprehended, there are some clear evidences showing the disruptions in enzymatic function and signaling mechanisms at cellular levels. DNA-based toxicity studies also indicate that pesticides affect gene expression and this may transferred to generations through epigenetic inheritance [119].

Organophosphate compounds (OCs) and OCPs have been widely used as pesticides in agricultural productivity. However, they have been proven to be extremely hazardous for human health. OCs and other pesticides may persist on Earth for a long time, adverse to the ecology. Therefore, pesticide residues in vegetables, fruits, water, and on Earth are drawing more and more attention [125–128]. Applied pesticide residues may persist within the tissues or on the surface of the crops when we buy from market. Scientists have developed a variety of techniques to both determine and quantify the pesticide levels in food. Data obtained from these studies suggested that nonstop monitoring is needed to ensure that pesticide residues do not exceed their acceptable values [99]. Most countries, on either a regional or a national basis, maintain a threshold maximum residue level (MRL) for each substance, above which the foodstuff is thought unacceptable for human consumption [119].

OCPs are among the substances restricted or banned globally under the Stockholm Convention on Persistent Organic Pollutants [129]. These compounds are environmentally persistent [130], toxic, and apt to bioaccumulation [131] and have adverse effects on animals and humans [132]. Some developing countries are still using these compounds because of their low cost and versatility in industry, agriculture, and public health [133]. Consequently, environmental problems associated with toxic contamination in these countries are of great concern [134]. As a result, organochlorines in various environmental media have received much attention [133]. They are well-known anthropogenic and lipophilic pollutants due to their high bioaccumulation potential in fatty tissues of living organisms [135]. Although these substances are generally stored in the fat and muscles of the animals, some can also be found in the brain, lungs, liver, and other offal. Additionally, because milk and other dairy products contain a range of fat, these foods may also contain a number of pesticides. This is important because cow's milk is one of the indispensable components of human diet [119,136,137]. OCPs can enter animal tissues through different pathways of ingestion, dermal contact of dust, and inhalation [138].

In the past decades, attention was focused on the determination and pollution levels of OCPs in human blood serum, maternal and cord serum, adipose tissue, human milk, and hair and other available tissues to study human exposure and assess health risk [139]. Human exposure to OCPs is through many routes: breathing OCP-contaminated air, working in or living beside OCP factories, drinking and taking a bath with OCP-polluted source water, eating vegetables and grains containing OCP residues, and eating especially fish and animal meats [140]. OCPs accumulated in the human body could cause various negative effects such as immunological function damage, endocrine disruption, female spontaneous abortions and preterm, and children neurodevelopmental delays [141].

Several studies showed that cancer risks could be induced by OCP exposures [142]. At the same time, OCPs could be transferred from maternal to fetal tissues through placenta and from mother to infant through breast milk. Exposure to OCPs could also lead to some adverse effects on human productivity, including spontaneous abortions and preterm [143], delayed neurodevelopment during childhood [144], and reproductive disorders of man [145] and other negative effects. In the fetus, as the rapid growth and development occur during early development, the organs of the baby can be sensitive to the toxic substances; especially, the brain is more susceptible to neurotoxicants [146]. Increasing evidence suggests that prenatal pesticide exposure may have a permanent effect on children's behavior and intelligence. Besides, organophosphates are also hazardous compounds in the environment and public health. When children are exposed to pesticides in various ways at a young age, there is an observed negative effect on the development of the central nervous system [147]. Developmental impacts were mainly described as behavioral or cognitive, particularly those related to attention-deficit disorders and motor skills [119].

Experimental research has shown that many pesticides are endocrine disruptors that can disturb the functioning of various hormones throughout the body [148]. The production of thyroid hormone is thought to be inhibited by substances such as cyhalothrin, amitrole, pyrimethanil, and fipronil. Other pesticides may also alter thyroid hormone levels and potentially cause thyroid disease. Experimental studies *in vitro* support observations that the balance of sex hormones can be disrupted by exposure to certain pesticides. There is also evidence that fertility of both women and men may be decreased with increased pesticide exposure [119].

Studies showed that there are evidences of pesticide exposure and disorders in both hormonal regulation imbalance and immune system activities. The statistical results are associated with pesticide exposure and occurrence of some diseases. This finding cannot be ignored. The mechanisms of pesticide-induced diseases are not yet fully understood, but we now know that some key enzymatic activities in main metabolic pathways and/or the permeability of the ion channels are affected by them [149].

Moreover, some people carry susceptibility genes to the health effects of pesticides, and for that reason, they are likely to be more at risk than others. The questions on these epigenetical differences and developing policy approaches to ensure a high level of protection for mankind may remain insurmountable for a long time. In the meantime, people will continue with the routine application of pesticides to get more crops. On the contrary, the next generations, even they if are not exposed to pesticides, may also be at risk to these diseases due to epigenetical inheritance [119].

As mentioned by Allsop et al., many synthetic pesticides used in agriculture are persistent and pervasive in the environment. As a result, mankind is exposed to the mixture of pesticides via the food consumed and the environment around. Evidences suggest that more exposure means more toxic effect we will face. Although assays have been made to describe the toxicity of these kinds of interactions, there are no validated international guidelines in assessing these risks. In this case, we need to essentially rethink and change our systems to get rid of the exposure of pesticides. We must protect the health of vulnerable groups as well as the general population and whole ecosystems [119].

Reducing the use of pesticide strategies will not help us protect human health, because there are enormous kinds of pesticides in the market to be sold. In this case, people need to go towards ecological farming. This is a critical act in avoiding all risks. Protecting crops via a multilevel approach will help us increase the heterogeneity of the agricultural areas and this will provide a natural habitat for pollinators and natural pest control species. Thus, a functional biodiversity can be created if we can achieve an active vegetation management. A variety of crop types and cultivars increase both the fertility of soils and resistance to pests. Natural control agents, such as beneficial bacteria, viruses, insects, and nematodes, can be used in improving crop protection successfully [150].

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