Cholinergic system (Parasympathetic system)

Part 1

By

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Msc pharmacology

Learning objectives

- **This system is covered in three lectures**

1. **Identify the neurotransmitter and the receptors on which it acts**
2. **Classify the drugs acting on parasympathetic system according to their mechanisms of action**
3. **List their main side effects**
4. **Correlate between the pharmacological effects of drugs and their main clinical uses and contraindications**
5. **Recognize the most common utilized drugs in clinical practice**

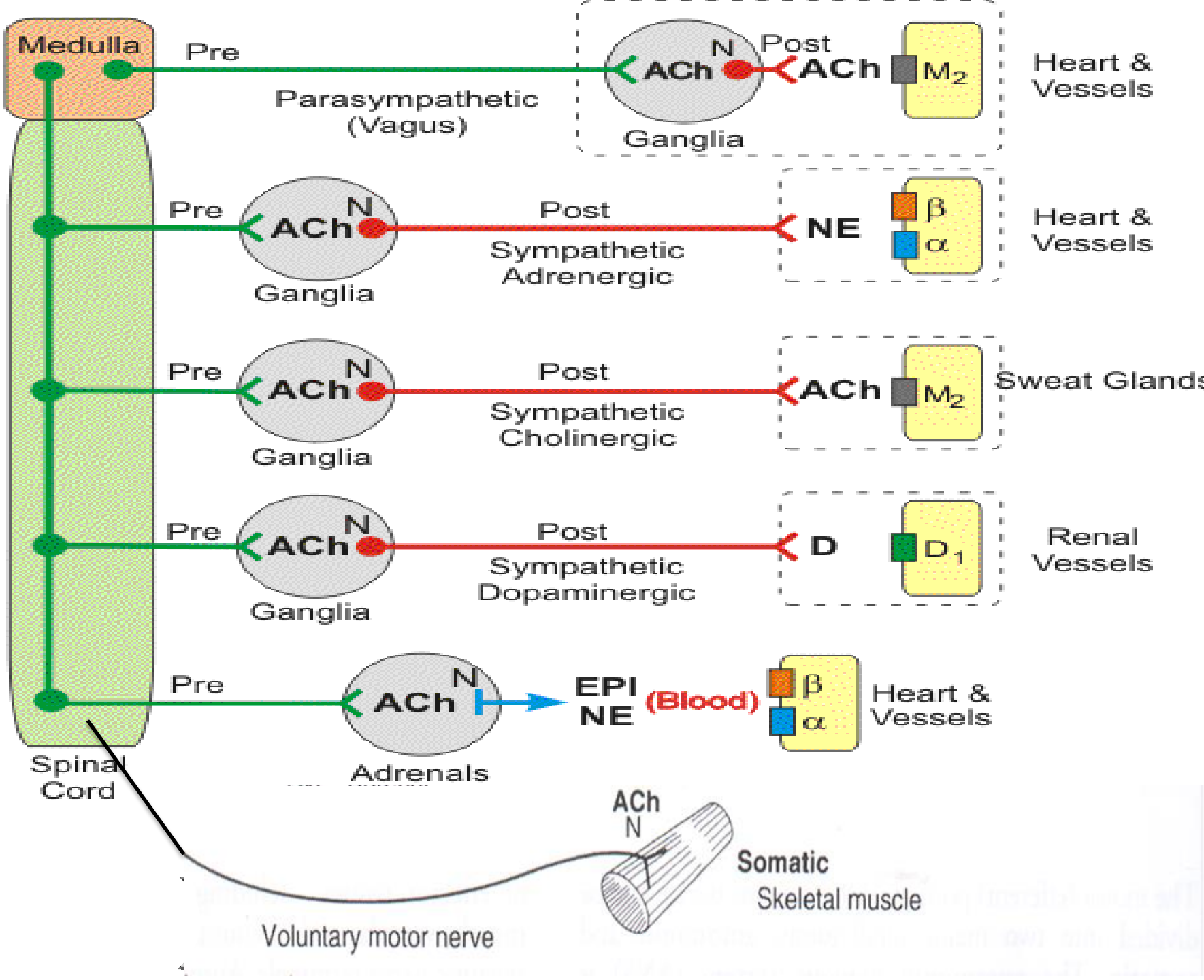
Autonomic nervous system (physiological view)

- **The autonomic nervous system ANS is a part of peripheral nervous system**
- **It control the involuntary body function**
- **ANS has two divisions**

1. **Parasympathetic system(cholinergic system)**
2. **Sympathetic system(adrenergic system)**

- **Both sympathetic and parasympathetic systems consist of**

1. **Preganglionic fiber: originate from brain and spinal cord**
2. **Autonomic ganglia**
3. **Post ganglionic fibers**


Medulla
Pre
Parasympathetic
(Vagus)
ACh
N
Post
ACh
M2
Ganglia
Heart &
Vessels
Pre
ACh
N
Post
Sympathetic
Adrenergic
NE
β
α
Ganglia
Heart &
Vessels
Pre
ACh
N
Post
Sympathetic
Cholinergic
ACh
M2
Ganglia
Sweat Glands
Pre
ACh
N
Post
Sympathetic
Dopaminergic
D
D1
Ganglia
Renal
Vessels
Pre
ACh
N
EPI
NE
(Blood)
β
α
Adrenals
Heart &
Vessels
Spinal
Cord
ACh
N
Somatic
Skeletal muscle
Voluntary motor nerve

- **The following fibers release acetylcholine as a main neurotransmitter**

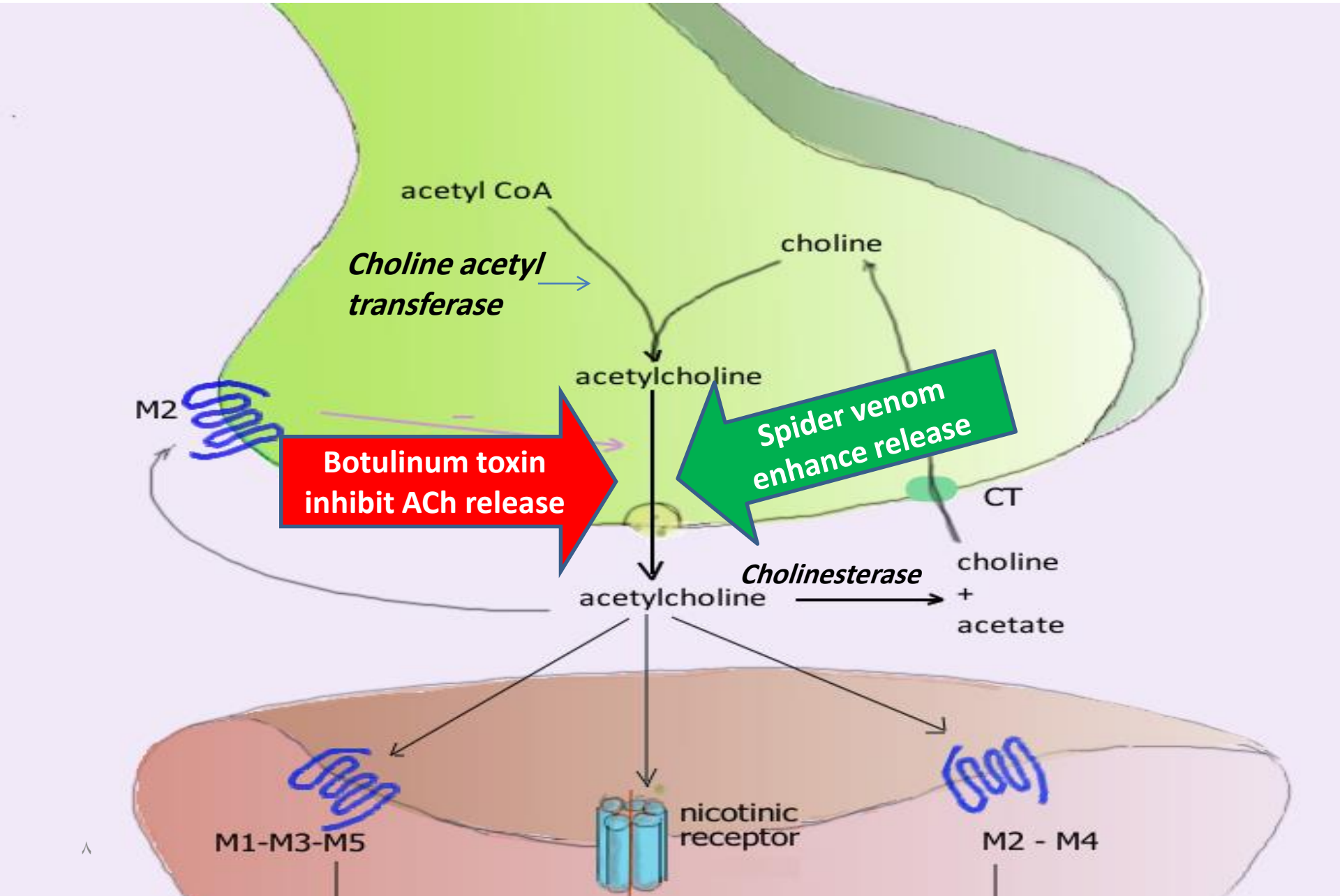
1. **All preganglionic fibers(sympathetic and parasympathetic)**
2. **All postganglionic parasympathetic fibers**
3. **Only postganglionic sympathetic fibers to sweat glands**
4. **Somatic nerve fibers at neuromuscular junction**

Cholinergic system
parasympathetic system

- **The neurotransmitter : acetylcholine ACh**
- **The receptors**

1. **Muscarinic receptors (M1-M5); present in CNS and other organs supplied by parasympathetic system**
2. **Nicotinic receptors (Nn,Nm); in CNS, autonomic ganglia, adrenal medulla and neuromuscular junction**

Acetylcholine



- **Most cholinergic synapses are richly supplied with cholinesterase so half-life of Ach is very short (seconds).**
- **Cholinesterase enzyme is of 2 types**

1. **True- found at cholinergic nerve endings & in RBC**
2. **False(pseudo cholinesterase)-has lower specificity for Ach & found in blood plasma, liver & many other tissues.**

Effects of acetylcholine

1- CNS

Contains both muscarinic & nicotinic receptors causing stimulation followed by depression.

2- Eye

1. **Contraction of circular muscles of iris---- miosis**
2. **Contraction of ciliary muscles--- accommodation for near vision**
3. **Decrease intraocular pressure IOP**

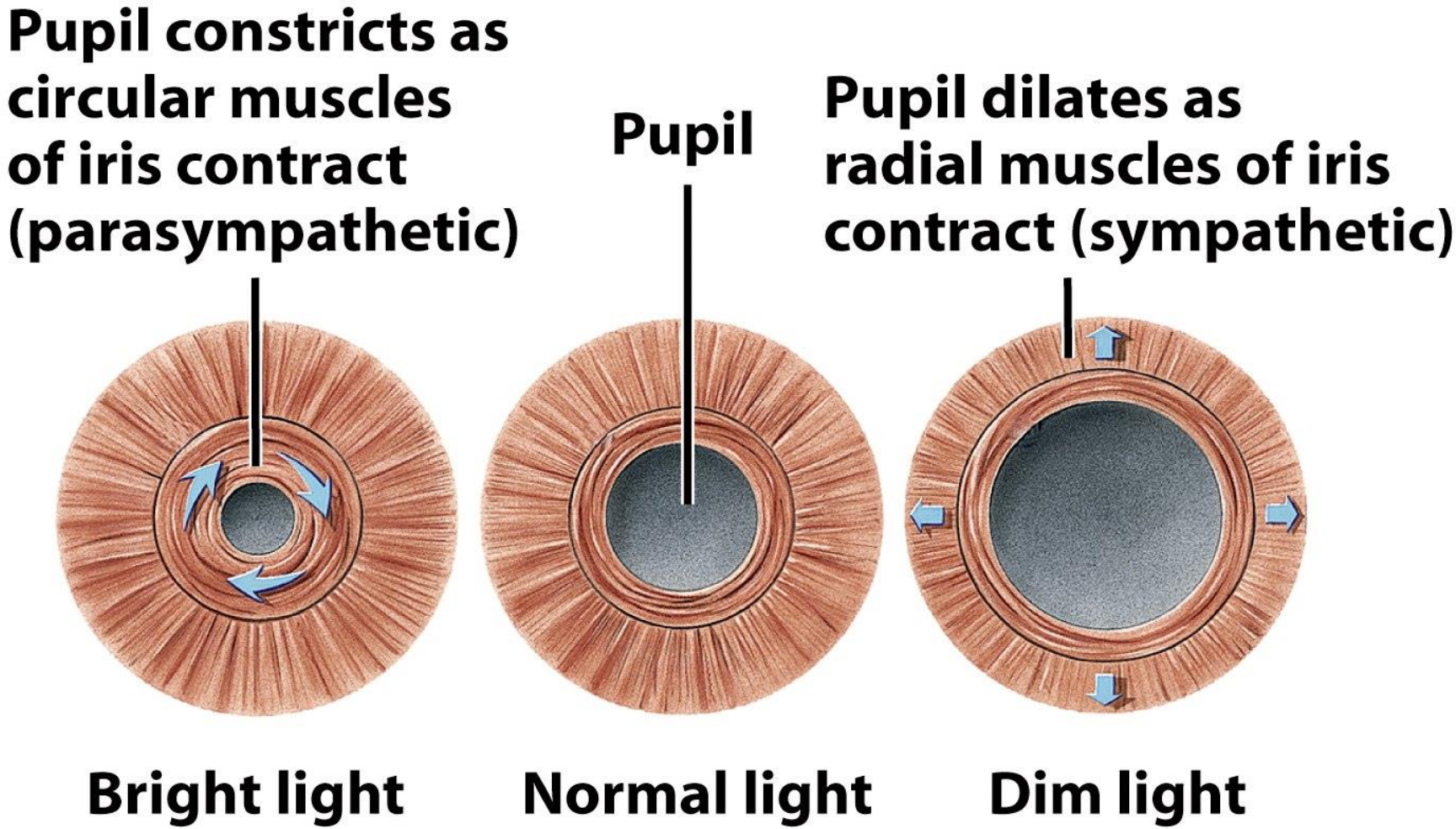
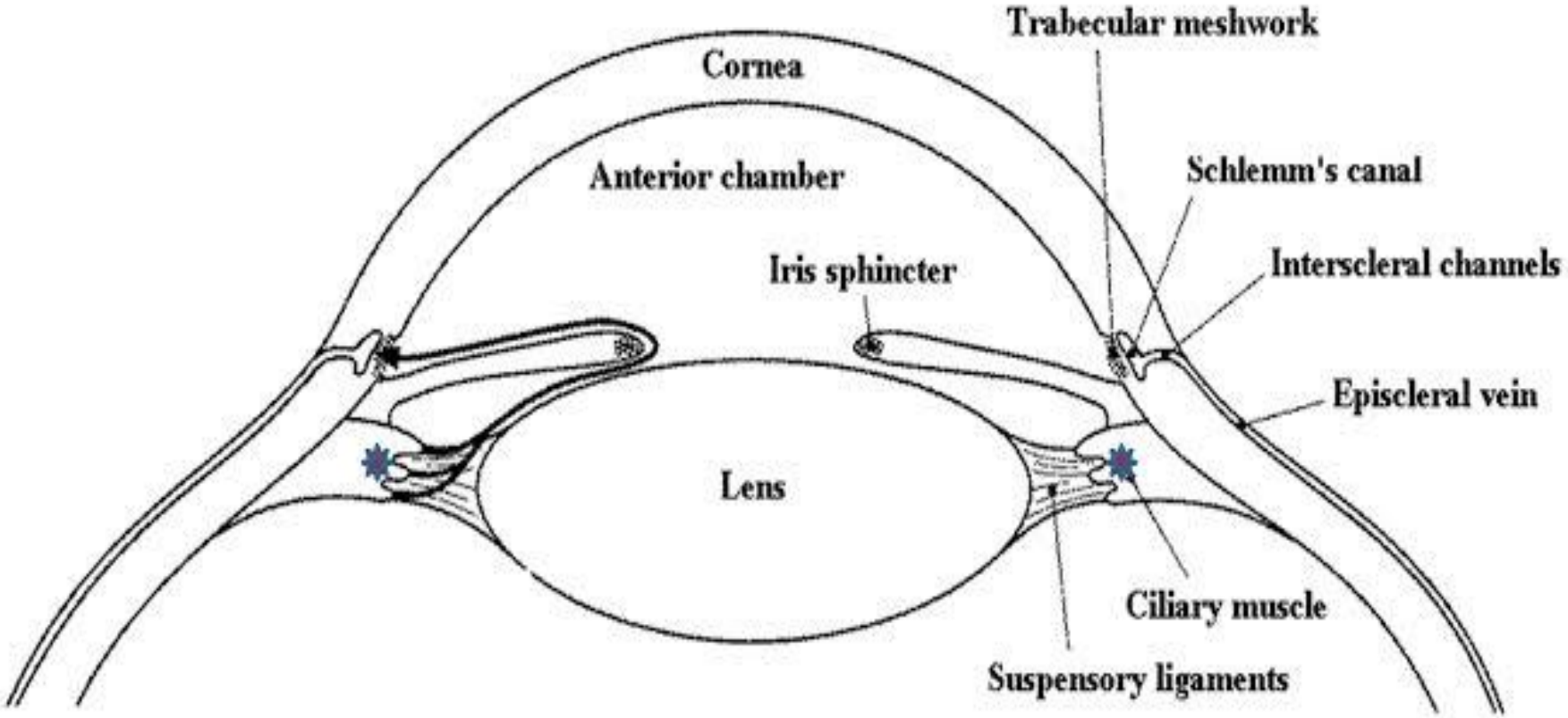


Figure 17-6 Principles of Anatomy and Physiology, 11/e

Diagram of eye & outflow of aqueous humor (arrow) which drains at Schlemm's canal



- **Intra-ocular pressure decrease by**

1. **miosis- the iris is pulled away from the angle of the anterior chamber**
2. **by contraction of ciliary muscle, the trabecular meshwork on the base of the ciliary muscle is opened**

Both these effects facilitate aqueous humor flow into canal of Schlemm.

3- Bronchi- bronchoconstriction & increase bronchial secretion (Bronchorrhea)

4- GIT

1. **increased tone and peristalsis of the gut and may cause colicky pain and diarrhea.**
2. **increased exocrine secretions mainly of salivary & gastric glands**
3. **Relaxation of sphincters**
   - **anal sphincter(causes defecation)**
   - **esophageal sphincter(causes regurgitation)**

5.CVS

On the heart: Causes bradycardia with AV block & eventually cardiac arrest.

On blood vessels—vasodilation through release of nitric oxide----hypotension

6- GUT

Contraction of detrusor muscle with relaxation of trigone & sphincter muscles ------micturition.

7.Exocrine glands- increase secretions mainly salivary, lacrimal, bronchial & sweat glands.

Sweat glands are cholinergic, but anatomically part of sympathetic system, axillary sweat glands are adrenergic.

Cholinergic drugs (Parasympathomimetic drugs)

They have acetylcholine- like effects, include:

1.Directly acting (act directly at cholinergic receptors)

- **a.cholinesters**
- **b.alkaloids**

2.Indirectly acting drugs(cholinesterase inhibitors) influence cholinergic receptors indirectly by preventing the breakdown of ACh including:

- **a. reversible anticholinesterases**
- **b. irreversible anticholinesterases**

Direct acting cholinomimetic drugs

- **Cholinesters**

1. **Acetyl choline; not suitable as drug because of its very short duration of action and wide range of activity(lack of selectivity)**
2. **Synthetic esters of choline**

- **Bethanecol**
- **Carbachol**

Bethanecol and carbachol

- Both resist hydrolysis by cholineasterase
- Act mainly on GIT and GUT
- Used mainly for treatment of intestinal and bladder atony
- Can be used for treatment of glucoma

Alkaloids

1)Nicotine- is absorbed through mucous membranes

- **At low dose—stimulate *autonomic ganglia**
  ***NMJ (fasciculation)**
- **In large doses- blocks *autonomic ganglia**
  *** NMJ causing paralysis.**
- **CNS is stimulated (including vomiting center, tremor, convulsion) & followed by depression.**

***clinical use- is a social drug used as an adjunct to stopping its own abuse as tobacco.**

2)Muscarine-

is of no therapeutic use.

***it has role in discovery of cholinergic receptor subtypes**

***has toxicological significance because of its presence in certain poisonous mushrooms.**

3)Pilocarpine

Is a direct acting muscarinic agonist

Clinical uses

1.Glaucoma , it decreases IOP by miosis & contraction of ciliary muscle

2.used orally for treatment of xerostomoia(dry mouth) following irradiation of head & neck tumors

Adverse effects –

Local effects: decreased visual acuity, eye irritation& pain

rarely is absorbed in amounts sufficient to cause systemic effects (bradycardia, bronchospasm, hypotension, urinary urgency, diarrhea, hyper salivation & sweating)

***Its systemic toxicity is reversed by atropine**

Questions

- **The following effects result from action of acetylcholine on muscarinic receptors except**
- **A- miosis** **b- sweating**
- **C- bradycardia** **d- skeletal muscle contraction**
- **What are the effects of acetylcholine on GIT?**
- **By which mechanism pilocarpine decrease intraocular pressure?**