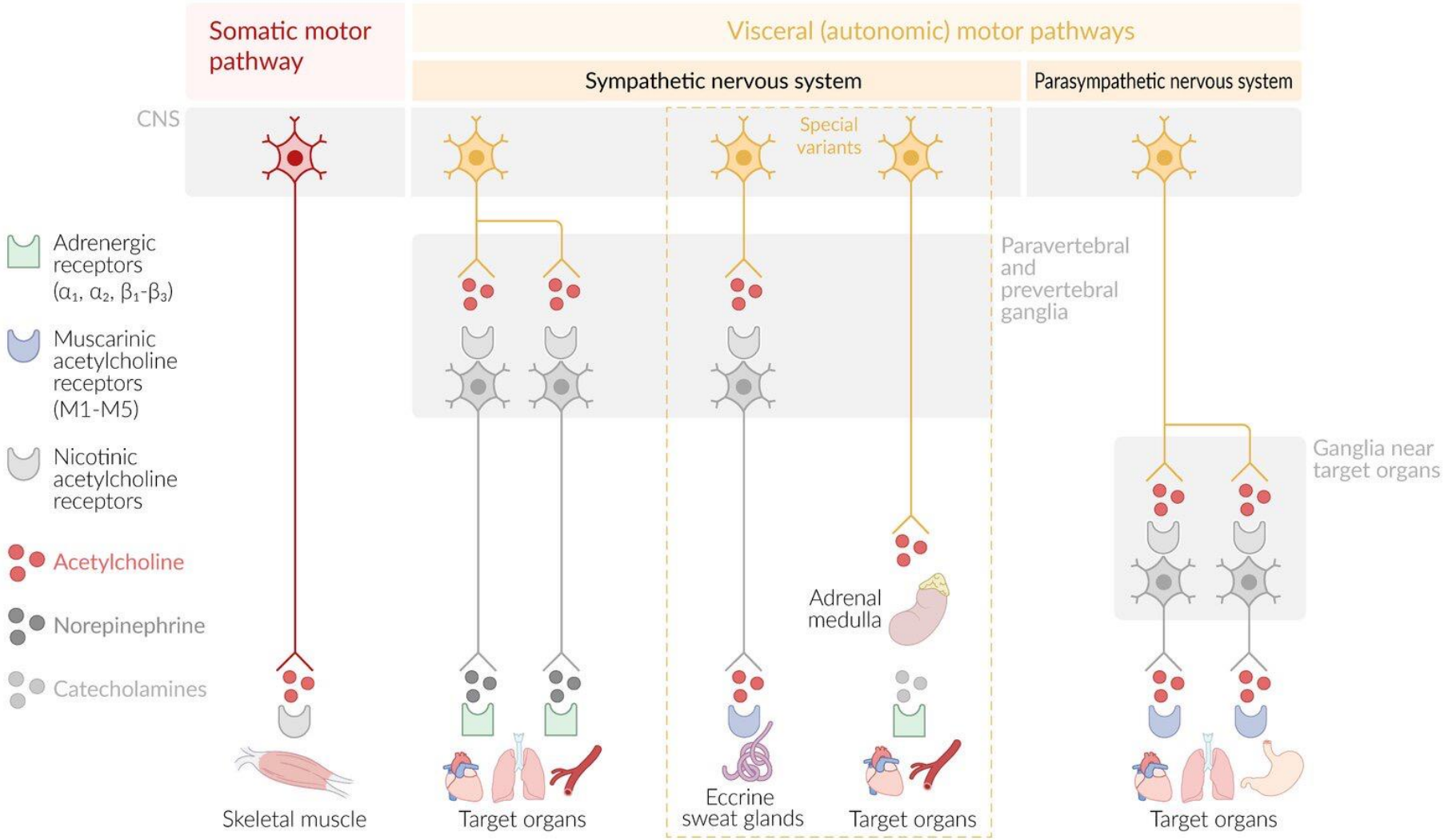
Parasympathetic system

Abdalrhman Froukh

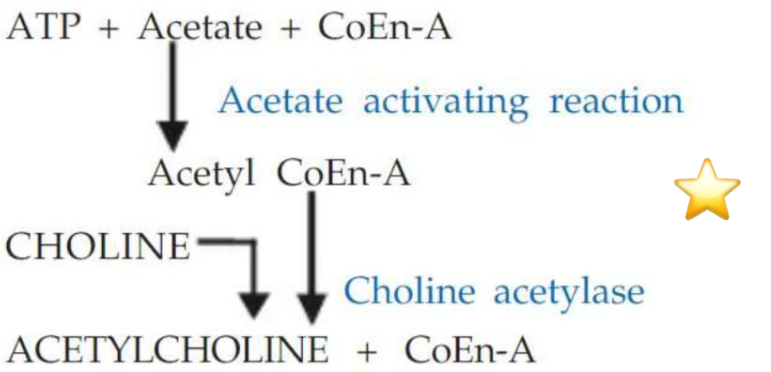

Somatic motor pathway
Visceral (autonomic) motor pathways
Sympathetic nervous system
Parasympathetic nervous system
CNS
Special variants
Adrenergic receptors (α_1, α_2, β_1-β_3)
Muscarinic acetylcholine receptors (M1-M5)
Nicotinic acetylcholine receptors
Acetylcholine
Norepinephrine
Catecholamines
Paravertebral and prevertebral ganglia
Ganglia near target organs
Adrenal medulla
Skeletal muscle
Target organs
Eccrine sweat glands
Target organs
Target organs

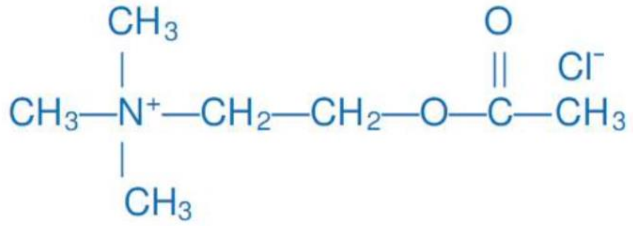
Synthesis and metabolism of ACh

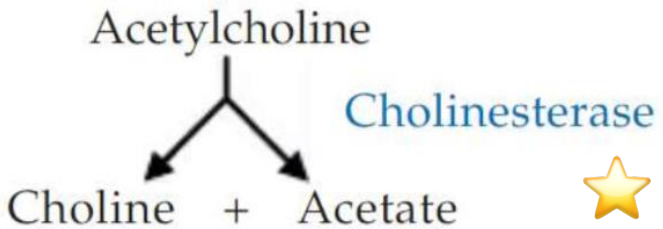
Acetylcholine (ACh) is a major neurohumoral transmitter at autonomic as well as somatic sites.

Choline is actively taken up by the axonal membrane and acetylated with the help of ATP and coenzyme-A by the enzyme cholineacetylase.

ACh is hydrolyzed by the enzyme cholinesterase, and choline is recycled immediately after release.







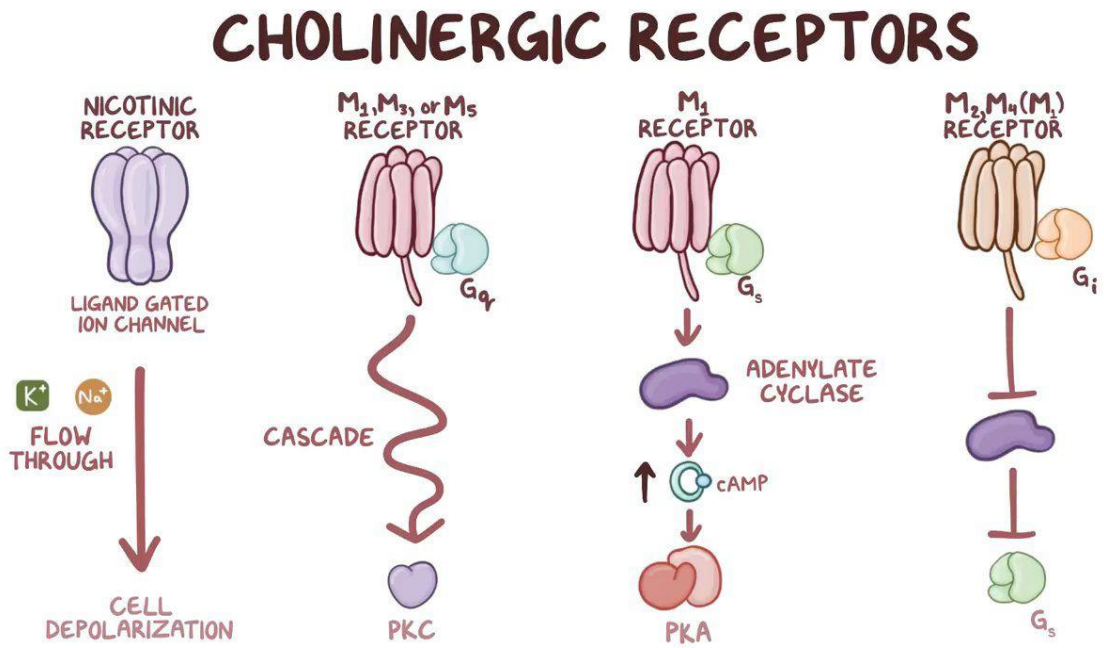
Cholinoceptors

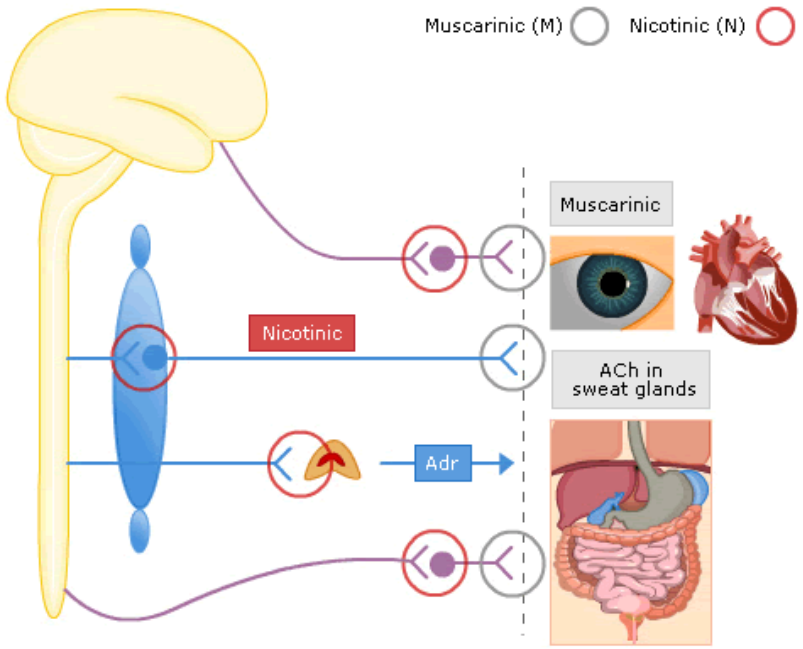
Two classes of cholinoceptors are muscarinic and nicotinic.

Muscarinic receptors: These receptors are selectively stimulated by muscarine and selectively blocked by atropine.

They are located in the heart, blood vessels, eye and glands of the gastrointestinal, respiratory, and urinary tracts, sweat glands, and in the CNS.

The muscarinic receptors have been divided into 5 subtypes: M1, M2, M3, M4, and M5





M1	M2	M3
AUTONOMIC GANGLIA: depolorization, alters autonomic nerve messaging GASTRIC GLANDS: histamine release, acid secretion BRAIN: increase memory, attention, emotional responses	HEART: reduces heart rate, slows AV node conduction, reduces force of contraction	GI TRACT & GALLBLADDER: smooth muscle contraction PUPILS: regulates pupil constriction GLANDS: promotes eye, mouth, sinus, lung and skin lubrication BLOOD VESSELS: increases vasodilation

Muscarinic cholinoceptors

The first 3 have been functionally characterized as following:

M1: has a major role in mediating gastric secretion and relaxation of the lower esophageal sphincter caused by vagal stimulation.

M2: Cardiac muscarinic receptors are predominantly M2 and mediate vagal bradycardia.

M3 :Visceral smooth muscle contraction and glandular secretions are elicited through M3 receptors.

Muscarinic actions

All blood vessels are dilated, though only a few (skin of face, neck) receive cholinergic innervation.

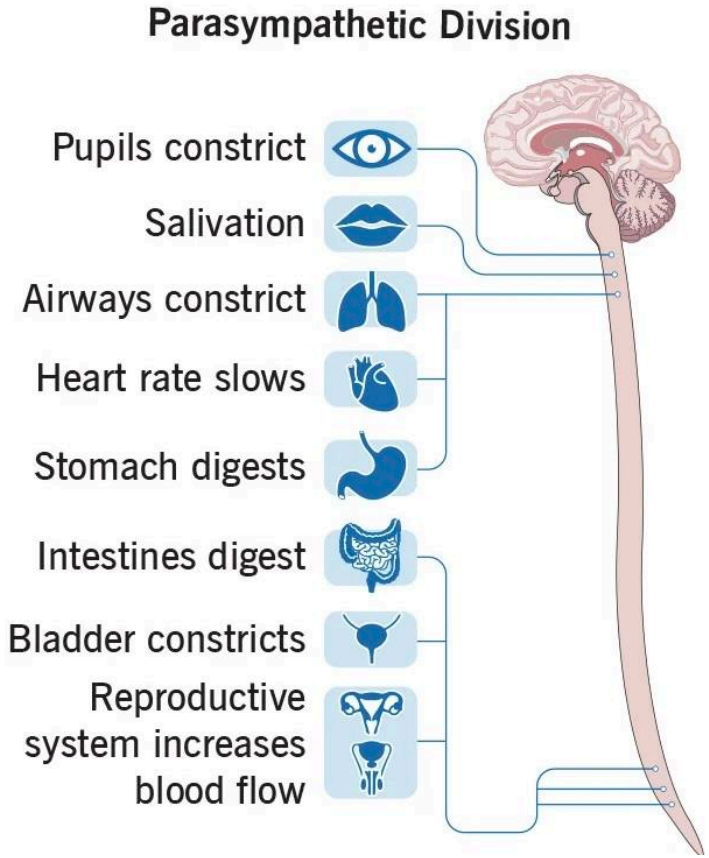
Smooth muscle contraction in most organs.

Secretion from all parasympathetically innervated glands is increased (sweating, salivation, lacrimation, and gastric secretion).

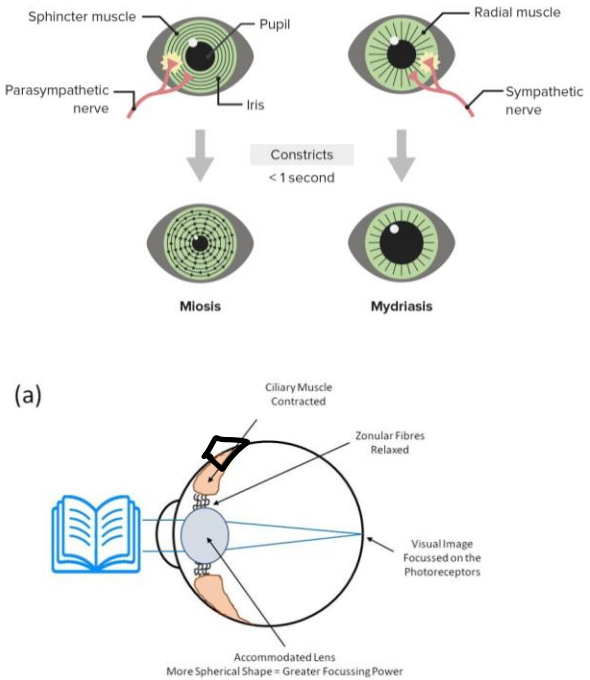
Bronchial muscles constrict (asthmatics are highly sensitive).

Contraction of circular muscle of iris →miosis.

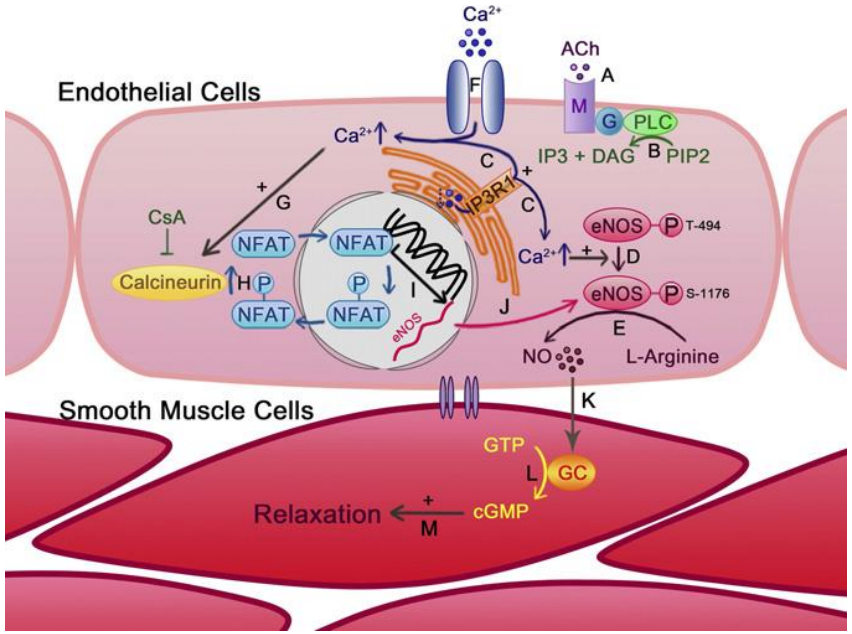
Contraction of ciliary muscle → reduction in intraocular tension (especially in glaucoma patients).



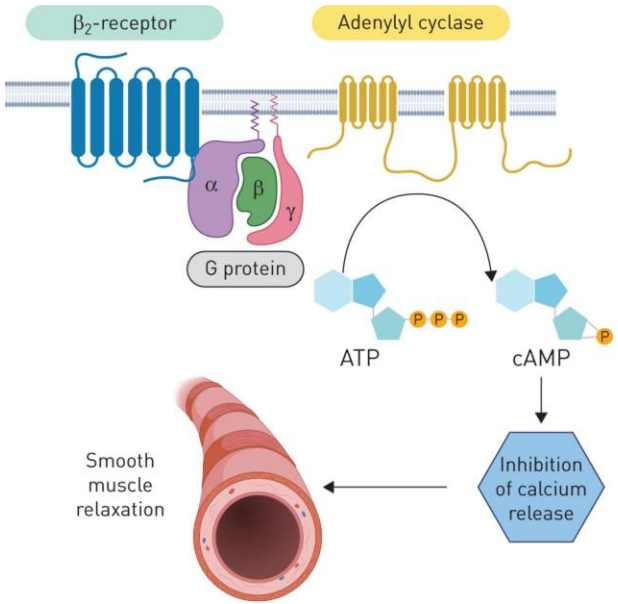
Eyes



Blood Vessels



Smooth Vessels



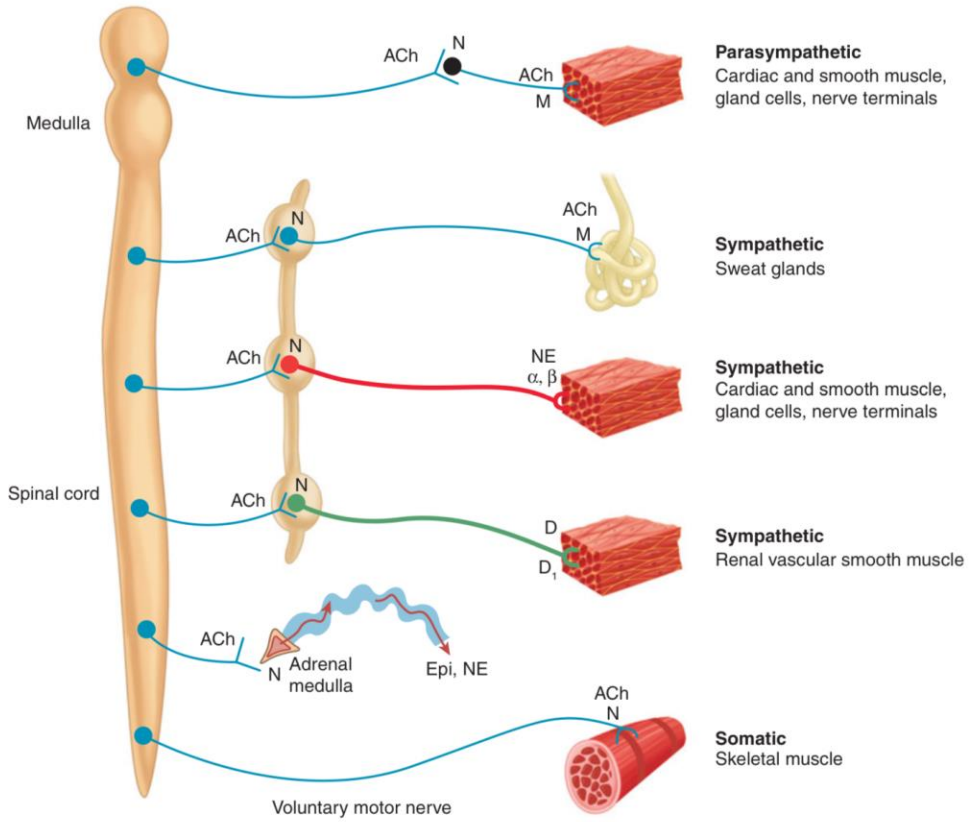
Muscarinic actions

Nicotinic receptors

Based on location and selective agonists and antagonists two subtypes:

Nm: are present in the skeletal muscle, mediate skeletal muscle contraction. They are selectively stimulated by phenyl trimethyl ammonium (PTMA) and blocked by tubocurarine.

Nn: are present on ganglionic cells of ANS, adrenal medullary cells,in the spinal cord and certain areas of the brain. They are selectively stimulated by dimethyl phenyl piperazinium (DMPP) and blocked by hexamethonium.



Nicotinic actions

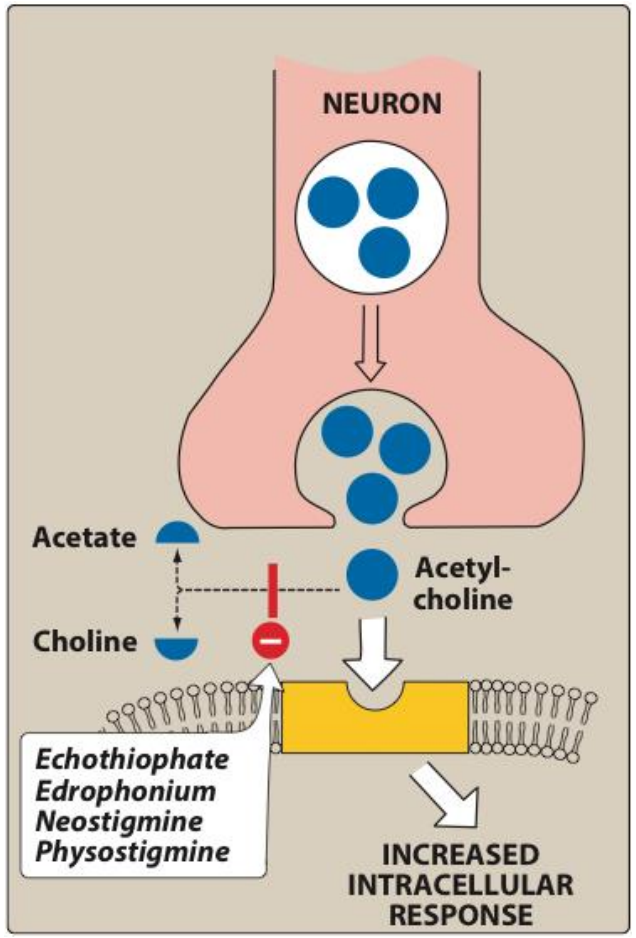
- Autonomic ganglia:
- High dose ACh stimulates both sympathetic and parasympathetic ganglia causing tachycardia and a rise in BP.
- Skeletal muscles:
- ACh causes contraction of the skeletal muscle fiber.

Cholinergic drugs (Parasympathomimetic)

They act similarly to ACh, either:

1) Directly by interacting with cholinergic receptors (agonists).

2) Indirectly by increasing the availability of ACh (anticholinesterases).



CHOLINERGIC AGONISTS

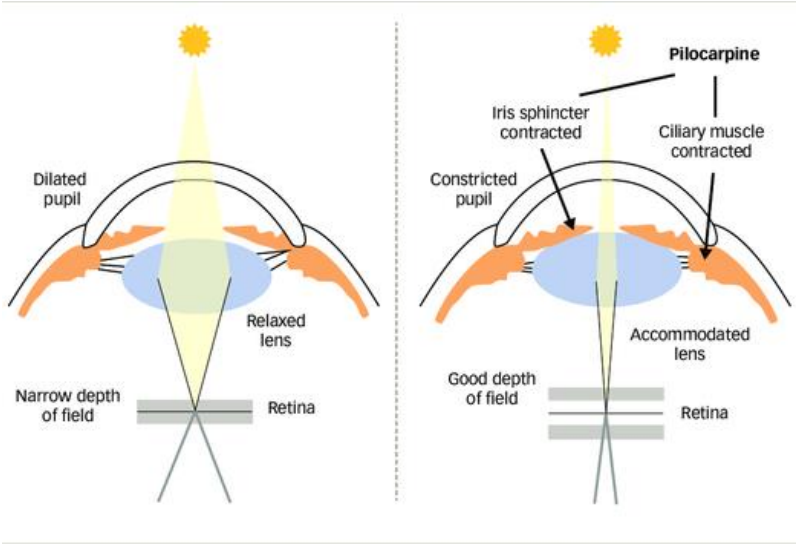
Choline esters	*Alkaloids*
Acetylcholine	Muscarine
Methacholine	Pilocarpine
Carbachol	Arecoline
Bethanechol	

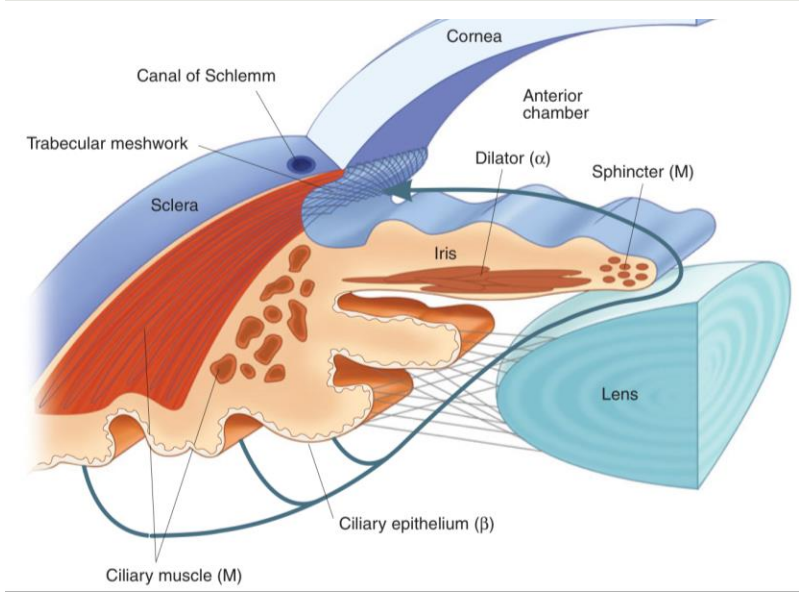
Cholinergic alkaloids

1. Pilocarpine: obtained from the leaves of Pilocarpus microphyllusIt has prominent muscarinic actionsIt causes marked sweating, salivation.

Applied to the eye, it penetrates the cornea and causes miosis, ciliary muscle contraction, thus decreasing intraocular tension (i.o.t.) (lasting 4–8 h).

Used primarily in glaucoma (0.5–4% drops).





Cholinergic alkaloids

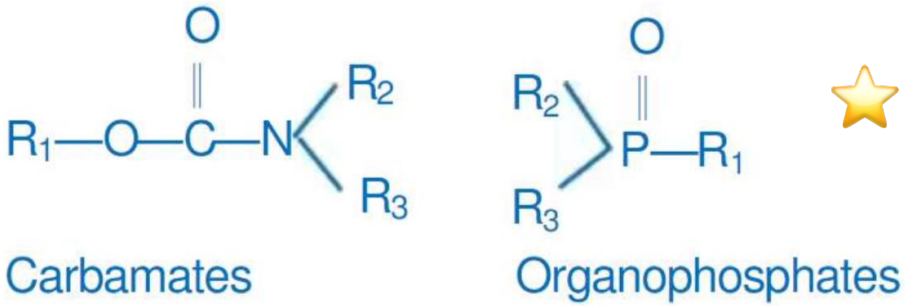
- 2. Muscarine: occurs in poisonous mushrooms Amanita muscaria and Inocybe species has only muscarinic actions.
- It is not used therapeuticallyIt is of toxicological importance in mushroom poisoning, Antidote is atropine.
- 3. Arecoline: found in betel nut Areca catechu.
- It has both muscarinic and nicotinic actions.
- Prominent CNS effects.

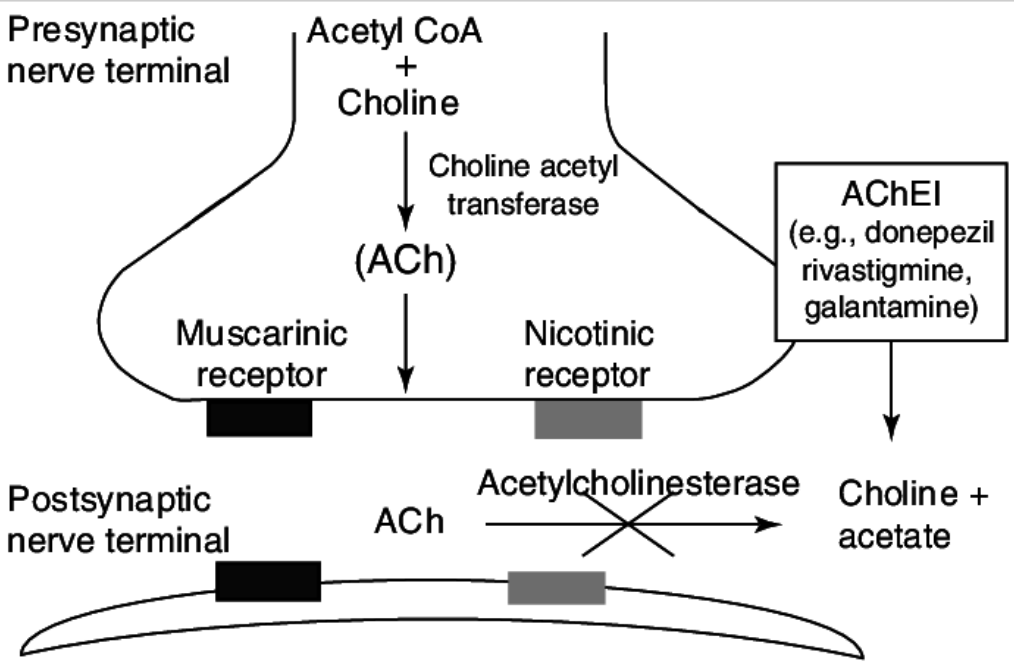
Anticholinesterases

Anticholinesterases (anti-ChEs)Agents which inhibit ChE thus protect ACh from hydrolysis → cholinergic effects.

They have similar but more intense actions as directly acting cholinoceptor stimulants.

Anti-ChEs are either esters of carbamic acid or derivatives of phosphoric acid.



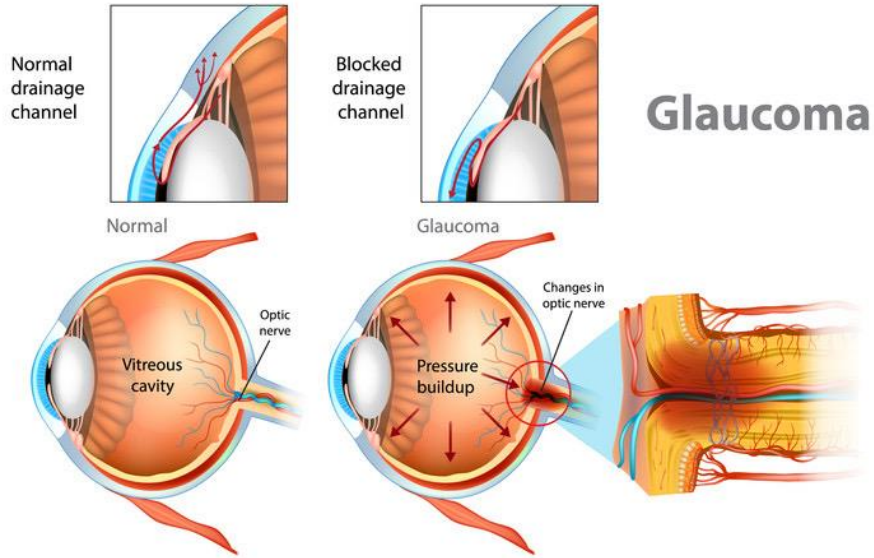


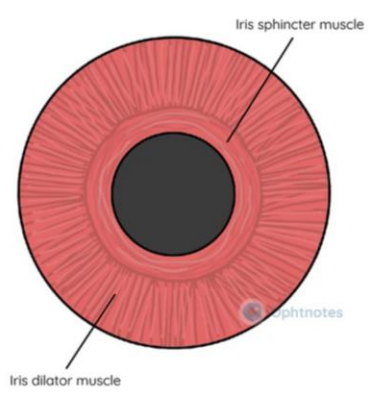
Therapeutic uses of anti-ChEs

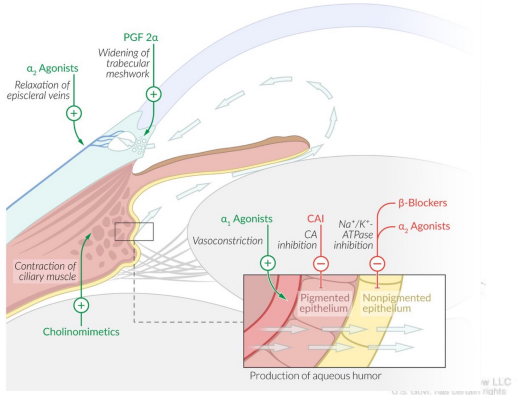
1) Glaucoma: It is a progressive form of optic nerve damage associated with raised intraocular tension (IOT). Miotics like pilocarpine and physostigmine are used to: Lower intraocular tension.

2) Reversal of Mydriasis: To reverse the effect of mydriatic after refraction testing.

3) Prevention of Adhesions: To prevent adhesions between the iris and lens/ cornea.







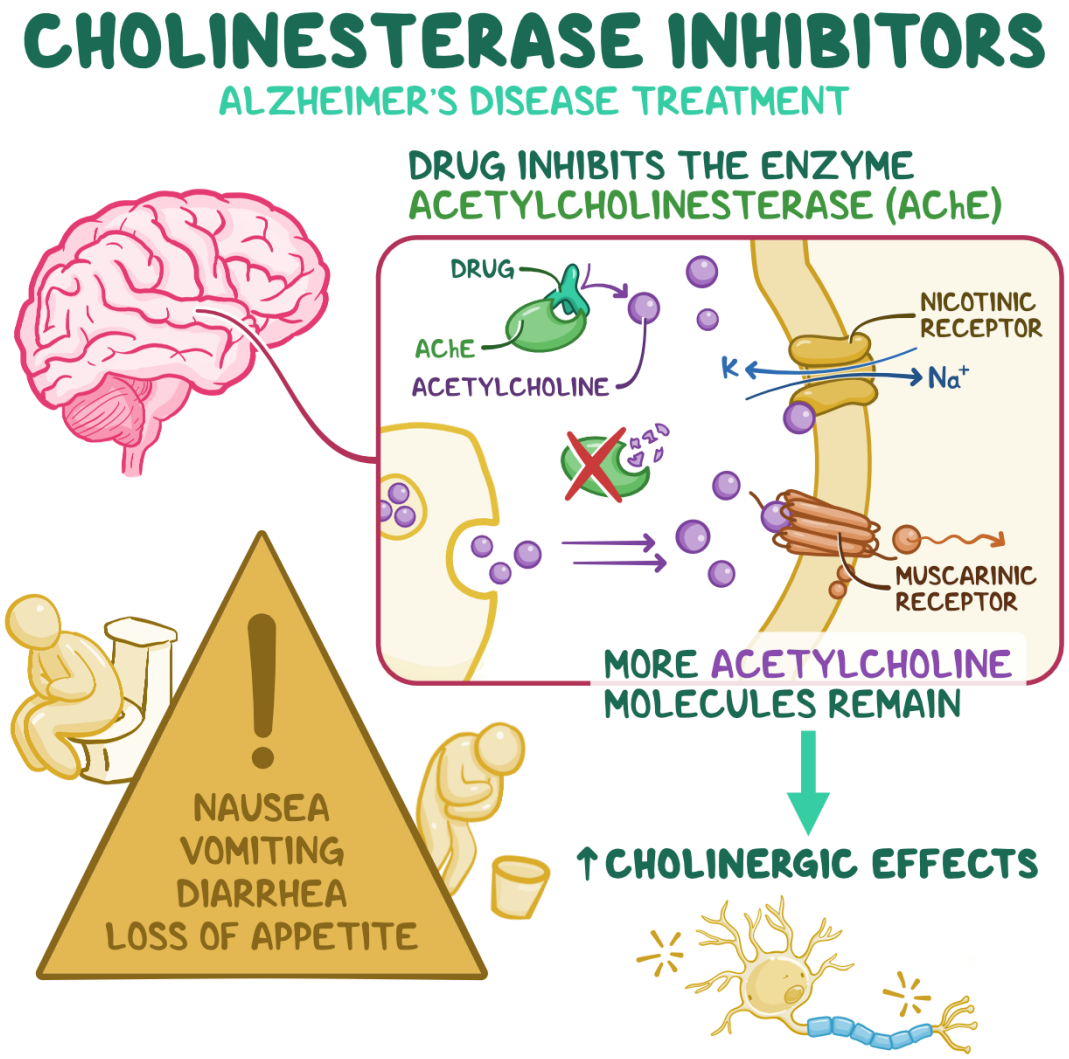
Therapeutic uses of anti-ChEs

4) Cobra bite: To antagonize the action of cobra neurotoxin.

5) Belladonna poisoning: Physostigmine is the drug of choice for poisoning with atropine and other anticholinergic drugs.

6) Alzheimer's disease: a neurodegenerative disorder affecting primarily the cholinergic neurons in the brain.

The relatively cerebroselective anti-ChEs (Tacrine, rivastigmine, and donepezil) improve some symptomatic improvement.

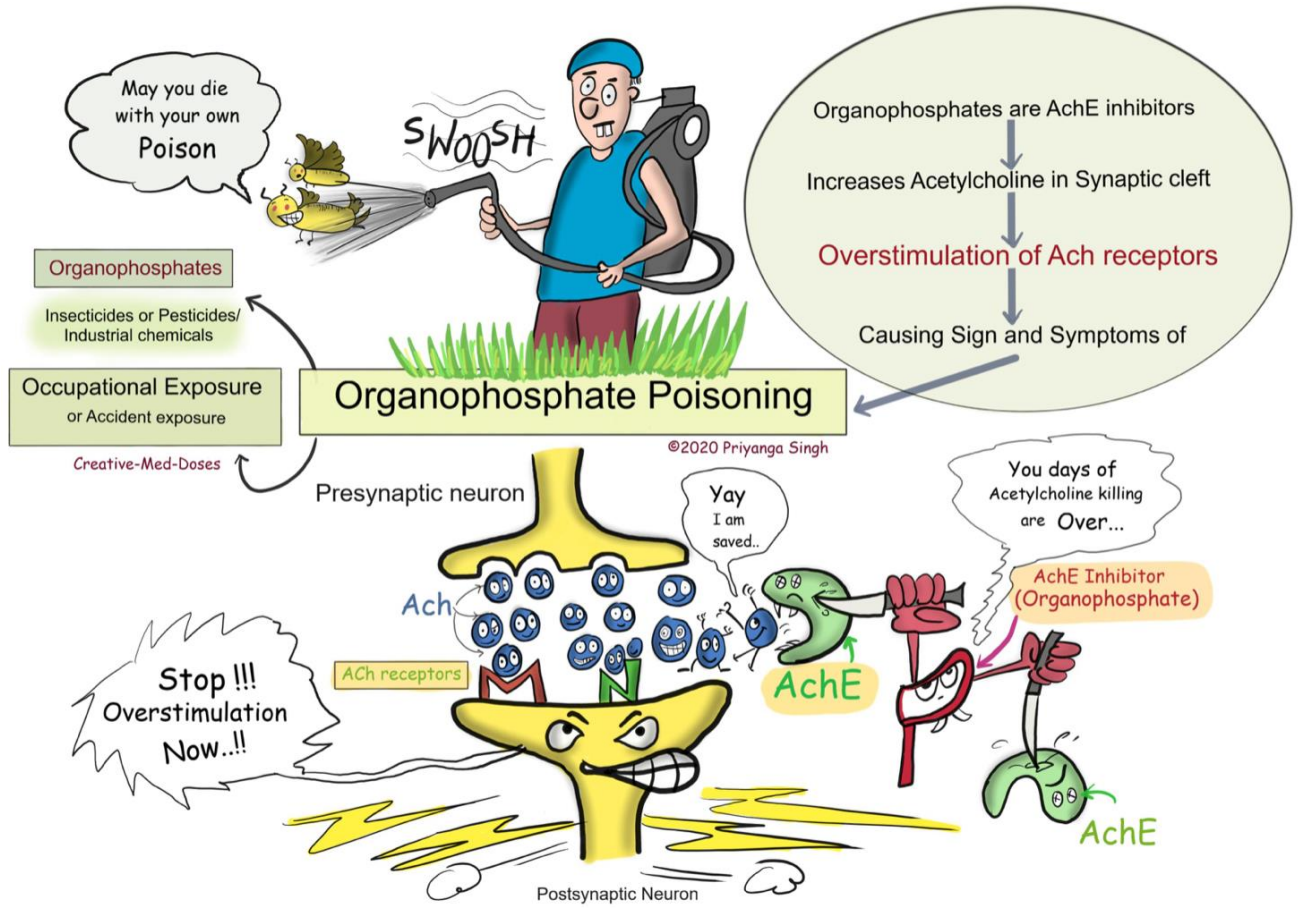


Anti-ChEs poisoning

Anti-ChEs are easily available and extensively used as agricultural and household insecticides.

Accidental as well as suicidal and homicidal poisoning are common.

Local muscarinic manifestations at the site of exposure (skin, eye, GIT) occur immediately, Followed by complex systemic effects due to muscarinic, nicotinic and central actions.



	Sympathetic	*Parasympathetic*
Origin	Dorso-lumbar (T_1 to L_2 or L_3)	Cranio-sacral (III, VII, IX, X; S_2-S_4)
Distribution	Wide	Limited to head, neck and trunk
Transmitter (neuroeffector)	Noradrenaline (major) Acetylcholine (minor)	Acetylcholine
Stability of transmitter	NA stable, diffuses for wider actions	ACh—rapidly destroyed locally
Important function	Tackling stress and emergency	Assimilation of food, conservation of energy

Differences between sympathetic and parasympathetic divisions of the autonomic nervous system