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Toxicity of Pesticides[1]

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This document describes how pesticides work on living things, so you can learn to reduce or eliminate exposure.

Background

Pesticides are designed to control pests, but they can also be toxic (poisonous) to desirable plants and animals, including humans. Some pesticides are so highly toxic that very small quantities can kill a person; while exposure to a sufficient amount of almost any pesticide can make a person ill. Since even fairly safe pesticides can irritate the skin, eyes, nose, or mouth, it is a good idea to understand how pesticides can be toxic so you can follow practices designed to reduce or eliminate your exposure and the exposure of others to them.

How Pesticides Enter the Body

Before a pesticide can harm you it must be taken into the body. Pesticides can enter the body orally (through the mouth and digestive system); dermally (through the skin) or by inhalation (through the nose and respiratory system).

Oral Exposure

Oral exposure may occur because of an accident, but is more likely to occur as the result of carelessness, such as blowing out a plugged nozzle with your mouth, smoking or eating without washing your hands after using a pesticide, or eating fruit that has been recently sprayed with a pesticide. The seriousness of the exposure depends upon the oral toxicity of the material and the amount swallowed.

Dermal Exposure

Dermal (skin) exposure accounts for about 90% of the exposure pesticide users receive from nonfumigant pesticides. It may occur any time a pesticide is mixed, applied, or handled, and it often goes undetected. Dry materials--dusts, wettable powders, and granules, as well as liquid pesticides--can be absorbed through the skin. The seriousness of dermal exposure depends upon:

- the dermal toxicity of the pesticide;
- rate of absorption through the skin;
- the size of the skin area contaminated;
- the length of time the material is in contact with the skin; and
- the amount of pesticide on the skin.

Rates of absorption through the skin are different for different parts of the body. Using absorption through the forearm as the standard, absorption is over 11 times faster in the lower groin area than on the forearm. (Absorption through the skin in the scrotal area is rapid enough to approximate the effect of injecting the pesticide directly into the bloodstream.)

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Absorption continues to take place on all of the affected skin area as long as the pesticide is in contact with the skin. The seriousness of the exposure is increased if the contaminated area is large or if the material remains on the skin for a period of time.

Inhalation Exposure

Inhalation exposure results from breathing pesticide vapors, dust, or spray particles. Like oral and dermal exposure, inhalation exposure is more serious with some pesticides than with others, particularly fumigant pesticides.

Inhalation exposure can occur from the applicator's smoking; breathing smoke from burning containers; breathing fumes from pesticides while applying them without protective equipment; and inhaling fumes while mixing and pouring pesticides.

Toxicity

Toxicity refers to the ability of a poison to produce adverse effects. These adverse effects may range from slight symptoms such as headaches to severe symptoms like coma, convulsions, or death. Poisons work by altering normal body functions, consequently toxicity can occur in as many ways as there are body functions. Most toxic effects are reversible and do not cause permanent damage if prompt medical treatment is sought. Some poisons, however, cause irreversible (permanent) damage.

All new pesticides are tested to establish the type of toxicity and the dose necessary to produce a measurable toxic reaction. In order to compare the results of toxicity tests done in different labs, there are strict testing procedures. Toxicity testing is extensive (involving many phases) and therefore, expensive. Humans, obviously, cannot be used as test animals so toxicity testing is done with animals. Since different species of animals respond differently to chemicals, a new chemical is generally tested in mice, rats, rabbits, and dogs. The results of these toxicity tests are used to predict the safety of the new chemical to humans.

Toxicity tests are based on two premises. The first premise is that information about toxicity in animals can be used to predict toxicity in humans. Years of experience have shown that toxicity data obtained from a number of animal species can be useful in predicting human toxicity, while data obtained from a single species may be inaccurate. The second premise is that by exposing animals to large doses of a chemical for short periods of time, we can predict human toxicity from to exposure to small doses for long periods of time.

Toxicity is usually divided into two types, acute or chronic, based on the number of exposures to a poison and the time it takes for toxic symptoms to develop. Acute toxicity is due to short-term exposure and happens within a relatively short period of time, whereas chronic exposure is due to repeated or long-term exposure and happens over a longer period. (Table 1).

Table 1. Types of Toxicity

Type	Number of Exposures	Time for symptoms to develop
Acute	usually 1	immediate (minutes to hours)
Chronic	more than a few	one week to years

Acute Toxicity

The acute toxicity of a chemical refers to its ability to do systemic damage as a result of a one-time exposure to relatively large amounts of the chemical. A pesticide with a high acute toxicity may be deadly if even a very small amount is absorbed. The signal words on the label (see Table 2) are based on the acute toxicity of the pesticide. Acute toxicity may be measured as acute oral (through the mouth), acute dermal (through the skin) and acute inhalation (through the lungs or respiratory system).

Acute Toxicity Measure

The commonly used term to describe acute toxicity is $LD_{50.}$ LD means Lethal Dose (deadly amount) and the subscript 50 means that the dose was acutely lethal to 50 percent of the animals to whom the chemical was administered under controlled laboratory conditions. The test animals are given specific amounts of the chemical in either one oral dose or by a single injection, and are then observed for 14 days.

Since LD_{50} values are measured from zero up, the lower the LD_{50} the more acutely toxic the pesticide. Therefore, a pesticide with an oral LD_{50} of 500 would be much less toxic than a pesticide with an LD_{50} of 5. LD_{50} values are expressed as milligrams per kilogram (mg/kg) which means milligrams of chemical per kilogram of body weight of the animal. *Milligram* (mg) and *kilogram* (kg) are metric units of weight similar to *ounce* and *ton*. Milligrams per kilogram is the same as parts per million.

Table 2. Acute Toxicity Measures and Warnings

		Categories of Acute Toxicity			
		LD_{50}	LD_{50}	LC_{50}	
Categories	Signal Word	Oral mg/kg	Dermal mg/kg	Inhale mg/l	Oral Lethal Dose[1]
I Highly Toxic	DANGER, POISON (skull & crossbones)	0 to 50	0 to 200	0 to 2,000	a few drops to a teaspoonful
II Moderately Toxic	WARNING	50 to 500	200 to 2,000	2,000 to 20,000	over a teaspoonful to one ounce
III Slightly Toxic	CAUTION	500 to 5,000	2,000 to 20,000	n/a	over one ounce to one pint
IV Relatively Non-toxic	CAUTION	5,000+	20,000 +	n/a	over one pint to one pound

[1] Probable for a 150 lb.-person.

For example, if the oral LD_{50} of the insecticide parathion is 4, a dose of 4 parts of parathion for every million parts of body weight would be lethal to at least half of the test animals.

LD_{50} values are generally expressed on the basis of active ingredient. If a commercial product is formulated to contain 50 percent active ingredient, it would take two parts of the material to make one part of the active ingredient. In some cases, other chemicals mixed with the active ingredient for formulating the pesticide product may cause the toxicity to differ from that of the active ingredient alone.

Acute inhalation toxicity is measured by LC_{50}. LC means Lethal Concentration. Concentration is used instead of dose because the amount of pesticide inhaled from the air is being measured. LC_{50} values are measured in milligrams per liter. Liters are metric units of volume similar to a quart. The lower the LC_{50} value, the more poisonous the pesticide.

Chronic Toxicity

Chronic toxicity refers to harmful effects produced by long-term, low-level exposure to pesticides. Less is known about the chronic toxicity of pesticides than is known about their acute toxicity, not because it is of less importance, but because chronic toxicity is much more complex and subtle in how it presents itself. While situations resulting in acute exposure (a single large exposure) do occur, they are nearly always the result of an accident or careless handling. On the other hand, persons may be routinely exposed to small amounts of pesticides while mixing, loading, and applying pesticides or by working in fields after pesticides have been applied.

Chronic Toxicity Measures

There is no standard measure like the LD_{50} for chronic toxicity. How chronic toxicity of chemicals is studied depends upon the adverse effect being studied. Chronic adverse affects may include carcinogenesis, teratogenesis, mutagenesis and reproductive toxicity.

Carcinogenesis (oncogenesis)

Carcinogenesis means the production of malignant tumors. Oncogenesis is a generic term meaning the production of tumors which may or may not be carcinogenic. The terms tumor, cancer, or neoplasm are all used to mean an uncontrolled progressive growth of cells. In medical terminology, a cancer is considered a malignant (potentially lethal) neoplasm. Carcinogenic or oncogenic substances are substances which can cause the production of tumors. Examples are asbestos and cigarette smoke.

Teratogenesis

Teratogenesis is the production of birth defects. A teratogen is anything that is capable of producing changes in the structure or function of the offspring when the embryo or fetus is exposed before birth. An example of a chemical teratogen is the drug thalidomide which caused birth defects in children when their mothers used it during their pregnancy.

Measles virus infection during pregnancy has teratogenic effects.

Mutagenesis

Mutagenesis is the production of changes in genetic structure. A mutagen is a substance which causes a genetic change. Many mutagenic substances are oncogenic, meaning they also produce tumors. Many oncogenic substances are also mutagens.

Reproductive toxicity

Some chemicals have effects on the fertility or reproductive rates of animals. Males or females can be affected.

Chronic Toxicity Testing

Chronic toxicity testing is both lengthy and expensive. EPA and regulatory agencies in other countries require an extensive battery of tests to identify and evaluate the chronic effects of pesticides. These studies, which may last up to 2 years, utilize several species of animals to evaluate toxicity from multiple exposures or continuous long-term exposure.

Label Identification of Acute and Chronic Toxicity

To alert pesticide users to the acute toxicity of a pesticide, a signal word must appear on the label. Four different categories are used (seeTable 2). Signal words are used to tell the user whether the chemical is highly toxic, moderately toxic, slightly toxic, or relatively non-toxic. These label warnings are based, for the most part, on the chemical's acute toxicity. For example, the acute oral and acute dermal toxicity of a pesticide may be in the slightly toxic category. But if the acute inhalation toxicity is in the highly toxic category, the pesticide label will have the signal words for a highly toxic pesticide. The degree of eye or skin irritation caused by the pesticide also influences the signal word.

For chronic toxicity there is no comparable set of signal words like those used for acute toxicity. Instead, a statement identifying the specific chronic toxicity problem is sometimes used on the label. Such a statement might read "This product contains (name of chemical) which has been determined to cause tumors or birth defects in laboratory animals." Chronic toxicity warning statements may be accompanied by label directions to wear certain kinds of protective clothing when handling or working with the pesticide to minimize or eliminate exposure to the pesticide.

It is important to read the label to look for signal words identifying the product's acute toxicity and for statements identifying any chronic toxicity problem. A pesticide may be low in acute toxicity (signal word caution), but it may have a label statement identifying potential chronic toxicity.

Safety Factors

In animal feeding studies, the pesticide under investigation is incorporated into the daily diet and fed to animals from a very young to a very old age. These, as well as the reproductive effects studies, are designed to arrive at a No-Observable-Effect-Level (NOEL); that is, a level in the total diet that causes no effect in treated animals when compared to untreated animals maintained under identical conditions. This NOEL is expressed on a mg/kg of body weight/day basis.

A Reference Dose (RfD), also known as Acceptable Daily Intake (ADD), is usually established at 1/100 of the NOEL, in order to add an additional margin of safety. The RfD (ADI) is the amount of chemical that can be consumed daily for a lifetime without ill effects.

Extensive residue trials are conducted to determine levels of the pesticide that remain in or on growing crops after treatment with the pesticide. These trials lead to the establishment of a tolerance for residues of the chemical on food commodities. A tolerance is the maximum allowable amount of the pesticide permitted in or on a specific food commodity at harvest. The directions for use found on the product label are written to assure that residues in food commodities are below the tolerance. The tolerance is set low enough to assure that even if someone ate only food items with residues of a given pesticide at the tolerance limit, there would still be a safety factor of at least 100 when compared to a level causing no observable effects in laboratory animals. This is, of course, a worst case situation, since all crops on which the pesticide is registered for use would not be treated with the chemical, and in most cases residue levels would be well below the tolerance due to pre-harvest intervals being longer than the minimum period stated on the label. Further reduction of residues may occur in storage or from washing, trimming, and processing.

Dose-response

Ironically, the extensive amount of data developed about a pesticide is often used against it by ignoring the dose-response. For example, some acute toxicity studies, which are designed to include dosage levels high enough to produce deaths, are cited as proof of the chemical's dangers. Chronic effects seen at very high doses in lifetime feeding studies are misinterpreted and considered as proof that no exposure to the chemical should be allowed. Major improvements in analytical chemistry permit detection of the presence of chemicals at levels of parts per billion (ppb) or even parts per trillion (ppt).

We may hear that a certain chemical has been found in a food or beverage and the amount found is expressed in parts per million or parts per billion. Often, no information is provided to assist us in comprehending the meaning of these numbers. Frequently, this information neglects the issue of dose-response, the key principle of toxicology which simply stated is "the dose makes the poison.". The concentration of a chemical in any substance is meaningless unless it is related to the toxicity of the chemical and the potential for exposure and absorption. Chemicals of low toxicity such as table salt or ethyl alcohol can be fatal if consumed in large amounts. Conversely a highly toxic material may pose no hazard when exposure is minimal.

Monitoring for Residues

Monitoring foods for pesticide residues is carried out by the Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA). Crops containing residues over the official tolerance (maximum legal level) established by the EPA must be destroyed. The threat of crop destruction with resultant financial loss is a strong incentive for farmers to observe use instructions on pesticide labels and thus assures that residues will be below established tolerances. Crops grown for export are often checked for residues by foreign residue laboratories to assure that local tolerance limits are not exceeded. Lastly, market-basket surveys (analyses of food items from grocery stores) have confirmed the low exposure of the general public to pesticides in foods.

Hazard

Hazard is a function of the toxicity of a pesticide and the potential for exposure to it. We do not have control of the toxicity of a pesticide since toxicity is a given characteristic of a particular pesticide; however, we can have control over our exposure to pesticides. This is done by following several safety practices including the use of protective clothing and equipment (PPE).

All pesticides are hazardous if misused, no matter what their toxicity. All pesticides can be handled safely by using safety practices that minimize or eliminate exposure to them.

Federal laws regulating pesticides have placed the burden of proving safety of pesticide usage on the manufacturer. Hazard evaluation studies are generally done by scientific laboratories maintained by the manufacturer or through outside contract laboratories. Few products are subjected to such extensive and vigorous testing as pesticides are before they are marketed. Many promising pesticide products are not marketed because they do not pass the extensive toxicology testing. Older pesticide products that were registered before the current toxicology testing standards were established are being re-evaluated under current standards. Precautions and other safety information found on the product's label are based on information from these tests. By reading and following the directions on the label, users can minimize or eliminate hazards due to use of the pesticide to themselves and others.

Bibliography

Some of the preceding material was adapted from Pesticide Toxicities, Leaflet 21062, Division of Agricultural Sciences, University of California and the *Dose Makes the Poison* by Alice Ottoboni, Ph.D., Vincente Books.