Organophosphate Poisoning [created by Paul Young 02/10/07]

general

- Organophosphorus pesticides are the most important cause of severe toxicity and death from acute poisoning worldwide, with more than 200 000 deaths each year in developing countries.

sources

Sources of organophosphorus pesticides

Domestic

- Garden sheds—in particular insecticidal preparations but also other products that are marketed as fertilisers but contain some organophosphorus pesticides, available as solid or liquid formulations
- Surface and room sprays
- Baits for cockroaches and other insects (for example, chlorpyrifos)
- Shampoos against head lice (for example, malathion)
- Pet preparations (for example, pet washes, collars)

Industrial or occupational

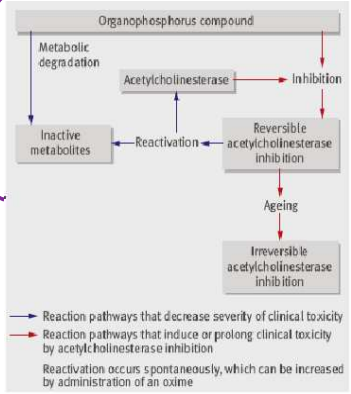
- Crop protection and livestock dipping
- Large scale internal control, including fumigation

Terrorism or warfare (nerve agents)

Sarin, for example, was used in the Tokyo subway attack, and both tabun and sarin were used during the Iraq-Iran conflict. Although nerve agents share a similar mechanism of toxicity with organophosphorus pesticides, their treatment is a specialised topic and not dealt with in this review

mechanism

- Organophosphorus compounds inhibit numerous enzymes, of which esterases seem to be the most clinically important.
- Inhibition of acetylcholinesterase leads to the accumulation of acetylcholine at cholinergic synapses, interfering with normal function of the autonomic, somatic, and central nervous systems.
- This produces a range of clinical manifestations, known as the acute cholinergic crisis



clinical features

DUMBELS (diarrhea, urination, miosis, bronchospasm, emesis, lacrimation, salivation)
SLUDGE (salivation, lacrimation, urination, defecation, emesis)

diagnostic tests

- When the diagnosis is in question or there is doubt about the significance of an organophosphorus exposure, quantification of butyrylcholinesterase or acetylcholinesterase activity is helpful.
- Cholinesterase activity that is less than 80% of the lower reference range is probably indicative of a significant exposure to an organophosphorus compound; with severe clinical toxicity, the erythrocyte acetylcholinesterase activity is less than 20% of normal.
- Butyrylcholinesterase has no relation to the severity of clinical toxicity

treatment - general

Suggested symptom based treatment recommendations for organophosphorus poisoning

Sign or symptom	Recommended therapy
Excessive salivation, lacrimation, nausea and vomiting, diarrhoea	Atropine, glycopyrrolate
Bronchorrhoea, bronchospasm	Atropine, ipratropium, glycopyrrolate
Hypotension	Fluids, atropine, vasopressors, inotropes
Bradycardia	Atropine, glycopyrrolate
Eye pain	Mydriatics, cycloplegics
Muscle weakness	Oximes
Respiratory failure	Intubation and ventilation, oximes
Seizures	Benzodiazepines

- all patients require decontamination

- The three most widely used classes of antidotes are muscarinic antagonists (usually atropine) oximes (usually pralidoxime or obidoxime), and benzodiazepines.
- oximes should be given as early as possible to prevent ageing

specific treatments

Atropine
- For poisoning in adults initially give 1-3 mg atropine intravenously (0.02 mg/kg in children).
- The main end points of atropinisation are a clear chest on auscultation with resolution of bronchorrhea (focal crepitations or wheeze may be noted when there has been pulmonary aspiration) and a heart rate of more than 80 beats/min.
- If these targets are not achieved by 3-5 minutes, double the intravenous dose. Continue to double the dose and give intravenously every 3-5 minutes until atropinisation has been achieved.
- Large doses (hundreds of mg) may be required in some patients.
- Maintain atropinisation by infusion, starting with 10%-20% of the loading dose every hour.
- Regular clinical observations are necessary to ensure that atropinisation is achieved without toxicity (delirium, hyperthermia, and ileus)

Oximes
- Several oximes have been developed, but two are more commonly used for treatment of acute organophosphorus poisoning. They are administered as an infusion which should be continued until recovery (12 hours after stopping administration of atropine or once butyrylcholinesterase is noted to increase)
- Pralidoxime chloride-loading dose of 30 mg/kg intravenously over 20 minutes, followed by an infusion of 8 mg/kg/h. In adults it is usually given as a 2 g loading dose followed by 500 mg/h. Various salts are available and their dose is determined by converting this dose into equivalent dosing units-for example, 1 g pralidoxime iodide is roughly equal to 650 mg pralidoxime chloride
- Obidoxime-loading dose of 4 mg/kg over 20 minutes, followed by an infusion of 0.5 mg/kg/h. In adults it is usually given as 250 mg loading dose followed by 750 mg every 24 hours

Benzodiazepines (LB)
- Benzodiazepines are usually given intravenously as required for agitation or seizures-with doses starting at: 5-10 mg diazepam (0.05-0.3 mg/kg/dose), lorazepam 2-4 mg (0.05-0.1 mg/kg/dose), or midazolam 5-10 mg (0.15-0.2 mg/kg/dose)

Decontamination
- Dermal spills-wash pesticide spills from the patient with soap and water and remove and discard contaminated clothes, shoes and any other material made from leather
- Gastric lavage-consider for presentations within 1 or 2 hours, when the airway is protected. A single aspiration of the gastric contents may be as useful as lavage
- Activated charcoal without cathartic-50 g may be given orally or nasogastrically to patients who are cooperative or intubated, particularly if they are admitted within one or two hours or have severe toxicity