**Pesticides**

Pesticides are a group of chemicals made for the purpose of killing or otherwise deterring “pest” species. The word pesticide may refer to insecticides, herbicides, fungicides, or other pest control formulations. Pesticides are inherently toxic and often associated with adverse health effects in non-target organisms.

* Pesticide exposures include:

(1) accidental and/or suicidal poisonings

(2) occupational (manufacturing, mixing/loading, application, harvesting, and handling of crops) exposure

(3) bystanders exposed to off-target drift from spraying operations,

(4) members of the general public who consume food items containing pesticide residues.

**Insecticides**

All chemical insecticides in use today poison the nervous systems of the target organisms. The central nervous system (CNS) of insects is highly developed and is similar to that of mammals. The peripheral nervous system (PNS) of insects is not as complex as that of mammals. Insecticides are not selective and affect non-target species as readily as target organisms.

Potential sites of action of insecticides include interference with membrane transport of sodium, potassium, calcium, and chloride ions; inhibition of selective enzymatic activities; and contribution to the release and/or persistence of neurotransmitters at nerve endings.

**1. Organochlorine Compounds:**

DDT (Dichlorodiphenyltrichloroethane) poisoning affects CNS function in humans, also many pathologic changes are observed in the liver and reproductive organs. Hypertrophy of hepatocytes and its subcellular organelles, and an increase in the incidence of hepatic tumors have been noted after exposure to high concentrations.

Site and Mechanism of Toxic Actions:

An insect or mammal poisoned with DDT-type agents displays periodic persistent tremor and/or convulsive seizures that are suggestive of repetitive discharges in neurons.

DDT reduces potassium transport across the membrane, inhibits neuronal adenosine triphosphatases (ATPase), which play vital roles in neuronal repolarization, also affect the release of neurotransmitters. All these inhibited functions reduce the rate of depolarization and increase the sensitivity of neurons to small stimuli that would not elicit a response in a fully depolarized neuron.

**2. Anticholinesterase Agents:**

Organophosphorus and carbamate ester insecticides elicit their toxicity through inhibition of acetylcholinesterase (AChE), the enzyme responsible for the destruction and termination of the biological activity of the neurotransmitter acetylcholine (ACh). With the accumulation of free, unbound ACh at the nerve endings of all cholinergic nerves, there is continual stimulation of electrical activity of the autonomic nervous system, the neuromusclar junction, and the CNS.

A second distinct manifestation of exposure to organophosphorus ester insecticides is a paralytic condition called the *intermediate syndrome.* Neurologic signs that appear 24 to 96 h after the acute cholinergic crisis include muscle weakness (neck, flexors, muscles of respiration as well as those of the limbs).

A third syndrome, organophosphate-induced delayed neurotoxicity (OPIDN), the characteristic OPIDN usually follows 7 to 14 days after exposure and progresses from ataxia to moderate to severe muscular weakness and paralysis.

The signs and symptoms of acute intoxication by carbamate insecticides differ from those described for organophosphorus compounds in regard to the duration and intensity of the toxicity. Carbamate insecticides are reversible inhibitors of nervous tissue AChE and are biotransformed rapidly in vivo. There is little evidence of prolonged neurotoxicity, and carbamate ester insecticides do not elicit OPIDN-type neurotoxicity.

organophosphorus esters can produce an irreversibly inhibited enzyme. So, the toxicity persists (20 to 30 days) until sufficient quantities of "newly synthesized" AChE are available.

In contrast, carbamic acid esters, which attach to the reactive site of AChE, undergo hydrolysis ( considered as reversible inhibitors).

**3. Pyrethroid Esters**:

They exert their mammalian and insect toxicity by extending the open time of sodium channels throughout the central and peripheral nervous systems. Symptoms of toxicity include loss of coordination, tremors, convulsions, burning and itching sensations. Pyrethroids can also act as dermal and respiratory allergens, and exposure can lead to contact dermatitis or asthma-like symptoms. Death, when it occurs in humans, is usually due to respiratory failure. Fortunately, the pyrethroids are much more toxic to insects due to their limited ability to eliminate these compounds.

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| **4. Nicotine:**  Nicotine has been used as a contact insecticide, and fumigant. It is extremely toxic, is readily absorbed through the skin, and mimics or blocks, depending on the dose, the action of acetylcholine at all ganglionic synapses and at neuromuscular junctions. As an insecticide, nicotine blocks synapses associated with motor nerves. |

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| **Herbicides**  A herbicide is any compound that is capable of killing or severely injuring plants. Herbicides may be classified by how and when the agents are applied. *Preplanting* herbicides are applied to the soil before a crop is seeded. *Preemergent* herbicides are applied to the soil before the usual time of appearance of the unwanted vegetation. *Postemergent* herbicides are applied to the soil or foliage after the germination of the crop and/or weeds. |
| Most herbicides are dermal irritants, causing skin rashes and contact dermatitis. Individuals who are prone to allergic reactions may experience severe contact dermatitis, asthma-like attacks, and even anaphylactic reactions after dermal contact or inhalation.  **1.** **Paraquat**:  It is still used in many countries and is one of the most specific pulmonary toxicants known. The signs and symptoms include lethargy, hypoxia, dyspnea, tachycardia, diarrhea, ataxia, hyperexcitability, and convulsions.  The ingestion of commercial paraquat concentrates is invariably fatal and runs a time course of 3 to 4 weeks. The initial irritation and burning of the mouth and throat, severe gastroenteritis with esophageal and gastric lesions, abdominal and substernal chest pains, and bloody stools give way to dyspnea, anoxia, opacity in the lungs seen in chest x-rays, progressive fibrosis, coma, and death. Although pulmonary damage is extensive, paraquat also induces multiorgan toxicity with necrotic damage to the liver, kidneys, and myocardial muscle plus extensive hemorrhagic incidents throughout the body.  **Diquat** is a rapid-acting contact herbicide that is slightly less toxic than paraquat; it has poor absorption from the gastrointestinal tract. The major target organs are the gastrointestinal tract, liver, and kidneys, and in a study there was an increased incidence of cataracts. Diquat can form free radicals, and tissue necrosis is associated with superoxide-induced peroxidation as is observed with paraquat. Diquat shows no special affinity for the lung.  **2. Glyphosate:**  Glyphosate inhibits the enzyme 5-enolpyruvyl-shikimate-3-phosphate synthetase (EPSPS), an enzyme of the aromatic amino acid biosynthesis pathway that is essential for protein synthesis in plants.  Mild intoxications are characterized by gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain) resulting from mucosal irritation and injury. In moderate intoxications, intestinal ulceration, esophagitis, and hemorrhage are seen, along with hypotension, some pulmonary dysfunction, acid-base disturbance, and evidence of hepatic and renal damage. Severe poisoning is characterized by pulmonary dysfunction, renal failure, cardiac arrest, repeated seizures, coma, and death.  **3. Glufosinate:**  Glufosinate irreversibly inhibits the plant enzyme glutamine synthetase, which decreases ammonia detoxification. Increased ammonia levels lead to impairment of photorespiration and photosynthesis.  Early clinical symptoms of glufosinate ammonium poisoning include nausea, vomiting, and diarrhea that followed by impaired respiration; seizures; muscle weakness, convulsions; and even death. |

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| **Fungicides**  Fungicides are chemical compounds used to kill fungi or fungal spores. They may be described as protective, curative, or eradicative according to their mode of action.  An effective fungicide must have the following properties: (1) low toxicity to the plant but high toxicity to the particular fungus, (2) activity or the ability to convert itself (by plant or fungal enzymes) into a toxic intermediate, (3) ability to penetrate fungal spores to reach a site of action, and (4) formation of a protective, tenacious deposit on the plant surface that will be resistant to weathering by sunlight, rain, and wind. All commercially available compounds lack persistence because of environmental degradation.  Most fungicides have low toxicity to mammals. However, all fungicides are cytotoxic and most produce positive results in in vitro microbial mutagenicity test systems. Public concern has focused on the positive mutagenicity tests obtained with many fungicides and the fact that nearly 90 percent of all agricultural fungicides are carcinogenic in animal models. |
| **1. Hexachlorobenzene:**  Hexachlorobenzene (HCB) causes a syndrome, called *black sore,* that is characterized by dermal blistering and epidermolysis, pigmentation and scarring, alopecia, photosensitivity, hepatomegaly, porphyria, suppurative arthritis, and osteoporosis of the bones of the hands.  HCB has chemical stability, slow degradation and biotransformation, environmental persistence, bioaccumulation in adipose tissue, and the ability to induce cytochrome P450 and conjugative enzymes. |

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| **Fumigants**  These agents are used to kill insects, nematodes, weed seeds, and fungi in soil as well as in silo-stored cereal grains, fruits and vegetables, clothes, and other consumables, with the treatment carried out in enclosed spaces because of the volatility of most of these products.  **1. Phosphine:**  Used extensively as a grain fumigant, phosphine (PH3) is released from aluminum phosphide (AlP) by the natural moisture in the grain over a long period, giving continual protection during transhipment of the grain. Symptoms of PH3 intoxication in adults include shortness of breath, cough and pulmonary irritation, nausea, headache, jaundice, and fatigue.  **2. Ethylene Dibromide/Dibromochloropropane:**  At relatively high (>200 ppm) concentrations, inhaled ethylene dibromide can cause pulmonary edema and inflammation in exposed animals. Repeated exposures to lower concentrations have produced centrolobular hepatic necrosis and proximal tubular damage in the kidneys. |

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| **Rodenticides**  The black rat, the brown or Norway rat, and the house mouse pose particularly serious problems because they act as vectors for several human diseases.  To be effective yet safe, a rodenticide must (1) not be unpalatable to the target species and must be potent, (2) not induce nervousness so that the animal will continue to eat it, (3) cause death in a manner that does not raise the suspicions of survivors, (4) make the intoxicated animal go out into the open to die (otherwise the rotting corpses create health hazards), and (5) be species-specific, with considerably lower toxicity to other animals that might inadvertently consume the bait or eat the poisoned rodent.  Accidental or intentional ingestion of most rodenticides poses a serious, acute toxicologic problem, and rodenticide poisoning is seen more frequently in children.  **1. Zinc Phosphide:**  Widely used in developing nations because it is both cheap and effective, zinc phosphide hydrolyzes with water, producing PH3 and causing widespread cellular toxicity with necrosis of the gut and injury to other organs, such as the liver and kidneys.  Signs of intoxication from accidental or suicidal poisonings include vomiting, diarrhea, cyanosis, tachycardia, restlessness, fever, and albuminuria several hours after exposure. Also, hypertension, pulmonary edema, dysrhythmias, and convulsions have been reported.  **2. Fluoroacetic Acid and Derivatives:**  Sodium fluoroacetate and fluoroacetamide have extreme toxicity, which is facilitated by their ready absorption from the gastrointestinal tract. Fluoroacetate incorporates inhibition of the Krebs cycle. These chemicals are uniquely effective in mice and rats because of the high metabolic rate in the tissues that are susceptible to inhibition.  In humans, gastrointestinal symptoms are seen initially some 30 to 100 min after ingestion. Initial nausea, vomiting, and abdominal pain are replaced by sinus tachycardia, ventricular tachycardia or fibrillation, hypotension, renal failure, muscle spasms, and CNS such symptoms as agitation, stupor, seizures, and coma.  **3. Anticoagulants:**  Coumadin (warfarin) antagonizes the actions of vitamin K in the synthesis of clotting factors II, VII, IX, and X. The onset of anticoagulation is delayed 8 to 12 h after the ingestion of warfarin owing to the half-lives of previously synthesized clotting factors. The safety of warfarin as a rodenticide rests with the fact that multiple doses are required before toxicity develops and the fact that single doses have little effect. Human poisonings are rare. Neverthless, after consumption over a period of days, bleeding of the gingiva and nose, bruising and hematomas developing at the knee and elbow joints, gastrointestinal bleeding with dark tarry stools, hematuria accompanied by abdominal or low back pain, epistaxis, and cerebrovascular accidents occur. The signs and symptoms persist for many days after the cessation of exposure owing to the prolonged biological half-lives of the warfarins. |