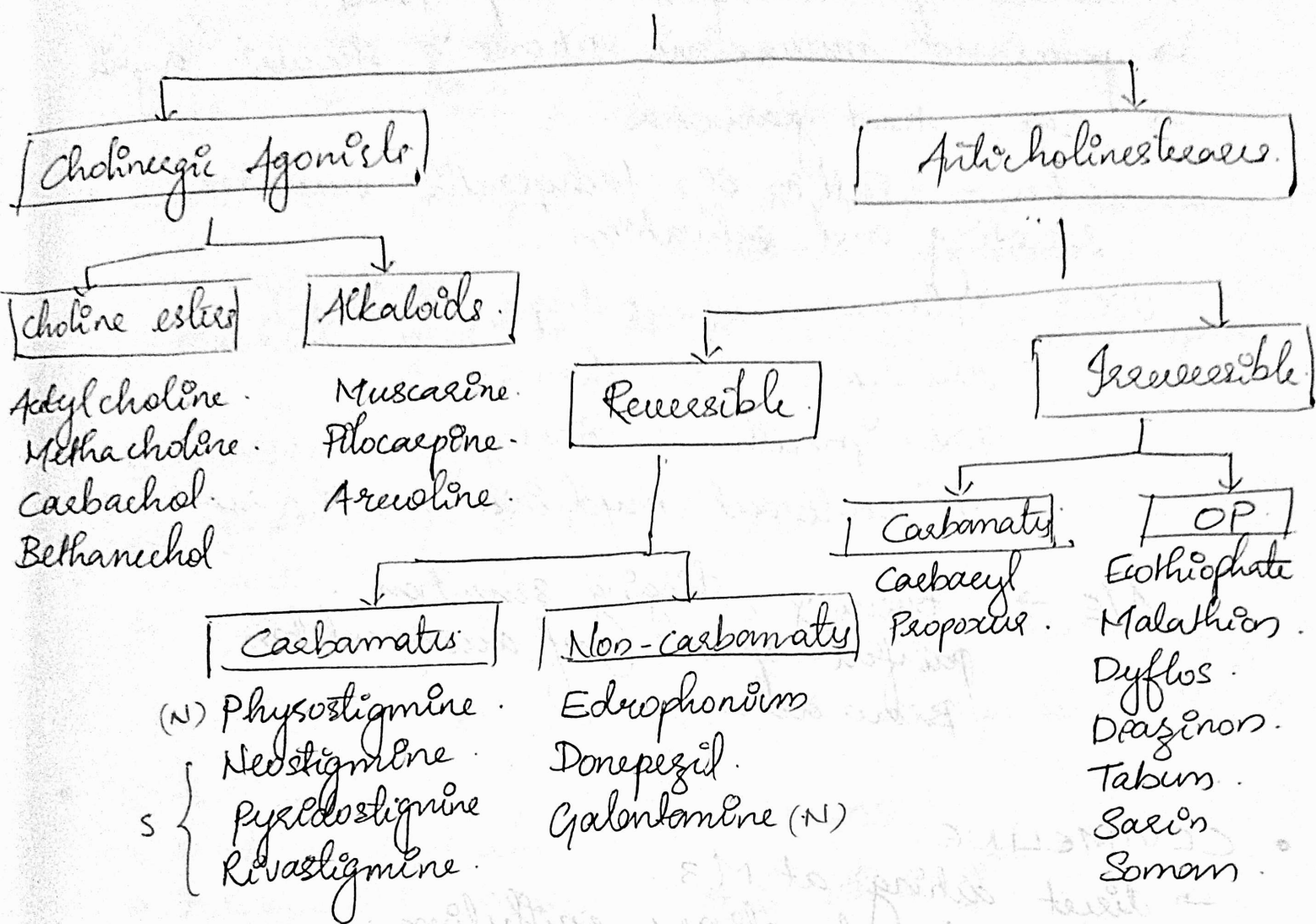


CHOLINERGIC DRUGS.



• ACETYLCHOLINE

cannot be given orally or IV.
used as eye drops - eye surgery.

• BETHANECHOL. (M3)

post operative paralytic ileus (rarely).

- post OP & post partum non obstructive urinary retention
- neurogenic bladder
- congenital megacolon
- GERD.

side effects prominent - hiccups, urticaria, involuntary urination / defecation, flushing, ↓ BP, sweating, bronchospasm.

• Pilocarpine

- leaves of *Pilocarpus microphyllus*.
- parasympathetic actions & stimulate parasympathetic.
- Eye - treat glaucoma.
- Salivary glands - salivary secretion.
- Sweating and salivation.

USE: Glaucoma (eye drops, ointment)

dry eyes - Xerostomia

Pdry mouth - xerostomia

to contract mydriators after refraction testing.

A/E → Sweating, shivering sensation, painful spasms of accommodation, Bradycardia.

• CEVIMELINE

- direct acting at M3.
- lacrimal and salivary epithelium.
- longer lasting anticholinergic action than pilocarpine.
- ↑ lacrimal secretion in Sjögren's syndrome.

MECHANISM OF ACTION - ANTICHOLINESTERASES

- structural similarity to ACh, hence bind to anionic and esteratic site of acetylcholinesterase enzyme, inactivate it.

The phosphorylated enzyme can undergo 'aging' by loss of one of the alkyl groups - totally resistant to hydrolysis - irreversible inhibition.

Pharmacological actions - similar to cholinergic stimulants.

* Lipid soluble agents (physostigmine, organophosphates) more muscarinic & CNS effects.

* Lipid insoluble agents (Neostigmine & other quaternary ammonium compounds) no CNS effects, marked effect on skeletal muscles & NMJ.

• EDROPHONIUM

- binds only to anionic site
- weak cholinergic bond.
- diffuses rapidly (10-20 min) - short acting

TENSILON TEST → diagnosis of myasthenia gravis

• NEOSTIGMINE

- binds to both sites
- intermediate action (30 min - 6 hours)
- For myasthenia gravis - 15mg orally, 6 hourly

USES (of anticholinesterases)

1. Myasthenia gravis

2. Myasthenia gravis (Neostigmine, Pyridostigmine)

3. Poisoning due to anticholinergic drugs

Atropine poisoning
Poisoning with tricyclic antidepressants, anticholinergics
P.O.C → Physostigmine

4. Curare poisoning - skeletal muscle paralysis
P.O.C → Neostigmine

5. Leads like neostigmine, skeletal muscle paralysis.

venom $\rightarrow$ Neostigmine + Atropine $\rightarrow$ to prevent resp. paralysis.

6. Post-operative paralytic plus 9 urinary retention.

7. Atropine $\rightarrow$ Nicotinic (prevented by atropine as glycopyrrate).

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ORGANOPHOSPHOROUS POISONING.

Mechanism of action.

OP $\rightarrow$ powerful inhibitor of AChE $\rightarrow$ continuous stimulation $\rightarrow$ ACh accumulates $\Rightarrow$ essential paralysis of nerve/muscle.

Symptoms

Respiratory like smell.

1) muscarinic $\rightarrow$ lacrimation, salivation, sweating, copious rhinobronchial secretions, miosis, etc.

2) nicotinic $\rightarrow$ ptosis, flaccidity of vision, tachycardia, weakness, fall in BP, tachy/bradycardia, arrhythmias, muscular collapse.

3) Nicotinic $\rightarrow$ muscle fasciculations, weakness, respiratory paralysis.

11) Central: Disorientation, ataxia, convulsions, coma, death.

Chronic poisoning - usually in occupational exposure $\rightarrow$ peripheral neuropathy, tremor, restlessness.

Treatment

(a) Decontamination and termination of further exposure to poison.

(b) Supportive measures.

- Airway, breathing, circulation.

- positive pressure ventilation (if needed).

- maintain BP, IV fluids (hydration).

- control of convulsions - Diazepam.

(c) Specific treatment.

(i) ATROPINE $\rightarrow$ specific antidote.

Anticholinergic $\rightarrow$ block N receptors $\rightarrow$ not effective to control N symptoms.

Dose: 2mg IV every 10 min till atropinisation (pupil dilates, reflexes return).

Max dose $\rightarrow$ 50-100mg.

(ii) Cholinesterase Reactivators $\rightarrow$ OXIMES.

PRALIDOXIME

MOA : Oxime binds to anionic site of AChE
↓
react with OP to form oxime-OP complex
↓
oxime-OP complex dissociates, sets the
enzyme free
↓
AChE reactivated.

Dose : PRALIDOXIME-

1-2g IV given within 5 minutes of
poisoning (not later than 24 hours).
before enzyme undergoes aging.
Not useful in carbamate poisoning