Pesticides

- **Pesticides: substances or mixtures of substances intended to prevent, destroy , repel or mitigate any pest.**
- **Pests: undesirable organisms…. Insects, fungi, herbs, rodents or worms.**
- **Poisoning occurs due to careless use, misuse or occupational exposure**
- **<u>Classification:</u>**

1. **Insecticides**
2. **Rodenticides**
3. **Herbicides : for weed control**
4. **Fungicides**

PESTICIDES – RISKS AND BENEFITS

BENEFITS

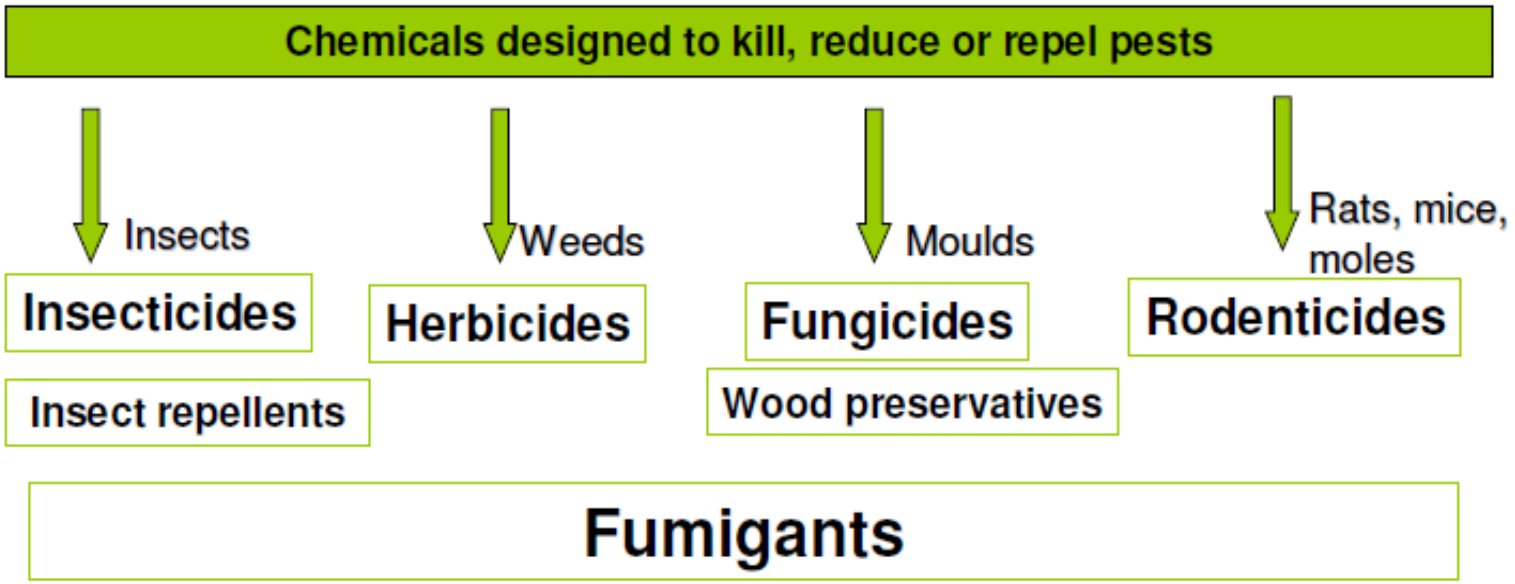
- Crop protection
- Food preservation
- Material preservation
- Disease control

RISKS

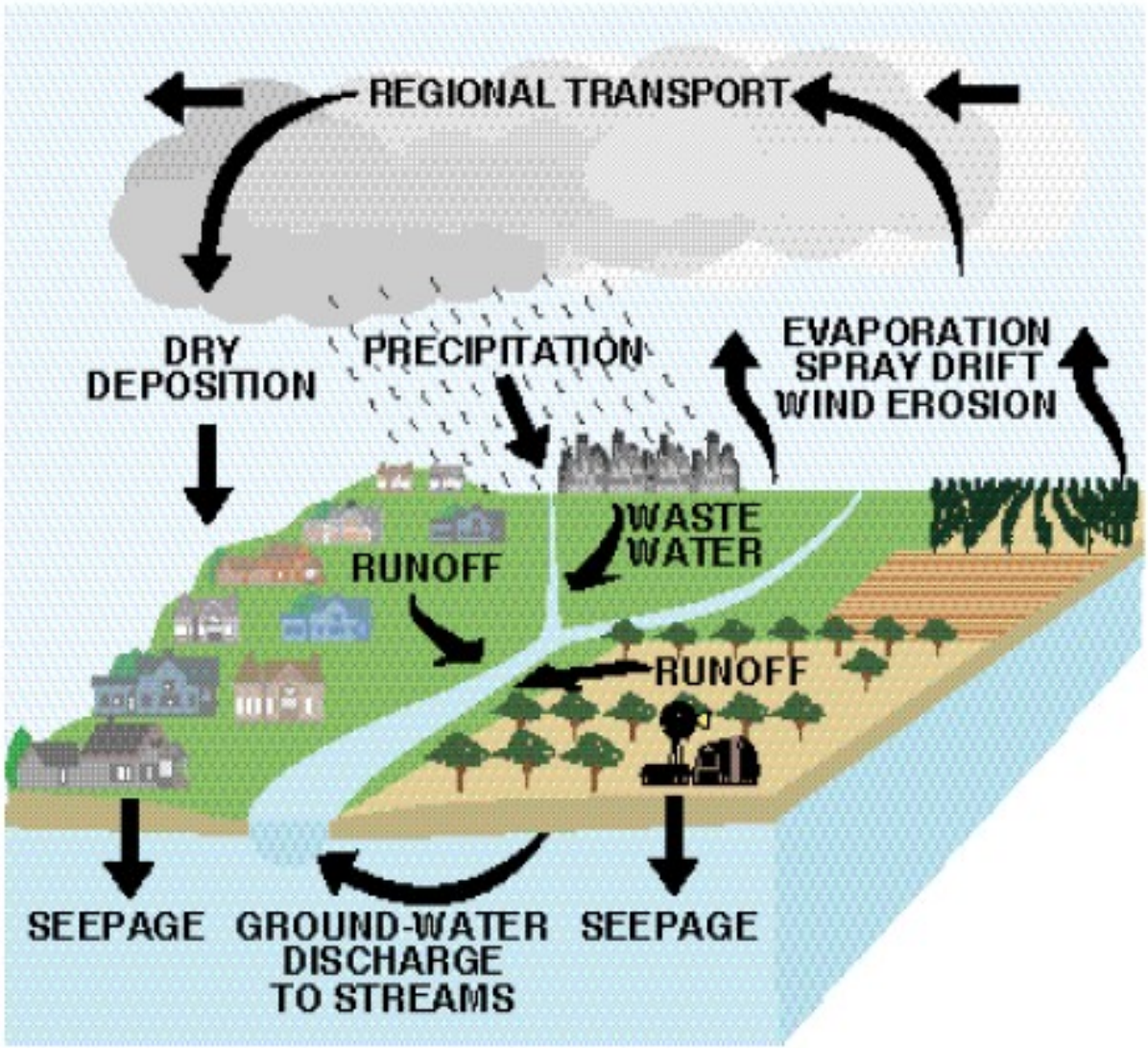
- Toxic to humans
- Impact on environment and ecosystems

Pesticides

PESTICIDES – CLASSIFICATION BY USE



PESTICIDES IN THE ATMOSPHERE AND WATER



USGS

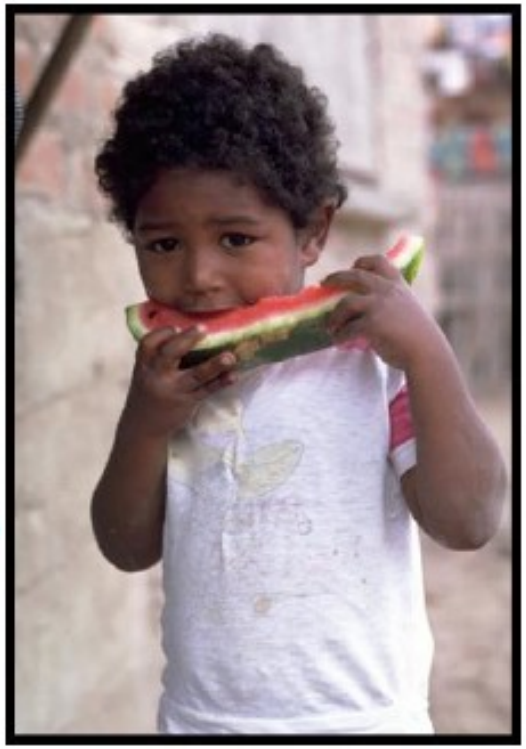
PESTICIDES IN DIFFERENT MEDIA

Water

- Pesticides in drinking water: tap, well

Food

- Crops routinely sprayed:
  - fruits, vegetables, grains
- Bioaccumulation in animals and products
  - fish, meat, eggs, dairy



WHO

I- Organophosphate Poisining

- Volatile substances,lipophilic , garlic odour.
- Used as nerve gases in World war II

- **Pathophysiology:**

Acetylcholine (ACh) is one of the main neurotransmitters of CNS. It is released at the cholinergic nerve endings and may be excitatory or inhibitory; it initiates muscular contraction at neuromuscular junctions. Acetylcholine receptors (cholinoceptors) fall into two main classes: muscarinic and nicotinic receptors. Once acetylcholine has been released it has only a transitory effect because it is rapidly broken down by the enzyme cholinesterase.

- **cholinesterase (acetylcholinesterase) An enzyme that hydrolyses the neurotransmitter acetylcholine to choline and acetate. Cholinesterase is secreted by nerve cells at synapses and by muscle cells at neuromuscular junctions. Organophosphoshates inhibit the action of cholinesterase**.
- **Organophosphates inactivate AChE by phosphorelation.**
- **Two forms of AChE:**
  - **True: RBCs, CNS, Skeletal muscles**
  - **Pseudo ChE: Plasma, liver.**
- **Once AChE has been inactivated, ACh accumulates throughout the nervous system, resulting in overstimulation of muscarinic and nicotinic receptors.**
- **Clinical effects are manifested via activation of the autonomic and central nervous systems and at nicotinic receptors on skeletal muscle (Cholineregic toxic syndrome).This syndrome persists until reactivation of the enzyme occurs by use of oximes or synthesis of new enzyme.**
- **Response to oximes declines with time due to aging of the enzyme.**
- **Although most patients rapidly become symptomatic, onset and severity of symptoms depend on specific compound, amount, route of exposure, and rate of metabolic degradation.**

- **Organophosphates are clssified into:**

1- Direct inhibitors: Malathion, Paraoxon, tetra-ethyl-pyro-phosphate (TEPP).

2- Indirect inhibitors : become active after being converted within body to other active metabolites : Parathion

- **Mode of Poisoning:**

- Organophosphates can be absorbed cutaneously, ingested, inhaled or injected.

1- Accidental: workers during spraying or dusting of trees OR manufacture of the compounds

2- Commonly suicidal: easy to obtain, rapid action, e.g. Drink Police El-Nagda (Parathion).

3- Homicidal: mix compounds with foods

Clinical Presentation:

1- Acute poisoning (Cholinergic crisis): classical presentation...episodes of relapse between episodes of control.Relapses are caused by redistribution in the body or delayed absorption from the gut.

- Other syndromes may follow cholinergic crisis or complicate the condition in some patients such as:

2- Intermediate syndrome: may occurs 2-3 days after exposure.

3- Delayed neuropathy: may occurs 2-3 weeks after exposure.

4- Cardiotoxicity

I- Acute poisoning (Cholinergic crisis)

- Can be divided into 3 broad categories, including:

(1) Muscarinic effects

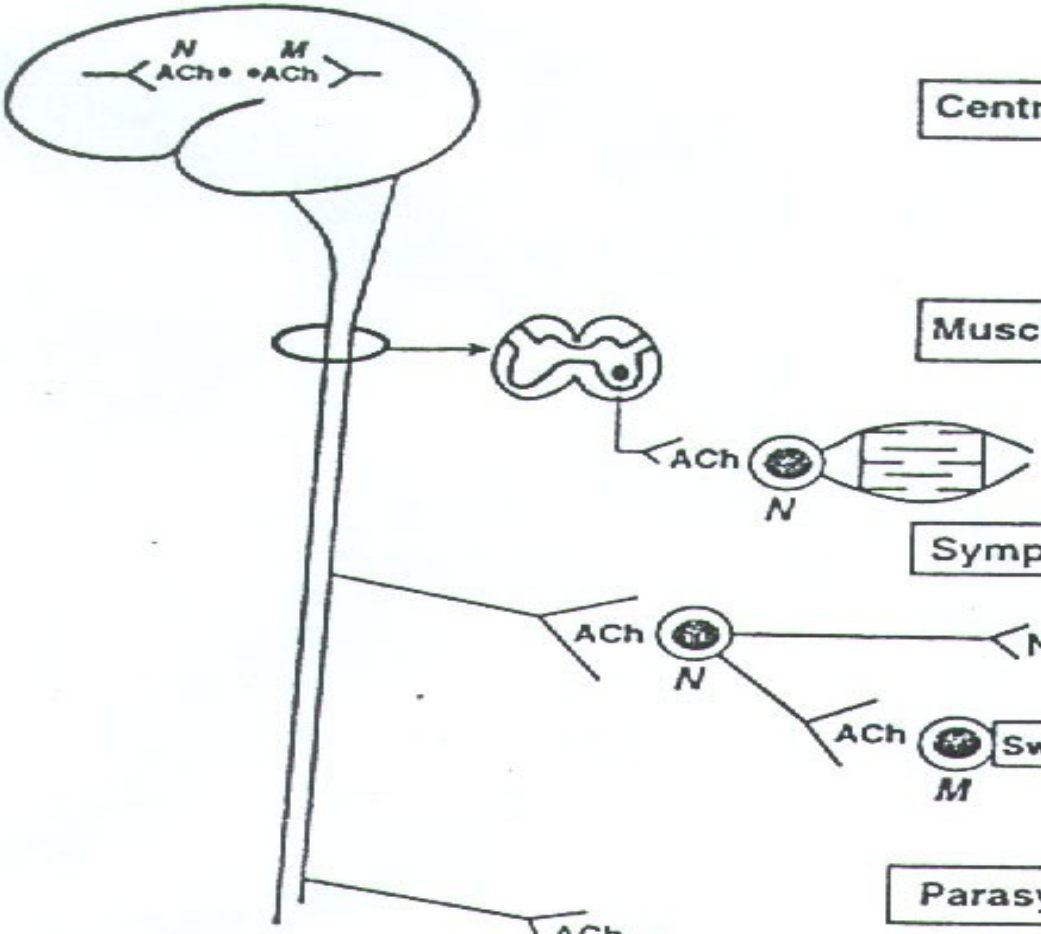
- GIT : Nausea, vomiting, abdomonal colic.
- SLUD syndrome : salivation, diaphoresis, lacrimation, urination, diarrhea,
- Respiratory system:Bronchial spasm, wheezing, increased broncheal secretion.
- Slow bounding pulse
- Miosis (pinpoint pupil)

(2) Nicotinic effects:

- Muscle weakness, fasiculation (around eye lid), twitches, tremors, convulsions may be followed by paralysis
- Hypertension and tachycardia due to the effect on sympathetic ganglia.

(3) CNS effects:

- anxiety, emotional lability, restlessness, confusion, ataxia, tremors, seizures, cyanosis and coma.
- Depression of cardiovascular and respiratory centers.... Coma



Central Nervous System

Symptoms:
Seizures
Coma
Respiratory depression

Muscle motor End-plate

Fasciculations
Weakness
Paralysis

Sympathetic Nervous System

Tachycardia
Hypertension
Adrenal Stimulation

Diaphoresis

Parasympathetic Nervous System

Miosis
Lacrimation
Salivation
Bronchorrhea
Bronchospasm
Bradycardia
GI Motility: vomiting
diarrhea
Detrussor Muscle Contraction

II-Intermediate syndrome:

- **Characterized by relapse of muscle weakness including cranial nerves palsies, respiratory, neck and proximal limb muscles weakness resulting in respiratory muscles paralysis.....treated by controlled ventilation**
- **It occurs between the acute cholinergic crisis and the usual onset of organophosphate induced delayed neurotoxicity.**
- **The weakness is due to muscle fiber necrosis and begins shortly after the initial decline in AChE activity.**
- **Maximal muscle involvement occurs within the first 2-5 days of poisoning.**
- **Its intensity is correlated with the degree of fall of True AChE**
- **Early treatment with oximes may prevent the occurrence of intermediate syndrome**

III- Delayed neuropathy:

- It usually occurs 2-3 weeks after exposure to some OPC even after a skin contact.
- It is a mixed sensory and motor neuropathy
- It usually begins in the legs, causing burning or tingling sensations, and then followed by weakness of the legs and feet.Thighs and arms also become involved.
- It is due to nerve demylenation and is usually permenant.

VI- Cardio toxicity:

- Parasympathetic cardiomyopathy:Foci of myocardial necrosis which correlate with the degree of accumulated acetylcholine.
- Increased QT interval favoring ventricular tachycardia.

Treatment

(A) Prophylactic

1. Wearing of protective clothes (Overalls, long boots, gloves, masks)
2. Exhaust ventilation, respirator for workers during mixing or spraying the insecticide compounds
3. Spraying must be through a long nozzle bottle or container and with the current of air.
4. Containers should be kept away from children
5. Washing facilities must be nearby to workers
6. Workers should not eat, drink or smoke during the hours of work.

(B) Curative :

- ABC resuscitation, oxygen therapy
- Decontamination: As early as possible after stabilization
  - Wash the whole body with water
  - Remove the contaminated clothes
  - Gastric lavage by sodium bicarbonate if the poison is ingested.

- Antidotes

1. Atropine: life saving

- 2-5 mg IV every 15 minutes until relieve bronchospasm and wheezes. Do not rely on HR. Titrate and keep the patient atropinized for 1-2 days trying to avoid atropine toxicity and relapse of cholinergic crisis. Atropine antagonize the muscarinic action but not the nicotinic action. It may protect from parasympathetic cardiomyopathy and reduce risk of arrhythmia.
- Optimizing oxygenation prior to the use of atropine is recommended to minimize the potential for dysrhythmias.

2. Oximes (Cholinestraze reactivator)

- They reactivate the inhibited AChE ….. Correct signs of AChE inhibition, muscarinic ,nicotinic and CNS effects.
- They must be given before aging of the enzyme
  - ❖ Pam (Pyridine Aldoxime Methiodide)…. Pralidoxime: 1-2 mg IV or infusion as a loading dose followed by half the loading dose every 6-8 hours for 2 days.
  - ❖ Dam (Diacetyl Monoxime); It is given by IV drip . Better than PAM because it crosses the BBB.
  - ❖ Obidoxim (Toxogonin): Similar to DAM

- The effect of oximes is adjusted by measuring the level of enzymes or the disappearance of muscle fasiculations.

(C) Supportive :

- Complete rest , antibiotics, a close observation for the fear of relapse. Workers return to work when cholinesterase returns to at least 75% of its normal level.

Avoid

1. CNS depressant
2. Physostigmine, neostigmine, pilocarpine as they have parasympathomimetic action
3. Phenothiazines, theophylline as they have anticholinestaersae activity
4. Succinyl choline muscle relaxants

II- Organonitrogenous Insecticide (Carbamates)

- They are reversible inhibitor of PseudoChE enzyme
- Nitrous radical binds to active enzyme site ….. Accumulation of acetylecholine.
- Duration of action is short
- They commonly used for domestic uses (Baygon).They have low dermal toxicity, and their toxicity is rarely fatal.
- The most potent types : Aldecarb (Temik) & Carbofuran (Lannate) are used as rodenticides.

Clinical picture & management:

Similar to OPC with the following differences:

1- Carbamates do not effectively penetrate CNS and thus they result in limited CNS toxicity

2- Signs and symptoms of poisoning are typically as muscarinic and nicotinic manifestations of OPC.

3- If symptoms develop, they do not persist for more than 2 hours.

4- NO intermediate syndrome, no delayed neuropathy, no cadiotoxic effects.

5- Atropine sulphate is the only antidote for carbamate poisoning.

6- Oximes are contraindicated because they increase the toxicity.

III- Organochlorine Insecticide

-Organochlorine pesticides are chlorinated hydrocarbons used extensively from the 1940s through the 1960s in agriculture and mosquito control (Malaria). Representative compounds in this group include DDT, methoxychlor, dieldrin, chlordane, toxaphene, mirex, kepone, lindane, and benzene hexachloride.

-They are CNS stimulants. Recently they are banned as they are non-biodegradable.

- Dicholoro-Diphenyl-Trichloroethane (DDT)

- ❖Used during world war ll in lice control and other insects by direct application to humans.
- ❖Poorly absorbed from intact skin
- ❖Good safety
- ❖Fatal period :several hours
- ❖Fatal dose: 10mg/kg

Clinical picture

I- Acute poisoning: may be accidental or suicidal

- **GIT manifestation**
- **The chief acute toxic action of the organochlorine pesticides is on the central nervous system, where these compounds induce a hyperexcitable state in the brain leading to convulsions or other less severe signs of neurologic toxicity such as myoclonic jerking, paresthesias, tremor, ataxia and hyperreflexia. More severe poisoning results in myoclonic jerking movements, often followed by generalized tonic-clonic convulsions. Coma and respiratory depression may follow the seizures.**

II- Chronic poisoning

-Liver necrosis, degeneration of the renal tubules and haemolysis of RBCs are distinct features of this class.

-Sensitization of the myocardium to catecholamines may lead to life threatning ventricular arrythemias.

- If DDT is ingested in low levels over a prolonged period , it will accumulate in high concentrations in the adipose tissue.On starvation ….. Acute toxicity.

Treatment : symptomatic

1. Monitoring of vital functions
2. Remove contaminated clothes
3. Washing of the skin
4. For ingestion, gastric lavage with activated charcoal or saline cathertic.
5. CNS depressant and anticonvulsant as Diazepam are necessary to control tremors and convulsions.
6. Calcium gluconate

VI- Insecticide of botanical origin (Pyrethrines)

Pyrethrins are commonly used to control mosquitoes, fleas, flies, moths, ants, and many other pests. Pyrethrins are generally separated from the flowers. However, they typically contain impurities from the flower. Whole, crushed flowers are known as pyrethrum powder. Examples are Raid & Ezalo

Clinical picture: may take several forms

1. **GIT manifestation**
2. **CNS stimulation followed by depression may occur with massive oral dose**
3. **Contact dermatitis: it is the most common**
4. **Asthematic like reactions**
5. **Severe anaphylactic reaction with peripheral collapse and difficult breathing**

- **Death is due to respiratory failure**
- **Management:**

  Epinephrine

V- Herbicides

- They are substances used for destruction of noxious weeds
  - Chlorophenoxy compounds
  - Paraquat &Diquate

Action:

- GIT irritation
- Increase basal metabolic rate and elevate body temperature

Treatment

- Decontamination lavage if ingested or skin washing by soap and water.
- Ice bags to reduce body temperature
- sedatives: 50 mg chlorpromazine IM.

VI- Rodenticides

- For control of rats and mice
  - Inorganic yellow phosphorous
  - Metal phosphide: Zinc and Aluminum phosphide
  - Strychnine sulphate
  - Warfarine
  - Red squill

-Toxicity results from ingestion of a large single dose.
-Zinc phosphide: highly toxic rodenticide. It is black in colour with a roten fish odour and taste making it unattractive to other animals but attractive to rats. On contact with water or gastric acid, phosphine gas is liberated (PH3) which inhibit cytochrome oxidase enzyme leading to inhibition of aerobic metabolism which in turn leads to lactic acidosis and cell death.

- Warfarine: It is a rodenticide pellets or tablets. It is a cumarine derivatives. It is anticoagulant so it inhibits the formation of prothrombine leading to haemorrhage through the body. It has also a direct action on the capillary wall (capillary damage).

VII- Moth repellent (naphthaline)

- Derivative of coal tar.
- It is solid volatile substance present as large crystalline plates with a characteristic odour

Uses:

1. As insecticide for moth repelling as moth balls
2. In industry for manufacture of some dyes
3. Toilet bowel deodorizer

Absorption

- It is absorbed through skin and from respiratory and GIT.

Mode of poisoning

- Accidentally among children

F.D.: 2 gm

F.P.: few hours in children, up to few days in adults

Action:

- It causes haemolysis of RBCs with subsequent blocking of renal tubules and hepatic necrosis. This occurs only with those with hereditary glucose-6-phosphate dehydrogenase deficiency enzyme in red cells.
- GIT irritation after ingestion.
- Dermatitis after contamination and eye irritation
- Initial stimulation then depression of CNS (more evident with inhalaltion)

Chronic toxicity:

- Causes aplastic anaemia and liver necrosis.

Treatment

1. Decontamination : gastric lavage by warm water or saline
2. Magnesium sulphate to clear the bowels. Avoid fatty substances
3. Alkalinization of urine by sodium bicarbonate solution, 5gm orally/ 4hours to prevent precipitation of acid haematin crystals which block renal tubules.
4. Activated charcoal
5. Haemodialysis or exchange transfusion.
6. Fresh blood transfusion until Hb reaches 60-80% of normal level.
7. Control convulsions by diazepam
8. Diet high in carbohydrates and vitamins , moderate in protein and low in fat .

PM picture:

- A characteristic odour of naphthaline.
- Yellow colouration of skin (Jaundice).
- Gastric mucosa may be yellow, congested or inflamed.
- Liver necrosis and kidney damage.
- Small quantity of dark urine in urinary bladder.
- Congestion and irritation of respiratory tract.