PESTICIDES *

Wesley E. Straub

This section deals with a discrete group of chemicals that are of particular importance in agriculture, pest control industries, and public health. Their use in crop production and disease control has increased with the expanding world population, and their complexity and number have increased in proportion to their expanded use.

No attempt is made to present the clinical effects of all pesticides currently in use nor to delineate definitive treatment. Some aspects of clinical treatment are presented, particularly where the information is of general application to more than one substance and is not generally available, and treatment must be rapidly instituted. Hazardous exposures may occur in both occupational and nonoccupational activities, and the physician should be on notice to consider both aspects of a worker's activities in checking for source of exposure.

In severe poisoning, the initial diagnosis and institution of appropriate treatment must be made on clinical grounds alone since there is generally insufficient time to wait for confirmatory laboratory results.

Essential to the correct diagnosis of pesticide poisoning is a high index of suspicion on the part of the physician based on 1) a history of opportunity for any adequate exposure compatible with time-dose relationships, 2) clinical manifestations, and 3) laboratory confirmation.

The toxic dose and clinical picture of poisoning vary with the compound and formulation, and possibly with the individual.

For purposes of the following discussion, the pesticides are grouped according to their chemical nature or use as organophosphates, carbamates, chlorinated hydrocarbons, bipyridyls, coumarins and indandiones, rodenticides, fungicides, herbicides, fumigants, and miscellaneous insecticides.

ORGANOPHOSPHATES

The more important organophosphates are:

Abate	Ethion
DDVP (Vapona)	Fenthion (Baytex)
Diazinon	Gardona
Dicathon	Malathion
Dimethoate (Cygon)	Naled (Dibrom)
Dursban	Parathion
EPN	

The organophosphate insecticides are characterized by the similarity of their mechanism of toxic action. They differ widely, however, in inherent toxicity and, to some extent, in rate of absorption and excretion.

The organophosphates act as irreversible inhibitors of the enzyme

*Based in some parts on the Chapter in the previous edition written by Roy L. Gibson, M.D., and Thomas H. Milby, M.D.

cholinesterase, thereby allowing the accumulation of acetylcholine at nerve endings. They are rapidly absorbed into the body by ingestion, through the intact skin, including the eye (even more efficiently through cuts, abrasions, areas of dermatitis, etc.), and by inhalation.

Dose and dose-interval affect the speed with which the toxic manifestations occur. Onset of symptoms more than 12 hours after the termination of exposure generally excludes the diagnosis of organophosphate poisoning. It must be remembered, however, that continuing exposure may occur from contaminated hair, shoes, and clothing.

The following table for parathion lists symptoms which are indicative not only for parathion, but for other organophosphate exposures.

Table 6. Signs and symptoms in patients with parathion poisoning as related to levels of cholinesterase activity.

Sign or symptoms	Total number of patients with signs or symptoms	Number of symptomatic patients in each of three levels of activity*		
		0-10% of normal	11-20% of normal	21-50% of normal
Weakness	47	14	11	22
Headache	46	14	11	21
Sweating	44	14	10	20
Nausea and vomiting	42	14	11	17
Salivation	31	13	8	10
Miosis	25	14	6	5
Dyspnea	23	14	6	3
Difficulty in walking	22	14	8	0
Diarrhea	21	9	4	8
Muscular fasciculation	20	14	6	0
Disturbance in speech	20	14	6	0
Disturbance in consciousness	19	14	5	0
Abdominal pain	15	5	4	6
Fever	15	9	6	0
Bronchopharyngeal secretion	14	10	4	0
Increased blood pressure	12	10	2	0
Loss of pupillary reflex	10	10	0	0
Cramp	9	9	0	0
Cyanosis	8	8	0	0

*As percent of value of each patient after recovery from poisoning.

Note: Modified from Nambe, T., C. T. Nolte, J. Jackrel, and D. Grob. 1971. Poisoning due to organophosphate insecticides: acute and chronic manifestations. Am. J. Med. 50:475-492. Reprinted with permission from author and publisher.

PERMISSIBLE EXPOSURE LIMITS

The Federal standards for parathion and malathion are 0.1 mg/m³ and 15 mg/m³, respectively. NIOSH has a recommended limit for parathion of 0.05 mg/m³ (TWA) and a limit for methyl parathion of 0.2 mg/m³ (TWA).

HARMFUL EFFECTS

Mild organophosphate poisoning causes symptoms of headache, fatigue, dizziness, blurred vision, excessive sweating, nausea and vomiting, stomach cramps, diarrhea, and salivation. These symptoms are similar to those of many diseases not related to pesticide exposure such as influenza, heat stroke, heat exhaustion, and gastroenteritis.

Moderately severe organophosphate poisoning causes all of the symptoms found in mild poisoning, but in addition, the patient is unable to walk, often complains of chest discomfort and tightness, exhibits marked miosis (constriction of the pupils), and exhibits muscle twitching. These symptoms might be reasonably mistaken for such conditions as pneumonia, myocardial infarction, and encephalitis.

Severe organophosphate poisoning may result in rapid onset of unconsciousness, local or generalized seizures, and other manifestations of a cholinergic crisis.

CLINICAL NOTES

An important clinical observation, in addition to those previously mentioned (high index of suspicion, history, clinical manifestations), which aids in the substantiation of the diagnosis of an anticholinesterase intoxication, is atropine refractoriness. When a larger than normal dose of atropine is given to a person not exposed to anticholinesterase pesticides, the early signs of atropine toxicity soon become apparent. These signs include dry mouth, flushed skin, increased heart rate, and dilated pupils. If the patient has anticholinesterase poisoning, large doses of atropine are required to produce these normal reactions.

The atropine test should be used with caution in patients with glaucoma. However, in acutely toxic patients suspected of organophosphate poisoning, immediate atropine therapy must be initiated even without tests of atropine refractoriness.

Acholest screening tests provide a simple but crude index of the degree of cholinesterase inhibition while offering the most immediate confirmation that is within the laboratory expertise of any hospital or clinic. Plasma cholinesterase determinations of this nature use filter paper impregnated with a pH-sensitive color reagent and can detect inhibition as low as 20 percent of serum cholinesterase. Plasma and red blood cell cholinesterase are more precise determinations, but errors have resulted from unfamiliarity of laboratory personnel with these procedures.

Treatment for parathion poisoning has been improved with the availability of 2-PAM (2-pyridine-aldoxime methiodide). Blood samples for cholinesterase determinations must be collected before 2-PAM treatment is started.

In severe cases it may be necessary to begin treatment with atropine

or 2-PAM before laboratory confirmation of significant cholinesterase depression is obtained.

TREATMENT

SPEED IS IMPERATIVE.

Principles of treatment include the immediate injection of atropine to block parasympathetic effects of the accumulated acetylocholine and of 2-PAM to reactivate the phosphorylated enzyme.

It is imperative to keep the airway open.

When the compound is ingested, it is important to act quickly to prevent any further systemic absorption.

When exposure is by skin contact, the compound should be rapidly removed by thorough rinsing or washing with water or soap and water. Compound splashed in the eye should be washed out with water, isotonic saline, or other ophthalmic irrigating solution, as available.

Wear rubber gloves while washing contact area to prevent any danger to medical personnel.

CARBAMATES

Carbamates are reversible cholinesterase inhibitors. Like organophosphates, they may be direct or delayed in action. Inhibition of the enzyme is reversed largely by hydrolysis of the carbamylated enzyme and to a lesser extent by synthesis of a new enzyme. Important carbamates are:

Baygon
Carbaryl (Sevin)
Thiram
Vapam
Zectran

PERMISSIBLE EXPOSURE LIMITS

The Federal standard for carbaryl is 5 mg/m^3.

HARMFUL EFFECTS

Signs and symptoms of intoxication may include miosis, salivation, profuse sweating, lassitude, muscle incoordination, nausea, vomiting, diarrhea, epigastric pain, tightness in the chest, etc.

CLINICAL NOTES

2-PAM and other oximes are contraindicated for routine use.

Cholinesterase reactivates rapidly after carbamate poisoning. Laboratory cholinesterase determinations may be misleading.

LABORATORY NOTES

1-Naphthol, normally found in traces, is excreted in the urine in much higher concentrations following carbaryl ingestion.

TREATMENT

SPEED IS IMPERATIVE

Principles of treatment are similar to those used in organophosphate poisoning (atropine and maintenance of adequate respiration) with the exception of the use of 2-PAM.

CHLORINATED HYDROCARBONS

Chlorinated hydrocarbon insecticides are more persistent in the environment than most other synthetic organic pesticides, and because of this, their use has recently decreased. Among the most important chlorinated hydrocarbons are the following:

Benzene Hexachloride (BHC)	Kepone
Chlordane	Heptachlor
DDT	Lindane (Isomer of BHC)
Dicofol (Kelthane)	Mirex
Dieldrin	Thiodan
Endrin	Toxaphene

HARMFUL EFFECTS

Chlorinated hydrocarbons are most efficiently absorbed by ingestion. In general, they act on the central nervous system to stimulate or depress. Signs and symptoms of toxicity, therefore, vary with the specific chemical. Symptoms have been reported as soon as 30 minutes after massive exposure, but generally develop more slowly; if this pattern of symptoms does not appear within a few hours after suspected acute exposure, another diagnosis or complicating feature must be sought.

Mild chlorinated hydrocarbon poisoning causes such symptoms as dizziness, nausea, abdominal pain, and vomiting. In chronic poisoning, loss of weight and appetite, and, in the case of endrin, temporary deafness and disorientation may occur.

Moderately severe chlorinated hydrocarbon poisoning presents mild signs followed by severe irritability, convulsive seizures, and coma. Seizures may be epileptiform in character with frothing at the mouth, facial congestion, violent convulsive movements or stiffness of the limbs, associated with stupor or coma. In severe cases, the convulsions may be continuous, with elevated body temperatures, unconsciousness, labored breathing with vigorous, rapid heart beat, and eventually death.

CLINICAL NOTES

Vomiting should NOT be induced when the ingested pesticide is in a hydrocarbon solvent. Epinephrine should not be given since chlorinated hydrocarbons may sensitize the heart to catecholamines.

LABORATORY NOTES

A high urinary level of organic chlorine or especially of p-chlorophenyl acetic acid indicates exposure to DDT or to one of the analogous compounds. The level, however, is not necessarily indicative of the severity of exposure.

TREATMENT

In cases of ingestion, gastric lavage should be performed.

Care should be taken to prevent aspiration of gastric contents. In some cases, induction of catharasis with aqueous solutions of sodium

sulfate has been of value in increasing fecal excretion and retarding absorption. Barbiturates are sometimes helpful in reducing convulsions. Respiration should be closely followed. Oil, oily cathartics (e.g., mineral oil), and epinephrine should be avoided.

BIPYRIDYLS

Bipyridyls include paraquat and diquat and are used in the form of the dichloride, dibromide, or dimethosulfate salt.

HARMFUL EFFECTS

Most reported cases involved accidental ingestion which produced proliferative changes in the lungs, cornea, lens, nasal mucosa, skin, and finger nails.

With the exception of eye lesion, illness due to occupational exposure is usually mild and is the result of skin contact.

CLINICAL NOTES

Diquat affects the lens and the gastrointestinal mucosa. It does not produce the lung changes characteristic of paraquat.

The clinical picture following accidental or suicidal ingestion of paraquat is very different. Paraquat ingestions are frequently fatal. Their management is unsatisfactory and largely symptomatic. Three clinical stages follow ingestion of as little as one ounce of paraquat.

The first is a gastrointestinal phase with burning in the mouth and throat, nausea, vomiting, abdominal pain, and diarrhea.

Several days after exposure, signs of hepatic and renal toxicity appear. These are due to central zone necrosis of the liver and acute tubular necrosis of the kidney.

Ten to 20 days after ingestion, progressive proliferative changes develop in the lungs. Hyperplastic changes in the terminal bronchioles occur with alveolar fibroblastic proliferation. Loss of lung surfactant has been demonstrated. Within a few days, death from respiratory failure occurs.

LABORATORY NOTES

Urinary studies have indicated that 90 percent of the ingested paraquat is excreted in the first 24 hours. Delayed pulmonary effects appear to be the result of an irreversible process that develops long after the initial stimulus has gone.

Paraquat is poorly absorbed from the gastrointestinal tract. Excretion data suggest that only 1 to 5 percent of the ingested material is absorbed in man. Maximal blood concentrations are reached within 4 to 6 hours after ingestion.

TREATMENT

Treatment is primarily directed toward decreasing the amount of paraquat absorbed and the concentration in the circulating blood. This may be achieved by appropriate repeated administration of large amounts of adsorbents and purgatives.

RODENTICIDES

Rodenticides of first importance include sodium fluoroacetate, strychnine, thallium sulfate, and warfarin. For information on rodenticides containing arsenic, barium, cyanide, and phosphorus, reference may be made to the appropriate chemical in the section on Chemical Hazards.

SPECIAL NOTES

Fluoroacetate is a highly toxic poison which causes central nervous system stimulation (convulsions) and cardiac arrhythmias. Specific treatment includes monacetin (monoacetin, glycerol monoacetate).

Strychnine poisoning is characterized by severe convulsion without loss of consciousness. Death is usually a result of asphyxia or involvement of vital brain centers. The compound may be identified in the urine soon after ingestion.

Thallium sulfate by ingestion or skin absorption may induce intoxication. Acute poisoning is characterized by severe gastroenteritis following a latent period of 12 to 24 hours. Other effects may include liver and kidney damage, encephalopathy, neuritis, ataxia, and alopecia. Recovery is slow. Thallium may be demonstrated in the urine.

Warfarin — See Coumarins.

Coumarins and *Indandiones* include Diphacin, Fumarin, Pival, (Pivalyn), PMP, Valone, and warfarin.

After repeated ingestion for several days, symptoms may include bleeding from the nose and gums, and into the conjunctiva, urine, and stool. Other possible symptoms are pallor, petechial rash, massive ecchymoses, hematoma of skin and joints, brain hemorrhage, etc. Shock and death may follow.

Laboratory determination of prothrombin time may be helpful in assessing the extent of exposure.

FUNGICIDES

The fungicides are a heterogeneous group of chemicals and, with the major exception of the dithiocarbamates, have been in use for many years. Many of the fungicides such as formaldehyde, furfural, phenol, tetramethylthiuram disulfide and compounds of boron, chromium, copper,

mercury, tin, and zinc (some of which are also used as herbicides and insecticides) are discussed in the section on Chemical Hazards.

The dithiocarbamates include ferbam (ferric dimethyldithiocarbamates), ziram (zinc dimethyldithiocarbamate), maneb (manganous ethylene bisdithiocarbamate), nabam (disodium ethylene bisdithiocarbamate), and zineb (zinc ethylene bis-dithiocarbamate). Their chief adverse effects are irritation of the skin, eyes, and upper respiratory tract.

HERBICIDES

Herbicides, or weed killers, may be classified as pesticide chemicals. They can kill plants on contact, or they can be translocated, that is, absorbed by one part of the plant and carried to other parts where they exert their primary toxic effect. Most of the commonly used herbicides (ammonium sulfamate, dalapon, phenoxyacetic acid derivatives (e.g., 2,4,5—T), carbamate derivatives, petroleum oils, sodium borate, Crag herbicide) have a low toxicity and have caused little difficulty among users.

Some herbicides pose more serious problems; for example, the methemoglobinemia and central nervous system depression produced by sodium chlorate. Pentachlorophenol, a metabolic stimulant, has been responsible for several deaths because of hyperthermia. Pentachlorophenol through skin absorption can also result in peripheral m otor neuropathies. Amino triazole has produced cancer in experimental animals, but there have been no untoward effects reported in man.

Herbicides with cutaneous effects include trichloroacetic acid, a corrosive irritant of the skin and mucous membranes; pentachlorophenol, a producer of a primary irritant type of contact dermatitis; and creosote, a primary irritant and photosensitizer.

Reference may be made to chemicals in the section on Chemical Hazards for the toxicity of the following herbicides: arsenic trioxide and sodium arsenate (see Arsenic), copper sulfate (see Copper and Compounds), creosote compounds, (see Cresol and Phenol), dinitrophenols (see Dinitrophenol), kerosene, and phenylmercuric acetate (see Mercury and Compounds).

FUMIGANTS

Fumigants are pesticides which may be applied in the solid, liquid, or gaseous state. A combination of high volatility with high pest toxicity is generally desired; however, compounds with low volatility may be preferred for soil fumigation. The possibility of excessive exposures exists wherever fumigants are used, as in fumigating grains, soils, clothes, furs, homes, warehouses, barns, ships, mills, freight cars, and greenhouses.

Each of the following compounds has found use as a fumigant.

Because they have other industrial applications as well, they are discussed individually in the section on Chemical Hazards.

Acrylonitrile
Carbon Disulfide
Carbon Tetrachloride
p-Dichlorobenzene (see Chlorinated Benzenes)
Dioxane
Ethylene Dibromide
Ethylene Dichloride
Ethylene Oxide
Hydrogen Cyanide
Methyl Bromide (see Bromine and Compounds)
Methylene Chloride
Methyl Formate
Naphthalene
Perchloroethylene
Propylene Dichloride
Sulfur Dioxide
Tetrachloroethane
Trichloroethylene

MISCELLANEOUS INSECTICIDES

Although the newer synthetic pesticides previously discussed in this section are becoming increasingly popular, the following compounds continue to find significant usage.

Lead Arsenate and Arsenite

These compounds enter the body by inhalation, ingestion, or percutaneous absorption. Signs and symptoms of poisoning are similar to those characteristic of lead or arsenic intoxication. Acute symptoms include nausea, vomiting, abdominal pain, diarrhea, muscle cramps, excitation, and disorientation. Chronic poisoning is manifested by anorexia, weakness, weight loss, pallor, colic, diarrhea, peripheral neuritis, hepatitis, and nephritis. A vesicular dermatitis has frequently been reported. The carcinogenic hazard from chronic arsenic exposure also cannot be ignored.

Nicotine

Nicotine is an extremely toxic alkaloid capable of producing nervous system stimulation followed by severe nervous system depression. The effects may result from ingestion, inhalation, or rapid percutaneous absorption of the material. Analysis for urinary nicotine may aid in the diagnosis.

Pyrethrum

Pyrethrum does not appear to be particularly toxic; however, pri-

mary contact dermatitis and allergic skin and pulmonary reactions have occurred following minimal exposure to the dust.

Rotenone

Rotenone is a plant extract which is more toxic than pyrethrum but, as normally used, is not excessively hazardous. Contact dermatitis and numbness of the oral mucous membranes may follow sufficient exposure.

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