Toxicology course

Part 4:

- Household products
- Pesticides

TOXICOLOGY

❑Household products

- Any chemical / mixture that may be harmful to the environment and to human health if inhaled swallowed or absorbed through skin.

- These toxic substance contained in everyday household products.

- Poisoning due to household substances is usually **mild**.

- Drugs and household cleaners are the most reported cases of poisoning.

- **Easy availability of household product** makes them one of the leading causes of poisoning.

- Usually target age: **under the age of five**, majority were children between the age of 1-3 years.

- Product warning label indicates level of toxicity

- ❑No label = LD50 > 5 g/kg
- ❑Caution = 0.5 – 5 g/kg
- ❑Warning = 50 – 500 mg/kg
- ❑Danger: Poison = <50 mg/kg

Commonly used harmful household products

- **Cleaners:**
- Used to remove dirt mostly contains fragrance, surfactants & pesticides.
- Surfactants remove dirt & pesticides kill germ like bacteria and viruses.
- Glass cleaners – Ammonia, Isopropanol
- Dish washers – Cationic, anionic or nonionic detergents
- Oven cleaners – Lye (Na/K hydroxide)

- All purpose cleaners – Ethylene glycol, Na hyperchlorite

- **Soaps, Shampoos, Detergents:**

- Most have low toxicity, Usually cause only vomiting and diarrhea
- **Cationic surfactants** are found in contact lens solutions, fabric softeners: can cause neuromuscular and ganglionic blockade as well as GI ulcerations, acidosis and shock
- **Anionic surfactants** are in many cleaning products like shampoos have the potential to cause hemolysis

N.B

- **Rust removers:**
- Mold and rust are kind of funguses.
- Pesticide chemicals found in these products are chlorine, alkyl ammonium chloride.
- Very caustic and corrosive.

- **Batteries:**

❑Dry cell – Carbon + Heavy metal

❑Wet cell – used for vehicles, lead and battery acid(H_2SO_4)

- **Button & Disk Batteries:**
- Button/Disk battery single cell batteries used as an energy source for digital watches, calculators, cameras etc.
- Contains **heavy metals** and potassium oxide solution.
- **If swallowed – majority no symptoms passed intact with feces.**
- **If impacted in esophagus – fever, dysphasia, vomiting and anorexia**
- **Tissue damage cause by flow of electric current, potentially fatal.**

- **Bleaches/ Disinfectants**:

- Used to kill germs
- Depending on the specific product usually do not cause serious harm if a small amount is swallowed.
- Average amount may cause serious poisoning and even death.
- Germicide chemical-acids, alkalis, pine oil, phenol.....

- **Paints/ Polishes**

- Paints:

  Water base - mostly used for indoors. Main solvent is water

  Oil base – mineral spirit and other petroleum distillate. Used for out doors.

- Polishes: Furniture polishes & metal cleaners – petroleum distillate.

- **Treating Household Cleaner Ingestions**

- If a potentially toxic amount of **a non-corrosive** compound ingested, **emesis should be induced**; no activated charcoal unless systemic effects are expected

- For corrosive compounds:

1) dilute with milk or water
2) determine exactly how much of what material was ingested

- **Treating Toxic Corrosive Ingestions**

- If there is pain, dysphagia, excessive drooling, or ulceration and the exposure was potentially toxic:
  - Establish airway and get esophagoscopy
  - If esophagus can't be examined quickly, start corticosteroids
  - Symptomatic and supportive care

Petroleum Products

- Gasoline, mineral spirits, kerosene, lighter fluid, nail polish remover, solvents, motor oil, furniture polish, Brake fluid, car coolant, antifreezer.
- Biggest worry is aspiration causing hydrocarbon pneumonia
- **Pneumonia risk related to viscosity; less viscous = more toxic.**
- Brake fluid, car coolant, antifreezer ethylene glycol, highly toxic – damage to heart, kidney & brain can cause death.

Systemic Toxicity of Hydrocarbons

- Most hydrocarbons are **CNS depressants**
- Some volatile hydrocarbons **sensitize the heart to catecholamines** and can cause sudden death due to cardiac arrest
- Many hydrocarbons cause **dermal irritation** and **hair loss**

Signs of Hydrocarbon Toxicity

- **CNS:** Depression, lethargy, ataxia, seizures, coma
- **Respiratory:** Dyspnea, coughing, wheezing, X-ray changes in lungs with pneumonia
  - Spontaneous vomiting and aspiration often occurs with more volatile compounds

Treating Hydrocarbon Ingestions

- Wash for dermal exposures
- Do not try to increase viscosity by adding heavier compound
- Do not induce emesis unless a large, life threatening ingestion (>1 ml/kg)
- Monitor for pneumonia; treat with antibiotics if present

❑Pesticides

- As any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating **pests**.

- **Pests** can be insects, rodents, weeds, and a host of other unwanted organisms.

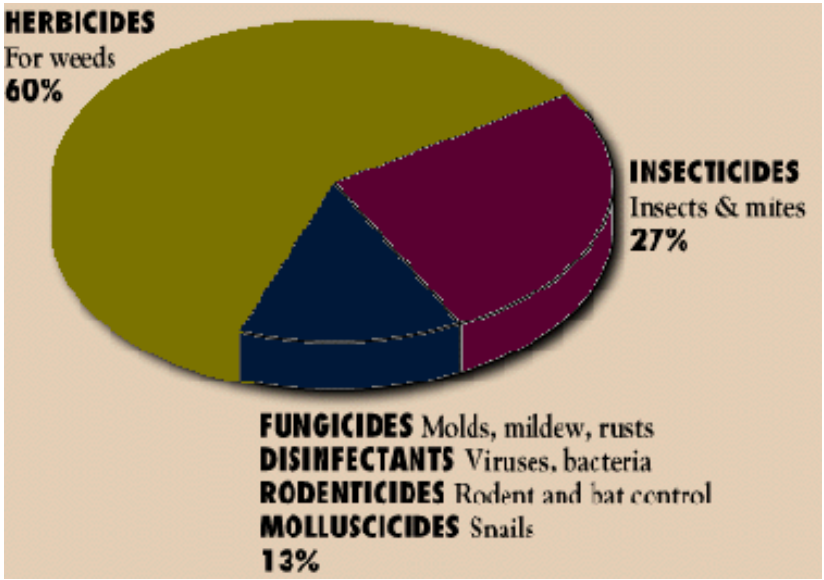
- About 800 compounds of active ingredients of pesticides have been registered world-wide.

- Most pesticides are not highly selective, but are generally toxic to many non target species

- there are a sufficient number of nonfatal poisonings from general pesticide use, averaging about 5000 cases annually in the United States.

- **The four major classes:**

1. Insecticides (insects)
2. Herbicides (weeds)
3. Fungicides (fungi, molds)
4. Rodenticides (rodents)



Texas center

- **Groups of pesticides include:**

- Organochlorine pesticides
- Organophosphates
- Carbamate pesticides
- Pyrethroids
- Phenoxyacetic acid – based pesticides
- Urea – based pesticides
- Diazine and triazine pesticides
- Bipyridil – based pesticides
- Phenylpyrazoles
- Metal – based pesticides

- With each class, there is several subclasses exist:
- Ex: insecticides… organochlorines….. DDT

- **Exposure to pesticides:**
- Exposure to pesticides can occur via the **oral** or **dermal** routes or by **inhalation**.

- **Oral route:**

➢ **High doses:** leading to severe poisoning and death (suicidal intents, or of accidental ingestion)

➢ **Chronic low doses:** are consumed by the general population as pesticide residues in food, or as contaminants in drinking water

- **The dermal route:**

➢ Is believed to offer the greatest potential for exposure for workers involved in the production, transport, mixing and loading, and application of pesticides, as well as in harvesting of pesticide-sprayed crops, or in case of accidental spilling.

➢ Slow penetration through the tissue and/ or to potential exposure of others, if clothes are not changed and washed on termination of exposure

- **Respiratory route:**

➢ When aerosols or aerial sprayings are used.

Pesticide degradation

- The most important factors are light, temperature, photolysis, free radicals produced in photochemical reactions, hydrolysis.

1. phase 2. phase

$$XH \longrightarrow X - OH \longrightarrow X - O - \text{conjugate}$$

The final products are inactive and are excreted.

Acute Toxicity – pesticides

- **Dermal:** skin irritation, reddening, itching
- **Oral:** nausea, muscle twitching, sweating, weakness
- **Inhalation:** burning of throat and lungs, coughing
- **Eye:** temporary or permanent irritation or blindness

Chronic toxicity of pesticides

- Cancer
- birth defects
- infertility or sterility
- Impotence
- blood disorders (anemia, inability to clot)
- brain damage
- Paralysis
- emphysema, asthma
- kidney problems

- **REMEMBER:**
- **Low-level exposure to chemicals that have potential to cause long- term effects may not cause immediate injury, but repeated exposures can greatly increase the risk of chronic adverse effects.**

INSECTICIDES

- Are **neurotoxicants**, and act by poisoning the nervous systems of the target organisms
- Insecticides play a most relevant role in the control of insect pests, particularly in developing countries.
- The organophosphates, are involved in a great number of human poisonings and deaths each year

Table 22-8

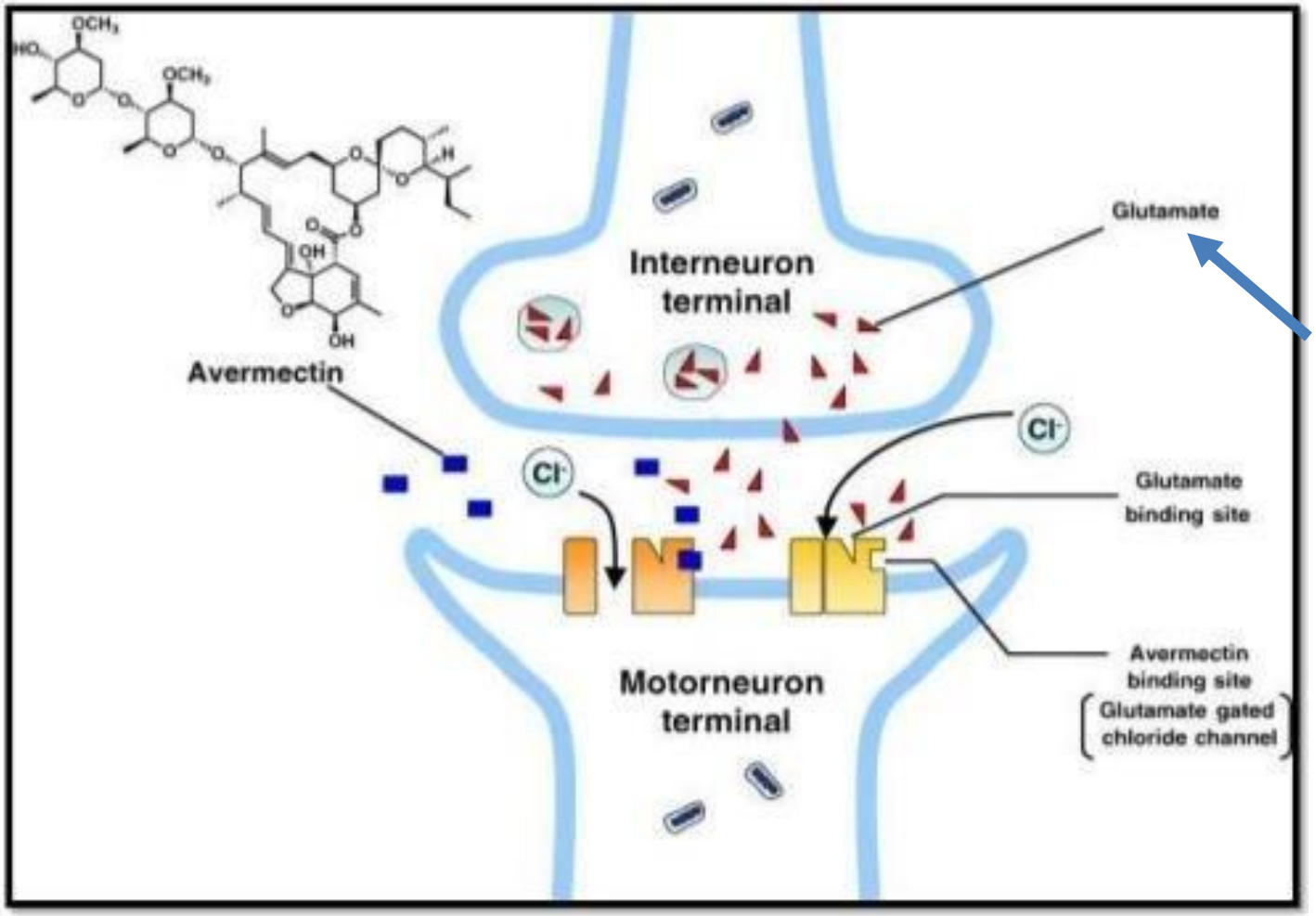
Molecular Targets of the Major Classes of Insecticides

TARGET	INSECTICIDE	EFFECT
Acetylcholinesterase	Organophosphates	Inhibition
	Carbamates	Inhibition
Sodium channels	Pyrethroids (types I and II)	Activation
	DDT	Activation
	Dihydropyrazoles	Inhibition
Nicotinic acetylcholine receptors	Nicotine	Activation
	Neonicotinoids	Activation
GABA receptor-gated chloride channels	Cyclodienes	Inhibition
	Phenylpyrazoles	Inhibition
	Pyrethroids (type II)	Inhibition
Glutamate-gated chloride channels*	Avermectins	Activation
Octopamine receptors†	Formamidines	Activation
Mitochondrial complex I	Rotenoids	Inhibition
Ryanodine receptors	Diamides	Activation

**Found only in insects. In mammals avermectins activate $GABA_A$ receptors.*

†In mammals, formamidines activate α_2-adrenoceptors.

Avermectins

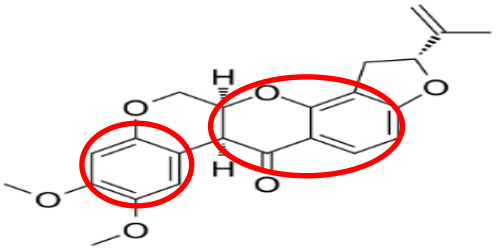


Excitatory

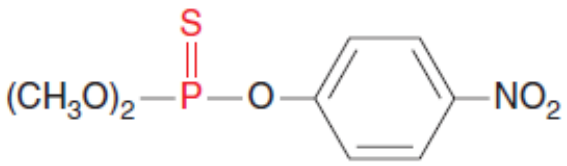
Rotenoids

Derris

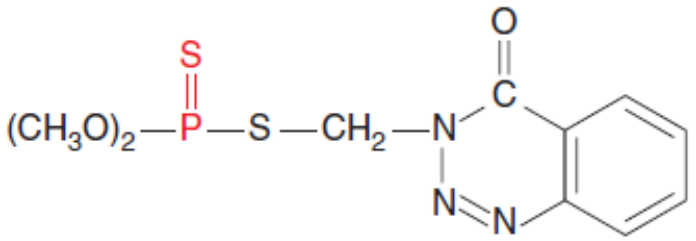
Lonchocarpus



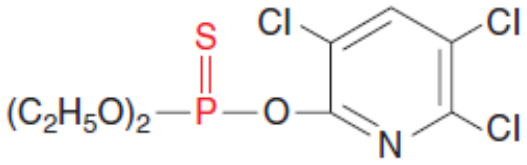
1. Organophosphorus Compounds



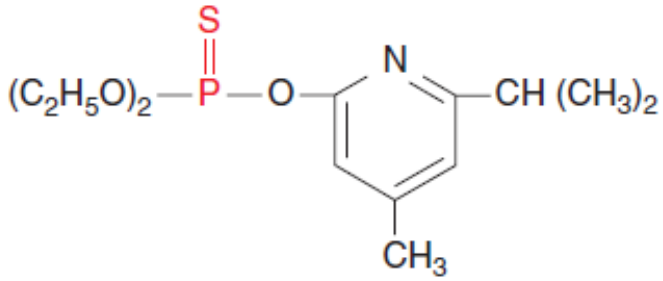
Methylparathion



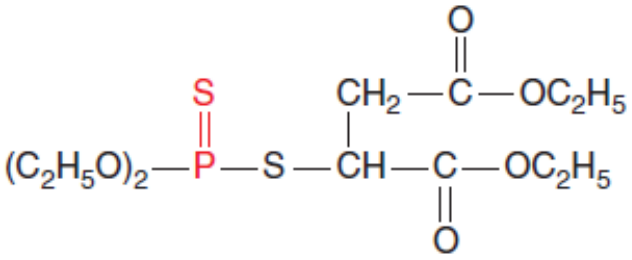
Azinphos-methyl (Guthion)



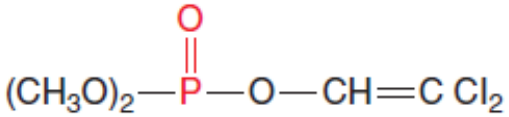
Chlorpyrifos



Diazinon



Malathion



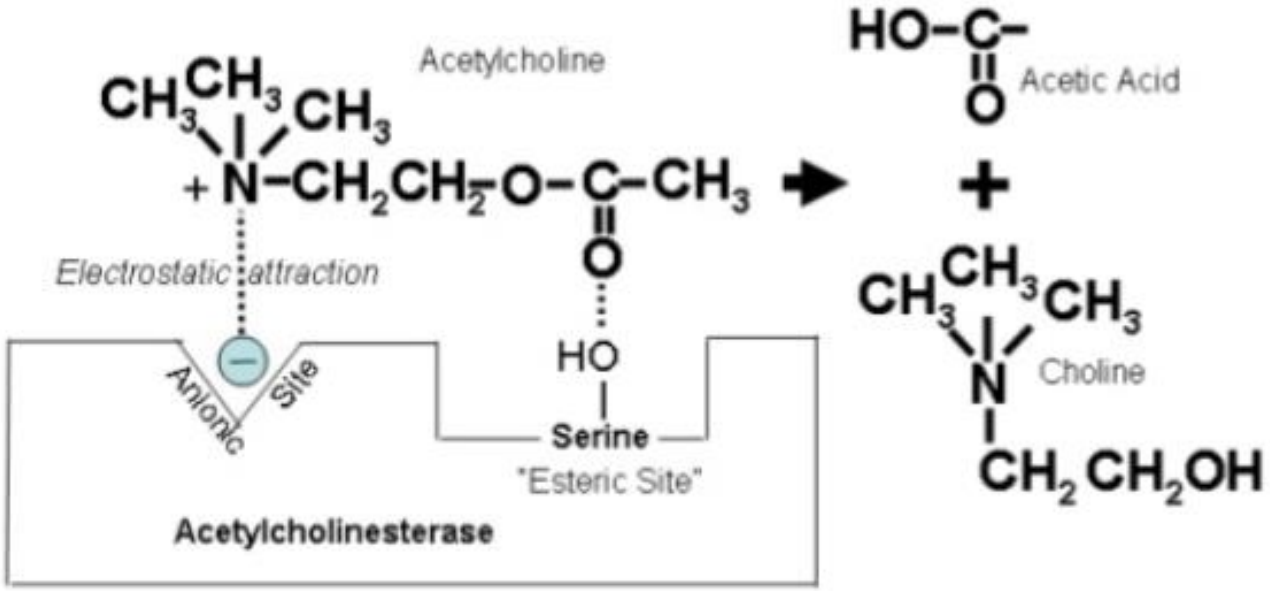
Dichlorvos

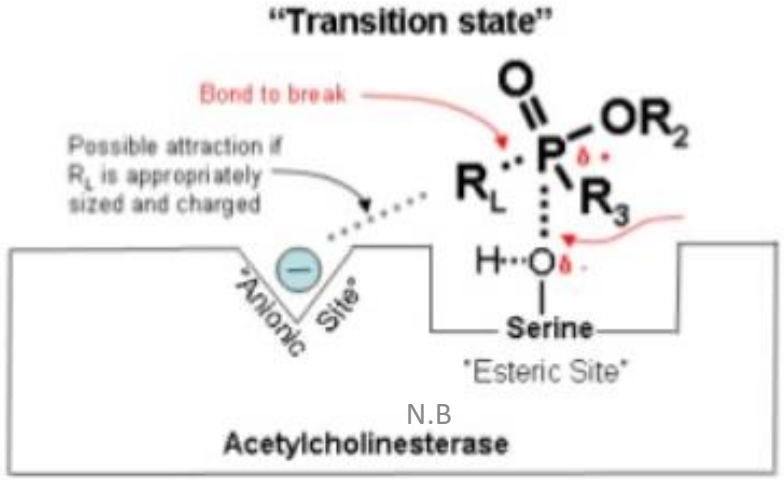
- **Insecticides and antiparasitics**
- Have high acute toxicity, with oral LD 50 values in rat often below 50 mg/kg.

- **Mechanism of toxicity:**

1. inhibition of Acetylcholine esterase enzyme causes accumulation of acetylcholine at cholinergic synapses, with over stimulation of cholinergic receptors of the muscarinic and nicotinic type

Ach & AChE


Acetylcholine
Acetic Acid
Electrostatic attraction
Anionic Site
Serine
"Esteric Site"
Acetylcholinesterase
Choline


"Transition state"
Bond to break
Possible attraction if
R_L is appropriately
sized and charged
"Anionic Site"
Serine
"Esteric Site"
Acetylcholinesterase

N.B

Muscarinic effects(post ganglionic parasympathetic nerve ending)

- Bronchospasm(wheezing)
- Bronchorrhoea
- Productive cough
- Dyspnoea
- Hypotension
- Bradycardia
- Cardiac arrhythmia
- Diarrhoea
- Vomiting
- Salaivation
- Tenesmus
- Miosis
- Lacrimation
- Blurred vision

Nicotinic effects (neuro muscular junction)

- Muscle weakness
- Fasciculation
- Paralysis
- Muscle twitching

Respiratory failure is a hallmark of severe OP poisoning
The agents are most rapidly absorbed after inhalation

1- Muscarinic effects: S*LUDGE/BBB*

S = Salivation	L = Lacrimation	U = Urination
D = Defecation	G = GI symptoms	E = Emesis
B = Bronchorrhea	B = Bronchospasm	B = Bradycardia

2. The Intermediate Syndrome:

- The syndrome develops one to several days after the poisoning, during recovery from cholinergic manifestations.
- weakness of respiratory, neck, and proximal limb muscles. Mortality due to respiratory paralysis and complications ranges from 15% to 40%, and recovery in surviving patients usually takes up to 30 days
- There is no specific treatment

3. Organophosphate-Induced Delayed Polyneuropathy:

- Tingling of the hands and feet, followed by sensory loss, progressive muscle weakness and flaccidity of the distal skeletal muscles of the lower and upper extremities, and ataxia.
- These may occur two to three weeks after a single exposure.

Management of organophosphate poisoning

1. check airway, breathing, circulation
2. monitor arterial oxygen saturation, cardiac rhythms, BP, Pulse rate.
3. look for signs & symptoms.
4. obtain IV access.

- **Treatment of Poisoning:**

- **Dermal :** contaminated clothing should be removed, and the skin washed with alkaline soap. rinsing the eyes

- **Oral:** procedures to reduce absorption from the gastrointestinal tract do not appear to be very effective….. give activated charcoal (50 g in 200 ml)

- **Atropine:** it is a muscarinic receptor antagonist, and thus prevents the action of accumulating acetylcholine on these receptors.

- Doses of atropine in adults are 1 or 2 to 5 mg in case of mild or moderate poison.

- 1.8-3.0 mg fast iv bolus-after 3-5minutes check the five parameters of cholinergic poisoning:

1. Poor air entry into the lungs due to bronchospasm
2. excessive sweating
3. bradycardia (<60)
4. hypotension
5. Miosis

- If above parameters are not corrected, double the dose of atropine every 5 minutes until at least 3/5 of below parameters corrected:

1. clear chest with no wheeze
2. heart rate 80-100 bpm
3. systolic BP > 90 mmhg
4. pupils no longer pinpoint

- Higher doses by continuous infusion may be required in severe cases
- Atropinization should be maintained for at least 48 hours

- **Oximes,** such as **pralidoxime** (2-PAM), are also used in the therapy of OP poisoning.
- Mechanism of action: 2-PAM contains a positively charged atom capable of attaching to the anionic site of AChE, and facilitates dephosphorylation of the enzyme.
- Dosing regimens for various oximes depend on the specific compound and the severity of OP poisoning (30mg/kg loading dose Iv over 10-20mins followed by continuous infusion of 8-10mg/kg/hr until clinical recovery)
- Inadequate dosing is major factor for lack of response to oxime therapy and aging of ACh

- **Diazepam**

- (10–20 mg) is also used in the treatment of acute OP poisoning to:

✓ relieve anxiety in mild cases
✓ to reduce muscle fasciculations
✓ antagonize convulsions in the more severe cases

Management of complications

1.Respiratory failure: ET intubation and mechanical ventilation required if - tidal volume <5mm/kg - vital capacity < 15 ml/kg -apnoic spells are present -PaO2 < 08 Kpa& FiO2 > 60%

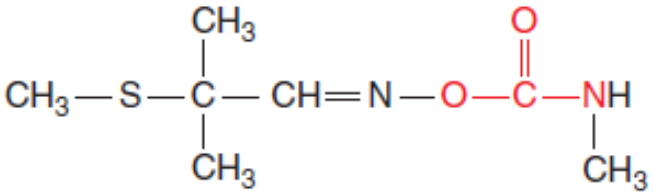
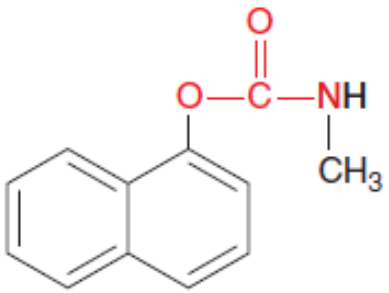
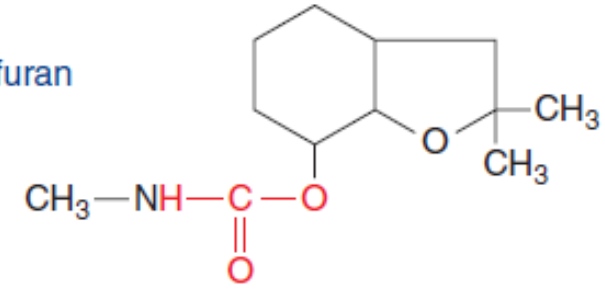
2.Pulmonary oedema: furosemide 40-80 mg iv

3.convulsion: 5-10 mg iv diazepam

4. ventricular tachycardia: temporary pacing

5. bronchopneumonia: antibiotics & chest physiotherapy

2. Carbamates

		LD_{50} in rats (mg/kg)		Water solubility (g/L)
		Oral	Dermal	
Aldicarb		0.8	3.2	6.0
Carbaryl		400	>5000	0.7
Carbofuran		10	>1000	0.7

- **Insecticides, herbicides, and fungicides**
- **Ex: Carbofuran: Birds**
- **Exposure:** oral and dermal (lower)
- **Mechanism of action**: inhibit AChE
- inhibition is transient and rapidly reversible, since there is rapid reactivation of the carbamylated enzyme in the presence of water.
- **Signs and symptoms**: include miosis, urination, diarrhea, salivation, muscle fasciculation, and CNS effects (poor penetration of the blood-brain barrier limits CNS toxicity of carbamates)
- **The treatment**: symptoms relive, the use of the muscarinic antagonist atropine.

3. Pyrethroids

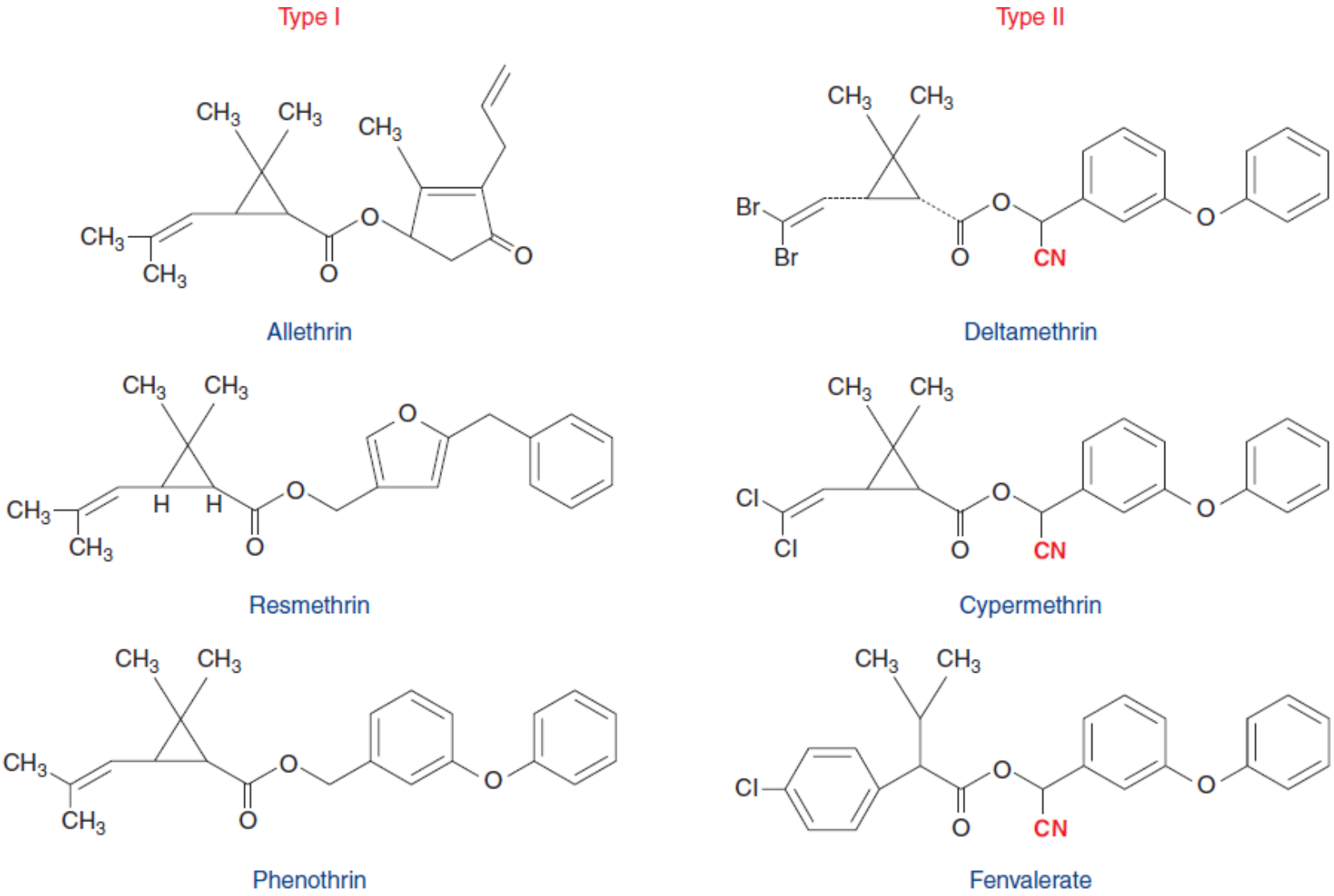


Figure 22-9. *Structures of type I (left) and type II (right) pyrethroid insecticides.* Note that all type II pyrethroids display a cyano (CN) group.

- Pyrethroids are used widely as **insecticides** both in the house and in agriculture

- in medicine for the topical treatment of scabies and head lice, and in tropical countries for malaria control, both in soaked bed nets to prevent mosquito bites and in indoor residual spraying.

- Values of LD_{50} are low: for example, from 100 mg/kg (deltamethrin) to 10,000 mg/kg (phenothrin).

- Insecticides and antiparasitics
- Toxic for fish and bees

<u>Mechanism of the toxic action</u> -

- pyrethroids T (tremor) – contain no α-cyano group

  cause reversible block of sodium channels (e.g. permethrin)
- pyrethroids CS (choreoatetosis, salivation) – contain α-cyano group

  cause reversible block of sodium channels and inhibition of GABA (e.g. deltamethrin)

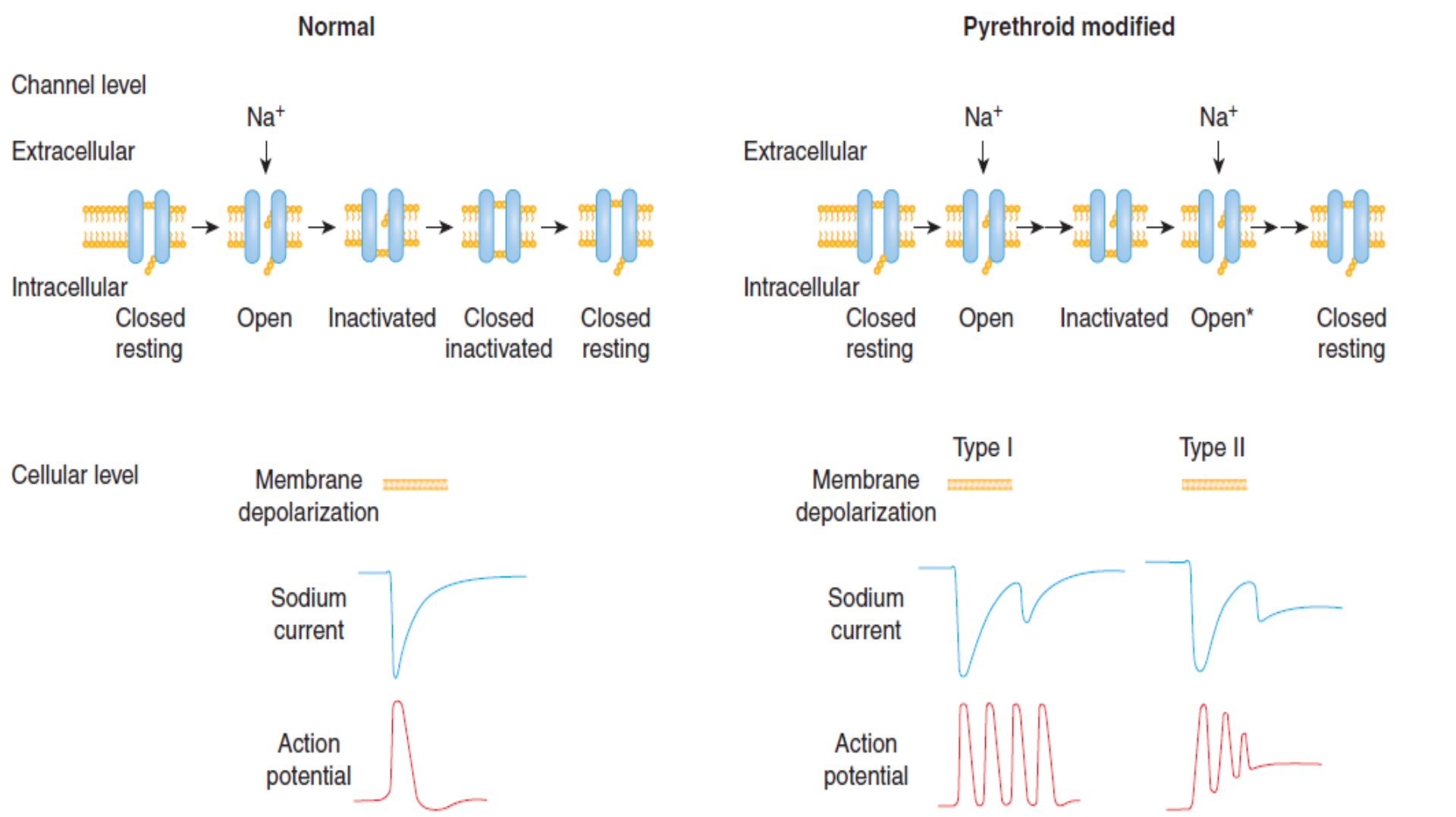


Figure 22-10. *Effect of pyrethroids on neuronal excitability.* Depolarization opens voltage-sensitive sodium channels (VSSCs) allowing Na^+ to enter the cell. To limit Na^+ entry and depolarization length, VSSCs inactivate and return to a "resting" state before reopening (top left). Pyrethroids delay inactivation (double arrows between states) of the channel and allow continued Na^+ flux (Open*) (top right). Under normal circumstances, depolarization leads to a rapidly inactivating current, and generates a single action potential (bottom left). Pyrethroid-modified VSSCs remain open when depolarization ends, resulting in a "tail" current. Type I compounds depolarize the cell membrane above the threshold for action potential generation, resulting in a series of action potential (repetitive firing). Type II compounds cause greater membrane depolarization, diminishing the Na^+ electrochemical gradient and subsequent action potential amplitude, eventually leading to depolarization-dependent block (bottom right). (From Shafer *et al.*, 2005, with permission.)

- **Signs and Symptoms:**

Table 22-12

Classification of Pyrethroid Insecticides Based on Toxic Signs in Rats

SYNDROME	SIGNS AND SYMPTOMS	EXAMPLES
Type I (T syndrome)	Aggressive sparring Increased sensitivity to external stimuli Whole-body tremors Prostration	Allethrin Bioallethrin Resmethrin Phenothrin
Type 2 (CS syndrome)	Pawing and burrowing Profuse salivation Coarse tremor Choreoatetosis Clonic seizures	Deltamethrin Fenvalerate Cypermethrin Cyhalothrin

N.B

4. Organochlorine Compounds (DTT)

- in agriculture, structure insect control, and malaria
- Their acute toxicity is moderate (less than that of organophosphates), but chronic exposure may be associated with A.E particularly in the liver and the reproductive system..fat soluble
- Have been banned in most countries in the past 30 years. Yet, because of their environmental persistence and high lipophilicity, exposure to these compounds continues, most notably through the diet

- DDT has a moderate acute toxicity when given by the oral route**(with an LD 50 of about 250 mg/kg)**
- Dermal absorption of DDT is very limited
- DDT distributes in all tissues, and the highest concentrations are found in adipose tissue.
- Extensively but slowly metabolized.
- Symptoms usually appear several hours after exposure, and death, usually due to respiratory failure, may follow after 24 to 72 hours.

- **Symptoms and signs: nervous system as the primary target**

❑Early:

- hyperesthesia of the mouth and lower part of the face, followed by paresthesia of the same area and of the tongue. Dizziness, tremor of the extremities, confusion, and vomiting,
- convulsions occur only in severe poisoning.
- myocardial arrhythmias

- **Mechanism of action:**

1. interferes with the sodium channels in the axonal membrane.
2. inhibits Na + ,K + -ATPase
3. inhibition of a Ca 2+ -ATPase
4. alters the levels of some neurotransmitters such as acetylcholine, norepinephrine, and serotonin
5. OCs alter membrane chloride ion permeability and interfere with normal GABA-ergic (g-aminobutyric acid) neuronal transmission

- **Treatment: acute exposure is rare**
- Decontamination (gastric lavage, and administration of activated charcoal reduce toxicity after oral ingestion).
- supportive treatment
- diazepam or phenobarbital may be beneficial to control convulsions, if present.
- Myocardial arrhythmias are managed with antiarrhythmics such as lidocaine
- Washing of the affected area may reduce absorption after dermal exposure
- **Chronic exposure**: target for DDT is the liver (increase enzymes levels, cancer)

5. Other Insecticides

- **Rotenoids:**

- Used in agriculture, fishing
- inhibit the mitochondrial respiratory chain,
- symptoms: increased respiratory and cardiac rates, clonic and tonic spasms, and muscular depression, followed by respiratory depression
- potential role in the etiology of Parkinson disease
- Management of poisoning is supportive and symptomatic.

Rotenone and rotenoids

DERRIS
(GENUS)
FABACEAE

Rotenone and rotesnoids

Lonchocarpus

(GENUS)

FABACEAE

- **Nicotine:** cured and dried leaves of the tobacco plant, Nicotiana
- to repel and kill insects, smoke was also used for fumigation.
- Mechanism: activating nicotinic acetylcholine receptors
- Toxicity: on large amounts (parasympathetic stimulation and ganglionic and neuromuscular blockade)
- Symptoms: nausea, vomiting, muscle weakness, respiratory effects, headache, lethargy, **and bradycardia or tachycardia**.

- Convulsions and respiratory paralysis are advanced complications of unattended nicotine toxicity.
- **Treatment** of poisoning:

1. Symptomatic
2. decontamination, induction of emesis (depending on the time of onset of symptoms)
3. maintenance of vital signs.

- **Metal – based pesticides**

arsenic compounds – insecticides, rodenticides

tributyltin – fungicide (xenoestrogenic effect)

thalium compounds – rodenticides

<u>Today</u>

Copper compounds – copper sulphate

– copper oxichloride

fungicides, algicides, molluscocides

Toxicity for fish – LC_{50} 1 – 10 $mg.l^{-1}$ depending on water quality

RODENTICIDES

- a rodenticide must satisfy several criteria:

(a) the poison must be very effective in the target species once incorporated into bait in small quantity

(b) baits containing the poison must not excite bait shyness, so that the animal will continue to eat it

(c) the manner of death must be such that survivors do not become suspicious of its cause

(d) it should be species-specific, with considerable lower toxicity to other animals

1. Fluoroacetic Acid and Its Derivatives

- The main targets of toxicity are the central nervous system and the heart.
- Symptoms of toxicity: gastrointestinal symptoms, severe cardiovascular effects (ventricular tachycardia, fibrillation, hypotension), as well as CNS effects (agitation, convulsions, coma)

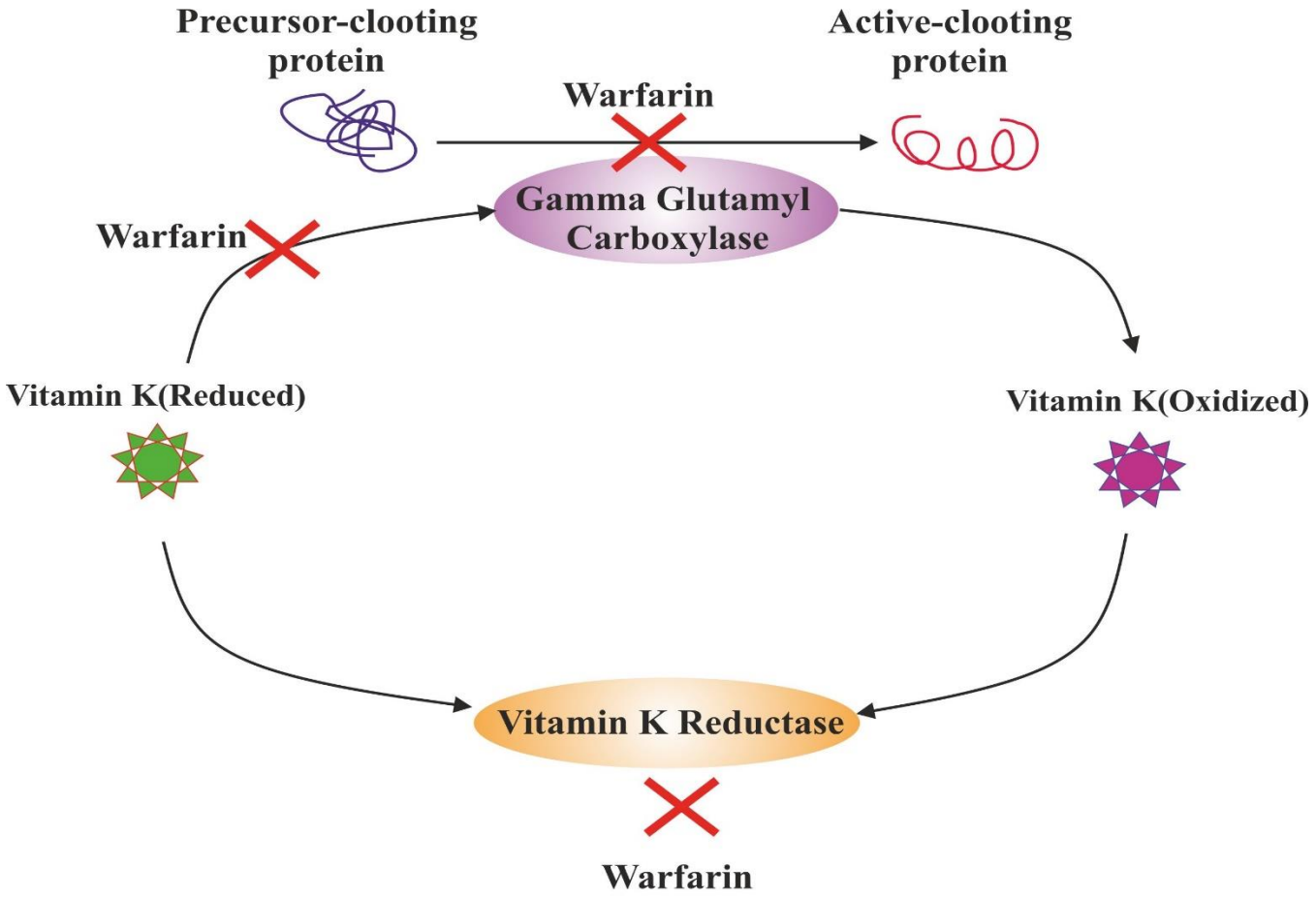
- Treatment:
- Monacetin (60% glycerol monoacetate) has proved beneficial in the treatment of poisoned primates
- Use of procainamide (for cardiac arrhythmia)
- Use of Barbiturates (to control seizures)

2. Anticoagulants

- **Toxicokinetics**
- Warfarins are rapidly and completely absorbed, reaching peak plasma concentrations within one hour. In circulation, warfarins are almost completely bound to plasma albumin (97–99%), localize to lipid and protein compartments (Vd ¼ 0.15 L/kg), and have a long half-life (about 35 hr).

- Mechansim: Coumarins antagonize the action of vitamin K in the synthesis of clotting factors (factors II, VII, IX, and X)….. Warfarin

Warfarin mechanism of action



Warfarin: Mode of action.

- Accidental exposure from ingested rodent bait mostly involves children, whereas intentional ingestion is associated with attempted suicides
- Symptoms : massive bruises, hematomata, gum and nasal hemorrhage… monitor INR
- “second- generation” anticoagulants: “superwarfarins” brodifacoum or difenacoum because of increase of resistance to warfarin.

- **Clinical Management of Acute Poisoning**
- Replacement of blood loss, A unit of fresh frozen replenishes lost multiple clotting factors and restores blood volume.

- **Chronic anticoagulant management** necessitates the administration of vitamin K1 (phytonadione).
- Subcutaneous or IV administration of this active form of vitamin K rapidly corrects PT within 24 hours. Maintenance with the oral dosage form may be continued for several weeks, as needed.

N.B

Drimia maritima and *indica*

FUNGICIDES

- Are surface or plant protectants, and are applied prior to potential infection by fungal spores.

- With few exceptions, fungicides have low acute toxicity in mammals.

1. Captan and Folpet

- chloroalkylthio fungicides: due to the presence of side chains containing chlorine, carbon, and sulfur
- low acute oral and dermal toxicity (LD 50 ≅ 5g/kg), while they are very toxic by the i.p. route (LD 50 = 40–50 mg/kg).
- They are potent eye irritants, but only mild skin irritants
- Both are extensively and rapidly metabolized in mammals
- Carcinogenic and reproductive studies

HERBICIDES

- are chemicals that are capable of either killing or severely injuring plants.
- Mechanism: act at a large number of sites of metabolic functions and energy transfer in plant cells (Inhibition of photosynthesis, Inhibition of respiration, Inhibition of lipid and protein synthesis,

1. **Preplanting herbicides**: applied to the soil before a crop is seeded
2. **Preemergent herbicides**: applied to the soil before the time of appearance of unwanted vegetation.
3. **Postemergent herbicides**: applied to the soil or foliage after the germination of the crop and/or weeds

- Herbicides are divided according to the manner they are applied to plants:

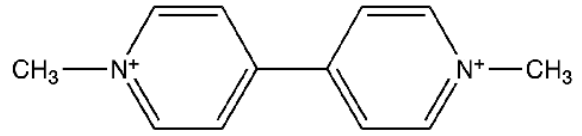
1. **Contact herbicides**: affect the plant that was treated
2. **Translocated herbicides**: applied to the soil or to above-ground parts of the plant, and are absorbed and circulated to distant tissues.

1. **Nonselective herbicides :** will kill all vegetation
2. **Selective compounds :** used to kill weeds without harming the crops.

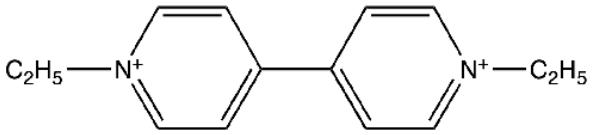
Bipyridyl Compounds

Paraquat:

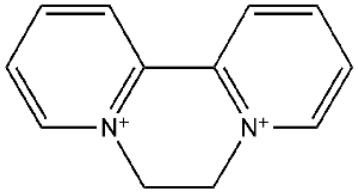
- Paraquat has one of the highest acute toxicities among herbicides; its oral LD 50 in rat is approximately 100 mg/kg.
- Target of toxicity: **lung** and **kidney.**
- Mechanism of toxicity: Forms free radicals (redox cycling reactions), mitochondrial damage.



Paraquat

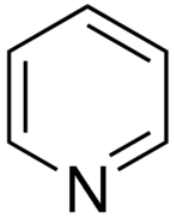


Ethyl paraquat (I.S.)



Diquat

Pyridine



Treatment:

- Prevention of **absorption** from the gastrointestinal tract, prevention of its **accumulation** in the lung, use of free radical scavengers [**catalases, glutathione peroxidase, superoxide dismutase (SOD), α-tocopherol (Vit. E), ascorbic acid (Vit. C), β carotene**] and prevention of lung **fibrosis**.

- Whole-bowel irrigation, forced diuresis and hydration, hemodialysis, hemoperfusion, surgical approaches, radiotherapy.

DIQUAT:

- Lower toxicity.
- It is not carcinogenic in rodents, has no effect on fertility, and is not teratogenic.
- No lung toxicity.
- Target organs for toxicity are the gastrointestinal tract, the kidney and particularly, the eye.
- Mechanism of toxicity: forms free radicals.

Symptoms:

- Nausea, vomiting, diarrhea, ulceration of mouth and esophagus, decline of renal functions, and neurologic effects, but no pulmonary fibrosis.

- **Treatment:** preventing absorption and enhancing elimination.

References

- Toxicology: the basic science of poisons, casarett and doulls, 8 ed ,2013,unit 1, chapters22,24,32
- Clinical toxicology , principles and mechanisms, 2 ed , Frank A. Barile,2010,chapter28,29,30