Organochlorines

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Introduction

- The organochlorine insecticides proved to be nonvolatile, inexpensive to manufacture, environmentally stable, and relatively less toxic than previous insecticides
- These properties led to the widespread use of this class of insecticides
- Utilization of organochlorines has had a tremendous impact on human health (bioconcentration) and environmental persistence
- These properties eventually led to a ban on DDT in the United States, and subsequent bans on other organochlorine insecticides

- Because Organochlorine insecticides are very effective and cheap, they are still widely used in developing countries

Classification

Organochlorine insecticides belong to four distinct structural classes:

1. Diphenyl aliphatics (e.g., DDT and related compounds),
2. Cyclodienes (e.g., aldrin, dieldrin, endrin, endosulfan, heptachlor),
3. Cyclohexanes (e.g., γ-hexachlorocyclohexane, known more commonly as lindane), and
4. Polychloroterpenes (e.g., toxaphene).

The organochlorine pesticides chlordecone and mirex are also called cage compounds; they do not fall into a distinct category, although they are sometimes classified with the cyclodienes.

Physical appearance

- These compounds are available as dusting powders, wettable powders, emulsions, granules and solutions.

Generic Name	Brand name
• Aldrin	Agroaldrin, aldrin 30, Alditon
• Chlordane DDT	Agrodane 20EC, chlordane, termex
• DDT	DDT sudarshan 50, ramdit, soltax, sunbrand, tafidex
• Endosulfan	Agrosulfan, hildon, thiodan
• Hepatochlor	Heptaf 50, Heptox
• Lindane	Lindane 20, lindex, scabex, Ultrascab

Common organochlorines

Fatal Dose

- **Extremely toxic**: endrin, aldrin, chlordane, and toxaphene

Dieldrin is placed in the extremely toxic category (LD50: 1 to 50 mg/kg)

- **Highly toxic**: kepone, heptachlor, mirex. DDT, endosulfan, and lindane are considered highly toxic(LD50: 51 to 500 mg/kg),

- **Least toxic**: methoxychlor, perthane, kelthane, chlorobenzilate, and hexachlorobenzene

Toxicokinetics

- All the organochlorines can be absorbed transdermally, orally, and by inhalation. The efficiency of dermal absorption is variable between different compounds.
- Gastrointestinal absorption increases in the presence of absorbable lipid (animal or vegetable) fat
- Most organochlorines are metabolized to some degree, being dechlorinated, oxidized, and then conjugated
- Metabolised slowly and persist in tissues (especially fat) for prolonged periods

Toxicokinetics

- The primary mode of elimination is through biliary excretion
- These organochlorines often undergo enterohepatic and enteroenteric circulation
- Nearly all organochlorines yield measurable urinary metabolites
- Excretion of organochlorine compounds does not follow first order kinetics.
- This may be due to complex lipoprotein binding

Mechanism of action

- Organochlorine insecticides kill insects is through their neurotoxicity.
- To humans, the predominant system affected is the nervous system.
- DDT and analogues affect the sodium channel and sodium conductance across the neuronal membrane which lead to sustained depolarization of the neuronal membrane, resulting in continued release of neurotransmitters and **central nervous system excitation.**
- They also alter the metabolism of serotonin, noradrenaline and acetylcholine.

Mechanism of action

- DDT may also have the effect of increasing serotonin and norepinephrine(inhibitory) breakdown as well as increasing levels of aspartate and glutamate (excitatory) in the central nervous system results in imbalance between them and leads to central nervous system excitation
- The cyclodienes and lindane appear to inhibit the GABAmediated chloride channels in the CNS which leads to increased nerve impulses
- Endosulfan involves inhibition of the calmodulin-dependant Ca2+ -ATPase activity, alterations in the serotoninergic system, and inhibition of GABA receptors.

Mechanism of action

- Chlorinated hydrocarbons, particularly toxaphene, chlordane, DDT, and lindane have enzyme induction capacity

- Most of these agents cause liver necrosis and they are potent enzyme inducers

Clinical Presentation

ACUTE

- GIT: nausea, vomiting, abdominal pain, hyperaesthesia or paraesthesia of the mouth and face

- CNS: headache, vertigo, myoclonus, tremor, ataxia, nervousness, amnesia, rapid and dysrhythmic eye movements, mydriasis, weakness, agitation, confusion, and convulsions. Occasional reports have associated peripheral neuropathy with exposure to organochlorines.

- Other systems: fever, aspiration pneumonitis, renal failure. Coronary spasm, hypotension, and sinus tachycardia, metabolic acidosis, respiratory depression

Clinical Presentation

CHRONIC

- Weight loss, tremor, weakness, opsoclonus, ataxia, pseudotumour cerebri, abnormal mental changes, oligospermia, and increased tendency to leukaemias, thrombocytopenic purpura, aplastic anaemia, hepatomegaly, centrilobular hepatic necrosis and liver cancer

Diagnosis

- History
- Abdominal radiograph may reveal the presence of certain Organochlorines which are radio opaque.
- Organochlorides can be detected in the serum, adipose tissue and urine by gas chromatography.
- Measurement of organic halogen compounds in urine is suggested as an indicator of exposure.

MANAGEMENT

- Specific Decontamination based on route of administration.
- Stabilize ABC
- Administer 100% humidified supplemental oxygen, Perform endotracheal intubation and provide assisted ventilation as required.
- Administer inhaled beta adrenergic agonists if bronchospasm develops.

MANAGEMENT

- Do not give oils by mouth. They tend to increase the intestinal absorption of these lipophilic toxicants.
- Seizures should be controlled with benzodiazepines, phenytoin or phenobarbitone in the usual way. If they are not effective enough, sodium thiopentone can be administered iv or neuromuscular blockade is done
- In one series of endosulfan poisoing, hydantoin and benzodizepines were not effective in controlling seizures, but phenobarbitone is effective.

Management

- Hypoxia, electrolyte disturbances, and hypoglycaemia should be treated

- Cholestyramine a non-absorbable bile acid binding anion exchange resin, is effective in enhancing the faecal excretion of organochlorine compounds, particularly chlordecone (Dose 16g/day for several days).

- Hyperthermia should be managed aggresively with cooling.

- Haemodialysis and haemoperfusion have not been proven effective.

Contraindications

- Oil-based cathartics, adrenaline, and atropine should not be given

THANK YOU