

**A Small Dose of Pesticide
Or
An Introduction to the Health Effects of Pesticides**

Dossier

Insecticides

Name: Insecticides
Use: kill insects
Source: synthetic chemistry, plants
Recommended daily intake: none (not essential)
Absorption: intestine, respiratory system (lungs), skin
Sensitive individuals: fetus, children, and elderly
Toxicity/symptoms: nervous system, range of problems depending on chemical
Regulatory facts: RfDs exist for many insecticides. Regulated by EPA.
General facts: billions of pounds used every year in agriculture, golf courses, around the home, and by commercial real estate
Environmental: pesticides are used globally; some are very persistent in the environment
Recommendations: minimize use, avoid exposure to children, and consider alternatives including Integrated Pest Management practices

Herbicides

Name: Herbicides
Use: kill or damage plants
Source: synthetic chemistry, manufactured by industry
Recommended daily intake: none (not essential)
Absorption: intestine, respiratory system (lungs), skin
Sensitive individuals: fetus, children, and elderly
Toxicity/symptoms: varies
Regulatory facts: Reference Doses (RfDs) exist for some herbicides. Regulated by the EPA.
General facts: long history of use; often used in combination with genetically modified plants
Environmental: widespread global use and contamination
Recommendations: minimize use, avoid exposure to children, and consider alternatives including Integrated Pest Management practices

Case Studies

Cats, dogs and fleas

Fleas are very small and annoying blood-sucking pests, capable of spreading serious human diseases. We come in contact with fleas, primarily through our cat and dog pets. Fleas have a complex life cycle and reproduce rapidly, so flea control is a challenging issue in any household with pets, particularly if pets spend any time outside. A common insecticide used to kill fleas on cats is *imidacloprid*. This insecticide is also used to control sucking insects such as aphids, whiteflies, termites and a range of other soil insects and some beetles. It is also very toxic to honey bees. *Imidacloprid* is toxic to the nervous system, causing an over stimulation of acetylcholine nicotinic nerves, resulting in the insect's paralysis and death. When used to control fleas, it is typically applied to the back of the animal's neck. *Imidacloprid* is absorbed through the skin and circulates in the blood. Fleas get exposed when biting and consuming the insecticide-infused blood. The average flea weighs between 0.5 mg and 1 mg, though they can double their body weight when feeding. It takes only a very small amount of the pesticide in the blood of the cat or dog to kill the flea. The flea, because of its very small size, receives a large dose relative to its body weight. The pet appears to be unaffected by its exposure to this pesticide primarily because it receives a very small amount of chemical relative to its larger body weight. However, if over exposed, the effect to an animal like a small cat would include muscle weakness, fatigue, and twitching.

Farm Worker Illness from Pesticides

The total use of pesticides in the United States is about 6 billion pounds a year, of that 1.2 billion pounds is used in agriculture. Worldwide agricultural pesticide use is an additional 5 billion pounds of active ingredient each year. The active pesticide chemical is often less than 1% of the material applied, so these estimates do not include other chemicals used to dissolve or apply the active pesticide chemical. These additional chemicals, sometimes called inert ingredients, may have their own hazards. Determining the exact amount of pesticides used by the agriculture industry is difficult because there is no national requirement for users to report the amount of pesticide applied. Commercial agriculture uses approximately 60% of pesticides and the rest is used by homeowners, commercial real estate managers, government, and industry use the rest on lawns, gardens, golf courses, and inside buildings.

The use of pesticides in large agricultural applications requires special training and knowledge to ensure that farm worker and crop picker's exposure is minimized. For example, *carbofuran* (n-methyl carbamate) is a broad-spectrum insecticide used on rice, alfalfa, table and wine grapes, cotton, potatoes, and soybeans. *Carbofuran* insecticide inhibits cholinesterase, causing an increase in the neurotransmitter acetylcholine.

Elevated acetylcholine levels cause tremor, paralysis, and death of the insect, and can have similar effects on wildlife such as birds, and humans. Farm workers come into contact with pesticides during pesticide application or when entering the fields too soon after an application. Due to its toxicity to humans and mammals, the US EPA moved to ban all use of *carbofuran* in 2008.

Here is an example of some of the problems with *carbofuran*. *Carbofuran* pesticide is used on cotton; however there is an EPA –required 48-hour waiting period after application before farm workers are allowed to enter the field. This is to allow the pesticide to dissipate and degrade, reducing the worker exposure to the active ingredient. In 1998, there was an aerial application of carbofuran to a California cotton field. Within hours of the spraying, 34 farm workers entered the cotton field to weed the cotton plants. Several hours later the workers reported symptoms including nausea, headache, eye irritation, muscle weakness, salivation, and decreased heart rate. These symptoms are consistent with poisoning from a cholinesterase inhibitor, such as *carbofuran*. The majority of the workers were decontaminated and hospitalized. Unfortunately several workers went home without being decontaminated, potentially exposing their families to the pesticide still on their work clothes and shoes. Infants or young children are more susceptible to pesticides than adults and are very vulnerable to this type of take home exposures from the workplace. For more information on this incident see the U.S. Centers for Disease Control report (MMWR, 1999).

Introduction and History

“Chlordane: America’s leading lawn and garden insecticide. Used extensively by pest control operators for termite control, because of its long lasting effectiveness.”
Velsicol Chemical Corporation – Advertisement – 1959

U.S. EPA lists chlordane as a persistent bioaccumulative toxic chemical. In 1978, EPA cancelled use of chlordane on food crops and in 1988 all use was banned.

The function of a pesticide is usually to destroy some form of life. Many plants and animals have evolved to develop their own sophisticated natural pest resistance as protection from other plants, insects, or animals bent on doing them harm. For example, both caffeine and nicotine are naturally produced chemicals manufactured by the plants to discourage pests. Humans have learned to use these naturally occurring pesticides, such as nicotine, to protect their crops. In the twentieth century new discoveries in chemical synthesis lead to a remarkable array of deadly synthetic pesticides designed to kill bacteria, fungi, plants, animals, and even other humans. The development and use of pesticides is a large and complex subject that includes chemistry, biology, environmental

fate, and governmental regulations. This chapter will provide a brief overview of this complicated group of compounds.

The two largest classes of synthetic pesticides are insecticides, which are designed to kill insects, and herbicides, which are designed to kill plants. Other major groups of pesticide compounds include fungicides, rodenticides, and antimicrobials. A word about antimicrobials, although many medications and antimicrobial products work by killing organisms such as parasitic worms, bacteria, or viruses, pharmaceuticals are not defined as pesticides and are regulated through a different mechanisms. For example, antibiotics are pesticides directed at bacteria. They are generally safe for humans and animals to consume at dosages prescribed by physicians or veterinarians. But as with many pesticides, antibiotics can cause problems. They are generally not specific to only one kind of bacteria and thus may kill helpful bacteria. Even more serious, bacteria adapt to the antibiotic and become resistant to its effects. In this chapter we will focus on the more traditional pesticides.

One of the first pesticides was sulfur, which was initially used by the Chinese in 1000 BC to control bacteria and mold (fungus). Sulfur is still widely used today. For example, in the wine industry sulfur is used to control unwanted bacterial growth in empty wine barrels and is commonly added to wine to kill unwanted yeast. The Chinese also pioneered the use of arsenic-containing compounds to control insects. Arsenic has a long history of use both as an insecticide and herbicide, and then as medicine (see chapter on arsenic). Arsenic trioxide was used as a weed killer in the late 1800s and lead arsenate was used as an insecticide particularly in orchards prior to the development of synthetic pesticides following WWII. Some of the first concerns about pesticide safety were raised over lead arsenate residue on fruit and in orchards. To this day some orchard soils remain contaminated with lead and arsenic. Arsenic in the form of chromated copper arsenate is used today to prevent wood that is in contact with soil from rotting.

Plants have provided several other important ‘natural’ pesticides. In the late 1600s nicotine, an extract from tobacco leaves was recognized as a potent insecticide and continues to be in limited use as a pesticide. Another group of ‘natural’ insecticides are pyrethrums, which are harvested and refined from chrysanthemums. The Strychnine tree, *nux vomica*, contains strychnine, which is used to kill rodents. Rotenone, another important insecticide and fish poison was extracted from the root of *Derris eliptica*, a climbing plant from Southeast Asia. Plant extracts are useful ways to control pests, but they are often difficult to purify and produce in large quantities. Consequently, it wasn’t until advances in synthetic chemistry and a better understanding of pest biology, did a significant increase in the use of pesticides occur.

Ready For Immediate Delivery! D.D.T., The Wonder Chemical In My-T-Kil Spray—49¢ quart – Bloomingdale’s Housewares, 6th Floor

My-T-Kil spray’s chief ingredient is the miraculous chemical called D.D.T. that’s fronts page news. The army has already proven its success in killing mosquitoes, bedbugs, cockroaches, etc., and seeing that they stay killed! Now you can use this wonder spray containing D.D.T. to combat bugs and insects. Warning: follow directions carefully.

From a 1945 advertisement in the New York Herald Tribune

Synthetic chemistry advanced rapidly in the 1930s and by the early 40s a range of new pesticides had been developed, including organochlorines like DDT. In 1937 the first organophosphorus compounds were synthesized by a group of German chemists. These very potent compounds were kept secret during World War II and were originally developed as potential chemical warfare agents. After the war, this class of compounds was re-purposed after some additional research and development into the insecticides we would recognize today.

Along with the development of insecticides was an effort to develop new herbicides to increase food production and to use as possible warfare agents. In 1946, the first commercially available chlorine-based herbicides were marketed to kill broad-leaf plants. This class of compounds includes 2,4-D (2,4-Dichlorophenoxyacetic acid), and 2,4,5-T (2,4,5-Trichlorophenoxyacetic acid) synthetic auxins that disrupt plant growth. These herbicides have been extensively utilized in agriculture, to clear roadsides and rights of way. Herbicides, notably 2,4,5-T was extensively used during the warfare to clear enemy hiding places, such as the jungles of Vietnam. During the manufacturing process 2,4,5-T was often contaminated with the persistent and very toxic dioxin, TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin). Dioxins, like other chlorinated compounds such as DDT, bioaccumulate in the fat and will persist for a long time. Dioxin are classified as carcinogens and are known also effect the reproductive and immune systems. Dioxin contamination ultimately lead to the cancellation of 2,4,5-T by the U.S. EPA, but 2,4-D is still one of the most widely used herbicides.

We have learned through bitter experience that we need to regulate the manufacture and use of pesticides. In the United States, regulation initially focused on protecting the consumer from pesticide residue on food, but it was also apparent that protection was need for the workers applying or working near pesticides. Congress passed the first federal act specifically dealing with pesticides in 1947. This act, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), was the first attempt to require pesticides be both safe and effective. Unfortunately, this law did not provide sufficient protection for

Table 7.1 Pesticide Use in the United States (2012 estimates)

	Agriculture	Industry/ Gov	Home & Garden
Herbicides	564	26	28
Insecticides	34	12	14
Fungicides	53	10	2
Fumigant	111	-	-
Sulfur & oil	122	-	-
Other	15		15

(Chlorine and hypochlorites are used in water purification)

Source: EPA Pesticides Industry Sales and Usage 2005 and 2012 Market Estiments

The history, development, toxicology, use, and regulation of pesticides make a fascinating story on many different levels. From a toxicology perspective, the principle of dose-response and individual sensitivity is demonstrated by unique sensitivity if small insects and children. The unique sensitivities of children and the subtle effects of pesticide exposure is driving the demand for more tightly regulated pesticides use and motivating efforts to reduce unintended exposures. Some communities are moving to ban the use of pesticides on lawns and landscaping and to ban the use of roadside herbicide spraying to control unwanted plant growth. People worldwide are recognizing the residual impact of pesticides on the environment. While pesticides may be needed to help protect crops and enable us to feed the world's expanding population; the challenge is to use these agents prudently and with knowledge of their potential harm. We need to continue to reduce unnecessary pesticide use, find safer and more selective pest management tools, and protect sensitive populations from exposure.

Biological Properties

Introduction

Exposures to pesticides can occur through foods, drinking water, home use of pesticides, indoor insect control, or through occupational exposure. Pesticides take advantage of two basic principles of toxicology: dose/response and individual sensitivity. They are designed to kill — and for insecticides this usually means toxicity to the nervous system — but size is important. A small amount of pesticide can be fatal to an insect, primarily

because the insect's small size and high rate of metabolism. For an insect a small exposure represents a very large dose on a body weight basis. The same small amount is relatively less harmful to an animal of much larger size because it is a small dose for the animal based on body weight. It is this same principle that makes children more vulnerable than adults to pesticides as well as their develop nervous systems. Table 6.2 illustrates how much of a chemical is need to achieve the same dose for an adult, a child, and insect. While a single exposure can be deadly, repetitive exposures to even small amounts of pesticides can cause adverse health effects.

Table 7.2 Comparison of body weight and dose

	Body Weight	Amount of chemical need for a dose of 10 mg/kg
Adult	70 kg (150 lbs)	700 mg
Child	10 kg (22 lbs)	100 mg
Insect	1 mg	0.00001 mg (1/100,000 mg)

mg = milligram, kg = kilogram

There is no perfect pesticide from the standpoint of the target organism and the unintended victims. Pesticides work by interfering with some basic biological function that is essential for life, and because all living organisms share many common biological mechanisms, pesticides are never specific to just one species. While killing a true pest, pesticides also kill other organisms that are either desirable or at least not undesirable, and we have a far from perfect understanding of what is undesirable. The ideal pesticide would be highly specific to only the target organism, be quick acting, and would degrade rapidly to non-toxic materials in the environment.

Insecticides

Most chemical insecticides act by poisoning the nervous system. The central and peripheral nervous system of insects is fundamentally similar to that of mammals. This means that given a sufficient exposure, insecticides will adversely affect human health. Insecticides are lethal to insects because of the high dose (exposure relative to body size). The similarities of nervous system structure make it nearly impossible to design insecticides that are highly specific for this mode of action; consequently, there are always a number of non-target organisms that may be affected by exposure. The newer insecticides are designed to be more specific and have the least amount of persistence in the environmental. We will discuss the most prominent classes of insecticides, organochlorines, pyrethroids, organophosphates, and carbamates in more detail.

Organochlorines, which include DDT, illustrate many of the challenges of insecticides. While they have the advantage of being cheap to manufacture and effective against serious target species, they have some serious unintended consequences. The chemical structure of organochlorines is diverse, but they all contain chlorine, which places them

in a larger class of compounds called chlorinated hydrocarbons. From the perspective of the nervous system, organochlorines disrupt the movement of ions such as calcium, chloride, sodium and potassium into and out of the nerve cells. Depending on the structure of the chemical, it may also have other effects on the nervous system as well. At one time organochlorines were thought to be ideal because they are very stable, persistent and slow to degrade in the environment, lipid soluble (therefore readily taken up by insects), and apparently harmless to mammals. Unfortunately it eventually became clear that the attributes of persistence and fat solubility were actually very undesirable for the environment and for mammals. Their persistence and solubility caused them to be passed up the food chain where they bioaccumulate in fat of large animals and humans and are passed on to nursing young. The global transport and use of these chemicals resulted in the contamination of wild life around the globe including in Arctic and Antarctic regions where these insecticides are rarely if ever used. A decline in the number of birds that prey on animals that came in contact with these chemicals was one of the first signs of the unintended consequences of DDT. Unexpectedly, DDT caused a thinning of the birds' eggshells and resulted in the death of their developing young. Organochlorines like DDT are largely banned now in North America and Europe, but are still manufactured and used in developing countries. Organochlorine insecticides provide many important lessons about the desirable and undesirable properties of pesticides.

Organophosphates and carbamates have very different chemical structures, but share a similar mechanism of action and will be examined here as one class of insecticides. Organophosphates were initially developed in the 1940s as highly toxic biological warfare agents (nerve gases). Modern derivatives, including sarin, soman, and VX, were stockpiled by various countries and now present some difficult disposal problems. Researchers created many different organophosphates in their search for ones that would target selected species and would be less toxic to mammals. When the organophosphate parathion was first used as replacement for DDT it was believed to be an improvement as it was more specific. Unfortunately there were a number of human deaths because workers failed to appreciate parathion's greater toxicity after working with much less acutely toxic DDT.

The problem with organophosphates and carbamates is that they affect an important neurotransmitter common to both insects and mammals. This neurotransmitter, acetylcholine, is essential to the way nerve cells communicate with each other. The acetylcholine that is released by one nerve cell initiates communication with another nerve cell, but that stimulation must eventually be stopped. To stop the communication, acetylcholine must be removed from the area around the nerve cells. This class of insecticides blocks an enzyme specifically designed to remove (break down) the no-longer-needed acetylcholine. The enzyme that breaks down acetylcholine is called acetylcholinesterase and this class of insecticides is commonly referred to as acetylcholinesterase inhibitors to acknowledge that they block this enzyme. Structural differences between the various organophosphates and carbamates affect the efficiency and degree to which the acetylcholinesterase is blocked. For example, nerve gases are

highly efficient and permanently block acetylcholinesterase, while the commonly used pesticides block acetylcholinesterase only temporarily. The human toxicity of these pesticides presents significant health hazards, and researchers continue to work to develop new insecticides that have fewer unintended consequences.

One of the newer class of insecticide, pyrethroids, is loosely based upon the naturally occurring pyrethrum that is found in chrysanthemum flowers. Synthetic pyrethroids were first developed in the 1980s, but the naturally occurring pyrethrum was first commercially used in the 1800s. Their use has increased significantly over the last 20 years. The chemical structure of pyrethroids is quite different from organochlorines and organophosphates, but the primary site of action is also the nervous system. Pyrethroids affect the movement of sodium ions (Na^+) into and out of nerve cells, causing the nerve cells to become hypersensitive to neurotransmitters. Structural differences between various pyrethroids can change their toxic effects on specific insects and even mammals. Synthetic pyrethroids are more persistent in the environment than natural pyrethrum, which is unstable in light and breaks down very quickly in the sunlight.

Herbicides

Herbicides are used to kill or damage a plant and are the most rapidly growing type of pesticide. Prior to the 1930s, herbicides were non-specific and often very toxic to humans as well as other animals. In the 1930s when they were developing new insecticides, researchers discovered several chemicals that selectively killed plants. These chemicals are now widely used to increase food production by killing weeds that choke out or compete with food crops and they have been used in warfare as defoliants. Herbicides have a variety of chemical structures and mechanisms of action, so they will be discussed in only general terms here. Interested readers are referred to the many web sites and the extensive research literature on herbicides (see below and the presentation).

The most famous (or infamous) of herbicides are the chlorophenoxy compounds that include 2,4-D and 2,4,5-T and its contaminant TCDD. This herbicide mixture, sometimes called Agent Orange in the 1960s, was widely used to kill broad-leaved plants in agriculture fields, along roadsides, and rights of way for power lines. It was also extensively used as a chemical warfare agent to kill unwanted vegetation, for example in jungles. The mechanism of action of this class of chemicals is poorly understood, but they appear to interact with plant growth hormones. Improvements in the manufacturing process of chlorophenoxy compounds and the cancellation of 2,4,5-T registration has reduced the amount of its related contaminants, such as dioxin, in the environment.

Paraquat and the related chemical diquat are nonselective herbicides that are also toxic to mammals. Occupational or accidental exposure to paraquat can occur with ingestion, skin exposure, or inhalation, all of which can cause serious illness or death. While seldom used in the United States at this time, paraquat is still widely used in developing countries. At one time it was used in marijuana plant eradication programs, but was

discontinued when a number of fatalities were observed in smokers of paraquat contaminated marijuana.

There are many other herbicides in widespread use, such as alachlor, glyphosate, and atrazine, that have a range of actions on plants and animals. Herbicides have become an essential part of the agriculture business and thought by some to be necessary to have the crop yields needed to feed the world's growing population. However, a serious limitation of many herbicides is their lack of specificity; in other words, herbicides can damage the crops of interest. The manufacturer of herbicides are working to address this problem and are increasingly turning to biotechnology to create genetically modify crops that are herbicide resistant. For example, the Monsanto company produces the glyphosate-based herbicide called RoundUp. The company also manufactures a genetically modified soybean that is resistant to RoundUp. This allows farmers to use RoundUp herbicide with the RoundUp Ready soybean plants and not have to worry about killing the soybean plants. The genetically modified 'RoundUP Ready' soybean is now widely planted though the practice has generated considerable controversy internationally.

Fungicides, rodenticides, molluscicides

Fungicides were developed to control the fungi and mold that in various forms are all around and on us. Early fungicides were sulfur, copper sulfate, and mercury based compounds. Chemical fungicides are now available for both medical treatment of human fungal disease and for use in agricultural applications. Control of plant fungus is important not only because they can damage the plant but also because some fungi produce toxic chemicals (mycotoxins) that are equally or more harmful. One of the more interesting fungi, *Aspergillus flavus*, often contaminates nuts (e.g. peanuts) and grains (e.g. corn). This fungus produces aflatoxin, which can cause liver disease and in some situations liver cancer. Another naturally occurring grain fungus produces an ergot alkaloid, which can cause hallucinations.

The chemical fungicide hexachlorobenzene was widely used in the 1940s and 1950s to protect seed grain from fungal rot. Mercurial compounds were also applied to seed grains to protect them from soil fungus. Both of these chemicals caused tragic human suffering when hungry people ate the treated grains rather than planting them for crops. The use of such potentially dangerous fungicides as these can be avoided through seed harvest and storage procedures that limit contamination or by modifying environmental conditions, such as controlling humidity and temperature.

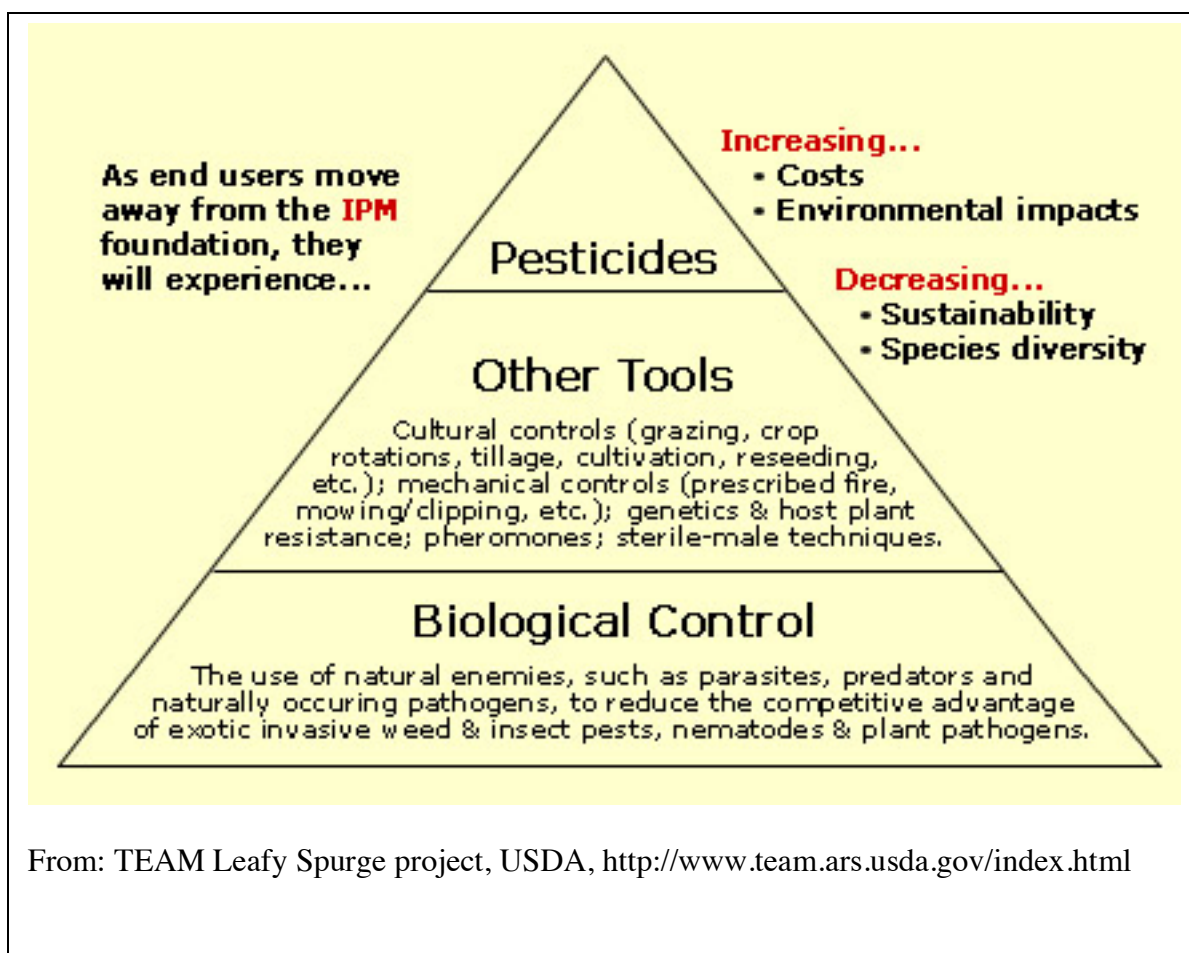
Rodenticides are a broad class of chemicals designed to kill small mammals such as rats and mice. Some rodenticides are anticoagulants and work by inhibiting blood-clotting; these are often used to control rat populations. One of the first anticoagulant rodenticides was warfarin, which is related to plant-derived coumadin (from spoiled sweet clover). In the 1950s rats developed resistance to warfarin, this promoted scientists to develop more potent anticoagulants. Other rodenticides include fluoroacetic acid and zinc phosphide

(very toxic), and thiourea based compounds. The primary alternative to using chemical rodenticides is trapping.

Molluscicides are used to control slugs and snails. Mollus are closely related to shellfish. The most common used active ingredient in molluscicides is metaldehyde, which disrupts the gastric organs of the mollus causing death. This product is often manufactured in the form of brightly colored pellets, which has the unfortunate unintended consequence of being attractive (and toxic) to children. The pellets are also attractive to other wildlife, such as dogs, cats, and birds. Some manufacturers have added a bitter agent to make the products unpalatable to children or other animals. Alternatives to using chemical molluscicides include trapping, barriers, or by designing gardens that is less attractive to slugs. Slug bait that is based on iron phosphate as the active ingredient is also available and appears to be somewhat less toxic.

Integrated Pest Management (IPM)

Integrated Pest Management (IPM) is an alternative and environmentally sensitive strategy for pest management. IPM uses the natural defense mechanisms of plants to combat pests and if necessary, uses pesticides in a highly selective manner. IPM also takes advantage of the life cycles of pests and relies careful planting of crops that are appropriate for the specific environment where they are planted. One of the goals of IPM is to minimize pesticide use and when pesticide use is necessary to use the least toxic pesticide. Pesticides can kill beneficial insects. IPM works to protect the overall ecological community, reduce human exposure to pesticides while maintaining crop productivity and plant beauty.



Health Effects

Introduction

Three of the most important health related issues with regard to pesticide use are 1) worker safety, 2) effects on children, and 3) unintended effects on other species and the environment. It is also important to remember some of the basic principles of toxicology: the differences between high-dose acute exposures and chronic exposure at lower levels and the potential impact on health related to the different routes of exposure (review Chapter 1).

All species have certain fundamental biological similarities and no matter how hard we try, pesticides cannot be designed to target just one species. Pesticides are designed to kill and because they are non-specific, they often kill or harm non target organisms, including humans. The World Health Organization estimates that there are 3 million cases of pesticide poisoning each year with up to 220,000 deaths, largely in developing countries.

Often the application of pesticides is not very precise and unintended exposures occur to other organisms in the general area of the pesticide application. Children, and indeed any young and developing organisms, are particularly vulnerable to the harmful effects of a pesticide. The consequence of even low levels of exposure during development is not well understood but may have adverse health effects.

Pesticide exposure can result in a range of neurological health effects such as memory loss, loss of coordination, reduced speed of response to stimuli, reduced visual ability, altered or uncontrollable mood and general behavior, and reduced motor skills. These symptoms are often very subtle and may not be recognized by the medical community as a clinical effect. Pesticide exposure also can result in asthma, allergies and hypersensitivity. Chronic exposure to pesticides is another problem. It can result in neurological effects as well as the possibility of an increased risk of cancer. In addition, the ingredients other than the specific active ingredients (sometimes referred to as inert ingredients) in many pesticide formulations include solvents that are toxic if inhaled or can be absorbed by the skin. These 'inert' ingredients may not be tested as thoroughly as active pesticide ingredient and are seldom disclosed on product labels. Thus, workers who apply pesticides and those who may be exposed do not know all the chemicals they are exposed to.

The Natural Resources Defense Council (NRDC) report, "Intolerable Risk: Pesticides in Our Children's Food" focused on the possible adverse effects of pesticides on children. The report notes that the smaller size of children relative to adults and different food consumption practices can result in the greater risk to children. Relative to their size, children eat, drink, and breathe more than adults. Their bodies and organs are growing rapidly which also makes them more susceptible. The use and regulation of pesticides illustrates the complexities of risk analysis and risk management and the difficulties in determining an acceptable level of exposure with acceptable risks, particularly for the wide range of populations that come in contact with these products.

Human Health Effects of Insecticides

All the major insecticides affect the nervous system so the health effects of human exposure can appear similar. Acute ingestion of organochlorines insecticides can result in a loss of sensation around the mouth; hypersensitivity to light, sound, and touch; dizziness; tremor; nausea; vomiting; apprehension; and confusion. Chronic exposure to insecticides can cause weight loss, muscle weakness, headache, anxiety and a range of other neurological complaints. DDT is an example of an insecticide that was thought to be relatively safe for humans because it was poorly absorbed through the skin. It is not uncommon to see pictures from the 1950s of people being dusted with DDT to kill insects and demonstrate its safety. Acute poisoning by oral ingestion of DDT can occur at a level of approximately 10 mg/kg which is a relatively large amount. But it was the environmental persistence, the accumulation of the insecticide in human and animal

tissue, and the effect on birds that caused DDT to be banned, along with most of the organochlorines.,.

Another organochlorine insecticide worthy of individual mention is Kepone or chlordane. In 1975, over 70 workers manufacturing Kepone in Hopewell, Virginia, developed a variety of neurological symptoms the most prominent of which became known as the “Kepone shakes”. Their symptoms started about 30 days after their first exposure to Kepone. Subsequent testing also revealed a decrease in sperm count and motility. Kepone was later found to be too environmentally toxic and its use was discontinued in favor of organophosphates.

Organophosphates, while environmentally less hazardous than the organochlorines, present their own challenges. Foremost, they are toxic to mammals. Unlike DDT, organophosphates are absorbed through the skin, which can lead to problems protecting workers from exposure. Acute organophosphate exposure causes signs and symptoms of excess acetylcholine, such as increased salivation and perspiration, narrowing of the pupils, nausea, diarrhea, decrease in blood pressure, muscle weakness, and fatigue. Usually (if the exposure is not too great) the symptoms of acute exposure decline within days after cessation of exposure as acetylcholine levels return to normal. Some organophosphates also have a delayed neurological reaction characterized by muscle weakness in the legs and arms. One example of the human health effects of organophosphates occurred during Prohibition when people consumed a homemade alcoholic drink made out of Jamaican ginger that was contaminated with the organophosphate triorthocresyl phosphate (TOCP). More than 20,000 people were affected by the condition called “ginger jake paralysis. Later research found that these effects could be reproduced in animals and the US government required testing for delayed effects as part of the registration of organophosphates. The human toxicity of organophosphates resulted in a steady decline in their use as new alternatives were developed.

Among the most promising alternatives were synthetic pyrethroids. However, pyrethroids, cause hyper-excitation, aggressiveness, uncoordination, whole-body tremor, and seizures. Acute exposure in humans, usually resulting from skin exposure due to poor handling procedures, usually resolve within 24 hours. While not particularly toxic to mammals, they can cause an allergic skin response in humans. Some pyrethroids may cause cancer, reproductive or developmental effects, or endocrine system effects.

Human Health Effects of Herbicides

Herbicides are designed to kill plants, not animals, and in general are less toxic to mammals than insecticides. Most herbicides interfere with plant hormones or enzymes that do not have any direct counterpart in animals. The most serious human health concerns have been related to contaminants in the active chemical ingredient. There is an enormous amount of animal and some human toxicity data on 2,4-D and 2,4,5-T, but it

now appears that much of this toxicity was caused by the contaminant dioxin (or TCDD). Military personnel and others exposed to Agent Orange, which was often contaminated with TCDD, reported birth defects, cancers, liver disease, and other illness. These concerns lead to improvement in the manufacturing process to reduce TCDD contamination and ultimately lead to a reduction in use of 2,4-D herbicides.

There is also concern that some herbicides may affect wildlife. For example, atrazine, a persistent herbicide may adversely affect frogs. Concerns about the effect of atrazine on amphibians resulted in its ban in the European Union, but atrazine remains one of the most widely used herbicides in the US at over 70 million pounds per year. Persistence of herbicides may also contaminate surface and ground water. There is an ongoing need for more alternatives to the use of herbicides.

Human Health Effects of Other Pesticides

Fungicides have caused a number of human health disasters. In the late 1950s, approximately 4,000 people in Turkey were poisoned by hexachlorobenzene that had been applied to seed grain to protect against soil fungus. Adults and particularly children who inadvertently ate the treated seed grain developed diseases of the skin and bone. In Iraq, a similar incident occurred when people consumed grain coated with a mercury based fungicide.

Rodenticides are clearly designed to kill mammals and thus (with the exception of thiourea compounds) are toxic to humans. Contact with these compounds should be avoided as much as possible. Environmental concerns occur when other animals consume a poisoned rodent and are in turn poisoned. Eagles, wolves, and other animals that eat rodents and are high in the food chain are particularly vulnerable.

Reducing Exposure

With estimates of 3 million people being overtly affected by pesticides each year, there is clearly much work to be done to reduce exposures. Many developing countries continue to use pesticides that have been banned in the United States and Europe.

Individually and collectively we need to examine our use of all forms of pesticides and consider alternatives to the use of pesticides. Home use of pesticides is widespread, and unfortunately there are many examples of home poisoning with pesticides. Consumers who use pesticides often apply them at much greater rates per acre than do farmers and professional pesticide applicators. Children are at particularly increased risk to pesticides that have been tracked in from outdoors as well as from pesticides that are used inside the home. Storage and proper disposal of pesticides also deserves special attention. Pesticide use around the home should be avoided as much as possible and consideration given to non-chemical methods of pest control. Integrated pest management (IPM) is an approach

that can significantly reduce pesticide use through prevention, monitoring, and less-toxic choices. Widely used in agriculture, landscape maintenance, and structural pest control, IPM can also be practiced by individuals in and around their homes. An IPM approach stresses proper food-waste management, landscape design, plant selection, natural pest controls, and physical controls such as traps, barriers, and mechanical removal.

Regulatory Standards

Experience has clearly demonstrated the need to regulate pesticide use. In the United States, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was passed in 1947 and allowed the U.S. Department of Agriculture to regulate appropriate labeling of pesticides. Later the U.S. Food and Drug Administration was given responsibility to ensure that food supply was safe from pesticides. In 1972, the administration of FIFRA was transferred to the U.S. Environmental Protection Agency. Subsequent revisions to FIFRA greatly expanded the testing requirements companies must comply with before pesticides could be registered for use. Current requirements include acute toxicity testing of full formulations (including inert ingredients); however, chronic and sub-chronic testing is only required for the active ingredients. Results of these tests, which are conducted by manufacturers and submitted to EPA, are used to estimate potential risks to human health and the environment. There is also an international effort to harmonize regulatory standards between the United States, Europe, and Japan.

Recommendation and Conclusions

Pesticides are widely used to help ensure an adequate food supply as well as to protect our health and safety from unwanted pests. But despite their attributes, these chemicals are not without their problems. There are several known and potential risks with the use of pesticides and more research needs to be done to find and test alternatives as well as to develop pesticides that do a better job targeting particularly species. Work also needs to be done to develop pesticides that cause the least amount of environmental damage. Businesses, schools, institutions, and the home gardeners that use pesticides should explore integrated pest management (IPM) methods to reduce pesticide use. An ongoing problem is the lack of data on the use of pesticides in agriculture, business or home. States and nations should consider adopting pesticide use registries to determine the actual volume of pesticides used, and to assist in the study of pesticide-related health effects and the unintended effects on the environment.

More Information and References

Slide Presentation

- A Small Dose of Pesticide presentation material and references online:
- www.asmalldoseoftoxicology.org
- Web site contains presentation material related to the health effects of pesticides.

European, Asian, and International Agencies

- European Union – Chemical and Pesticide Information. Online: <https://ec.europa.eu/food/plant/pesticides_en > (accessed: 02 September 2020). European site contains policy and other information on the use of pesticides in agriculture.
- World Health Organization - WHO Pesticide Evaluation Scheme (WHOPES). Online: <<https://www.who.int/whopes/resources/en/>> (accessed: 02 September 2020).
WHOPES is an “international programme which promotes and coordinates the testing and evaluation of new pesticides proposed for public health use.”
- World Health Organization - WHO Pesticide Information Online: <<https://www.who.int/topics/pesticides/en>> (accessed: 02 September 2020).
WHO high level information on international use and health related to pesticides.
- International Programme on Chemical Safety (IPCS). Online: <<http://www.who.int/pcs/index.htm>> (accessed: 02 September 2020).
“IPSC main roles are to establish the scientific basis for safe use of chemicals, and to strengthen national capabilities and capacities for chemical safety.”

North American Agencies

- Health Canada – Pesticides and Pest Management. Online: <<https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management.html>> (accessed: 02 September 2020).
Health Canada provided a range of information on pesticides in English and French.
- U.S. Environmental Protection Agency (EPA) - Office of Pesticides Programs (OPP). Online: <<http://www.epa.gov/pesticides/>> (accessed: 02 September 2020).
OPP’s mission is “to protect public health and the environment from the risks posed by pesticides and to promote safer means of pest control.” (2008).

- U.S. Geological Survey – National Water-Quality Assessment (NAWQA) Program. Pesticides and Water Quality Online: <<http://water.usgs.gov/nawqa/pnsp/>> (accessed: 02 September 2020). NAWQA provides an assessment water use in the U.S. and of pesticides in the streams, rivers, and ground water of the United States. Also - Estimated Annual Agricultural Pesticide Use – maps and graphs <https://water.usgs.gov/nawqa/pnsp/usage/maps/> (accessed: 02 September 2020).
- California Department of Pesticide Regulation. Online: <<http://www.cdpr.ca.gov/>> (accessed: 02 September 2020). The mission of this Department is “to protect human health and the environment by regulating pesticide sales and use, and by fostering reduced-risk pest management.”

Non-Government Organizations

- Pesticide Action Network North America (PANNA). Online: <<http://www.panna.org>> (accessed: 04 September 2020). “PANNA works to replace pesticide use with ecologically sound and socially just alternatives.”
- Pesticide Action Network International (PANI). Online: <<http://www.pan-international.org/>> (accessed: 04 September 2020). “PANI is a network of over 600 participating nongovernmental organizations, institutions and individuals in over 60 countries working to replace the use of hazardous pesticides with ecologically sound alternatives (English, French, Spanish).”
- Pesticide Database site – by Pesticide Action Network North America (PAN). Online: <<http://www.pesticideinfo.org/>> (accessed: 04 September 2020). “The PAN Pesticide Database brings together a diverse array of information on pesticides from many different sources, providing human toxicity (chronic and acute), ecotoxicity and regulatory information for about 6,400 pesticide active ingredients and their transformation products, as well as adjuvants and solvents used in pesticide products.”
- National Pesticide Information Center (NPIC) Call 1-800-858-7378. Online: <<http://npic.orst.edu>> (accessed: 04 September 2020). NPIC provides objective, science-based information about pesticides and pesticide-related topics to enable people to make informed decisions about pesticides and their use. NPIC is a cooperative agreement between Oregon State University and the U.S. Environmental Protection Agency.

- Beyond Pesticides. Online: <<http://www.beyondpesticides.org/>> (accessed: 04 September 2020).
Beyond Pesticides is a national network works with allies in protecting public health and the environment to lead the transition to a world free of toxic pesticides
- EXTOXNET InfoBase. Online: <<http://ace.orst.edu/info/extoxnet/>> (accessed: 04 September 2020).
EXTOXNET provides a variety of information about pesticides, including - the Pesticide Information Profiles (PIPs) for specific information on pesticides and the Toxicology Information Briefs (TIBs) contain a discussion of certain concepts in toxicology and environmental chemistry.

Integrated Pest Management (IPM) Principles

- U.S. Environmental Protection Agency (EPA) - Integrated Pest Management (IPM) Principles. Online: <<https://www.epa.gov/safepestcontrol/integrated-pest-management-ipm-principles>> (accessed: 04 September 2020).
Defines IPM principles and provides additional resources.
- University of California Statewide Integrated Pest Management Program (UC IPM). Online: <http://www.ipm.ucdavis.edu/IPMPROJECT/about.html> (accessed 04 September 2020).
“The University of California Statewide IPM Program (UC IPM) helps residents, growers, land managers, community leaders, and other professional pest managers prevent and solve pest problems with the least unintended impacts on people and their surroundings.”
- US Federal IPM Coordinating Committee. <http://www.ipm.gov/>. (accessed 04 September 2020).
- The National Integrated Pest Management (IPM) Coordinating Committee (NIPMCC) provides information to/from the United States Federal IPM Coordinating Committee.
- IPM Institute of North America, Inc. <http://www.ipminstitute.org/>. (accessed 04 September 2020).
“An independent non-profit organization formed in 1998 to foster recognition and rewards in the marketplace for goods and service providers who practice Integrated Pest Management, or IPM.”

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<<https://cfpub.epa.gov/ncea/risk/recorddisplay.cfm?deid=48865>> (accessed: 4 September 2020).

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