
بسم الله الرحمن الرحيم

Cholinergic Drugs;

(Parasympathomimetic Drugs)

By

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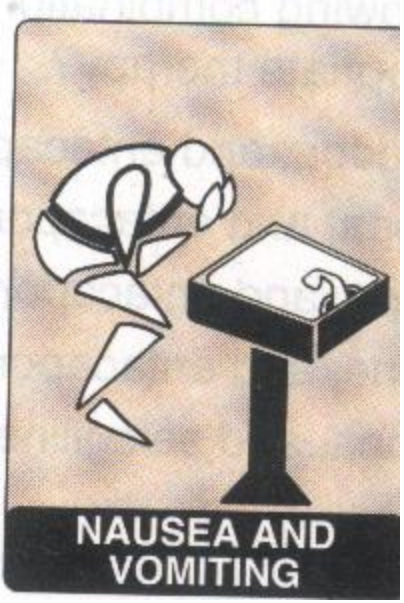
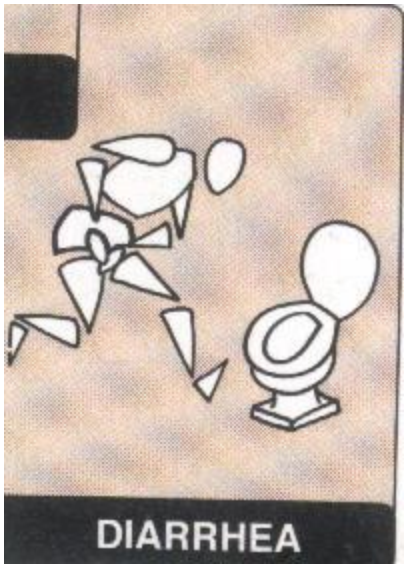
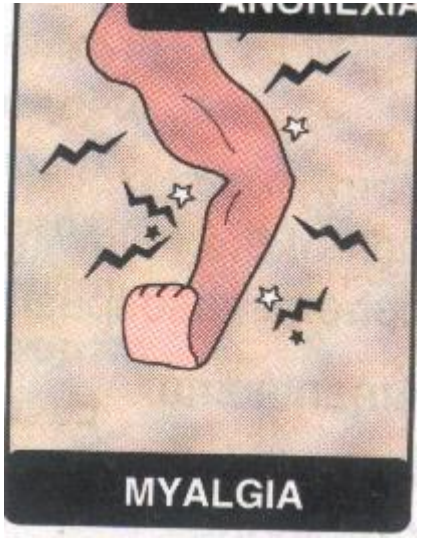
Adverse effects of Ach E inhibitors;

peripheral Cholinomimetic effects.







Contraindications of Cholinomimetics;

- **Bronchial asthma,**
- Mechanical Obstruction of GIT & Urinary Bladder.
- **Peptic ulcer** --- M_1 receptors on vagal ganglion
- **Cardiac disease**
  - ve chronotropic effect (SA node).
  - ↓ conduction velocity through AV node.
  - No effect on force of contraction of ventricles (no M receptors in ventricles).
- **Parkinson's disease**
- Hyperthyroidism -- Predispose to arrhythmia

Toxicity of organophosphates;

- Muscarinic symptoms, Nicotinic symptoms, &CNS symptoms.
  - (DUMBLESS)
    - D diarrhoea
    - U urination
    - M miosis
    - B bronchoconstriction
    - B bradycardia
    - L lacrimation
    - E excitation (of skeletal muscles and CNS)
    - S salivation
    - S sweating

- Muscarinic – smooth muscles + glands + CVS;
  - Eye --- pupillary constriction.
  - GI tract --- cramps, N, V, & diarrhea.
  - Urinary tract --- incontinence, urination.
  - Bronchoconstriction --- wheezing, dyspnea.
  - ↑ed glandular secretions --- sweating, salivation, lacrimation.
  - Heart and BV --- bradycardia and hypotension.
- **Nicotinic;**
  - Skeletal muscle fasciculations and then paralysis (e.g., respiratory muscles)
  - Autonomic ganglionic stimulation.
- **CNS effects;**
  - behavioral excitation, depression of cardiovascular [CV] and respiratory centers).

How will you Treat organophosphate poisoning;

- Termination of further exposure.
- Maintain patent airway, artificial ventilation.
- Supportive measures.
  - BP, hydration, control of convulsions.
- **Specific antidotes;**
  - **1) Atropine**
  - **2) Cholinesterase reactivators**
    - **Pralidoxime (PAM)**
    - **Diacetylmonoxime(DAM)**
    - obidoxime

Atropine in organophosphate poisoning

- **Atropine Counter only muscarinic effects.**
- **Does not reverse nicotinic effects.**
- Higher doses -- can **reverse the central effects.**
- It is given in large doses parenterally
  - 1-2 mg I/v every 5-15 minutes until signs of effects appear(dry mouth, reversal of miosis)
  - 1 g/day for as long as 1 month.

Cholinesterase reactivators – oximes;

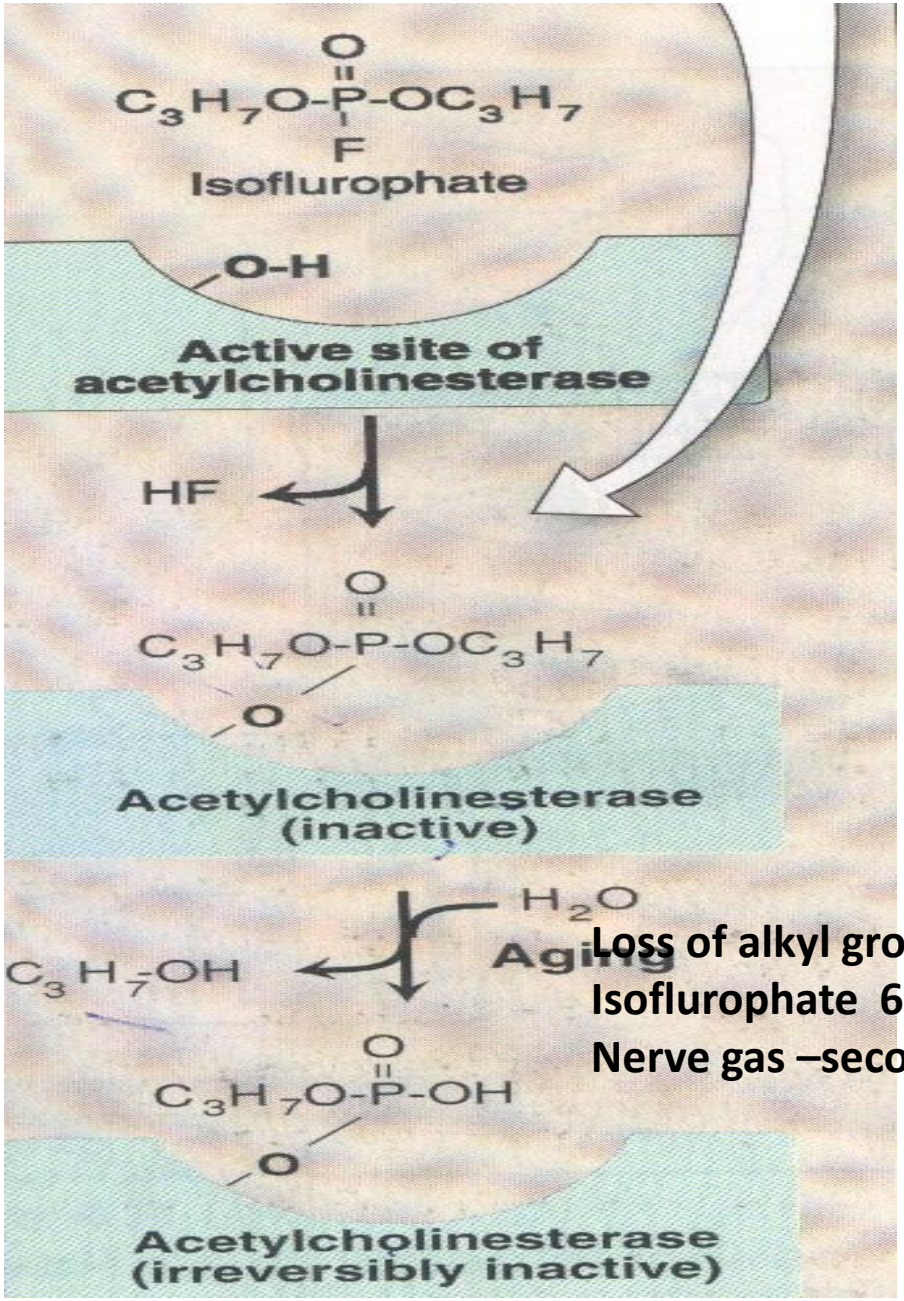
- Acetylcholinesterase enzyme has two binding sites **anionic and esteratic site.**
- **Oxime group (=NOH)** has very high affinity for phosphorous atom at the esteratic site.
- **It hydrolyse the phosphrylated enzyme that has not aged.**

  the site become free → reactivation of the enzyme → metabolism of the Ach resumes.

Cholinesterase reactivators – oximes;

- Effective only if given within 24 hours as after that “aging” occurs.
- **Organophosphate aging** -- a process whereby the organophosphate, after binding to cholinesterase, is **chemically modified and becomes more firmly bound to the enzyme.**
- Pralidoxime does not reverse the central effects.
- Diactylmonoxime (DAM) can cross the BBB.

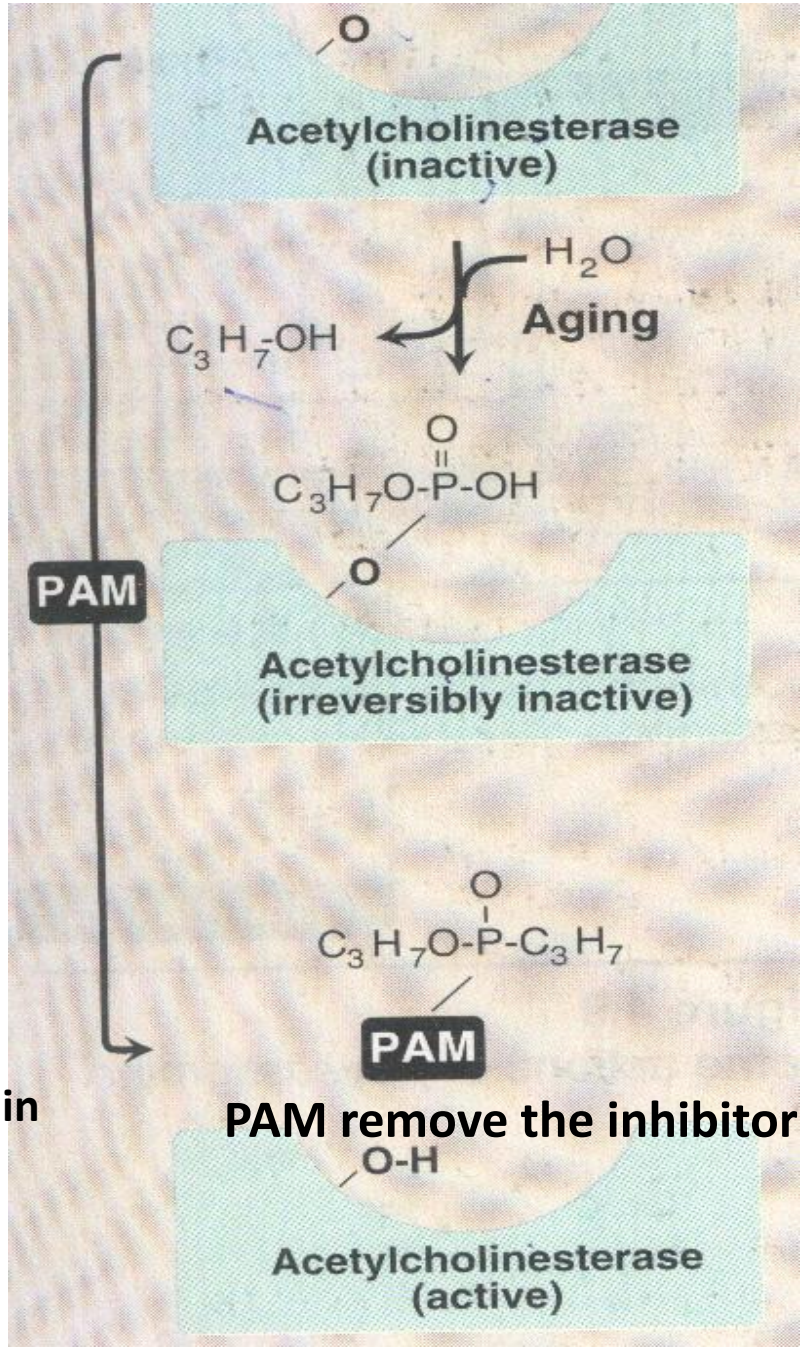
Phosphorylation of enzyme



Loss of alkyl group

Isoflurophate 6-8 hrs

Nerve gas –seconds to min



PAM remove the inhibitor

Can oximes (pralidoxime & Diacetylmonoxime) be used be used in reversible anticholinesterase poisoning?

- Oximes react at esteretic site whereas reversible anticholinesterase (physostigmine, neostigmine) react at the anionic site. **Hence they are not effective in neostigmne / physostigmine poisoning.**
- Oximes are ineffective, and are in fact contraindicated in over dosage with neostigmine, physostigmine, or the carbamyl-esters


Thank You