Protocol for organophosphate poisoning management

Category/Use: Used as an insecticide

Specific substances: Mentioned in the range of toxicity table

Range of toxicity:

<table>
<thead>
<tr>
<th>HIGHLY TOXIC (LD₅₀&lt;50mg/kg)</th>
<th>INTERMEDIATE TOXIC (LD₅₀ 50-100mg/kg)</th>
<th>LOW TOXIC (LD₅₀&gt;1000mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) TEPP</td>
<td>1) Coumaphos</td>
<td>1) Dichlorvos</td>
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<tr>
<td>2) Phorate</td>
<td>2) Crufomate</td>
<td>2) Chlorpyrifos</td>
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<td>3) Mevinphos</td>
<td>3) Famphur</td>
<td>3) Fenthion</td>
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<td>4) Fensulfothion</td>
<td>4) Fenitrothion</td>
<td>4) Diazinon</td>
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<tr>
<td>5) Demeton</td>
<td>5) Ronnel</td>
<td>5) Dimethoate</td>
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<tr>
<td>6) Disulfoton</td>
<td>6) Trichlorfon</td>
<td>6) Malathion</td>
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<tr>
<td>7) Parathion</td>
<td>7) Acephate</td>
<td>7) Abate</td>
</tr>
<tr>
<td>8) Fonophos</td>
<td>8) Crotosyphos</td>
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<tr>
<td>9) Monocrotophos</td>
<td>9) Cynophos</td>
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<td>10) Cythioate</td>
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</tbody>
</table>

Mortality rate: Not available

Clinical presentation: Similar toxicities can occur regardless of the route of exposure.

Common signs and symptoms of acute toxicity:

DUMBELS: Diarrhea, Urination, Miosis, Bronchospasm, Emesis, Lacrimation, Salivation
SLUDGE: Salivation, Lacrimation, Urination, Diarrhea, GI distress, Emesis

Other common signs and symptoms include muscle fasciculations and weakness, seizures, respiratory depression, tachycardia, and elevated blood pressure. Symptoms may occur within 5 minutes following a large ingestion and death is possible within 15 minutes. Most patients will be symptomatic within 8 hours of exposure, nearly all within 24 hours.

Population-dependent:

Pediatrics: Children often do not present with the classic DUMBELS/SLUDGE syndrome. More commonly, they experience CNS effects with seizures, lethargy, stupor, coma, and muscle weakness and flaccidity.
Comprehensive listing by system (listed alphabetically):

**Cardiovascular:** Asystole, AV block, bradycardia (less common in children), chest tightness, hypertension, hypotension, myocarditis, pallor, QT prolongation, tachycardia, ventricular arrhythmia

**Central nervous system:** Agitation, anxiety, ataxia, coma (more common in children), confusion, depression, dizziness, dysarthria, headache, lethargy (more common in children), loss of consciousness, memory loss, restlessness, seizures (adults: 2% to 3%, children: 22% to 25%), toxic psychosis

**Endocrine & metabolic:** Hyperglycemia (severe poisoning), metabolic acidosis (severe poisoning)

**Gastrointestinal:** Abdominal pain, cramps, diarrhea, fecal incontinence, nausea (early symptom), salivation (early symptom; common in adults and children), vomiting

**Hematologic:** Decreased platelet count and red blood cell count

**Neuromuscular & skeletal:** Choreoathetosis, muscle twitching, muscle weakness, paralysis (common in children), skeletal muscle fasciculations (less common in children), paresthesia, tremor, unsteadiness, weakness

**Ocular:** Blurred vision, lacrimation (early symptom; less common in children), miosis (unreactive to light; common in adults and children), myopia (children)

**Renal:** Urinary incontinence

**Respiratory:** Acute lung injury, bronchorrhea, bronchospasm, chemical pneumonitis, cough, diaphragmatic paralysis, pulmonary edema (noncardiogenic), respiratory depression, respiratory arrest, respiratory failure, rhinorrhea (early symptom), tachypnea, wheezing

**Miscellaneous:** Diaphoresis (early symptom; less common in children)

**Mechanism of Toxicity:**

If the patient does not receive an oxime, organophosphates cause irreversible inhibition of cholinesterase enzymes, resulting in excess accumulation of acetylcholine at muscarinic and nicotinic receptors, and in the periphery and central nervous system. The signs and symptoms of organophosphate poisoning are an expression of acetylcholine excess at a variety of nerve terminals - a combination of muscarinic and nicotinic effects. The central nervous system effects (eg, seizures) may be mediated by activation of N-methyl-D-aspartate (NMDA) glutamate receptors and inhibition of central GABA neurotransmission.
**Pharmacokinetics:**

Route of exposure: Inhalation, oral ingestion, dermal contact
Onset of action: Toxicity: Oral: Within 2 hours; dermal: Delayed up to 12 hours; inhalation: Within 30 minutes of exposure
Absorption: May occur through multiple routes; most organophosphates are absorbed from the conjunctiva, skin, GI tract, respiratory tract. The rate of dermal absorption may be dependent upon the solvent used.
Distribution: Pesticides may be secreted in breast milk.
Metabolism: Hepatic hydrolysis; conversion from thions to oxons (more toxic); oxons break down more readily to less toxic metabolites
Elimination: Renal

**Criteria for hospital admission:**

If major toxicity has occurred, the patient will require admission to an intensive care unit. Patients should have continuous cardiac monitoring for 12-24 hours after their last dose of antidote and then can be moved to an unmonitored bed.

**Monitoring parameters:**

Monitor ECG, pulse oximetry or arterial blood gases, serum amylase isoenzymes and cholinesterases.

**First aid measures:** Oral exposure: None of the decontamination methods are recommended at prehospital set up and patient needs medical assessment. For other types of exposure, same as decontamination method explained in treatment part.

**Treatment:**

**Oral exposure:**

**Stabilization**

Initially, evaluate and correct immediate life-threatening complications (eg, airway, breathing, and circulation). The most common serious complications are seizures, seizure-related hypoxia, and respiratory failure. Ensure that a clear airway exists. Suction excess secretions. Assess adequacy of oxygenation; close monitoring for sudden respiratory failure. Patients with significant bronchial secretions, severe muscle weakness, or significant CNS depression should receive supplemental oxygen and be intubated early if necessary.
Decontamination method

Emesis: Emesis is not recommended.

If the patient presents within 1 hour of ingestion, consider the following decontamination procedure(s):

Activated charcoal: Minimum of 240 milliliters of water per 30 grams charcoal.
- Adults and Adolescents dose: 25 to 100 grams
- Children aged 1 to 12 years: 25 to 50 grams
- Infants up to 1 year old: 0.5 to 1 gram/kilogram.

Gastric lavage: Gastric lavage is recommended (generally within 60 minutes).

Specific antidote:

Atropine: Effective for the treatment of the muscarinic effects (e.g., hypersecretion, bronchoconstriction, pulmonary edema, nausea, vomiting, cramps, bradycardia, hypotension, miosis, frequent urination) of poisoning. Atropine will not reverse nicotinic effects (e.g., muscular weakness).
- If muscarinic symptoms are present administer IV atropine until atropinisation is achieved

Therapeutic Dose:
- Adult: 2 to 5 milligram slowly IV until full atropinization.
- Child: 0.05 milligram/kilogram slowly IV until full atropinization.

Severe poisonings: Atropine infusion rates of 0.02 to 0.08 milligram/kilogram/hour

Pralidoxime: Primarily effective for nicotinic effects (muscular weakness including diaphragmatic and respiratory muscles) of poisoning.
- Indications for use: Muscle fasciculations and weakness, respiratory depression; if possible, begin therapy early to reactivate acetylcholinesterase enzyme.
- Bolus: 30 milligrams/kilogram followed by an infusion of more than 8 milligrams/kilogram/hour.
- Alternative Adult dose: 1 to 2 grams diluted in 100 milliliters of normal saline infused over 15 to 30 minutes.
- Alternative Child dose: An alternative initial dose for children is 20 to 50 milligrams/kilogram (maximum 2 gram/dose) infused over 30 minutes as a 5% solution in normal saline.
Continuous Infusion:
**Adult:** 8 milligrams/kilogram/hour following the initial loading dose.
An alternative is infusion of 500 milligram/hour as a 2.5% solution. A 5% solution may be used in patients with pulmonary edema.

**Child:** 10 to 20 milligrams/kilogram/hour of a solution containing 10 to 20 milligrams of pralidoxime/millitre.

**Duration of intravenous dosing:** Continued for at least 24 hours after cholinergic manifestations are resolved.

**Maximum dose:** 12gm in 24 hours for adults and dose may be exceeded in severely poisoned patients.

Glycopyrrolate:
**Adult:** 2ml of 0.4mg strength IV over 3 to 5 minutes along with atropine 1ml of 1 mg strength and repeated until the secretion dry up.

**Supportive treatment:**

Seizures

Diazepam:
**Adult:** 5 to 10 milligrams initially, repeat every 5 to 10 minutes. Can go up to 30 milligram. If seizures persist or recur after diazepam 30 milligram consider second agent.

**Child:** 0.2 to 0.5 milligram per kilogram (5 milligrams maximum), repeat every 5 to 10 minutes as needed. If seizure persist in children above 5 year 10 milligram and age below 5 year 5 milligram.

Recurring seizures:

Midazolam:

**Child:** 0.2 milligram/kilogram IM (max 7mg) or intranasally.

Lorazepam:

**Adult:** 2 to 4 milligrams IV. Initial dose may be repeated twice at intervals of 10 to 15 minutes if seizures persist.

**Child:** 0.05 to 0.1 milligram/kilogram IV (max 4mg/dose). Initial dose may be repeated twice at interval of 10-15 min if seizure persists.

Phenobarbital:

**Adult:** 20 milligrams per kilogram diluted in 0.9 percent saline given at 25 to 50 milligrams per minute. An additional 10mg/kg may be given if seizure persist or recur.
Child: 15 to 20 milligrams per kilogram IV is given.

Inhalation exposure:
Decontamination: Remove the patient from the source of exposure and bring into fresh air. Monitor for respiratory distress.
Treatment: Monitoring Parameters and Treatment and management of complication same as oral exposure

Eye exposure:
Decontamination: Remove the patient from exposure and irrigate exposed eyes with copious amounts of water or room temperature 0.9% saline for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persists after 15 minutes of irrigation, an ophthalmologic examination should be performed. Carefully observe patients with eye exposure for the development of systemic toxicity.
Treatment: Treatment should include recommendations listed in the oral exposure section when appropriate.

Dermal exposure:
Decontamination: Remove contaminated clothing. Wash the skin, including the hair, beneath the nails and umbilical for three times.
Treatment: If systemic toxicity develops treatment should include recommendation listed in oral exposure.

Elimination enhancement method:
Dialysis and hemoperfusion are not indicated. Hemoperfusion, hemodialysis, and exchange transfusion have not been shown to affect outcome or duration because of the large volume of distribution.

Criteria for emergency department discharge:
If the patient has ingested or inhaled a nonfat-soluble organophosphate and is not symptomatic 12 hours after exposure, then the patient is probably safe for discharge.

Complications of Exposure:
Intermediate syndrome: Occurs 24-96 hours after exposure; characterized by acute respiratory paresis and muscular weakness (primarily facial, neck, and proximal limb muscles). May be accompanied by cranial nerve palsies and depressed tendon reflexes. The syndrome lacks muscarinic symptoms (eg, diarrhea, urinary frequency, miosis, bradycardia, bronchorrhea, bronchoconstriction, lacrimation, salivation).
Organophosphate-induced delayed neuropathy (OPIDN): Weakness/paralysis and paresthesia of the extremities (primarily legs); may persist for weeks to years. Rarely occurs but is more common with several classes of organophosphates (eg, phosphonates, phosphoramidates, phosphates).

**Chronic effects:** Long-term neuropsychiatric sequelae with decreases in memory and concentration and mood disturbances.

**Contraindications:**
Avoid the use of cholinesterase inhibitors; concurrent use can worsen symptoms of poisoning. Avoid use of succinylcholine as it may prolong paralysis (Selden, 1987). Avoid use of central nervous system depressants; they may further decrease respiratory drive.

**References:**