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Pesticides

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World pesticide use exceeded 5.6 billion pounds of active ingredient (AI) in 1999, the latest year for which figures are available. Herbicides (chemicals used to control plants, usually weeds) accounted for the largest proportion (38%). Insecticides and fungicides were 25% and 10% of the total used, respectively (1).

The United States used 1.2 billion pounds of AI or more than 20% of the world's pesticide consumption. Herbicides were the largest category of use (46%), but insecticides were only 9% and fungicides 7% of the total pesticide market. While fungicide use in the United States and world markets is similar, insecticides are much more heavily used globally primarily due to the need for more widespread mosquito control (1).

Other pesticides account for 27% and 38% of the world and United States pesticide use, respectively. Categories included in other pesticides category are nematicides, fumigants, rodenticides, molluscicides, aquatic and fish/bird pesticides, plus other chemicals used as pesticides (e.g., sulfur and oils) (1).

Specialty biocides (used for recreational and industrial water treatment and as disinfectants and sanitizers), chlorine and hypochlorites (used as disinfectants for potable, waste, and recreational water), and wood preservatives are also considered pesticides. If the amount of AI used for these purposes is included in pesticide use data, total AI used in the world and the United States is four times higher (e.g., 5 billion pounds of AI in the United States).

Gross AI figures do not accurately reflect what has happened in world and U.S. agriculture over the past 20 years. Total pesticide use has dropped by about 20% over that time period—herbicides by 10% and insecticides by 50% (this does not reflect the likely increase in use of insecticides for West Nile virus prevention that has occurred in the last 5 years), and fungicides by 30%. In addition, the specific types of AI have also changed. The trend, generally, has been to decrease use of more toxic pesticides of all types and replace them with lower risk products (lower risk to humans, birds, fish, and beneficial insects) (1).

Approach to Pesticide Poisoning

Before discussing individual chemicals, a few principles of pesticide poisoning management should be addressed. The most important issue is proper diagnosis. Without it, all other interventions are potentially ineffective and possibly harmful.

Whenever possible, get the label of the suspected poison. It will contain principles of management and contact information for the manufacturer. The local poison control center and the National Pesticide Telecommunications Network (1-800-858-7378 Monday to Friday 9:30 a.m. to 7:30 p.m.) are also available for further advice. If coworkers have not been able to identify the suspect chemical, Cooperative Extension Service agents may also serve as a resource for commonly used chemicals at particular times of the year on specific crops.

Remember that careful decontamination of the patient is necessary to prevent possible further injury to the patient and possible injury to emergency department staff. Physical decontamination by removing clothing that has been in contact with the chemical, washing the skin with soap and water, and copiously irrigating the eyes is important. Recent evidence-based position statements from the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists suggest that gastric lavage, activated charcoal, cathartics, and ipecac should not be used routinely in poisoned patients. They can be considered within 60 minutes of presentation if a potentially life-threatening amount of poison has been ingested. Even in this circumstance, contraindications exist for the use of each: lavage is contraindicated in hydrocarbon ingestion; cathartic in volume depletion, hypotension, electrolyte imbalance, or ingestion of a corrosive substance; activated charcoal in an unprotected airway, a nonintact gastrointestinal (GI) tract or hydrocarbon ingestion; and ipecac in a nonalert patient or with ingestion of a hydrocarbon or corrosive substance (2).

Herbicides

The most widely used pesticides in the world, herbicides are designed to kill plants and attack plant metabolic pathways that do not exist in humans and other animals. Therefore, in general, they have relatively low animal toxicity. There are hundreds of herbicides and herbicide mixtures on the market in the United States and throughout the world. Seven of the top 10 pesticide active ingredients (by amount used) are herbicides. Chlorophenoxy herbicides are plant growth regulators. They are commonly used for broadleaf weed control on cereal crops and pastures. Common chlorophenoxy herbicides include 2,4-D; Dicamba; and Silvex. Many products available to consumers include a mixture of salts in a petroleum base. Most toxicity from contact with skin or eyes or ingestion involves mucous membrane irritation. Very high dose

exposure may result in neurological symptoms including muscle twitching, seizures, and coma. Renal and hepatic dysfunction may occur with large ingestions. Long-term health effects of low to moderate exposure include alleged, but not confirmed, carcinogenicity, teratogenicity, and reproductive abnormalities. Although no specific antidote is known, alkaline diuresis has been reported to be of value in severe overdose. Otherwise, aggressive supportive care including protection of the airway, correction of hypotension, and treatment of arrhythmias, hyperthermia, and seizures may be required (3).

Atrazine and glyphosate, triazine, and phosphonate herbicides are also widely used for weed control. Glyphosate was developed specifically as a much safer alternative to paraquat (discussed in a subsequent paragraph). Mucous membrane irritation is the most common adverse reaction to exposure to these chemicals and their many relatives. Gastrointestinal tract erosions were the primary adverse events in large-volume ingestions (all accidental or intentional), but renal, hepatic, central nervous system, and pulmonary involvement was sometimes noted. Since no antidote is known, supportive care is also indicated for these groups of agents (4,5).

Carbamate herbicides, unlike carbamate insecticides, do not produce inhibition of cholinesterase enzymes or the "all faucets on" cholinergic syndrome. Toxicity is uncommon. Common generic names for carbamate herbicides include asulam, terbucarb, butylate, pebulate, triallate, and thiobencarb. Mucous membrane irritation is the most common adverse effect. After removal of the chemical by soap and water, flushing the eyes, and increased fluid intake, treatment is supportive.

Urea-substituted herbicides are photosynthesis inhibitors, mainly used for weed control in noncrop areas. Chemicals in this class have names ending in "-uron" or "-oron"—e.g., chlorimuron, diuron, siduron, tebuthioron, and tetrafluoron. Urea-substituted herbicides have low systemic toxicity based on animal feeding studies; they may, however, produce methemoglobinemia with heavy ingestion. Methemoglobin and sulfhemoglobin levels should be measured in patients with dyspnea or cyanosis and a history of urea-substituted herbicide ingestion. Otherwise treatment of these ingestions is decontamination and supportive care.

The most dangerous group of herbicides is the bipyridyls. Paraquat is the most important of the bipyridyl group. Others in the group include diquat, chlormequat, and morfamquat. Bypyridyls exert their herbicidal activity by interfering with reduction of nicotinamide adenine dinucleotide phosphate (NADP) to reduced nicotinamide adenine dinucleotide phosphate (NADPH) during photosynthesis, producing superoxide, singlet oxygen, and hydroxyl and peroxide radicals. This eventually destroys lipid cell membranes, including those in the lungs, leading to late and irreversible pulmonary fibrosis. Major local effects of paraquat are due to its caustic properties. Corneal ulceration has been reported after paraquat concentrate was splashed in the eyes. Gastrointestinal tract ulceration including esophageal ulceration with

perforation has occurred. After ingestion of >30 mg/kg of paraquat concentrate, pulmonary, cardiac, renal, and hepatic failure can occur within hours. Ingestion of 4 mL/kg or more may cause renal failure, resulting in impaired paraquat excretion and higher serum concentrations. Pulmonary involvement is the major target of ingested paraquat with an adult respiratory distress syndrome (ARDS)-like syndrome developing 1 to 2 days after ingestion, progressing to pulmonary fibrosis in a few days.

Treatment of paraquat ingestion is aimed at several points along the toxicity pathway—removing toxin from the GI tract, increasing excretion from the blood, and preventing pulmonary damage with anti-inflammatory agents. Cautious aspiration with a nasogastric tube is appropriate if the patient presents within the first hour after ingestion. Because of the possibility of severe toxicity, some authorities still recommend activated charcoal (1 to 2 g/kg) if the patient is seen within 1 to 2 hours, repeated 4 hours later. Hemodialysis is effective for removing paraquat from the blood. Pulmonary damage is increased by oxygen supplementation, so low-oxygen breathing mixtures are recommended. Immunosuppression has been attempted with corticosteroids and cyclophosphamide or other similar agents, with limited success. Deferoxamine and *N*-acetylcysteine have been used as antioxidants. Prospective studies supporting immunosuppressive and antioxidant therapies are lacking. Diquat is felt to have much less pulmonary toxicity, but pulmonary fibrosis may also occur, especially if oxygen supplementation is used. Chlormequat toxicity resembles organophosphate toxicity but should not be treated as such (see the discussion of organophosphate pesticides in the next section). Treatment is by GI decontamination and supportive care. Morfamquat is rarely used. No human or animal toxicity has been reported with morfamquat, but poisoning with the chemical should probably be treated initially as a paraquat poisoning (6).

Insecticides

Organophosphates are still the most widely used insecticides in the United States and the world, but botanical insecticides and insect growth regulators are becoming much more widely used, due to their lower toxicity. Also included in this category are the organochlorines (such as DDT), the carbamates, and insect repellants (DEET and p-dichlorobenzene).

Organophosphates (OPs) are the most common cause of insecticide poisoning and cause a few deaths each year in the United States. OPs are used for suicide in both the United States and particularly in the Third World, where more than 100,000 people per year are estimated (by the World Health Organization) to take their own lives using this group of chemicals.

Organophosphates are so widely used because of their effectiveness against a wide variety of insects and their lack of persistence in the environment (compared to organochlorines). The toxicity of OPs varies greatly—a drop of

the OP nerve agents VX, soman, or sarin may be lethal, while malathion has an oral median lethal dose (LD_{50}) of approximately 1 g/kg. Most of the OPs are rapidly absorbed by all routes. They may be classified as direct (the nerve gases) or indirect (most commercially used crop, animal, and home products) cholinesterase inhibitors. Metabolism, primarily by the CYP450 system, is required to activate the indirect inhibitors. Direct inhibitors may have almost immediate effects, or up to 2 to 3 hours delay after dermal absorption. Indirect inhibitors may not produce symptoms until 6 to 24 hours after exposure.

The toxicologic effects of OPs are almost entirely due to inhibition of acetylcholinesterase in the nervous system, which causes acetylcholine to accumulate in the synapses and myoneural junctions. Muscarinic, central nervous system, and nicotinic effects are produced as outlined in Table 16.1, usually in that order. The most common clinical presentation is a patient with an odor similar to garlic, with miosis, increased airways secretion, lacrimation, bradycardia, and GI complaints (7). This constellation of findings should be managed as OP poisoning until proven otherwise (8).

Serum and red blood cell (RBC) cholinesterase levels should be obtained early, but therapy should not be delayed pending laboratory confirmation. Treatment should include attention to the airway and adequate oxygenation with atropine administered until secretions dry. The initial dose of atropine should be 1 to 2 mg for adults and 0.05 mg/kg for children, administered intravenously if possible, and repeated every 15 to 30 minutes until signs of atropinization develop (flushing, drying of secretions, and dilation of pupils, if they were miotic at presentation). Atropine may be required for 24 hours and should be tapered, rather that abruptly stopped. Pralidoxine (2-PAM) is a specific OP antidote. It should be administered as soon as possible in all

TABLE 16.1. Clinical effects of organophosphate poisoning.

Site	Physiologic Effect
Muscarinic effects	
Sweat glands	Sweating
Pupils	Miosis
Ciliary body	Blurred vision
Lacrimal glands	Lacrimation
Salivary glands	Salivation
Bronchi	Constriction with wheezing
Gastrointestinal	Cramping, vomiting, diarrhea, tenesmus
Cardiovascular	Bradycardia, hypotension
Bladder	Incontinence
CNS Effects	
	Anxiety, restlessness, ataxia, convulsions, coma
*Nicotinic Effect*s	
	Decreased reflexes, respiratory/circulatory depression
Striated muscle	Fasciculations, cramps, weakness, paralysis, respiratory depression, hypoxia, respiratory arrest
Sympathetic ganglia	Tachycardia, hypertension

clinically significant poisonings. The initial dose is 1 to 2 mg for adults and 25 to 50 mg/kg for children given intravenously over 15 to 30 minutes. A continuous infusion of 10 to 20 mg/kg, up to 500 mg/h, is then used in severe OP poisoning. More detailed information on OP poisoning management is found in standard texts on poisoning and drug overdose. Severe OP poisoning has been associated with chronic neurological sequelae including cognitive impairment, depression, and peripheral neuropathies. An intermediate syndrome, termed organophosphate-induced delayed-onset neuropathy (OPDIN) associates hyperreflexia and hypertonicity with long-term, low-dose exposure to OPs. Both syndromes are rarely recognized (7,9).

Carbamates are also cholinesterase inhibitors, producing the syndrome of cholinergic crisis as described for OPs. The syndrome is of shorter duration and more benign than with OPs because carbamates dissociate from the cholinesterase much more readily than OPs, producing a reversible inhibition. Carbamates also poorly penetrate the central nervous system (CNS), rarely producing seizures, ataxia, and central depression of the respiratory and circulatory centers. Red blood cell and serum cholinesterase levels return to normal within hours of exposure. Treatment of carbamate poisoning is also with atropine (in doses identical to those used for OPs but for only 6 to 12 hours because of the shorter duration of enzyme inhibition) and oxygen supplementation. Pralidoxime is not indicated in pure carbamate poisoning, but if the poison is not known for certain and cholinergic symptoms exist, it can be used, pending identification of the poison.

Because of their persistence in the environment, organochlorine insecticides are in limited use in the United States. They are, however, used around the world in mosquito control. Lindane is still used in the United States as a general garden insecticide, for control of ticks, scabies, and lice and for extermination of powderpost beetles. It is absorbed by inhalation and ingestion and less well by dermal contact, unless the skin is abraded or treated repeatedly.

Lindane interferes with normal nerve impulse transmission by disruption of sodium and potassium channels in the axon membrane, leading to multiple action potentials for each stimulus. Clinically this may result in confusion, apprehension, tremors, muscle twitching, paresthesias, dizziness, seizures, or coma—usually in the face of a history of repeated treatment for scabies or lice. Wheezing, rales, or cyanosis may be found if hydrocarbon (a frequent vehicle) aspiration has occurred. Diagnosis is based on a history of exposure or intentional ingestion with physical manifestations of CNS hyperexcitability. Treatment is decontamination with supportive and symptomatic care. Seizures may require lorazepam or diazepam. Arrhythmias should be treated with lidocaine.

Commonly used botanical insecticides include pyrethrum, nicotine, rotenone, and *Bacillus thuringiensis*. Other botanicals are used in small quantities but are rarely associated with adverse health effects. Pyrethrum is the oleoresin extract of dried chrysanthemum flowers. It contains about 50%

active insecticidal ingredients known as pyrethrins. Synthetic derivatives of these compounds, called pyrethroids, are much more widely used today. Most insecticides containing pyrethroids also contain piperonyl butoxide, a synergist that increases their effectiveness by retarding enzymatic degradation of the active ingredient.

Pyrethrum-based insecticides are considered to have low toxicity, but they can produce nausea, vomiting, diarrhea, tremors, muscle weakness, and paresthesias. Very high levels of exposure can produce temporary paralysis and respiratory failure. Treatment is supportive. Allergic reactions to the pyrethroids are more common, with about 50% of patients sensitive to ragweed, and cross-reacting to pyrethrum. Pyrethrum and the pyrethroids are well absorbed from the GI tract and minimally absorbed from dermal exposure. They are rapidly metabolized by the liver, leading to their relative lack of systemic toxicity in humans. Persons exposed to prolonged contact with high concentrations of pyrethroids report paresthesias in unprotected skin. Vitamin E oil has been reported to relieve these paresthesias, by an unknown mechanism. Otherwise treatment of toxicity is symptomatic and supportive. Allergic symptoms are treated as with other allergens, by avoidance and antihistamines for mild symptoms, and corticosteroids and epinephrine for severe bronchospasm (10).

Nicotine, usually derived from tobacco, was used as an insecticide in the past. Now rarely used, most nicotine poisoning is as a result of ingestion of tobacco products or incorrect use of nicotine patches, gum, or nasal sprays. Decontamination is the treatment of choice. Care is supportive, since there is no specific antidote for nicotine. Severe hypersecretion or bradycardia may be treated with atropine.

Rotenone, prepared from the roots of derris, *Lonchocarpus*, and *Tephrosia* plants, is used as a household and horticultural insecticide. Piperonyl butoxide is also used as a synergist with this compound. Toxic to fish, bird, and insect nervous systems, it has produced little human toxicity in decades of use. However, fresh derris root from Malaya has been used for suicides. Numbness of mucous membranes has been reported in exposed workers, along with dermatitis and respiratory tract irritation. Treatment of these symptoms is with decontamination and supportive care.

Several subspecies of *Bacillus thuringiensis* (BT) are pathogenic to some insects. The product is used both as a spray to be applied to certain food crops and, incorporated into the genetic material of certain plants as a "built-in" insecticide. Infections of humans with these organisms is extremely rare. One volunteer ingesting a BT variety not used as a pesticide developed fever and GI symptoms. A single corneal ulcer has been associated with a splash of BT suspension in the eye. The GI symptoms resolved spontaneously; the ulcer resolved with antibiotic treatment (11).

Insect repellants are intended for human use and are therefore designed to be nontoxic in routine use. Two insect repellants have produced poisoning syndromes: DEET (*N,N*-diethyltoluamide) and *p*-dichlorobenzene. DEET is

minimally absorbed through the skin and is rapidly eliminated, primarily in the urine. Excessive use of high concentrations of this compound has been associated with a idiopathic toxic encephalopathy, particularly in girls and female infants. Symptoms may include lethargy, anxiety, opisthotonos, athetosis, ataxia, seizures, and coma. Ingestion of 50 mL of high concentration DEET (50% to 90%) has produced coma, seizures, and hypotension within an hour of ingestion and death in at least two cases. Irritant contact dermatitis and conjunctivitis have also been reported, as has an anaphylactic reaction in one case. There are no characteristic physical findings. Treatment is symptomatic and supportive.

Originally used as a moth repellant and insecticide, *p*-dichlorobenzene is now more commonly used as a deodorizer. Ingestion is fairly common when children eat a part of a deodorant cake in a toilet bowl or diaper pail. It is a mucous membrane irritant and can produce allergic symptoms. Massive ingestions may produce tremors and hepatic or renal injury. There are no characteristic features on physical examination or laboratory studies. Diagnosis is by history of ingestion, and treatment is supportive.

Fungicides

Widely used in industry, agriculture, home, and garden, fungicides are used for many purposes—protection of seed grain during storage, transport, and germination; protection of crops, seedlings, and grasses in the field, in storage, and during shipment; suppression of mold; control of slime in paper processing, and protection of carpets and fabrics. Fungicides, used properly, rarely cause severe poisonings. Most have inherently low mammalian toxicity and are absorbed poorly (at least partly because they are formulated as suspensions of wettable powders or granules). Most are applied using methods that intensively expose only a few individuals. Irritant injuries to skin and mucous membranes are relatively common in heavily exposed individuals, however (12).

Of the substituted benzene herbicides, only hexachlorobenzene has produced systemic toxicity. This occurred when hexachlorobenzene-treated seed wheat was used instead for human consumption. In 4 years, approximately 3000 persons developed porphyria due to impaired hemoglobin synthesis. Most affected individuals recovered, but some infants nursed by affected mothers died.

Thiocarbamates, unlike the *N*-methyl carbamates, have little insecticide activity. Instead they are used to protect seeds, turf, ornamentals, vegetables, and fruit from fungi. Bisdithiocarbamates, represented by thiram, are structurally similar to disulfuram. With heavy exposure an Antabuse-like reaction can be produced if alcohol is ingested subsequently. This reaction is characterized by flushing, sweating, headache, tachycardia, and hypotension.

Other thiocarbamates—ziram, ferbam, and metam-sodium—should theoretically predispose to the Antabuse reaction, but no occurrences have been reported. Metam-sodium decomposition in water yields methyl isothiocyanate, a gas that is extremely irritating to mucous membranes. Inhalation of the gas may cause pulmonary edema. Metam-sodium is considered a fumigant and should be used in outdoor settings only. Persons caring for a victim with metam-sodium ingestion should avoid inhalation of evolved gas. Treatment of exposure is with skin and GI decontamination, oxygen supplementation, fluid support, and avoidance of alcohol.

Ethylene bisdithiocarbamates (EBDC compounds) are another group of fungicides that may irritate skin, respiratory tract, and eyes. Maneb, zineb, nabam, and mancozeb represent this class. Treatment of the irritant effects of these chemicals is by decontamination. Thiophthalimides, represented by captan, captafol, and folpet, are agents used to protect seed, field crops, and stored produce. All of these fungicides are moderately irritating to the skin, eyes, and respiratory tract. They may produce skin sensitization. No systemic poisonings have been reported with these chemicals.

Copper compounds, both inorganic and organic, are irritating to skin, respiratory tract, and eyes. Soluble copper salts, such as copper sulfate and acetate, are corrosive to mucous membranes and the cornea. Systemic toxicity is low, probably due to limited solubility and absorption. Treatment of poisoning is with GI and skin decontamination. Ophthalmologic consultation should be obtained if eye irritation persists after flushing the eyes with saline. Intentional ingestions of large volumes of these compounds may result in hemolysis with circulatory collapse and shock, with renal and hepatic failure. In these severe cases, fluid replacement, alkalinization of the urine, chelating agents, and hemodialysis may be required.

Organomercury compounds have been used primarily as seed protectants. Toxicity has occurred primarily when methyl mercury–treated grain intended for planting was consumed in food. Poisonings have also occurred from eating meat from animals fed mercury-treated seed. Organic mercury is efficiently absorbed from the gut and is concentrated in the nervous system and red cells. Early symptoms of mercury poisoning are metallic taste, distal paresthesias, tremor, headache, and fatigue. Further symptoms target the CNS with incoordination, slurred speech, spasticity, rigidity, and decline in mental status. Treatment is by skin and GI decontamination and chelation.

Cadmium has been used to treat fungal diseases of turf and bark of orchard trees. Cadmium salts and oxides are very irritating to mucous membranes of the respiratory and GI tracts. Inhaled cadmium dust or fumes can produce a mild, self-limited respiratory illness with fever, cough, and malaise, similar to metal fume fever. More severe symptoms with labored breathing, chest pain, and hemorrhagic pulmonary edema are associated with heavier exposure and resemble chemical pneumonitis. Cadmium ingestion may produce severe nausea, vomiting, diarrhea, abdominal pain, and tenesmus. Chronic obstructive pulmonary disease (COPD), renal and hepatic injury,

and pathological fractures have been associated with chronic cadmium exposure. Treatment is skin and GI decontamination, respiratory support, and chelation therapy (for severe, acute poisoning, though the possibility of inducing renal failure with a large load of cadmium exists).

A long list of miscellaneous organic fungicides is in use in many crop, ornamental, and turf applications. Reports of adverse effects on humans are rare or absent entirely. As with all pesticides, following label directions for use is the key to prevention of adverse events, even with these low-risk chemicals.

Rodenticides

Rodenticides are designed to kill nuisance rodents such as rats, mice, moles, voles, ground squirrels, gophers, and prairie dogs. These animals may damage crops in the field or in storage and can transmit disease to humans and other animals through their droppings or bites. A wide variety of organic and inorganic chemicals have been used to control rodents. Plant-derived materials such as strychnine and red squill or inorganic compounds such as thallium or arsenic trioxide were among chemicals used early for rodent control. Newer agents tend to be synthetic organic compounds. All pose particular risks for accidental poisonings. Since these agents are designed to kill mammals, their toxicity is often similar for the target rodents and for humans. Also, since rodents often share environments with humans and other mammals, the risk of accidental exposure to the rodenticide is high because of their placement in those environments. As rodents have become resistant to some chemicals, more toxic chemicals have been developed, exposing those applying them and those living in areas where they are used to increased risk of toxicity. There are over 150 trade name rodenticides in the United States alone, many with very similar names. While important for all poisonings, in rodenticide poisoning, having the label to guide therapy is critical.

Long-acting anticoagulants are responsible for nearly 80% of human rodenticide exposures reported in the United States. Introduced in the 1970s, they have essentially replaced warfarin-based products. They have the same mechanism of action as warfarin but are more potent and have longer half-lives. They are effective in a single feeding (or a limited number of feedings) and in animals that have developed resistance to the older anticoagulants.

Treatment of superwarfarin ingestion depends on the dose. A child who ingests a few pellets or grains of the material can be observed at home for the development of bleeding. A person with a bleeding disorder or who takes an anticoagulant is at much greater risk of excess bleeding, even with a small exposure. Patients with large ingestions (>0.1 mg/kg) should have gastric decontamination if they are seen within an hour or two of the ingestion. If there has been a longer delay, activated charcoal is indicated. Prothrombin

time (PT) and partial thromboplastin time (PTT) should be measured at 24 and 48 hours after a significant ingestion. If any value is elevated, phytonadione (vitamin K_1) should be started (1 to 5 mg for children and 15 to 20 mg for adults) by subcutaneous injection and repeated as necessary. Critically ill adults can be given 50 to 200 mg via slow intravenous infusion (0.5 mg/min). The PT and PTT should be checked every 4 hours until stable and then every 24 hours. Once the PT and PTT are stable, the phytonadione may be switched to the oral form (15 to 25 mg daily for adults, 5 to 10 mg for children), tapering the dose as the PT levels decline to normal (over a period sometimes as long as 6 months).

Warfarin-based products are still available, but single exposures, unless large amounts (>0.5 mg/kg) are ingested, can be observed without therapy. Recent large exposures should be treated with activated charcoal. The PT and PTT should be measured at 12 and 24 hours. If the PT is two times normal or more, phytonadione should be given (1 to 5 mg for children, 10 mg for adults orally or intramuscularly and repeated as necessary. The PT should be measured every 4 hours until stable, then every 24 hours until normalized (13).

Bromethalin, a relatively new rodenticide introduced in 1985, is a neurotoxin that produces its effect by uncoupling mitochondrial oxidative phosphorylation. This results in increased intracranial pressure, decreased nerve impulse conduction, paralysis, and eventual death. No human exposures have been reported. Its effectiveness as a rodenticide is based on the rodent's consuming a relatively larger dose per kilogram than other larger animals. There is no antidote, so treatment of poisoning would be symptomatic and supportive.

Cholecalciferol (vitamin D_3) takes advantage of the fact that rodents are sensitive to small percentage changes in calcium levels in their blood. Cholecalciferol increases serum calcium by mobilizing calcium from bone, resulting in calcium deposition in tissues and nerve and muscle dysfunction and cardiac dysrhythmias. Ingestion of several bait pellets or treated seeds should not be toxic, and no treatment is necessary. Larger ingestions should be treated with gastric lavage if recognized early and activated charcoal in several doses if after 1 to 2 hours of ingestion. Serum calcium should be checked at 24 and 48 hours and treatment initiated if hypercalcemia develops. Forced diuresis with furosemide and a low-calcium diet should be initiated along with prednisone (5 to 15 mg every 6 hours). Calcitonin and/or mithramycin may be necessary for patients unresponsive to above measures.

Red squill is a botanic rodenticide derived from the red sea onion (*Urginea maritima*). It contains two cardiac glycosides that produce effects similar to digitalis. Treatment of ingestion is the same as for digitalis toxicity, including the use of Digibind.

Strychnine is another botanical, found in seeds of *Strychnos nux-vomica,* a tree native to India. Used in Germany in the 16th century as a poison for rats and other animals, it is still available in many rodenticides. It is a neurotoxin, producing twitching of facial (*risus sardonicus*) and neck muscles, reflex

excitability and generalized seizures. Treatment should include activated charcoal and anticonvulsants (diazepam, phenobarbital, or phenytoin if unresponsive to diazepam). Stimulation of the patient should be minimized; respiratory support including intubation and mechanical ventilation may be required.

Thallium rodenticides are not used in the United States, but are available around the world. Treatment of poisoning is difficult. Gastric decontamination should be attempted with lavage and activated charcoal. Fluid support with potassium chloride theoretically displaces thallium and increases its excretion.

Zinc and aluminum phosphides are used to protect stored grains from rodents and other pests. On contact with moisture, phosphides release phosphine gas, which is the primary cause of toxicity. Oral exposures to phosphides occur as a result of intentional ingestion for suicidal purposes. Phosphine inhibits oxidative phosphorylation, leading to cell death, manifested by severe GI irritation, hypotension, and cardiac and respiratory dysfunction. Management is by activated charcoal and gastric lavage. Intragastric sodium bicarbonate and/or potassium permanganate have been suggested to decrease phosphine gas release. Oxygen should be supplemented (100% via rebreather). Treatment is otherwise symptomatic and supportive (14).

The fifth edition of *Recognition and Management of Pesticide Poisoning,* edited by Drs. Routt Reigart and James Roberts of the Medical University of South Carolina, contains a table that lists manifestations caused by specific pesticides, which may be useful in evaluating possible pesticide exposures and toxicities. The entire textbook is available on the Environmental Protection Agency Web site at http://www.epa.gov/pesticides/safety/healthcare/handbook.htm (see "Index of Signs and Symptoms" or pages 213 to 224) by request from the Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances at 703-305-7666.

Miscellaneous Solvents and Adjuvants

The liquids in which pesticides are dissolved and the solids on which they are adsorbed are chosen by the manufacturers to make handling and application easy and to achieve maximal stability and effectiveness of the active ingredient. The most commonly used solvents are petroleum distillates. The petroleum distillate may produce toxicities in itself in large-volume ingestions. Most adjuvants (emulsifiers, penetrants, and safeners) are potentially skin and eye irritants but with very low or no systemic toxicity.

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