
# Pesticides Poisoning

TOXICOLOGY LAB.

4TH STAGE / 2ND SEMESTER

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Very low chance of toxicity






High Chance of Toxicity

# Introduction:

- **Pesticide is a word that is considered of 2 parts:**
  - Pest = unwanted creature or living
  - Cide = killing or elimination
- **Pesticide can be defined as:**
  - Any substance or mixture of substances intended for repelling, destroying, preventing any insects, rodents, fungi or weeds, or any other forms of life declared to be pests
- **Classifications of pesticide:**
  - Insecticides (organophosphates, carbamates, organochlorines [chlorinated hydrocarbons], pyrethroids)
  - Herbicides (paraquat, chlorophenoxy, glyphosate, thiocarbamates)
  - Rodenticides (anticoagulants [warfarin], metal phosphides [ zinc phosphide], coumarins, indandiones)

# Introduction:

- **Types of poisoning with pesticide:**
  - Accidental
  - Suicidal
  - Homicidal
  - Occupational

- **Route of poisoning with pesticide:**
  - Oral (ingestion)
  - Dermal (skin contact)
  - Inhalation
  - Eye contact

# Insecticides:

## Organophosphates & Carbamates:

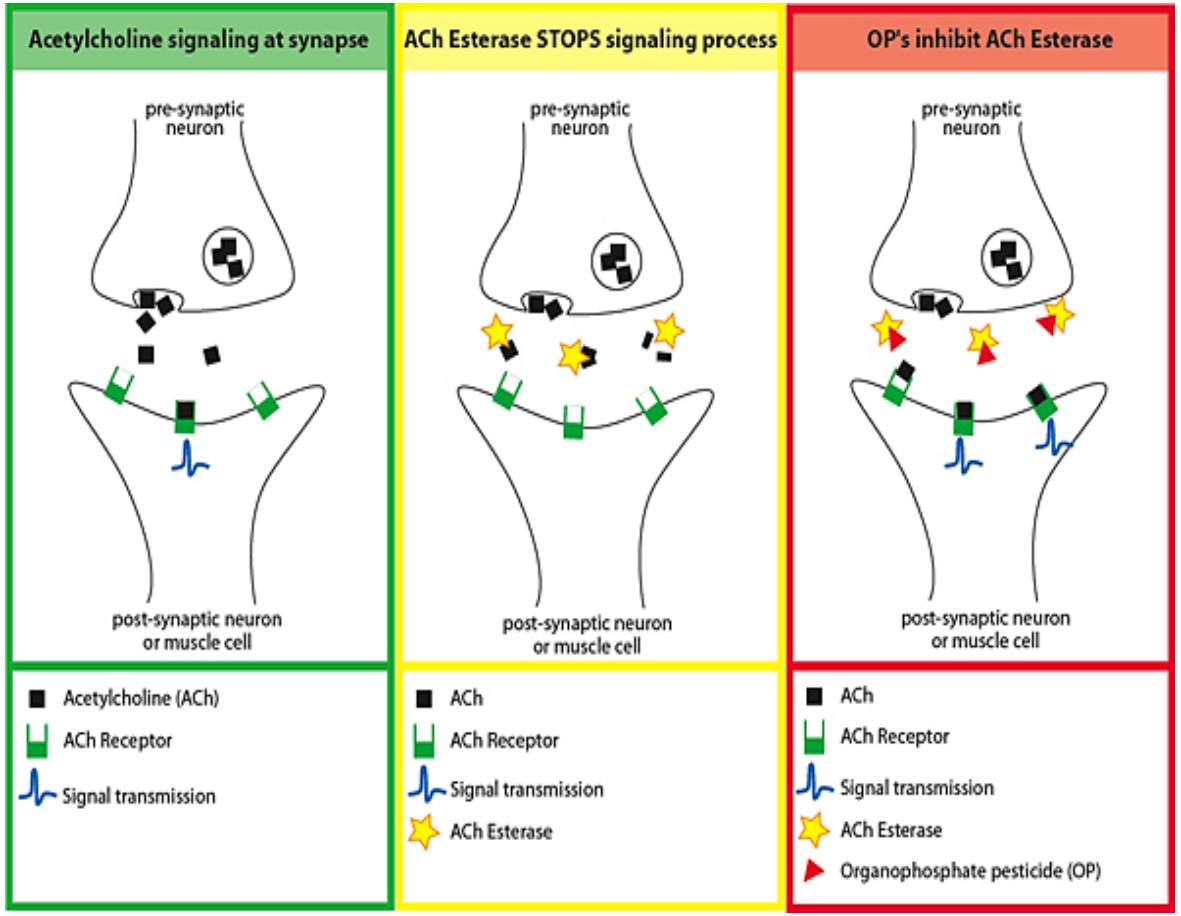
- Both of them share the same mechanism of action (inhibitors of Ach esterase enzyme)
- Organophosphates (eg/ parathion & echothiophate) irreversible inhibitors of AchE
- **Two organophosphates have medicinal uses. What are they??**
- Carbamates are reversible inhibitors of AchE (medicinal uses only)

- **Mechanism of Toxicity:**
  - They bind to AchE enzyme (the enzyme responsible for the degradation of Ach) by phosphorylation and inhibit its function, leading to accumulation of excess of Ach in the synapses and NMJ, thus resulting in muscarinic and nicotinic signs and symptoms
  - At postsynaptic muscarinic receptors leads to SLUDGE/DUMBELS symptoms
  - At nicotinic motor end plates (NMJ) causes persistence depolarization of the skeletal muscle resulting in fasciculation, progressive weakness and hypotonicity
  - Organophosphates can cross the blood brain barrier, they may cause seizures, CNS depression and respiratory depression in unknown mechanism

# Continue:

**Important notes:**

- Binding of *OP with AchE* for more than 10 hours results in an irreversible OP-AchE complex through strong covalent bonding; this phenomenon is called ***[aging]***
- ***Aging*** of the enzyme can not be reversed by an antidote, but requires the synthesis of new enzymes
- OP also binds AchE found in RBCs and plasma (pseudocholinesterase)
- ***Carbamates poisoning*** tends to be short duration because inhibition of AchE enzyme is reversible



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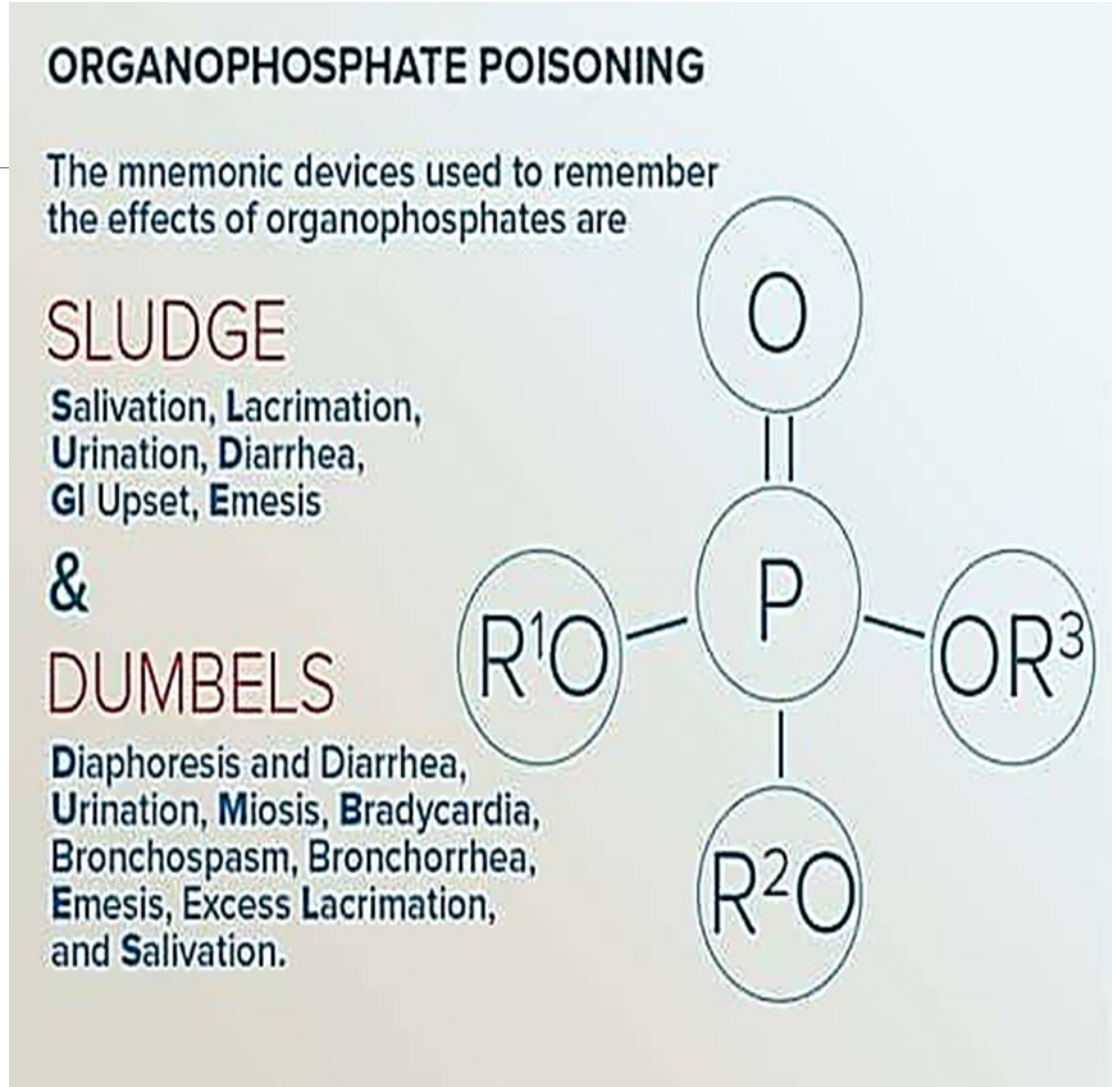
**Management of OP Poisoning:**

- Decontamination
- Suppurative care (airway, breathing, and circulation) = ABC
- Atropine (muscarinic blocking agent)
- Pralidoxime (activation of AchE enzyme), should be administered within 6 hours of the exposure, otherwise useless
- Correction of metabolic abnormalities



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**Organochlorines (chlorinated Hydrocarbons):**

- They are synthetic pesticides widely used all over the world
- These compounds are known for their high toxicity, slow degradation, and bioaccumulation

- **Mechanism of Toxicity/** they cause opening of neuronal sodium (Na) channels causing continuous and spontaneous firing of these neurons resulting in spasms and convulsions and finally death

- **Clinical signs/**
  - Skin = dermatitis
  - Inhalation = respiratory distress, cough, eye and nose irritation
  - GIT = nausea, vomiting, diarrhea, abdominal pain, convulsions, coma and death

# Continue:

**Pyrethroids:**

- The active ingredient extracted from the flower of *(Chrysanthemum cinerariaefolium)*
- Synthetic compounds Structurally related to pyrethrin are known as pyrethroids
- These are widely used for insect control both at home and in agricultural fields. In addition, they are used for the treatment of scabies and lice in humans.

- **Mechanism of Toxicity/**
  1. Pyrethroids without cyano group (Type I)/ modify the gating characteristics of voltage-sensitive sodium channels, thereby delaying their closure thus increases sodium influx and causes repetitive firing (excitable nerve and muscle cells are hence the key targets of pyrethroid toxicity) [eg/ permethrin]
  2. Pyrethroids with cyano group (Type II)/ decreased chloride currents on the voltage-dependent chloride channels, pyrethroids can also act on gamma amino butyric acid (GABA)-gated chloride channels [eg/ deltamethrin]

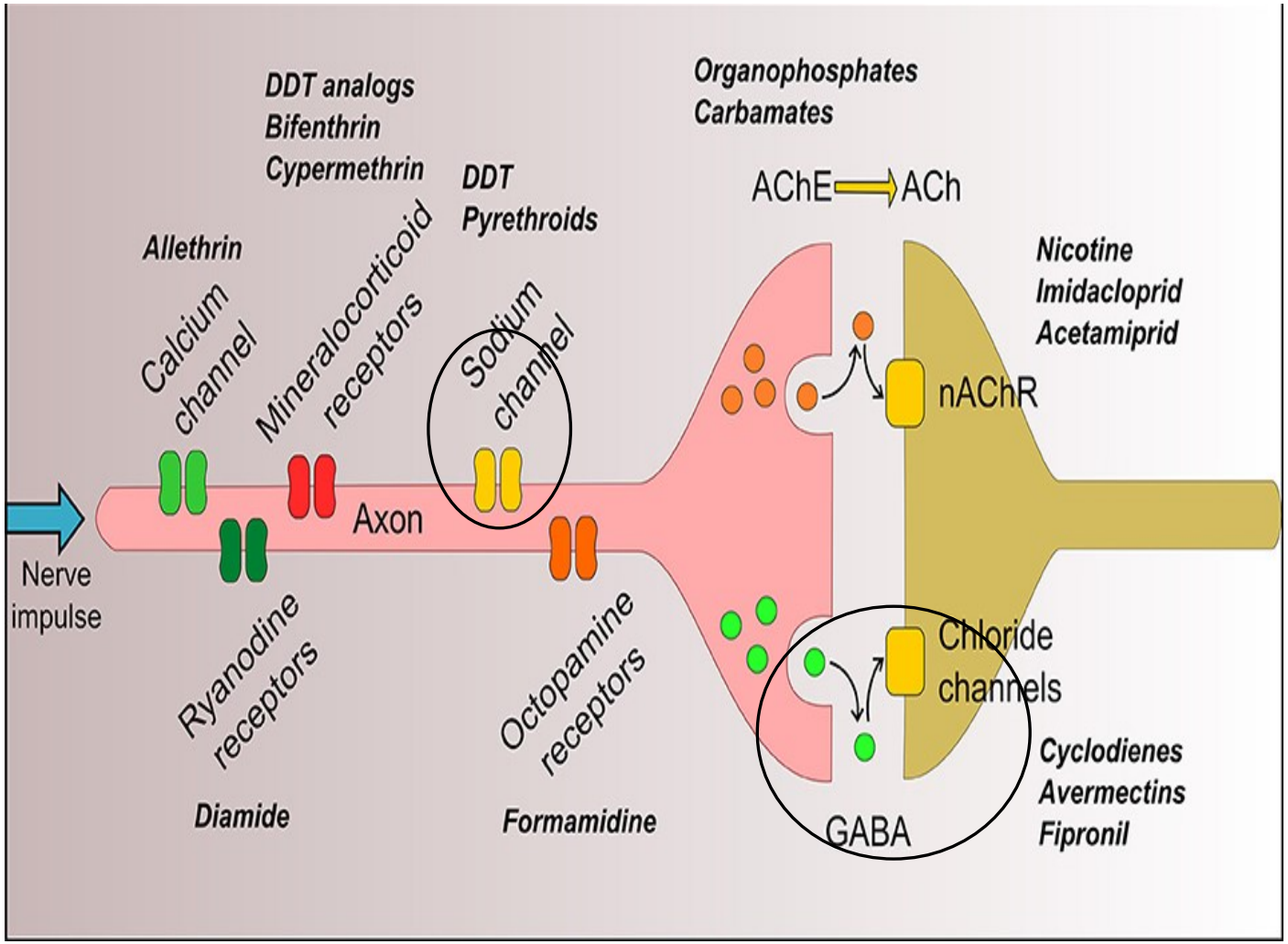
# Clinical signs of Toxicity:

Skin/ low absorption causes dermatitis

Inhalation/ allergic signs, cough and wheezing

Eye contact/ lacrimation and edema

Ingestion/ salivation, abdominal pain, vomiting, diarrhea



# Herbicides:

**Paraquat:**

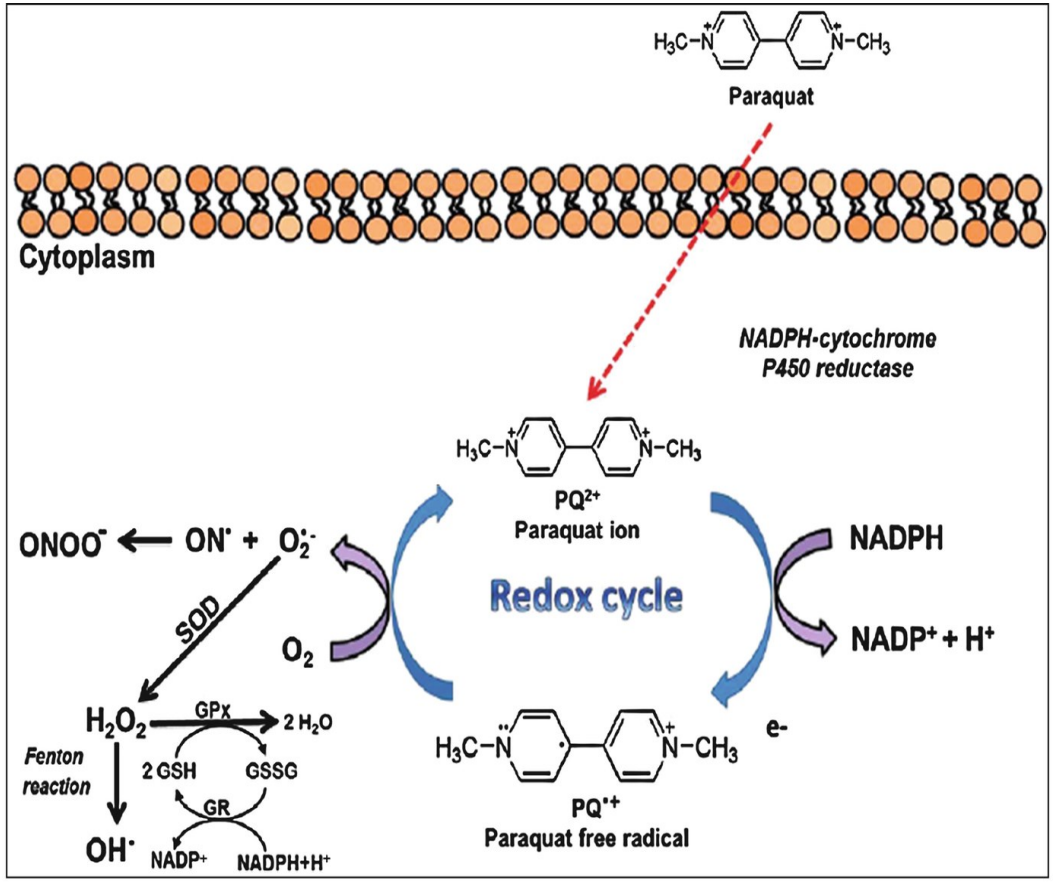
- It is the most widely used herbicides, but when it comes in contact with the soil becomes inactive
- It is largely used in suicidal attempts because of its high toxicity when ingested
- Water soluble herbicide, available as aqueous concentrate and granular formulation

- **Mechanism of Toxicity/**
  1. Known as **(redox cycling)** through oxidation/reduction cycle producing peroxides and free radicals
  2. Paraquat is reduced by cellular CYTP450 reductase to form free radicals
  3. Oxygen molecules is then reduced to superoxide that then can be converted to other toxic oxygen species
  4. These reactive compounds may cause peroxidation to the cellular phospholipids bilayer membrane, mitochondria, and DNA
  5. Lungs are the main organ for paraquat toxicity due to high pulmonary oxygen tension, and the presence of active energy – dependent uptake by alveolar cells type I & type II
  6. Paraquat has other life-threatening effects on GIT, kidney and liver

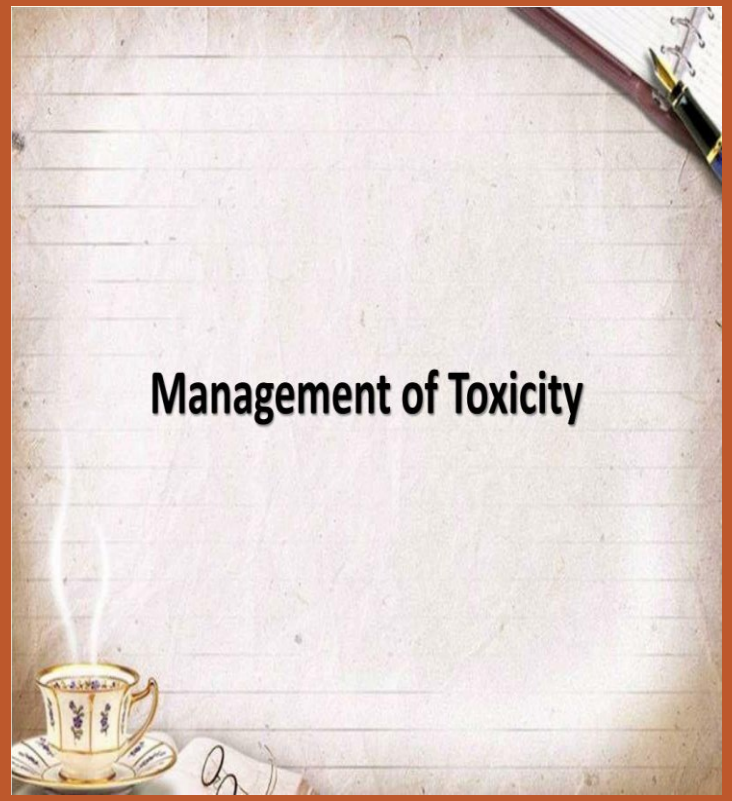
# Herbicides:

**Clinical signs of Toxicity/**

- Phase (1): GIT symptoms
  - Gastric and esophageal irritation and ulceration
  - Intense pain in mouth and pharynx
  - Hematemesis and diarrhea
- Phase (2): liver and renal impairment depending on the dose ingested
- Phase (3): Respiratory symptoms
  - Cough
  - Cyanosis
  - Pulmonary edema
  - Fibrotic pneumonia



# Management:




**Management of Paraquat poisoning:**

- Suppurative therapy:
  - Fluid replacement
  - Analgesia
  - Assessment of hepatic and renal function
  - **No oxygen supply or very low concentration oxygen supply (why?)**

- Gastric lavage with activated charcoal
- Antioxidant administration
- Anti-fibrotic (collagen synthesis inhibitors)/ pirfenidone
- Charcoal hemoperfusion
- **Hemodialysis and forced diuresis are less effective (why?)**

# Rodenticides:

- They are pesticides designed specially to kill rodents
- Example/ coumarins, warfarin, metal phosphides (Zinc & Aluminum)
- Since they are used to kill rodents, they pose a threat to human beings

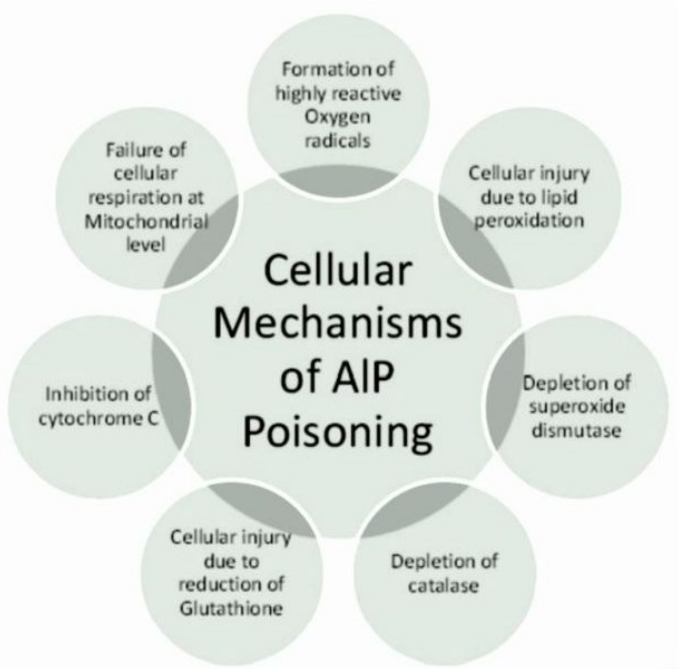
## Warfarin & Coumarin (anti-coagulants):

- **Mechanism of Toxicity/**
  - They inhibit hepatic synthesis of essential coagulation factors, causing disruption of normal blood coagulation
  - Increased capillary permeability, internal bleeding and tissue hypoxia, and finally death

- **Clinical Signs of toxicity/**
  - Massive internal bleeding, nose and gum bleeding, blood in urine and stool, skin bruises, ruptured blood vessels
  - GIT bleeding, hemoptysis
  - Depression and loss of appetite

**Management of such poisoning?**

# Rodenticides:




## Metal Phosphide (Zinc & Aluminum):

- Common means in suicidal attempts
- Mortality rate for Aluminum Phosphide = 60%, while for Zinc Phosphide = 2%

- **Mechanism of Toxicity/**
  - Metal phosphide when comes in contact with moisture (water, mucus membranes, gastric juice), it liberates phosphine gas
  - Phosphine gas is extremely cytotoxic to the pulmonary and GIT, resulting in extreme cellular alterations

- **Clinical signs of Toxicity/**
  - Severe GIT disturbances
  - Extreme respiratory symptoms: cough, breathlessness, chest tightness,  ARDS and respiratory failure
  - Hypotension, tachycardia, metabolic acidosis, hypoglycemia, electrolyte disturbance
  - Tremors, convulsions, and coma

# Continue:

**Management of Metal Phosphide Poisoning:**

- Suppurative therapy:
  - Ventilation and breathing
  - Fluid replacement
  - Remove contaminant
- Gastric lavage with vegetable oil (why?)
- Correct electrolyte disturbance (guided fluid therapy)
- Administer Na bicarbonate to reduce stomach acidity
- Vasoactive agents and antiarrhythmic drugs
- Antioxidants (Vit C or NAC)
- Hemodialysis

# General Principles of Poisoning Management:

**Standard toxicologic emergency procedures:**

- Recognize the poisoning promptly
- Assess the patient thoroughly to identify the toxin and the measures required to control it
- Initiate standard treatment procedures:
  - Protect the patient safety
  - Remove the patient from the toxic environment
  - Support ABC
  - Decontaminate the patient
  - Administer antidote if one exist

| **Supportive Care** | |
|---|---|
| Airway protection | Treatment of seizures |
| Oxygenation/ventilation | Correction of temperature abnormalities |
| Treatment of arrhythmias | Correction of metabolic derangements |
| Hemodynamic support | Prevention of secondary complications |
| **Prevention of Further Poison Absorption** | |
| Gastrointestinal decontamination | Decontamination of other sites |
| Gastric lavage | Eye decontamination |
| Activated charcoal | Skin decontamination |
| Whole-bowel irrigation | Body cavity evacuation |
| Dilution | |
| Endoscopic/surgical removal | |
| **Enhancement of Poison Elimination** | |
| Multiple-dose activated charcoal administration | Extracorporeal removal |
| Alteration of urinary pH | Hemodialysis |
| Chelation | Hemoperfusion |
| | Hemofiltration |
| | Plasmapheresis |
| | Exchange transfusion |
| | Hyperbaric oxygenation |
| **Administration of Antidotes** | |
| Neutralization by antibodies | Metabolic antagonism |
| Neutralization by chemical binding | Physiologic antagonism |
| **Prevention of Reexposure** | |
| Adult education | Notification of regulatory agencies |
| Child-proofing | Psychiatric referral |

# Wash Fruits and Vegetables Very Well

**Be careful & Be Safe**