

# pharmacolog pharmacolog



By:.

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# Indirect acting cholinomimetic drugs

**The students should know:**

- ✓ **Classification of indirect acting cholinomimetics.**
- ✓ **Mechanism of action, kinetics, dynamics and uses of anticholinesterases.**
- ✓ **Adverse effects & contraindications of anticholinesterases**
- ✓ **Symptoms and treatment of organophosphates toxicity.**

# Indirect cholinomimetics (also called anticholinesterases)

**Mechanism of action:**

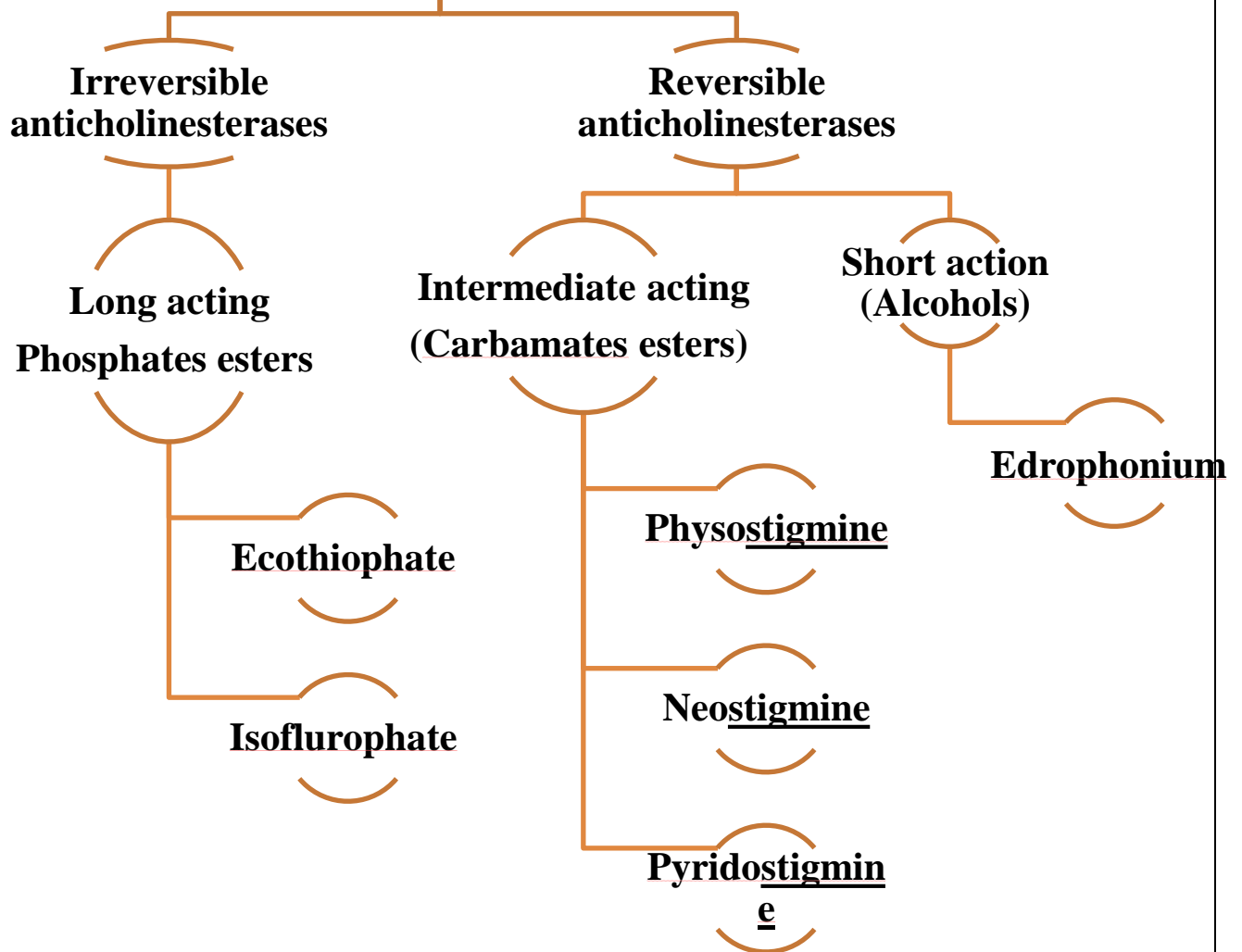
**Anticholinesterases** prevent hydrolysis of Ach by binding to cholinesterase thus increase Ach concentrations and actions at the cholinergic receptors (both nicotinic and muscarinic).

Note: Cholinesterase has two active site and anticholinesterases will bind to either one or both active site depending on the location and chemistry

**Anticholinesterases** are similar in structure to Ach so combine with cholinesterase instead of Ach

Note: Cholinesterase will bind to anticholinesterase then after a while it will starts to break Anticholinesterase down.  
(So it has long duration of action)

# Classification of anticholinesterases



# Reversible anticholinesterases

## Neostigmine

Quaternary ammonium comp.

Polar compound. Can be used orally but without good absorption

### Uses

1/ Treatment of myasthenia gravis (because it has long duration of action)

2/ Paralytic ileus & Urinary retention

3/ Competitive neuromuscular blockers intoxication

## Physostigmine

Tertiary ammonium compound (lipid soluble)

Good oral absorption

cross BBB (*has CNS effects*)

### Uses

1/ Glaucoma

2/ atropine toxicity (atropine is anti parasympathetic it blocks the muscarinic receptor)

## Edrophonium

NOT absorbed orally (*given by injection*) Because it is polar

attach mainly to anionic site of cholinesterase by weak hydrogen bond. (due to weak hydrogen bond it has short duration)

Has short duration of action (5-15 min.)

Used for diagnosis of myasthenia gravis (because of its short duration)

\* To treat patient who has overdose from atropine, we should give something that stimulates the parasympathetic system.

(Physostigmine)

\* Anticholinesterases in general:

- ✓ Decrease intraocular pressure.
- ✓ Increase GIT motility.
- ✓ Stimulate urination.

## Irreversible anticholinesterases or (Organophosphorous compounds)

الحشرية المبيدات منها

- ✓ It has phosphate group so it going to bind to cholinesterase with strong covalent bond (long duration)
- ✓ Irreversible anticholinesterases are very toxic.
- ✓ E.g. **Ecothiophate - Isofluorophate**
- ✓ All phosphates are lipid soluble except **ecothiophate**, which is polar.

## Ecothiophate

**Aging make bond extremely stable** (After 24 hours, the bond get old and become very stable bond, so the cholinesterase will not break the drug rapidly and that may cause toxicity)

**Used for glaucoma.**

## Organophosphates toxicity

1. Sever bradycardia, hypotension.
2. Bronchospasm.
3. Increased GIT motility → cramps & diarrhea.
4. CNS effects → convulsion, coma and respiratory failure.
5. Initial twitching of skeletal muscles → muscle weakness & paralysis.

## The treatment:

- ✓ We should first support the respiration; by taking the patient away from the source of contamination and do Artificial respiration
- ✓ Give him the medication as soon as possible.

## **Treatment of organophosphate toxicity**

**Support respiration**

**Cholinesterase reactivators (Oximes)**

**Atropine (to block muscarinic & central actions).**

### **OXIMES**

#### **Pralidoxime (PAM)**

**Cholinesterase reactivator**

**Acts by regeneration of cholinesterase enzyme.**

**Reactivates recently inhibited enzymes before aging.**

**(We cannot use after 24 hours because of aging).**

**Uses**

**I.V. → over 15-30 min for organophosphate intoxication.**