

Chemical Hazards of the Workplace

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ing a transverse white line to loss of nail. Ingestion of the gastrointestinal and kidney damage; acute natory reaction. By analogy in animals, severe pulmonary edema. *Diagnosis:* Differentiate from conjunctivitis and mucous discharge, such as viral infection of the eye and allergies. The bronchial tree becomes inflamed and signs must be sought. In cardiogenic pulmonary edema or bacterial pneumonia. If severe exposure is suspected, studies should include chest x-ray, sputum gram stain and differential white blood cell count. If pulmonary edema occurs, there is an increase in arterial blood gas. Institute appropriate procedures for removal from exposure and treatment of eyes and skin with water. If dermatitis occurs, see the section on treatment of Contact Dermatitis. If severe, hospitalization for 72 hours for delayed onset of edema is advisable. *First Aid:* Maneuvers in Treatment of Victims, Chapter 6. *Preplacement and annual testing:* Emphasis on the eyes and skin; 14" x 17" chest x-ray and FVC and FEV (1 sec.).

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PARATHION



1977 TLV 0.1 mg/m³

Synonyms: O,O-Diethyl O-p-nitrophenyl phosphorothioate; Akron; Niran; Amer. Cyan. 3422; BAY E-605; BLADAN; FOLIDOL E605

Physical Form: Brown or yellowish liquid

Uses: Acaricide; insecticide

Exposure: Inhalation; skin absorption; ingestion

Toxicology: Parathion is an anticholinesterase agent.

Signs and symptoms of overexposure are caused by the inactivation of the enzyme cholinesterase, which results in the accumulation of acetylcholine at synapses in the nervous system, skeletal and smooth muscles, and secretory glands. The sequence of the development of systemic effects varies with the route of entry. The onset of signs and symptoms is usually prompt but may be delayed up to 12 hours.¹⁻⁴ After inhalation, respiratory and ocular effects are the first to appear, often within a few minutes after exposure. Respiratory effects include tightness

in the chest and wheezing due to bronchoconstriction and excessive bronchial secretion; laryngeal spasms and excessive salivation may add to the respiratory distress; cyanosis may also occur. Ocular effects include miosis, blurring of distant vision, tearing, rhinorrhea, and frontal headache.

After ingestion, gastrointestinal effects, such as anorexia, nausea, vomiting, abdominal cramps, and diarrhea, appear within 15 minutes to two hours. After skin absorption, localized sweating and muscular fasciculations in the immediate area usually occur within 15 minutes to four hours; skin absorption is somewhat greater at higher ambient temperatures and is increased by the presence of dermatitis.

With severe intoxication by all routes, an excess of acetylcholine at the neuromuscular junctions of skeletal muscles causes weakness aggravated by exertion, involuntary twitchings, fasciculations, and eventually paralysis. The most serious consequence is paralysis of the respiratory muscles. Effects on the central nervous system include giddiness, confusion, ataxia, slurred speech, Cheyne-Stokes respiration, convulsions, coma, and loss of reflexes. The blood pressure may fall to low levels, and cardiac irregularities, including complete heart block, may occur.

Complete symptomatic recovery usually occurs within one week; increased susceptibility to the effects of anticholinesterase agents persists for up to several weeks after exposure.⁵ Daily exposure to concentrations which are insufficient to produce symptoms following a single exposure may result in the onset of symptoms. Continued daily exposure may be followed by increasingly severe effects.

The minimum lethal oral dose of parathion for humans has been estimated to range from less than 10 mg up to 120 mg.⁷ In a study of 115 workers exposed to parathion under varying conditions, the majority excreted significant amounts of *p*-nitrophenol (a metabolite of parathion) in the urine, while only those with heavier exposures had a measurable decrease in blood cholinesterase.⁸

Parathion itself is not a strong cholinesterase inhibitor, but one of its metabolites, paraoxon, is an active inhibitor. Paraoxon in-

activates cholinesterase by phosphorylation of the active site of the enzyme to form the "diethylphosphoryl enzyme." Over the following 24 to 48 hours there is a process, called aging, of conversion to the "monoethylphosphoryl enzyme." Aging is of clinical interest in the treatment of poisoning because cholinesterase reactivators such as pralidoxime (2-PAM, Protopam) chloride are ineffective after aging has occurred.

The TLV was set at a level to prevent systemic intoxication.¹⁰

Diagnosis: Initial signs and symptoms include headache, blurred vision, pallor, weakness, sweating, abdominal pain, nausea, vomiting, and diarrhea. The signs of moderate to severe intoxication are miosis, lacrimation, excessive salivation, muscle fasciculation, dyspnea, cyanosis, convulsions, shock, cardiac arrhythmias, and coma.

Differential Diagnosis: Diagnosis is based primarily on a history of exposure and clinical evidence of diffuse parasympathetic stimulation.⁴ Careful observation of the effect of atropine and pralidoxime may be valuable. Patients with organophosphate poisoning are resistant to the action of atropine; failure of 1 to 2 mg of atropine administered parenterally to produce signs of atropinization (flushing, mydriasis, tachycardia, or dryness of mouth) indicates organophosphate poisoning. Intravenous injection of 1 g. pralidoxime generally causes some recovery from signs and symptoms of organophosphate poisoning.

Special Tests: The following two types of cholinesterase are clinically significant: true acetylcholinesterase, found principally in the nervous system and the red blood cell; and pseudo- or butyrylcholinesterase, found in the plasma, liver, and nervous system. Although the action of both types is inhibited by organophosphates, the level of depression of red blood cell cholinesterase is a better indicator of clinically significant reduction of cholinesterase activity in the nervous system.

Laboratory evidence of depression of red blood cell cholinesterase to a level substantially below pre-exposure levels (at least 50 per cent and usually much lower) is verification of organophosphate poisoning.

There are many different methods for estimation of cholinesterase content of blood, and associated with each method is a differ-

ent set of normal values and a different set of reporting units. The laboratory report of a cholinesterase determination should state the units involved along with the appropriate normal range. Based on the Michel method, the normal range of red blood cell cholinesterase activity (delta pH/hour) is 0.39 to 1.02 for men and 0.34 to 1.10 for women.¹¹ The normal range of the enzyme activity (delta pH/hour) of plasma is 0.44 to 1.63 for men and 0.24 to 1.54 for women.

Treatment: Treatment of organophosphate poisoning ranges from simple removal from exposure in very mild cases to the provision of very rigorous supportive and antidotal measures in severe cases.^{4,6} In the moderate-to-severe case, because of pulmonary involvement, there may be need for artificial respiration using a positive-pressure method. Careful attention must be paid to removal of secretions and to maintenance of a patent airway. Anticonvulsants such as thiopental sodium may be necessary. Maintenance of respiration is critical, since death usually results from weakness of the muscles of respiration and accumulation of excessive secretion in the respiratory tract.

As soon as cyanosis has been overcome, 2 to 4 mg of atropine should be given intravenously. (Atropine may induce ventricular fibrillation in the presence of cyanosis.) *This dose of atropine is approximately ten times the amount which is administered for other conditions in which atropine is considered therapeutic.* This dose should be repeated at five- to ten-minute intervals until signs of atropinization appear (dry, flushed skin, tachycardia as high as 140 beats per minute, and pupillary dilatation). A mild degree of atropinization should be maintained for at least 48 hours.

Pralidoxime (2-PAM, Protopam) chloride is a cholinesterase reactivator which complements the action of atropine. In the moderate-to-severe case the dose for adults is 1 g. injected intravenously at a rate not in excess of 500 mg/minute. After an hour, a second dose of 1 g. is indicated if muscle weakness has not been relieved. Treatment with pralidoxime chloride will be most effective if given within 24 hours after poisoning. Morphine, aminophylline, and phenothiazines are contraindicated.

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25 April 1966

Defoliant Money from Army
Research Office

Conference, SDX, J. R. Key and
Col. Klinker, ARD, 21 April 1966

A. W. Lasley, Washington

J. R. Key, Washington
F. J. Winslow, Boston
T. L. Gossard/C. J. Lby, Da:
L. E. Hardy, Dayton
P. C. Mann, St. Louis
J. D. Early, Washington

J. R. Key and I visited Lt. Col. Louis G. Klinker, Dr. Joseph Rajerwicz, and Dr. Eugene M. Sporn of the Army Research Office in Arlington, Virginia, 21 April 1966.

The purpose of the visit was to see how we could get more Army funds for further Defoliant work, presumably from a source other than Ft. Detrick.

Col. Klinker described a technique for getting money out of places like the Limited War Laboratories at Aberdeen. If a company has a product they think can perform a real service now in Vietnam, they can send a description (really a proposal) to Klinker, who will send it to Gen. Cowan in Vietnam. If Cowan thinks it might meet the need, but still falls outside any definite military specification, he will endorse it back to Klinker with a request that it be tested in Vietnam even though it doesn't meet an officially stated specification or need. Klinker will then be in a position to get money and permission for a field test. Our original memorandum to Klinker should show Statement of Objective; Operational Concepts; Justification; and Other Considerations in a form similar to that described on p. 10 of AR 71-1, revised 18 June 1964.

Klinker stressed that the company must be willing to lay its reputation on the line. This should be an item which is already in a state of advanced development.

It sounded to me as though this procedure is made to order for a situation like Dow and "Tordon" a year ago.

Two possibilities were discussed here. One was Monsanto Company's rice sterilants, developed entirely on proprietary money. Yes, if Ag. Division agreed to, they could present a proprietary rice sterilant to the Army on this basis. I don't feel that MRC should take any position pro or con on this. If Col. Klinker and Gen. Cowan were suitably impressed, this could result in a small sale of chemical immediately, and potential development of a large application.

The other possibility was that we might wish to state that one of our fastest acting cyanide compounds (or trialkyltin cyanide) coupled with a herbicide like 2,4-D would give faster knock-down plus a long-term effect. (I have suggested to Detrick last week that they could have re-evaluated such a combination.) If we sold this to Army Research Office by the above-described procedure, it is at least possible that we could get an order for enough of the iodide for a field test. If the field test were successful this might become ~~the new Army defoliant~~

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ues: a different set of laboratory report of amination should state the ing with the appropriate d on the Michel method, red blood cell cholinesterase pH/hour) is 0.39 to 1.02 to 1.10 for women.¹¹ The enzyme activity (delta) is 0.44 to 1.63 for men women.

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It is of great importance to decontaminate the patient. Contaminated clothing should be removed at once, and the skin should be washed with generous amounts of soap or detergent and a flood of water; this is best accomplished under a shower or by submersion in a pond or other body of water if the exposure occurred in the field. Careful attention should be paid to cleansing of the skin and hair.

The patient should be attended and monitored continuously for not less than 24 hours, since serious and sometimes fatal relapses have occurred because of continuing absorption of the toxin or dissipation of the effects of the antidote.

Regeneration of cholinesterase is primarily by synthesis of new enzyme and takes place at the rate of approximately 1 per cent/day.³ A patient who has recovered from the acute phase of poisoning remains hypersusceptible to anticholinesterases for up to several weeks.

Medical Control: Preplacement and annual physical examination with determination of pre-exposure red blood cell cholinesterase activity. A person whose red blood cell cholinesterase falls to or below 40 per cent of the pre-exposure baseline should be removed from further exposure until the activity returns to within 80 per cent of the pre-exposure baseline.

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PENTABORANE

B₅H₉ 1977 TLV 0.005 ppm

Synonyms: Dihydropentaborane (9); pentaboron undecahydride

Physical Form: Volatile liquid

Uses: Reducing agent in propellant fuels

Exposure: Inhalation; skin absorption; ingestion