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Tikrit University
College of Vet. Medicine

First Term - M.Sc Pharmacology
Advanced Pharmacology

Prof Dr Husamuldeen Alnajjar
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Autonomic nervous system – PHARMA 1

THE NERVOUS SYSTEM

- The nervous system is a **complex part of the human body** concerned with the **regulation and coordination** of body activities **such as** movement, digestion of food, sleep, and elimination of waste products.

The nervous system has **two main divisions**: the central nervous system (CNS) and the peripheral nervous system (PNS).

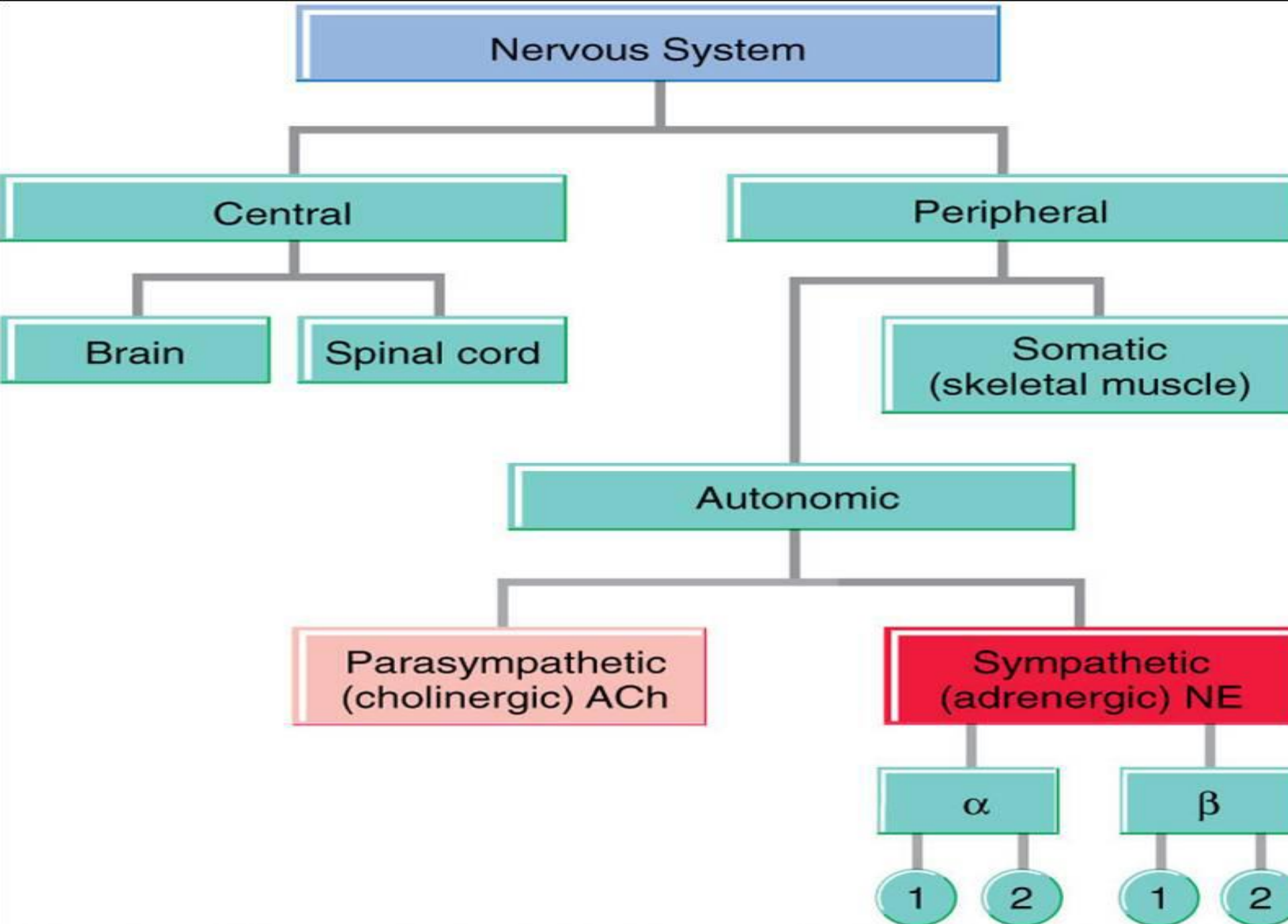


Fig. 17-1. The sympathetic nervous system in relation to the entire nervous system. *ACh*, Acetylcholine; *NE*, norepinephrine.

• **Autonomic nervous system:** The component of the CNS (Central Nervous System) that functions below the unconscious level, controlling several physiological **processes:**

1. **Distribution of blood flow & tissue perfusion**
2. **Regulation of blood pressure**
3. **Control of visceral smooth muscle (eyes, bladder, bowels)**
4. **Control of endocrine and exocrine glands**
5. **Control of metabolic energy (glycolysis, neoglucogenesis etc)**

Autonomic nervous system division to :

1. Sympathetic or
(thoracolumbar)

Neurotransmitter: (epinephrine,
norepinephrine)

Receptor : α_1 , α_2 , β_1 , β_2

2. Parasympathetic or (cholinergic):
(craniosacral)

Neurotransmitter :(acetylcholine)

Receptors: M1, M2 , N1, N2

Autonomic Nervous System

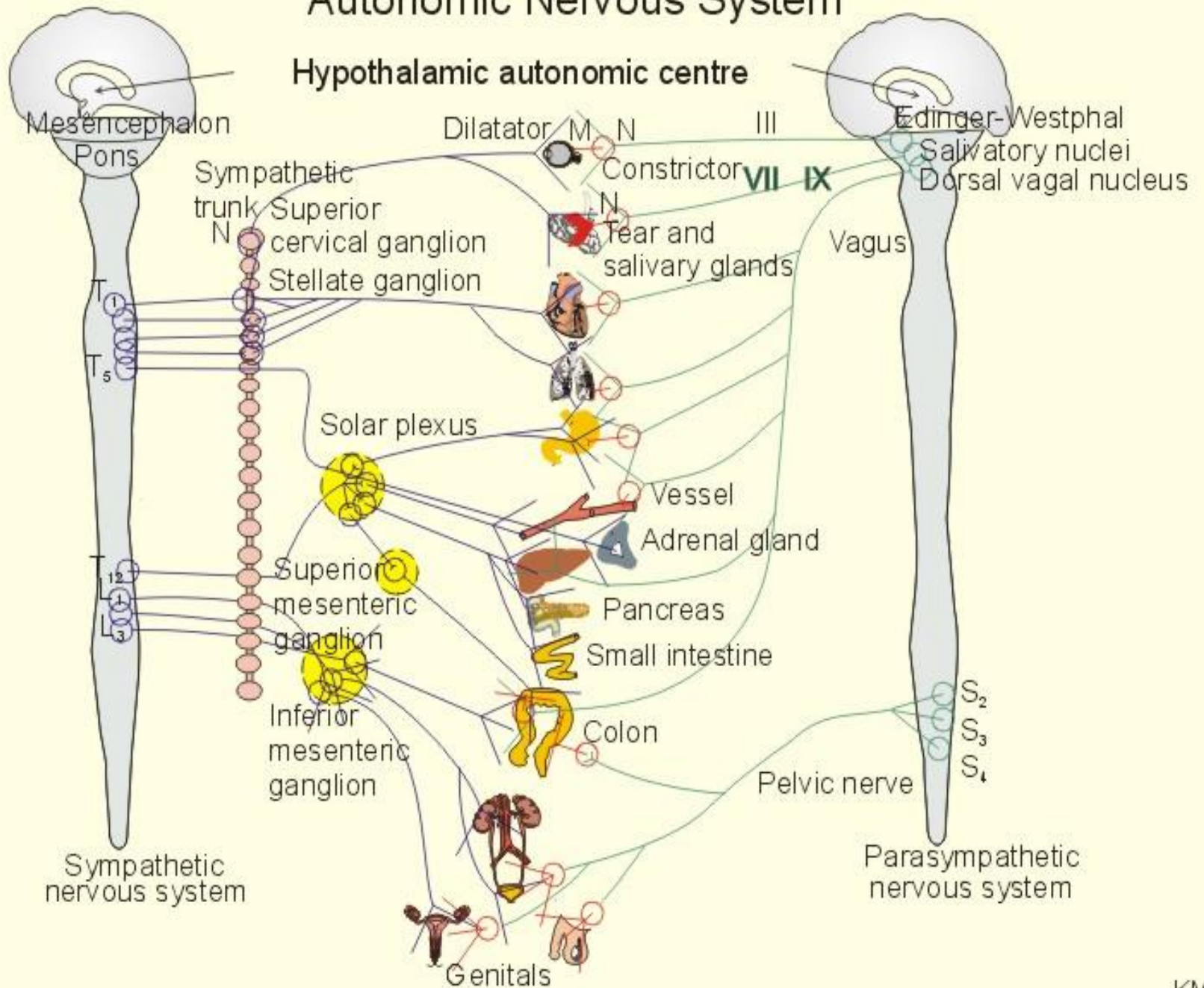
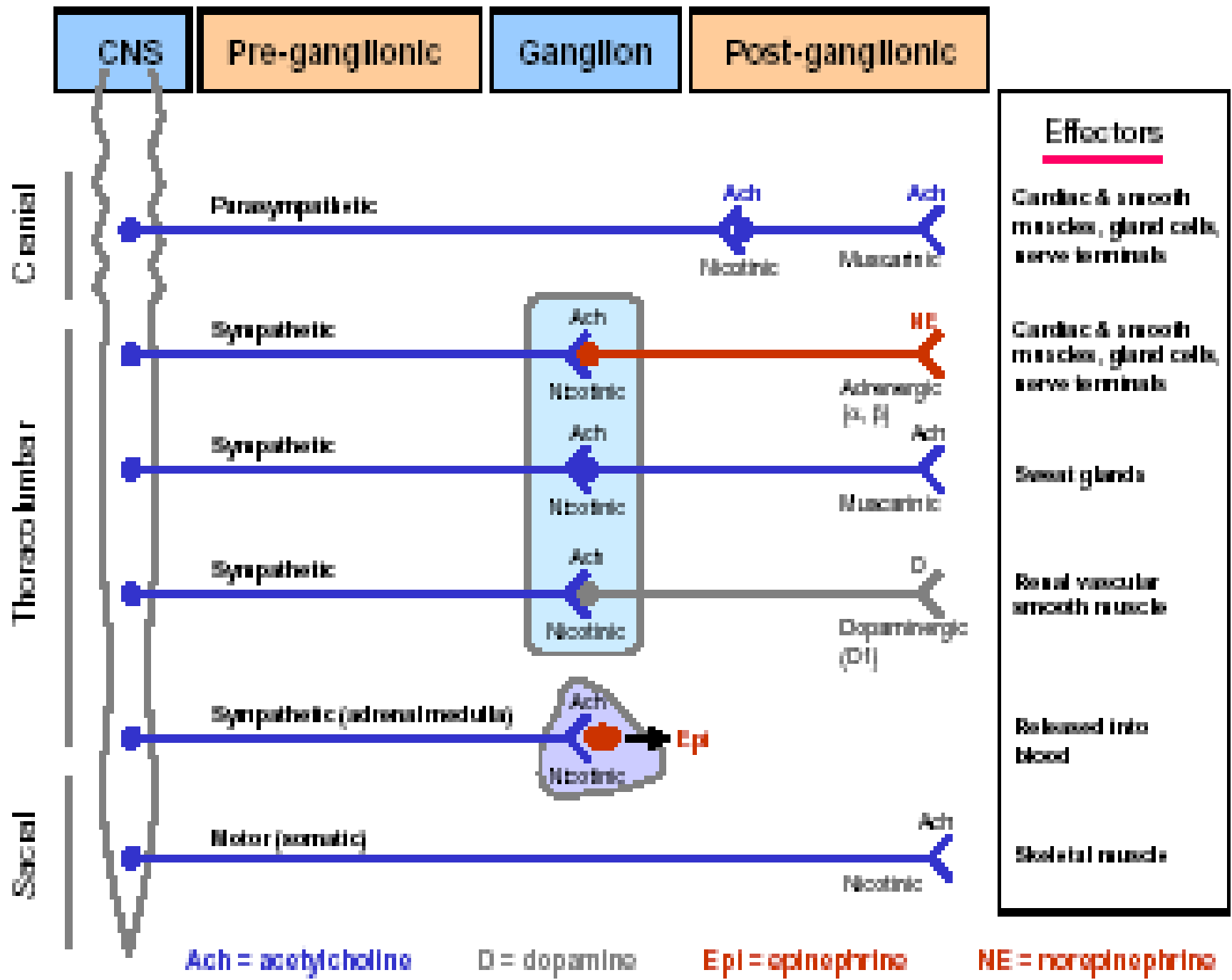


Fig. 6-1



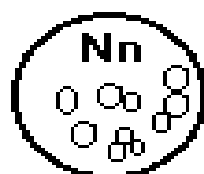
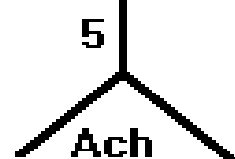
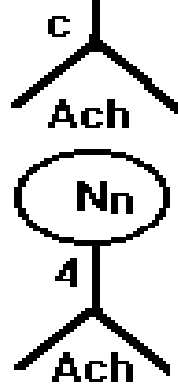
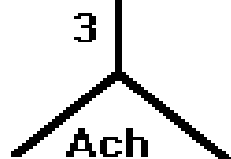
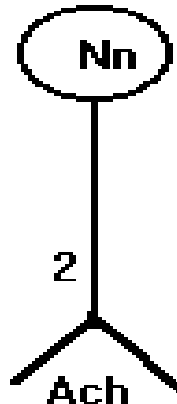
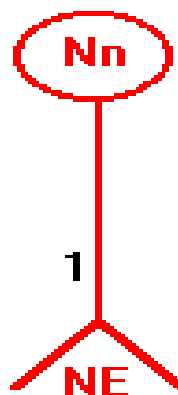
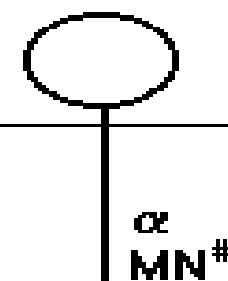
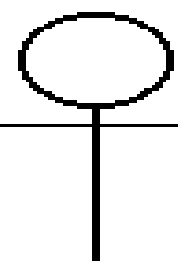
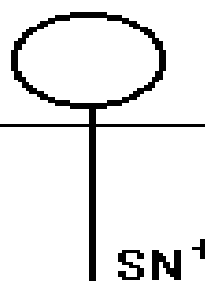
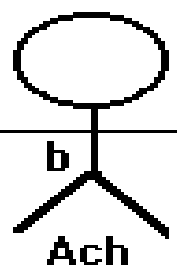
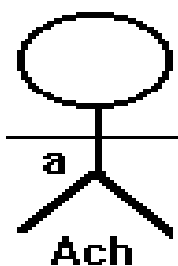
NEURONAL INNERVATION TO ORGANS

Sympathetic N.S.

Parasympathetic

Somatic

CNS



cardiac muscle
smooth muscle
glands

eccrine
sweat
glands;
b.v.s.m.*

adrenal
medulla

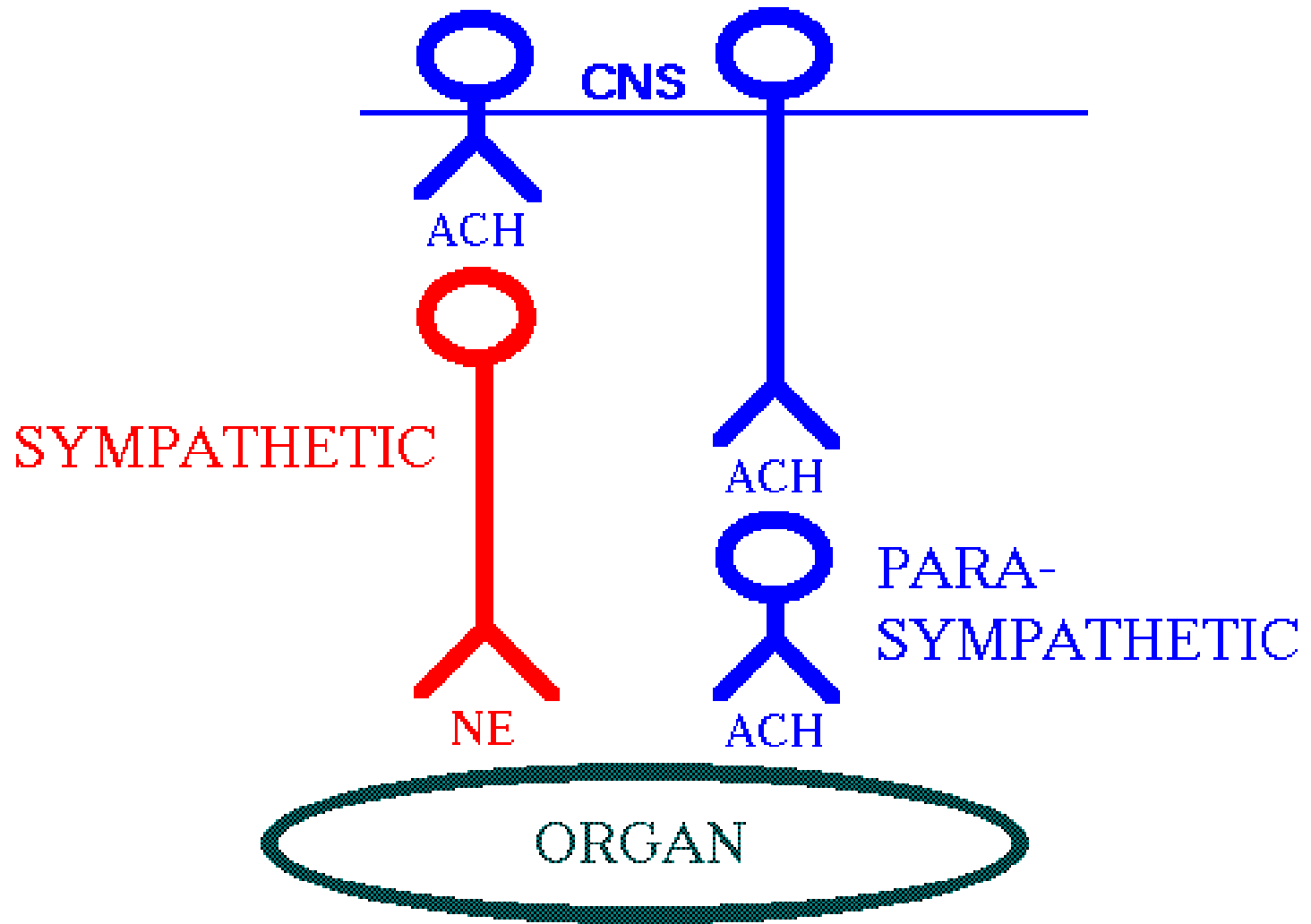
cardiac muscle
smooth muscle
glands


skeletal
muscle
fiber

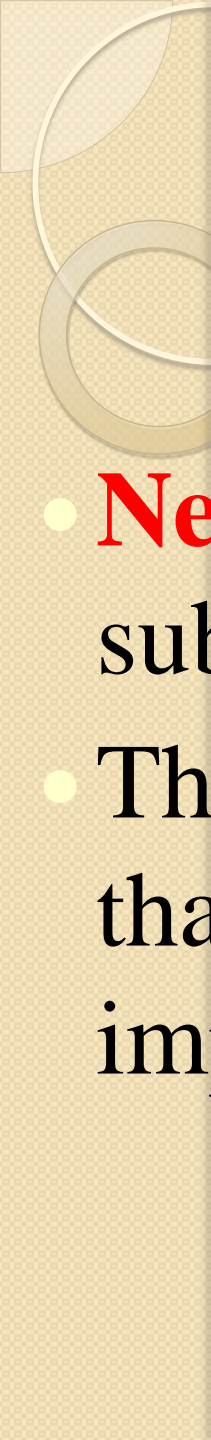
*blood vessels of skeletal muscle
†splanchnic nerve


#alpha motor neuron

INNERVATION AT MOST SITES



- 
- The **sympathetic division** stimulates functions involved in “**fight or flight**” reactions (fear, anger, etc), whereas the **parasympathetic division** stimulates more tranquil functions (“**rest-and-digest**”).

- 
- **Neurotransmitters** are chemical substances called neurohormones.
 - These are released at the nerve endings that facilitate the transmission of nerve impulses.

- 
- **Sympathetic:**
 - **Norepinephrine (mainly) and epinephrine (in adrenal gland) released at the postganglionic neurotransmitters.** These neurons are also called ‘Adrenergic’.
 - **Acetylcholine** is the preganglionic neurotransmitter in the sympathetic system.
 - A few sympathetic (sweat glands and salivary glands) have Acetylcholine as the postganglionic neurotransmitter.

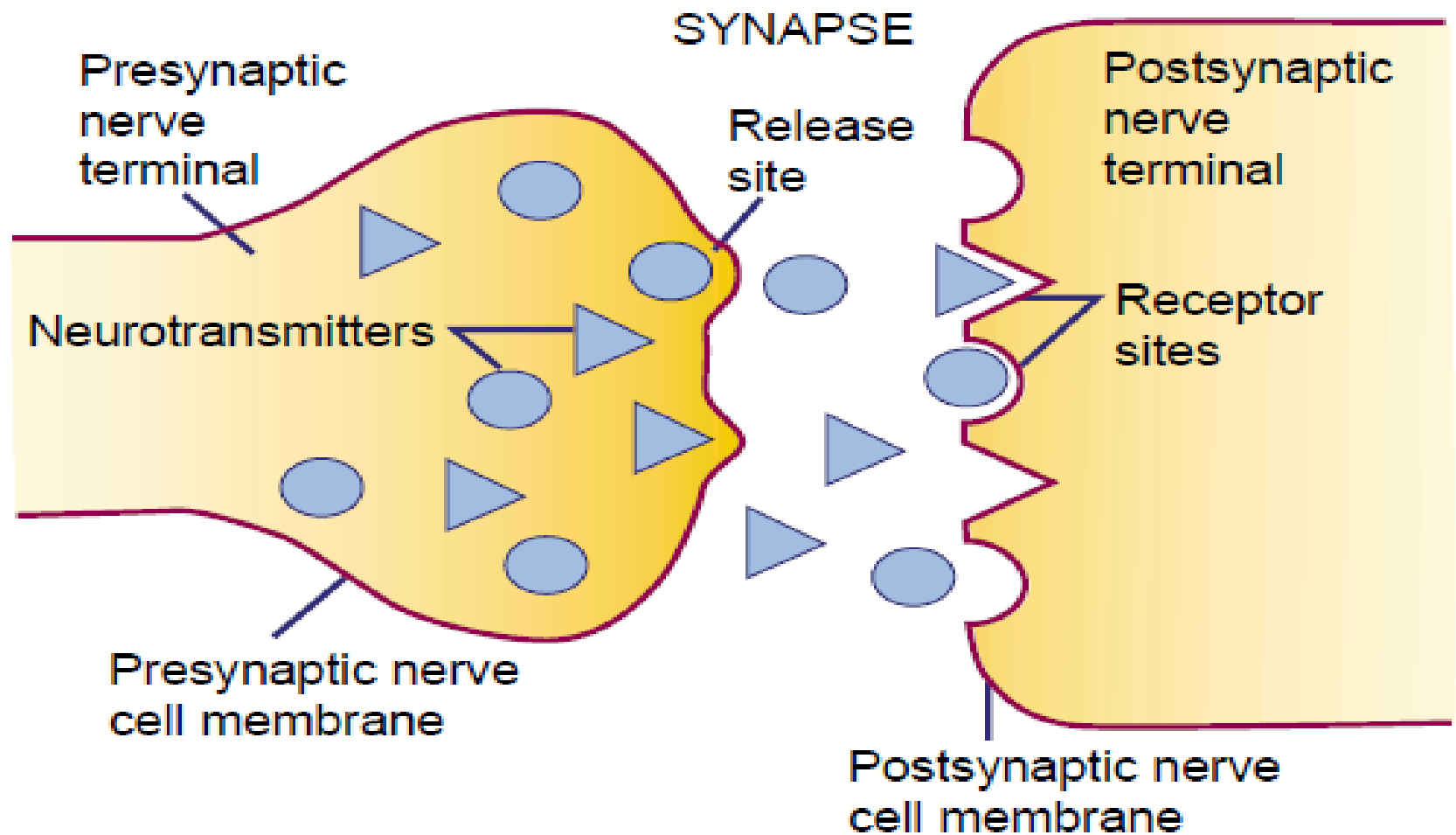


FIGURE 22-2. Neurotransmission in the central nervous system. Neurotransmitter molecules (eg, norepinephrine), released by the presynaptic nerve, cross the synapse and bind with receptors in the cell membrane of the postsynaptic nerve, resulting in the transmission of the nerve impulse.

Parasympathetic:

The **parasympathetic nervous system** helps **conserve body energy** and is partly responsible for such activities as **slowing the heart rate, digesting food, and eliminating body wastes.**

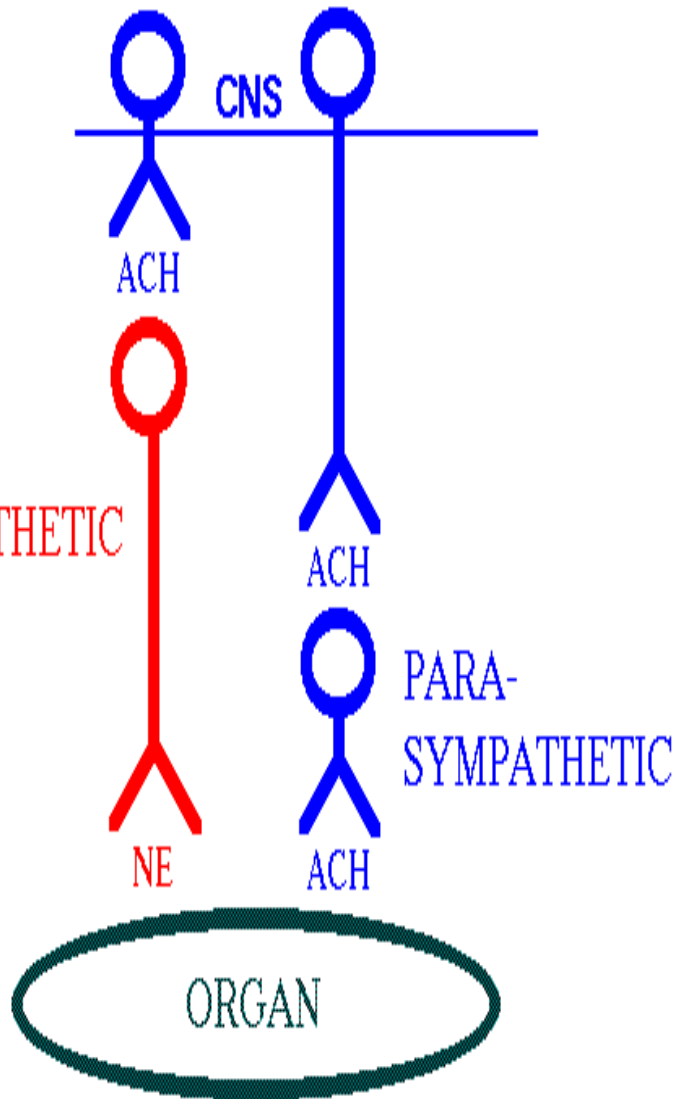
The ganglia are usually **close to or embedded in the target organ.**

Acetylcholine is both preganglionic and postganglionic neurotransmitter (Cholinergic).



Parasympathetic Nervous System

INNERVATION AT MOST SITES



- **Cholinergic Nervous System:**
- **Acetylcholine neurotransmitter releasing nerve fibers (parasympathetic).**
- **The parasympathetic nervous system innervates both smooth and cardiac muscle as well as exocrine glands.**

Function of The Parasympathetic Nervous System

- Protects the retina from excess light
- Decreases heart rate
- Promotes the emptying of hollow organs
- Promotes the conservation of energy
- Promotes rest and repair
- Physiologically antagonizes the sympathetic nervous system



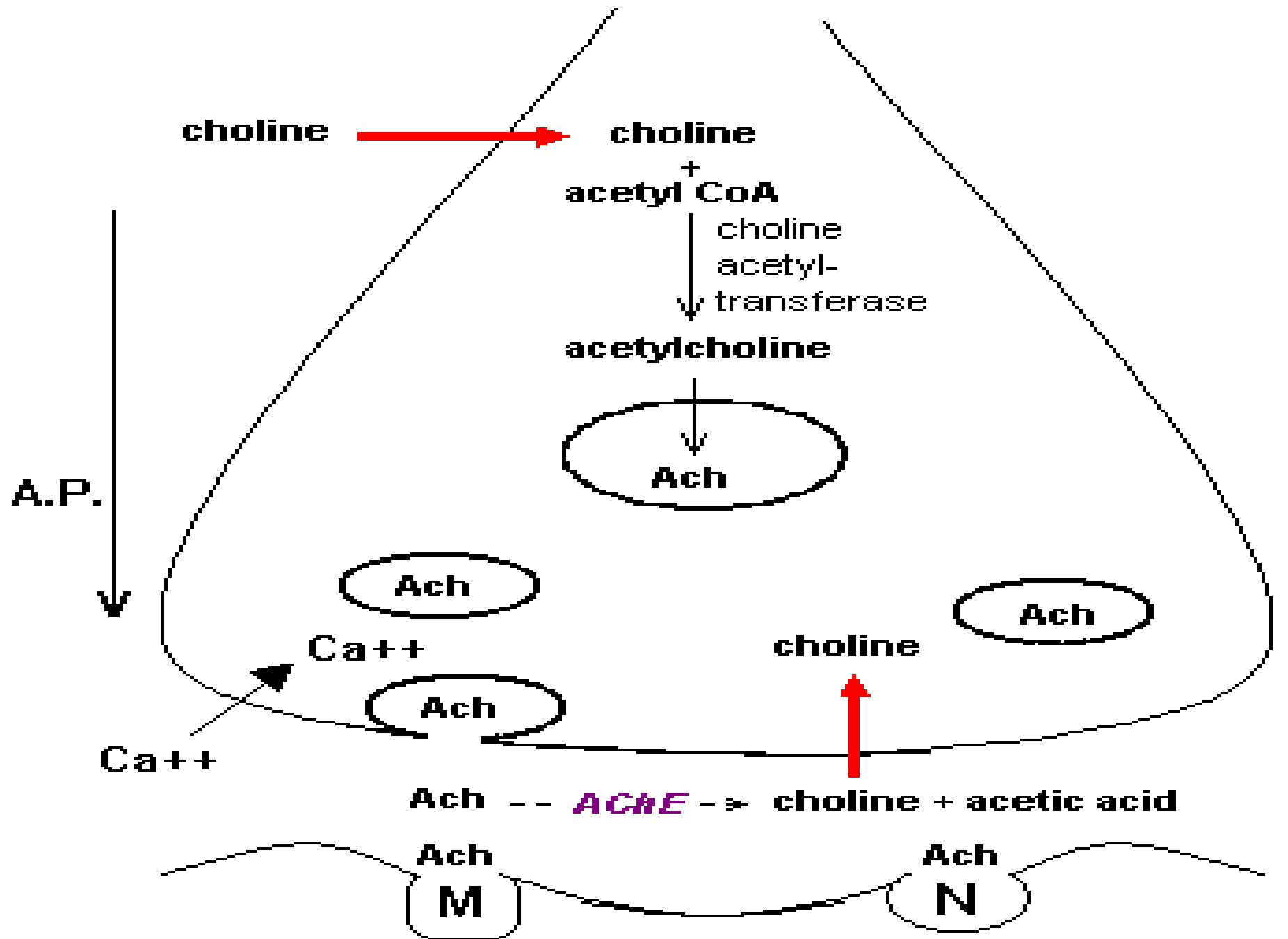
- **Biologic responses to parasympathetic stimulation:**

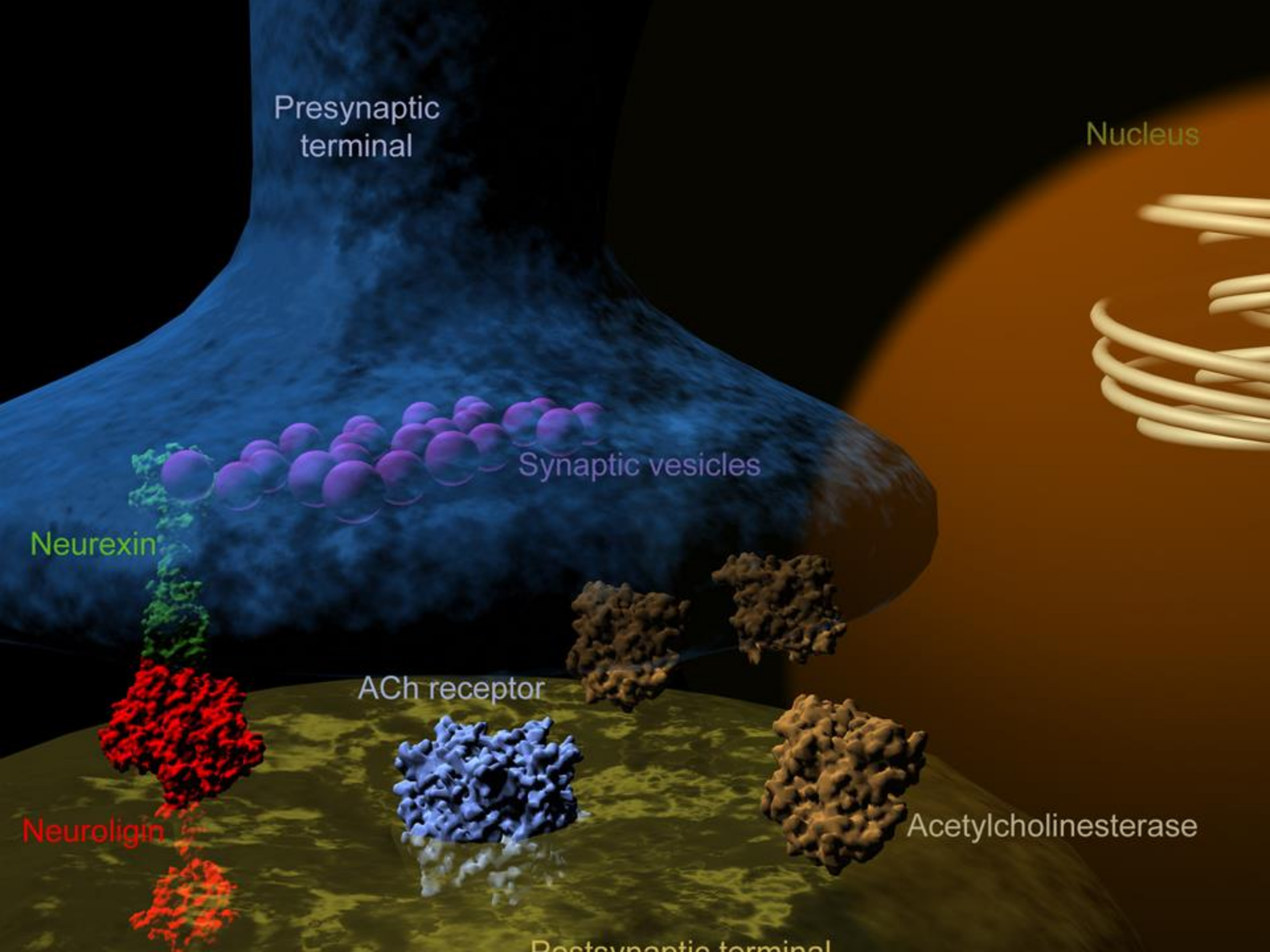
- Constriction of pupil (miosis), ciliary body (“accommodation” of lens)
- Contraction of smooth muscle in the GI (“peristalsis”) and urinary tract
- Constriction of the bronchioles (“bronchoconstriction”)
- Slowing of heart rate (“bradycardia”)
- Increased secretion by the glands

Neurotransmission **Acetylcholine**

neurotransmitter in cholinergic neuron involve 6 steps :

1. Synthesis of Ach
2. Storage of Ach in vesicles
3. Release of Ach
4. Binding to receptor
5. Degradation of Ach
6. Recycling of choline





DRUG ACTING ON A.N.S

- **1- cholinergic drugs**
 - A- Parasympathomimetic D
 - B- Parasympatholytic D
- **2- adrenergic drugs**
 - A- sympathomimetic D
 - B- sympatholytic D

Parasympathetic drugs :

- **A- Parasympathomimetic D**

Cholinergic agonist: Agents that bind to acetylcholine receptors and stimulates the parasympathetic system

(“parasympathomimetic”).

- **B- parasympatholytic D**

Cholinergic antagonist: Agents that bind to acetylcholine receptors but exhibit no intrinsic activity (“parasympatholytic” – competitive to endogenous Ach)

Parasympathomimetic drug:

- 1- direct acting cholinergic agent
- 2- Indirect acting cholinergic agent: **divided into reversible & irreversible**



Parasympathomimetic drugs: direct

either

choline esters

or

naturally occurring alkaloids

- **cholinergic Drugs (Muscarinic Agonists):**
- Pharmacological responses to the interaction of cholinergic agonists with **muscarinic receptors** include:
 - Contraction of smooth muscles
 - Vasodilation of vascular system
 - Increased secretion from exocrine glands
 - Decrease in heart rate and force of contraction
 - Constriction of pupil

A- cholin esters

I-Acetylcholine

- **Effect of ACH :**

1. on the **intestine** : Increase S.M contraction
2. on the **urinary tract** : Increase in muscle tone and contraction
3. on **blood vessels** : vasodilatation





4. on the **secretary gland** :increase secretion

5. on the **S.M of trachea** :contract , increase
bronchial secretion,

6. on the **skeletal Muscle** : increase Muscle tone

7. On the **heart** : bradycardia

8. On the **eye** : miosis , decrease in I.O.P

9 .On the **adrenal gland**

- Prototypical muscarinic (and nicotinic) agonist, Nonselective action.
- but a poor therapeutic agent.
- Chemical/enzymatic instability; Low bioavailability (poorly absorbed); Quick onset and short duration of action.
- Use: In ocular surgery, causes complete miosis in seconds.

2- carbachol

- **Potent** agonist activity.
- direct act :Nonselective (Muscarinic / Nicotinic)
- Also acts indirectly by promoting ACh release and anticholinesterase (weak) activity.



- **USES:**

- 1. Topically for glaucoma;
- 2. intraocular for miosis in surgery.
- 3. expel gases
- 4. stimulate intestinal motility.
- 5. relieve urinary retention
- **Side Effects:** Corneal edema; decreased vision.

3- bethanechol

4-Methacholine -----

More stable than acetylcholine.

- More selective action (muscarinic > nicotinic).

B- Natural alkaloid :

- muscarine , arecolin , pilocarpine

5- Pilocarpine

- Natural product. Isolated from the leaves of *Pilocarpus jaborandi*.
- **Actions :**
- decrease in IOP , miosis
- stimulator of secretions.
- Available as ophthalmic solution, gel, tablet .



- **Systemic effects:** include copious sweating, salivation and gastric secretion.

- **Uses:**

- lowering of IOP therefore Used in the treatment of glaucoma
- treatment of xerostomia (dry mouth).

- **Adverse effects:**

- 1-blurred vision
- 2- lacrimation
- 3- sever sweating
- 4-bronchospsm

