



Drugs Acting On Autonomic Nervous System (ANS)

Nervous system

Peripheral nervous system

Central nervous system

**Efferent Division
(Motor)**

**Afferent Division
(Sensory)**

Autonomic nervous system

**Somatic system
(skeletal muscles)**

Enteric nervous system

Parasympathetic nervous system

Sympathetic nervous system

What are the differences between the somatic and the autonomic nervous system?

Somatic N.S

Control skeletal muscles

Voluntary

Somatic nerve is one fiber

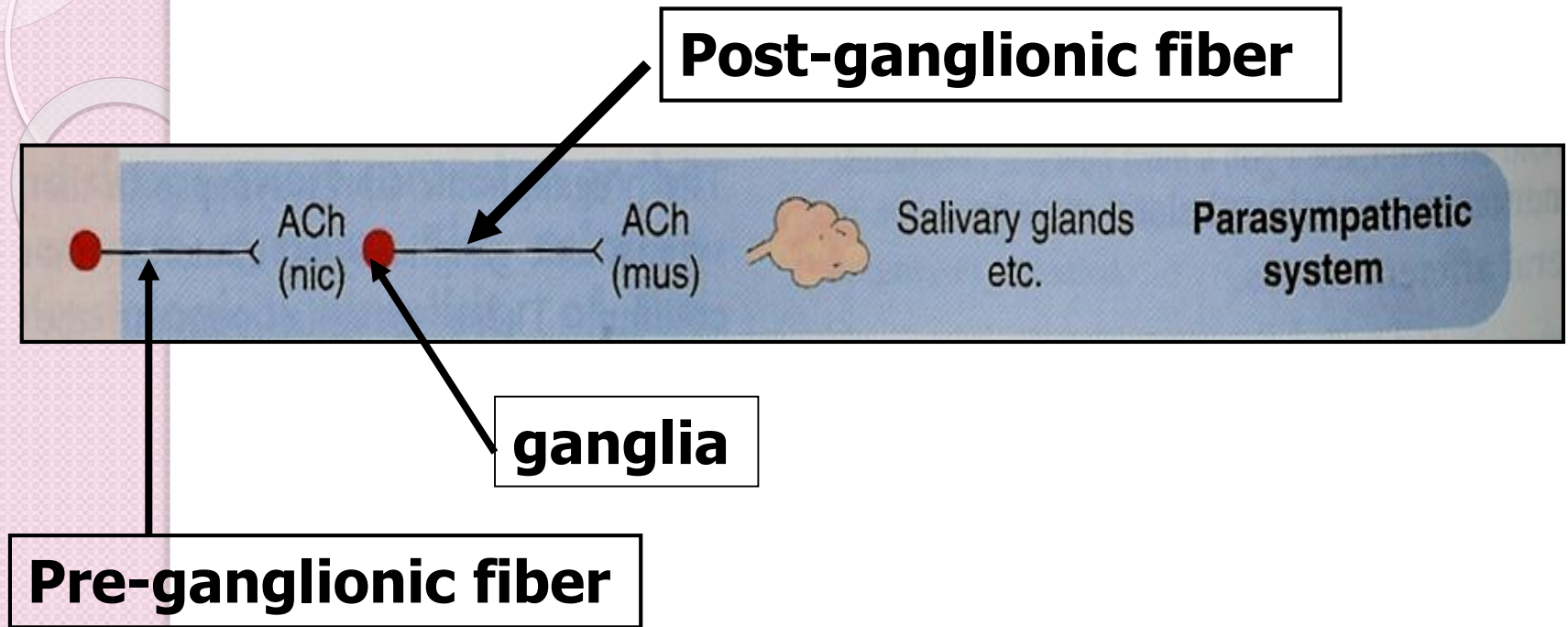
Autonomic N.S

Control internal viscera

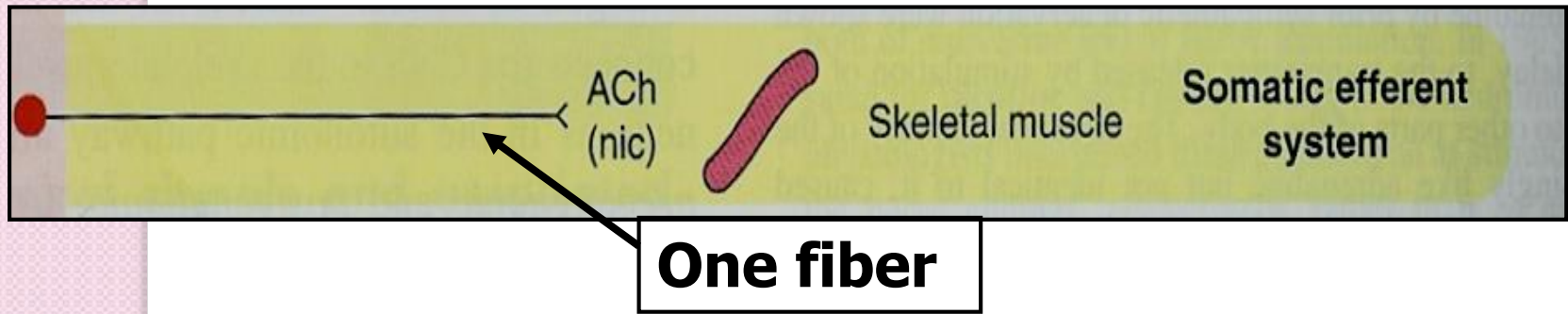
Involuntary

**autonomic nerve is two
fibers (*Preganglionic &
Postganglionic*)**

Autonomic nerve



Somatic nerve

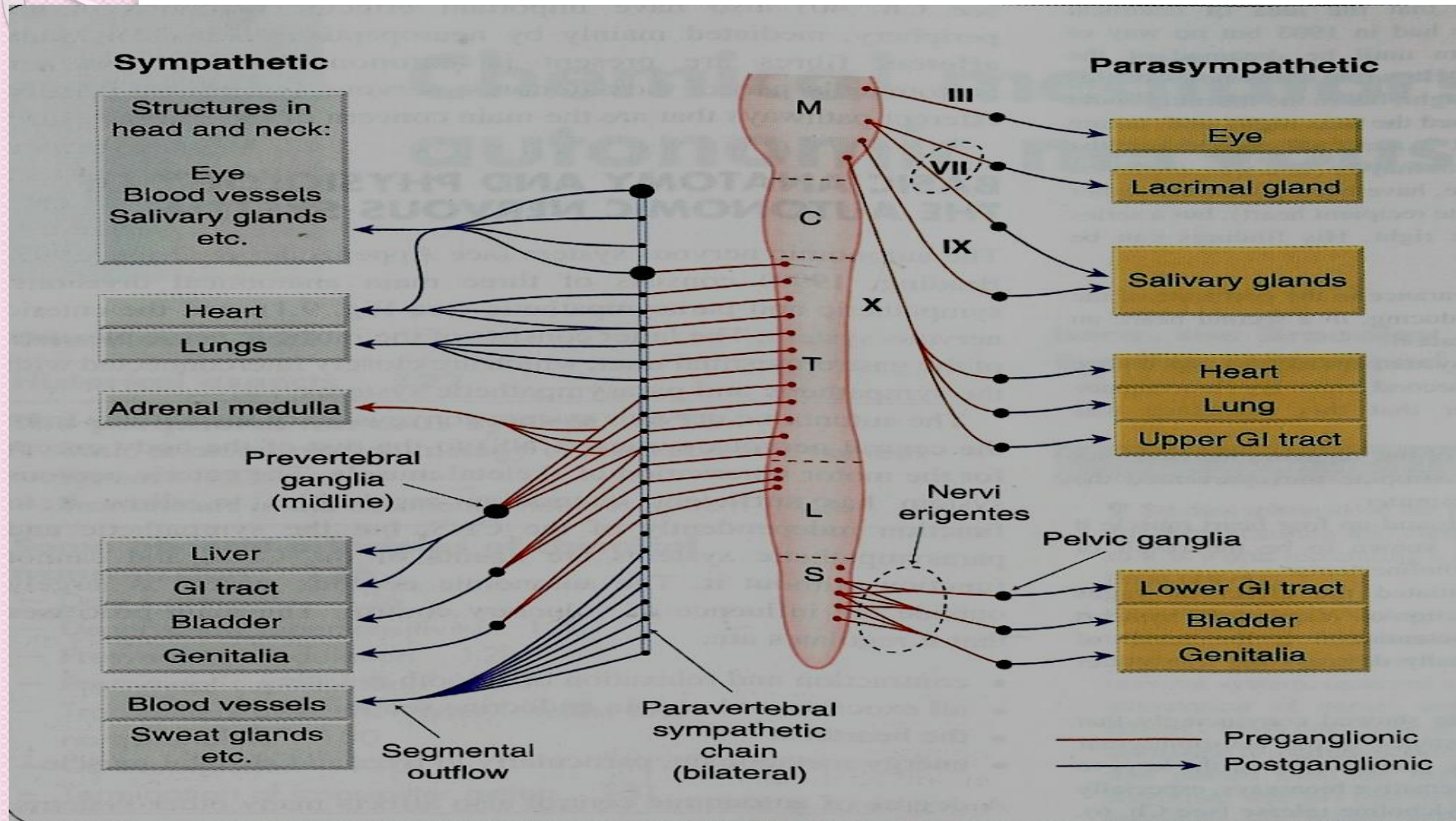


Division of Autonomic Nervous System

- **Sympathetic nervous system.**
- **Parasympathetic nervous system.**
- **Enteric nervous system.**

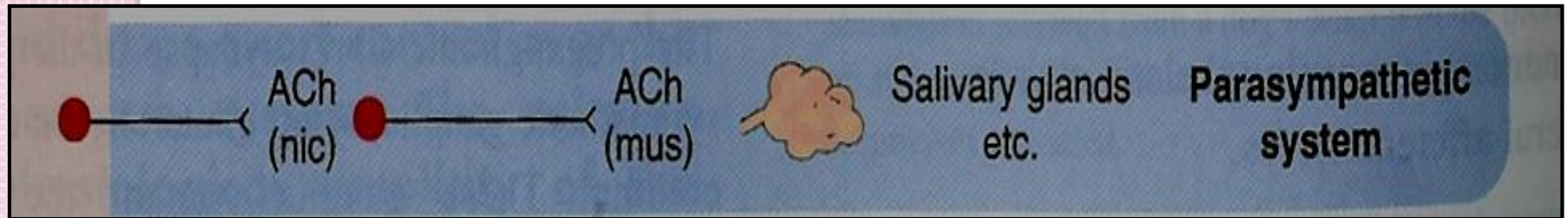
Parasympathetic Nervous System

Is a craniosacral outflow



Neurotransmitters

Neurotransmitter in parasympathetic nervous system or cholinergic system is **acetylcholine** and nerves are called **cholinergic nerves**



Cholinergic transmission

- **The release of neurotransmitter Ach from cholinergic nerves include the following steps:**
 - 1) Synthesis of Ach**
 - 2) Storage of Ach in storage vesicles**
 - 3) Release of Ach**
 - 4) Binding of Ach to postsynaptic receptors to give actions**

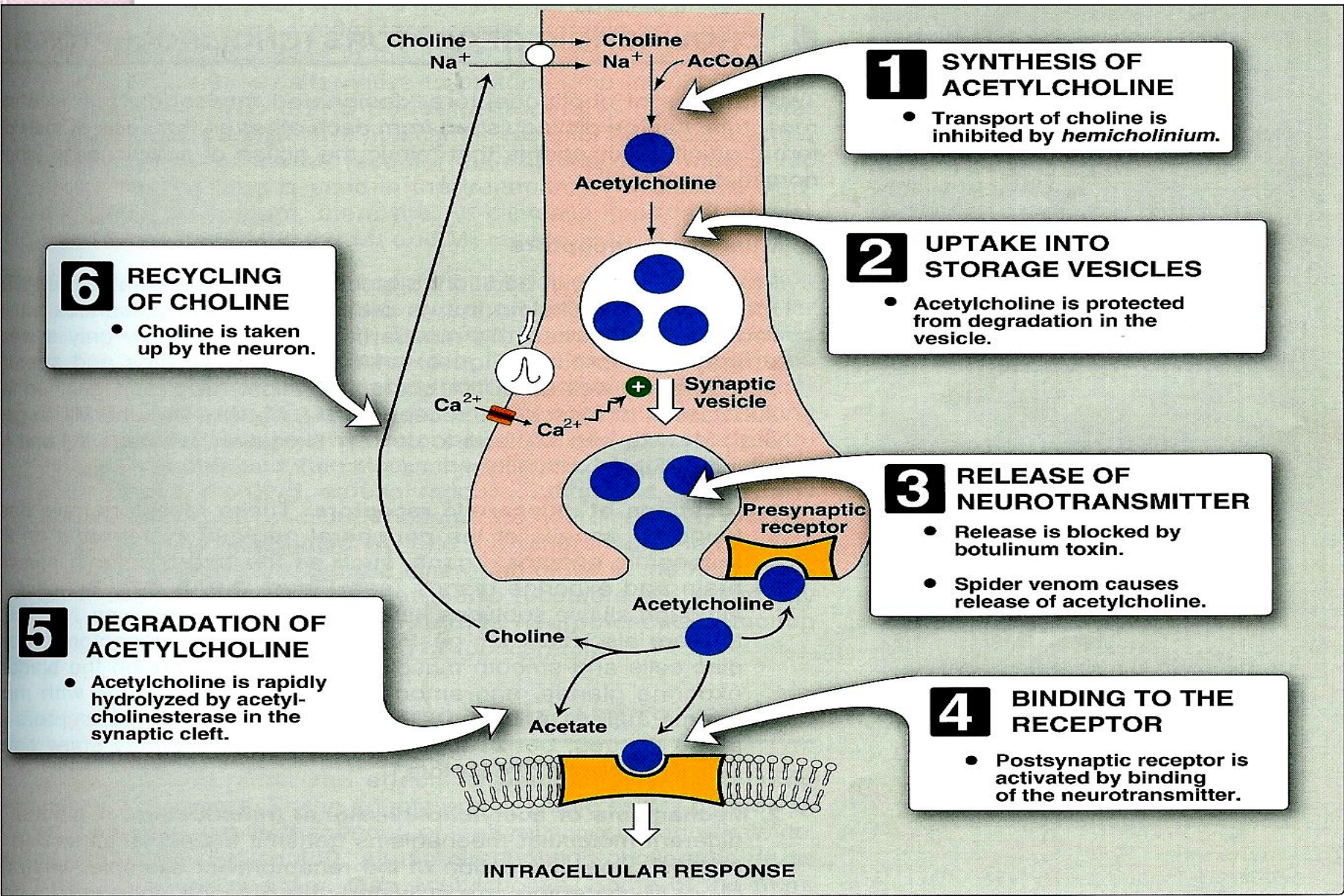
Cholinergic transmission

5) Metabolism by **acetyl cholinesterase** in synaptic cleft to give **choline and acetate**.



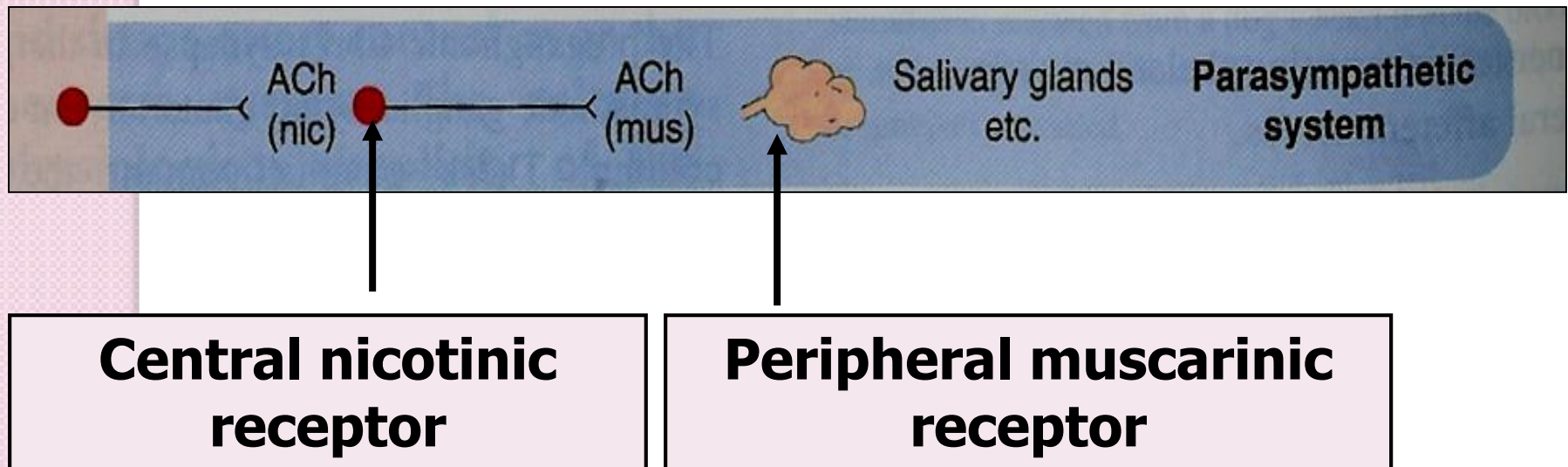
6) Recycling of choline

Cholinergic transmission



Cholinergic or parasympathetic receptors

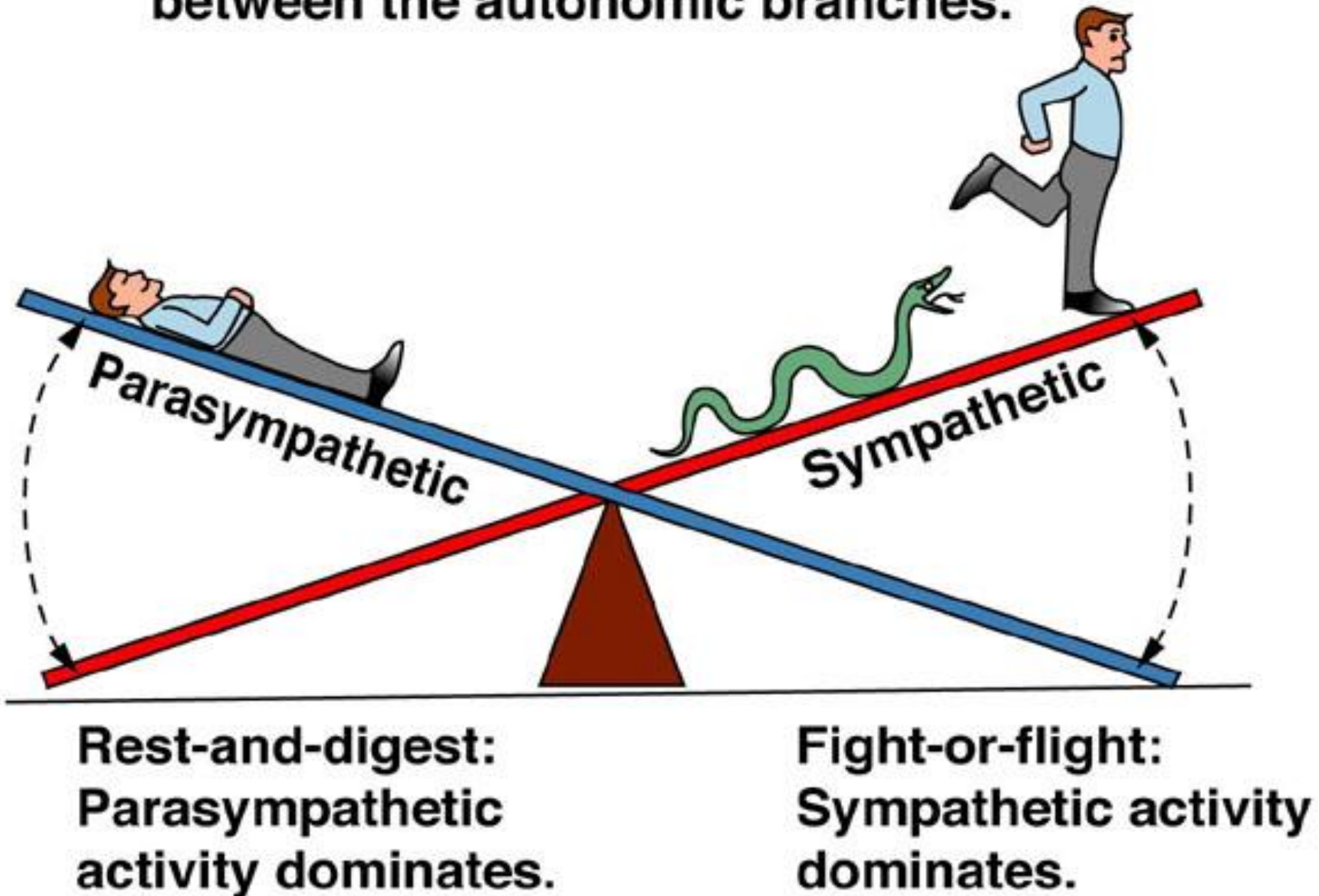
- Nicotinic receptors (**N**) = central receptors.
- Muscarinic receptors (**M**) = peripheral receptors



Neurotransmitters

- Sympathetic: noradrenaline (norepinephrine)
- Parasympathetic : acetylcholine

Homeostasis is a dynamic balance between the autonomic branches.



Cholinergic receptors

- ❑ Muscarinic: $M_1 - M_5$
Activated by muscarine
- ❑ Nicotinic: N_M, N_N
Activated by nicotine

Actions of Ach

- Acetylcholine - major neurotransmitter of PNS

Actions of Ach

Characteristics	M ₁ (neuronal)	M ₂ (cardiac)	M ₃ (glandular)
Location & Function			

Actions of Ach

Characteristics	M ₁ (neuronal)	M ₂ (cardiac)	M ₃ (glandular)
Location & Function	• Ganglia – impulse transmission		

Actions of Ach

Characteristics	M ₁ (neuronal)	M ₂ (cardiac)	M ₃ (glandular)
Location & Function	• Ganglia – impulse transmission	• SA node - Decreased rate of impulse generation • AV node – decreased conduction velocity • Atrium, ventricle- decreased contractility	

Actions of Ach

Characteristics	M ₁ (neuronal)	M ₂ (cardiac)	M ₃ (glandular)
Location & Function	• Ganglia – impulse transmission	• SA node - Decreased rate of impulse generation • AV node – decreased conduction velocity • Atrium, ventricle- decreased contractility	• Exocrine glands (salivary, sweat) - secretion • Visceral smooth Muscle (bronchus, bladder, GIT) – contraction

Actions of Ach

Characteristics	N_M (muscle type)	N_N (neuronal type)
Location & Function	Skeletal neuromuscular junction (NMJ) – contraction	• Autonomic ganglia– impulse transmission

Actions of ACh on eye

Muscarinic:

- **Eye:**

- Circular muscle of iris (M_3)- contraction-miosis
- Ciliary muscle (M_3) - contraction- eye's focus is accommodated for near vision - spasm of accommodation
- Better drainage of aqueous humor - reduced intraocular pressure
- Lacrimal glands (M_3) - lacrimation

Acetylcholine

- No therapeutic use because
 - i) Ultra short action: rapidly hydrolyzed by cholinesterases
 - ii) Widespread and nonselective activity: act on all receptors

- 
- **Drugs which mimic the actions of Ach are called as cholinergic drugs or parasympathomimetic drugs or cholinomimetic or cholinergic agonists**

Classification

A. Pharmacologically: by their spectrum of action.

1. Muscarinic agonists: Bethanechol, methacholine, pilocarpine.
2. Nicotinic agonists: nicotine

Cholinergic Agonists

Direct-acting

Receptor agonists

Choline esters

ACETYLCHOLINE
BETHANECOL

Alkaloids

PILOCARPINE

Indirect acting

Cholinesterase inhibitors

Carbamates

PHYSOSTIGMINE
NEOSTIGMINE
PYRIDOSTIGMINE
EDROPHONIUM

Phosphates

ISOFLUROPHATE
Antidote
PRALIDOXIME

Classification

B. mode of action

1. **Direct-acting**: bind directly to and activate muscarinic or nicotinic receptors,

Also subdivided chemically:

1. **Esters of choline** (including acetylcholine, bethanechol, methacholine and carbachol)
2. **Alkaloids** (such as muscarine, pilocarpine, nicotine and cevimeline).

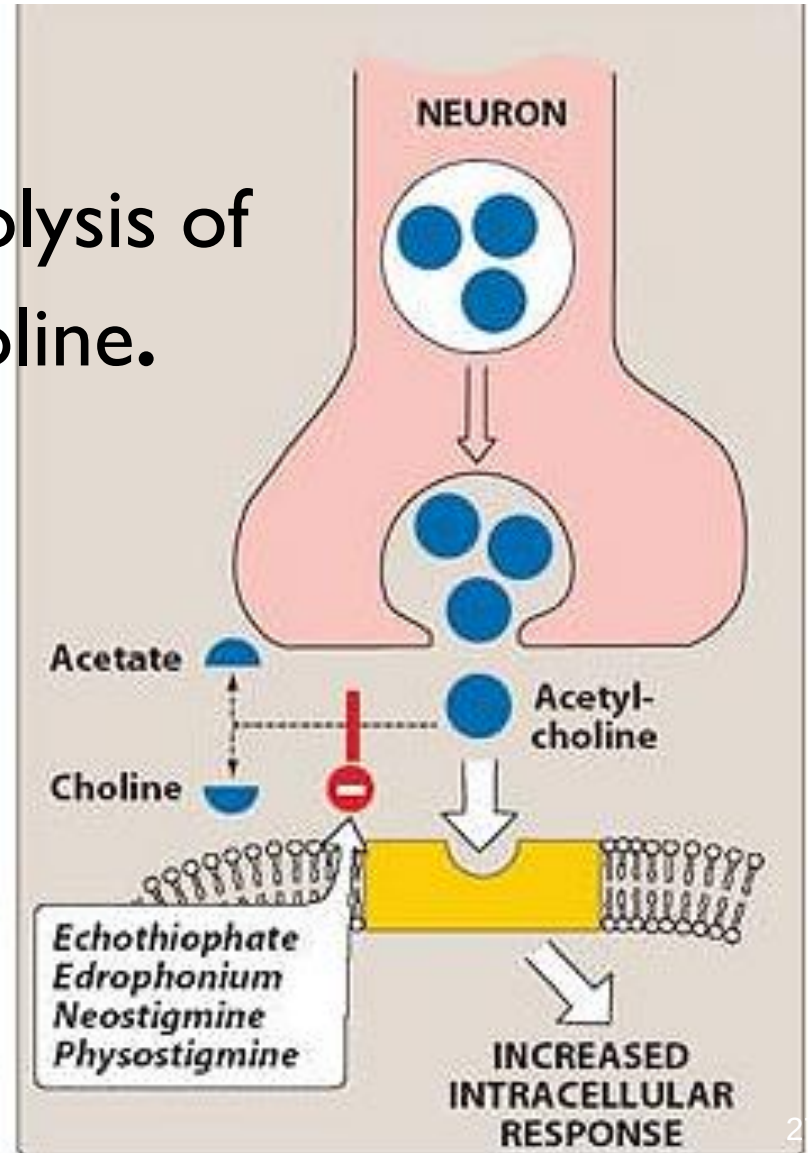
Classification

2. Indirect-acting:

by inhibiting the hydrolysis of endogenous acetylcholine.

also subdivided to

- **reversible**
- **irreversible**



Classification

a. Indirect acting (reversible):

eg., neostigmine, physostigmine.

b. Indirect acting (irreversible):

e.g., echothiophate, isofluorophate

Indirect and direct

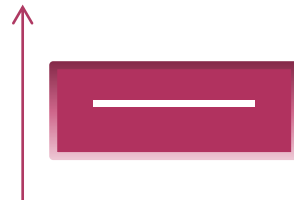
Some quaternary cholinesterase inhibitors also have a modest **DIRECT** action as well,

eg, **neostigmine**, which activates neuromuscular nicotinic cholinceptors directly in addition to blocking cholinesterase.

Mechanism of action of Anticholinesterases

- Inhibit acetylcholinesterase (AChE) enzyme

- Ach -----> Choline + acetate
AChE



Neostigmine

- Accumulation of Ach → Action

Adverse effects of cholinergic drugs:

The adverse effects result from excessive generalized cholinergic stimulation
DUMBLES.

- **D**iarrhea and decreased BP,
- **U**rination,
- **M**iosis,
- **B**ronchoconstriction,
- **L**acrimation
- **E**xcitation of skeletal muscle,
- **S**alivation and **S**weating

Diarrhea



Diaphoresis



Miosis



Nausea



Urinary urgency

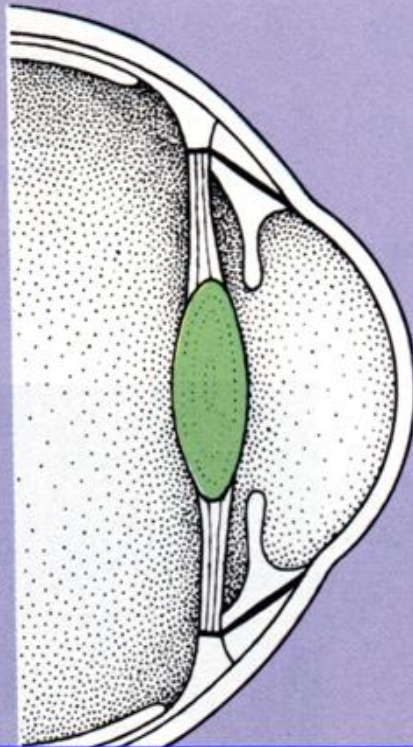


Pilocarpine (an alkaloid)

- The pilocarpine is a tertiary amine, and is stable not hydrolyzed by AchE.
- It is far less potent compared with Ach and its derivatives.
- Pilocarpine exhibits muscarinic activity and is used primarily in ophthalmology and dentistry.

Pilocarpine actions:

- topically produces a rapid **miosis and contraction of the ciliary muscle**; a spasm of accommodation; the vision is fixed at some particular distance, making it impossible to focus.



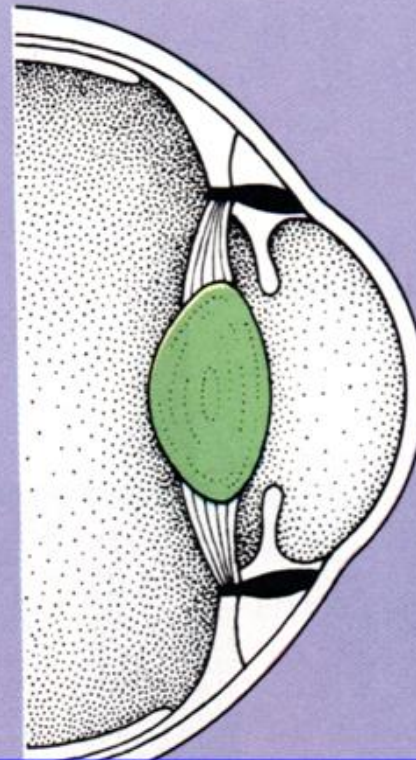
Normal:

Ciliary Muscle Relaxed

Suspensory Ligaments Under Tension

Lens is Flattened

Focus on Distant Objects



Accommodation:

Ciliary Muscle Contracts

Reduced Tension on Suspensory Ligaments

Lens becomes Round

Focus on Near Objects

Pilocarpine actions:

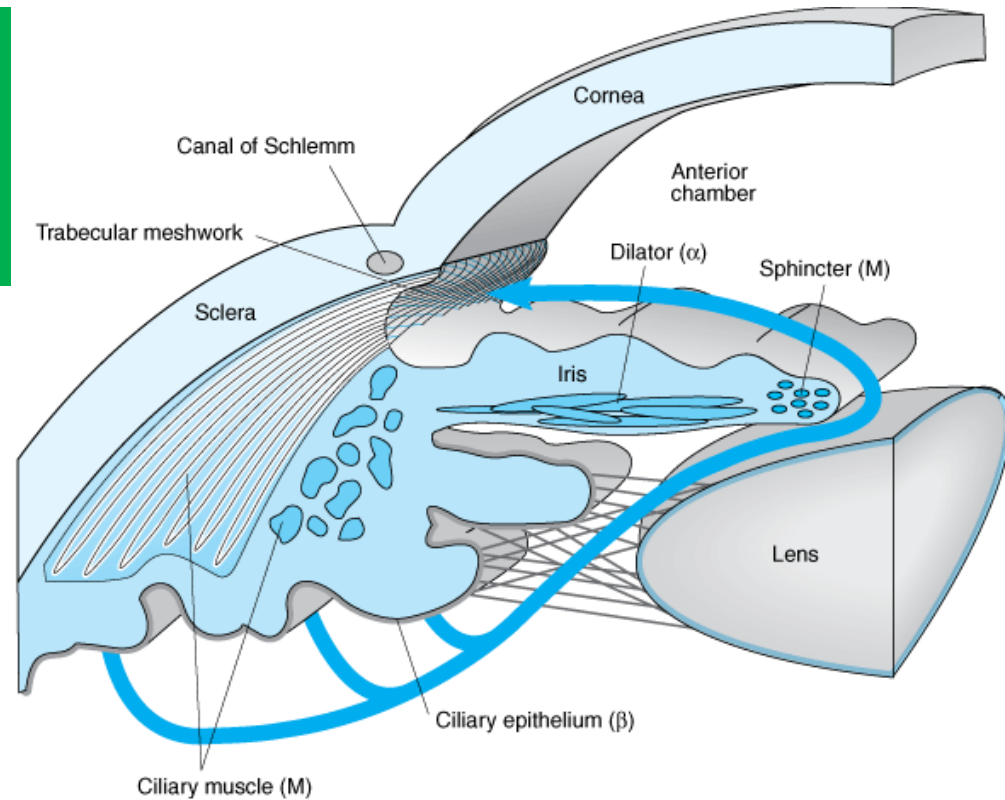
- Pilocarpine is one of the most potent stimulators of secretions such as sweat, tears, and saliva,
 - but its lack of selectivity (adverse effects) limited its use:
1. can enter the brain and causes CNS disturbances.
 2. It stimulates profuse sweating and salivation.

Sjogren syndrome

- Sjogren syndrome, immunologic disorder with destruction of the exocrine glands leading to the mucosal dryness (dry mouth and lack of tears)
- is usually treated with **cevimeline**, a cholinergic drug that also has the drawback of being nonspecific.
- Recent studies have shown that mouth sprays of **Pilocarpine** are beneficial in promoting salivation in patients with Xerostomia (dryness of the mouth).

Therapeutic use in glaucoma:

- is the DOC in the emergency Lowering of IOP of both narrow-angle and a wide-angle glaucoma.



is extremely effective in opening the trabecular meshwork around Schlemm canal result in an increased drainage of aqueous humor