Pharmacology lab

Lab 4

Drugs acting on the eye

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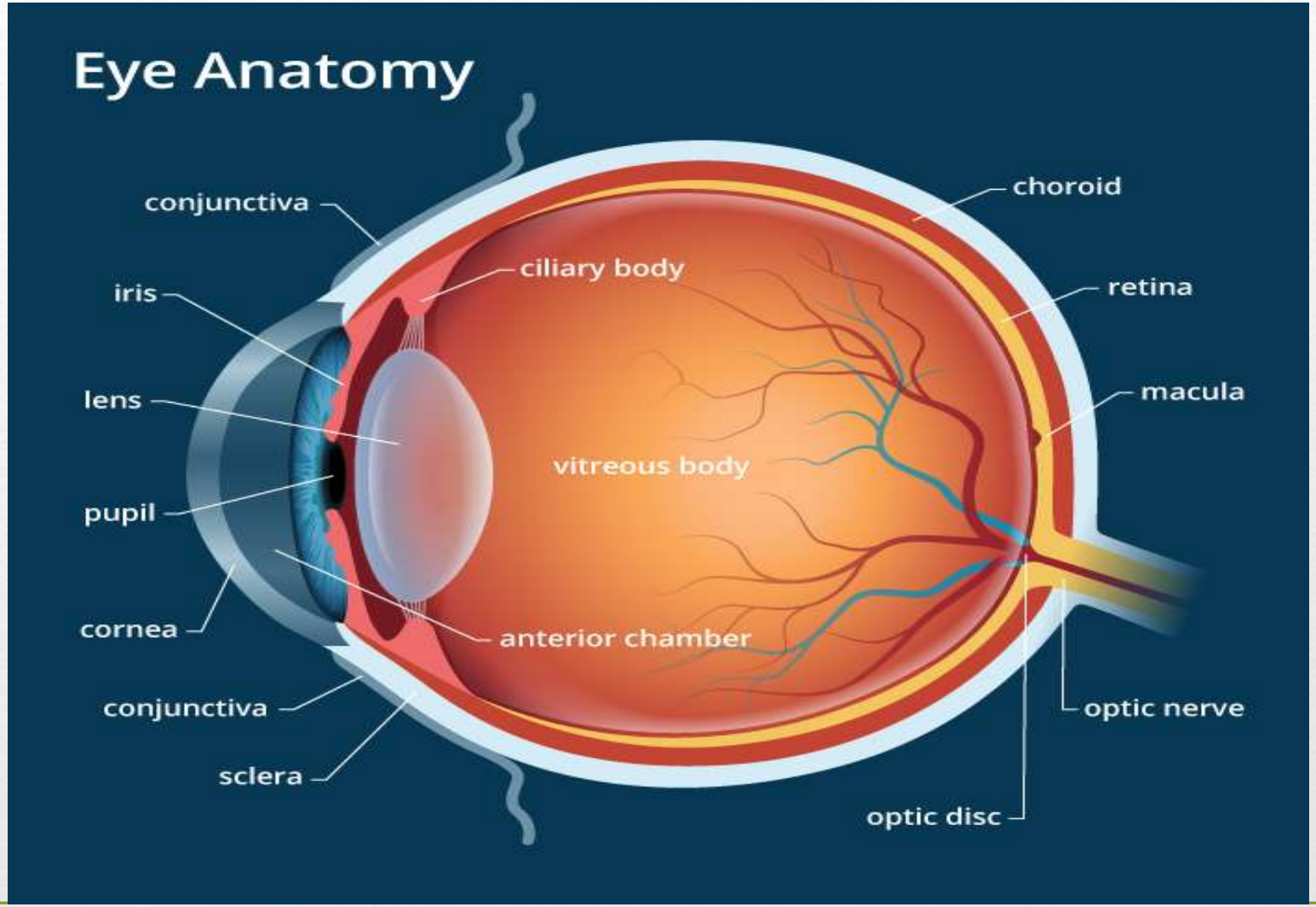
The composition of the human eye

The main compartments of the human eye are :

- Cornea
- Iris
- Lens
- Ciliary body and vitreous humor.

The composition of the human eye



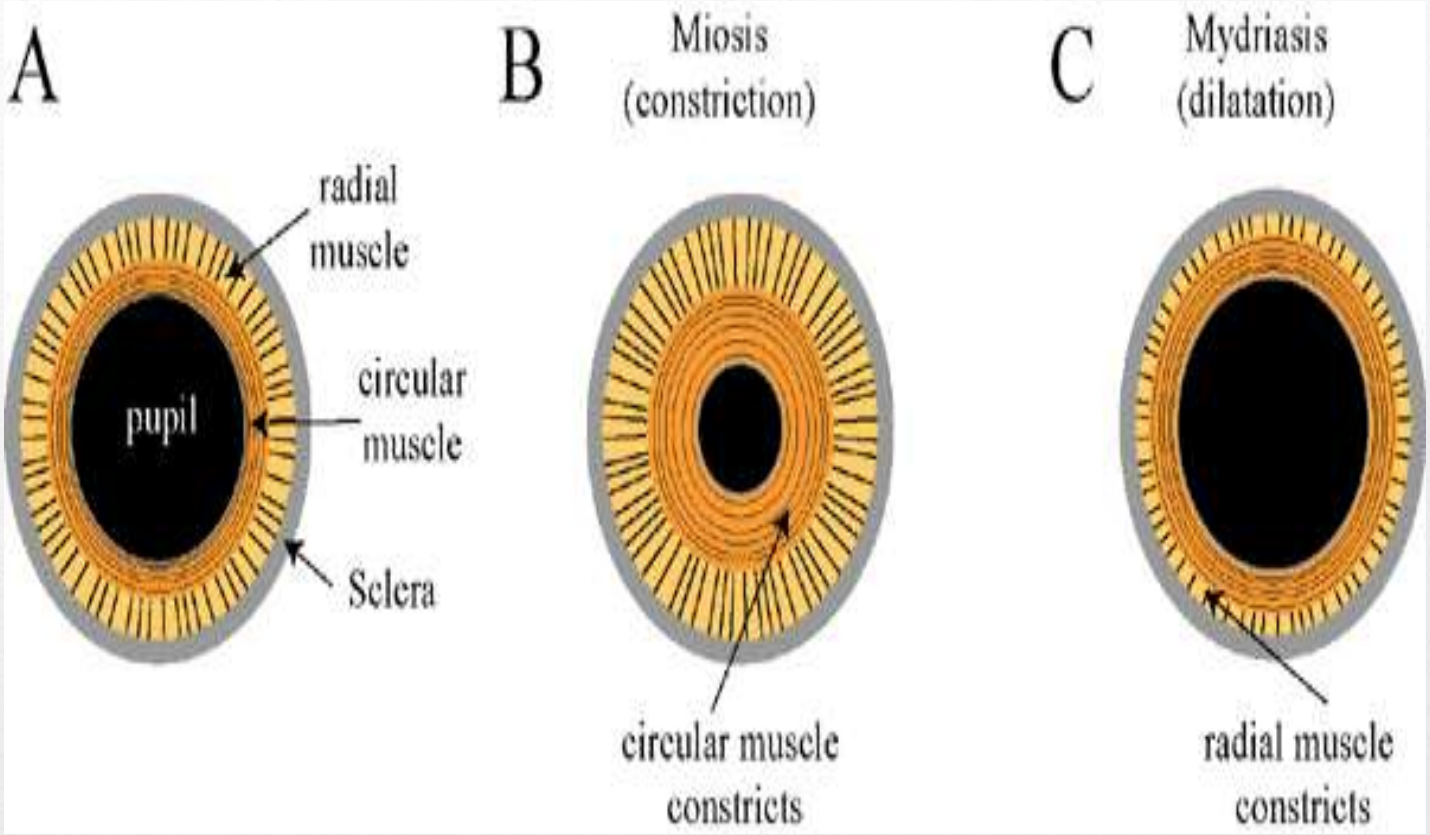
Iris

Iris involve;

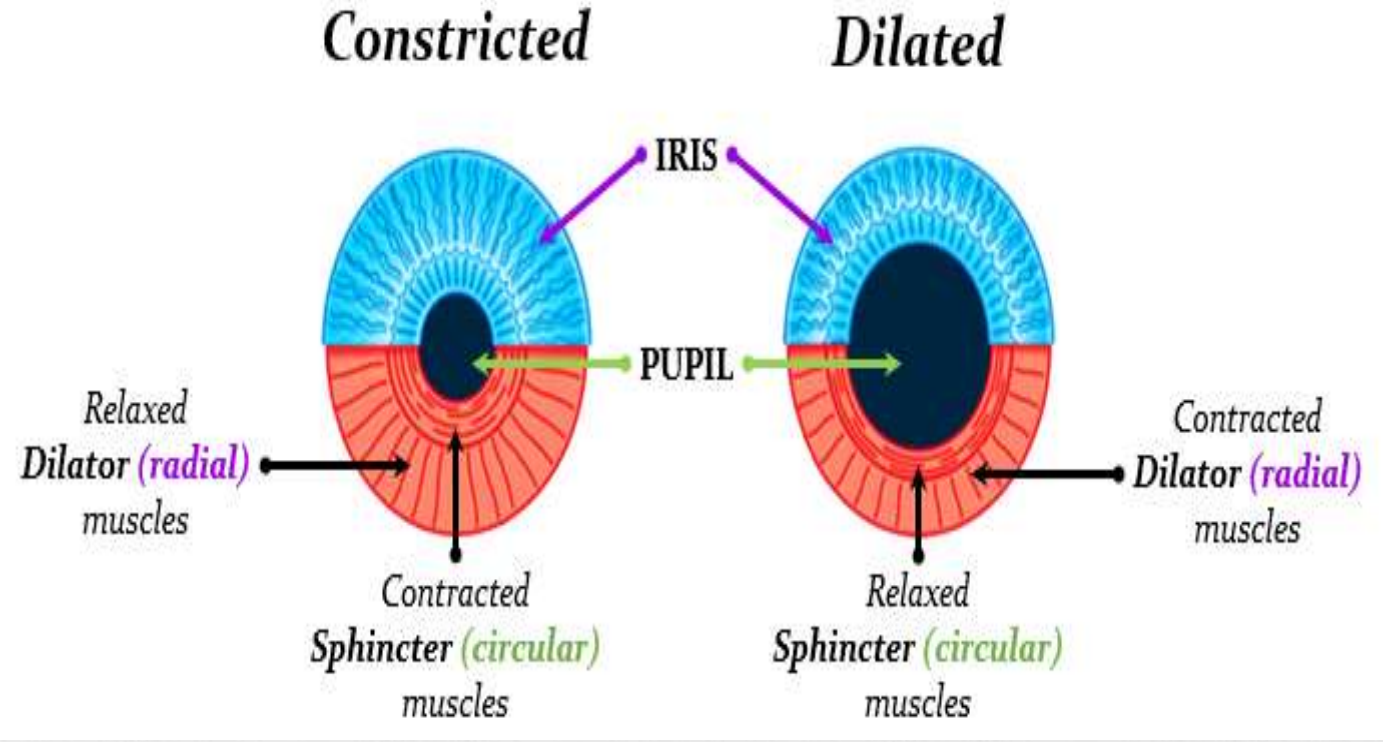
- **Circular muscle** (Muscarinic receptors).
- **Radial muscle** (Alpha-receptors).

- **Miosis**: smallness of the pupils of the eyes, is due to either contraction of circular muscle or relaxation of radial muscle.

- **Mydriasis**: dilatation of the pupils of the eyes , is due to either contraction of radial muscle or relaxation of circular muscle.


A
radial muscle
pupil
circular muscle
Sclera
B
Miosis (constriction)
circular muscle constricts
C
Mydriasis (dilatation)
radial muscle constricts

Working of Iris



Autonomic Nervous System

ANS Drugs & Pupil

	Miosis	Mydriasis
Cholinergic System	⊕ Cholinergics	⊖ Anticholinergics
Adrenergic System	⊖ Antiadrenergics	⊕ Adrenergics

Eye muscle	Receptor	Effect (muscle)	Effect (pupil)
Radial muscle (iris)	α_1 (SNS)	Contraction	Mydriasis
Circular muscle (iris)	M_1 (PNS)	Contraction	Miosis
Ciliary muscle	β_2 (SNS) M_2 (PNS)	Relaxation Contraction	– Accommodation

Alpha-receptors in iris

- **Alpha-agonist** → Contraction of radial muscle of iris (**Mydriasis**).
- **Alpha 1 agonist** such as **phenylephrine** → mydriasis, also increase the out flow of aqueous humor from the eye and reduce IOP.
- **Alpha-blocker** → Relaxation of radial muscles of iris (**Miosis**)

Alpha agonist

- **Alpha agonist** eye drops help reduce redness & irritation of the eyes by vasoconstriction of swollen blood vessels in the eye.
- Some ophthalmic alpha agonist used by ophthalmologists target the contraction of radial muscle to dilate the pupils (mydriasis) for examination or surgery. **Example**:
- **Naphazoline hydrochloride**
- **Phenylephrine hydrochloride**
- **Oxymetazoline hydrochloride**

Ciliary body

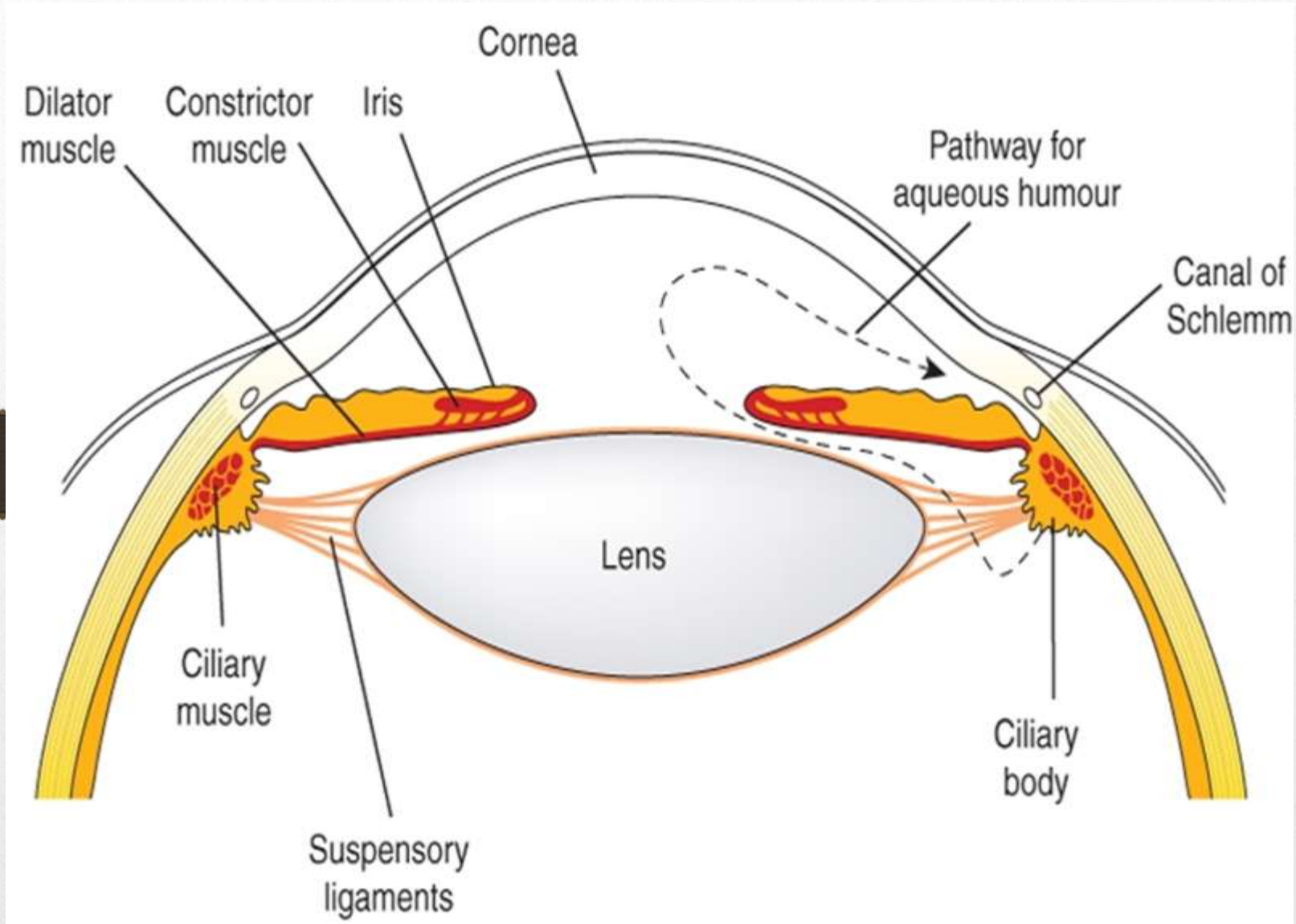
Ciliary body involve:

- **- Ciliary epithelium (B2 receptors):**

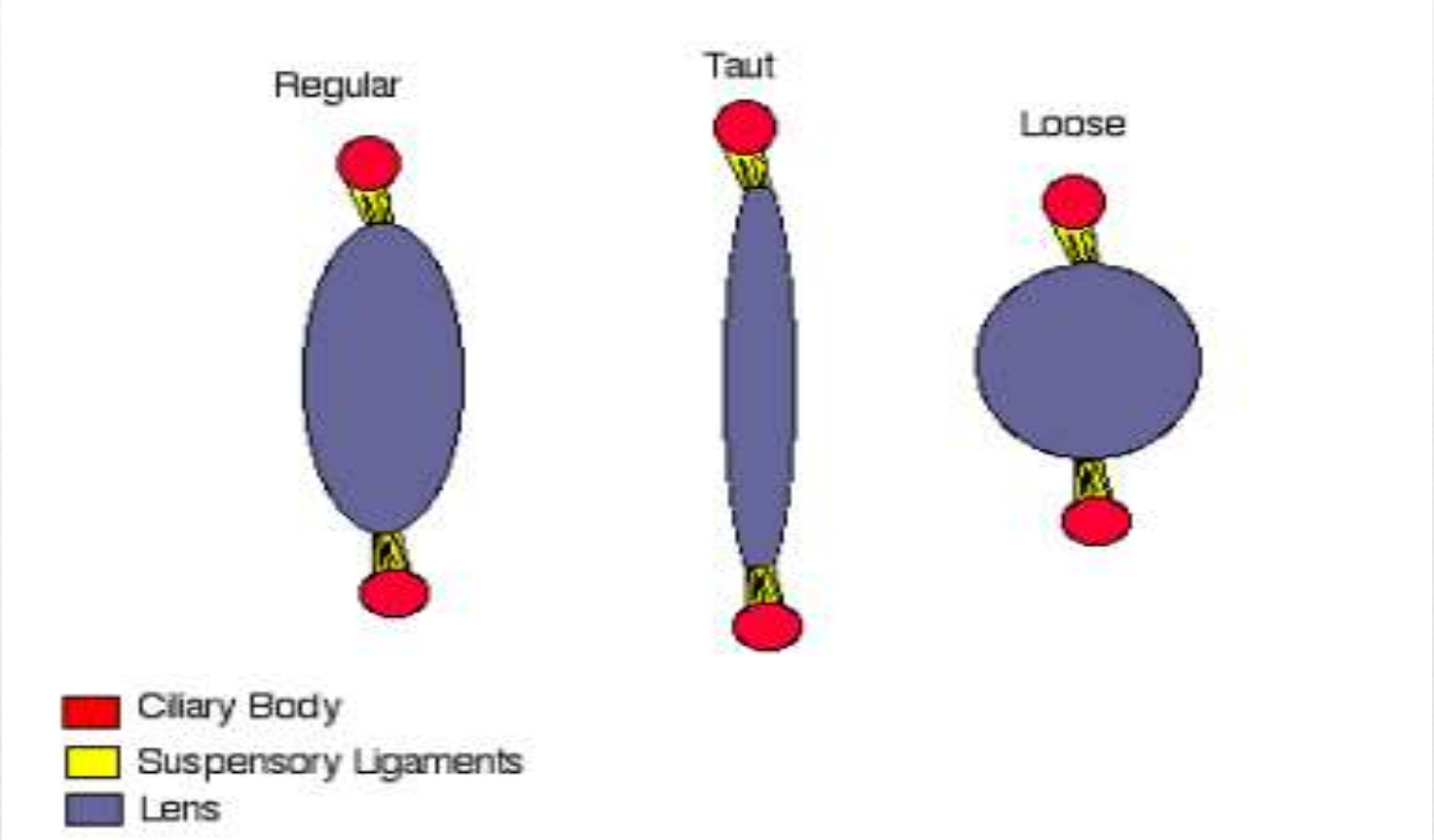
responsible for secretion of aqueous humor.

- **- Ciliary muscle (M2 receptors):**

responsible for near or far vision.


Cornea
Dilator muscle
Constrictor muscle
Iris
Pathway for aqueous humour
Canal of Schlemm
Lens
Ciliary muscle
Ciliary body
Suspensory ligaments

The contraction and relaxation of the lens

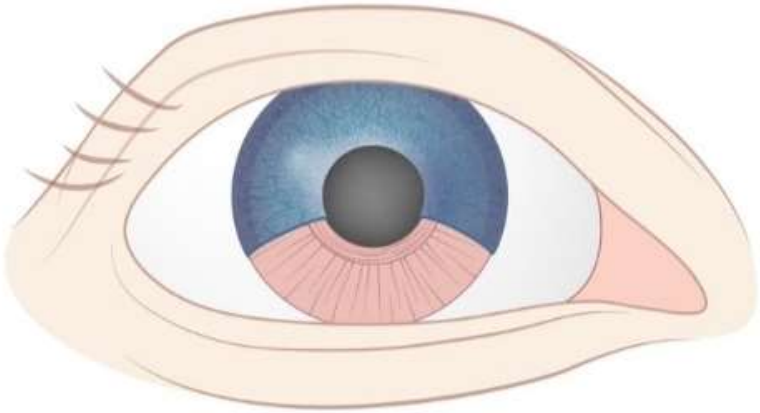


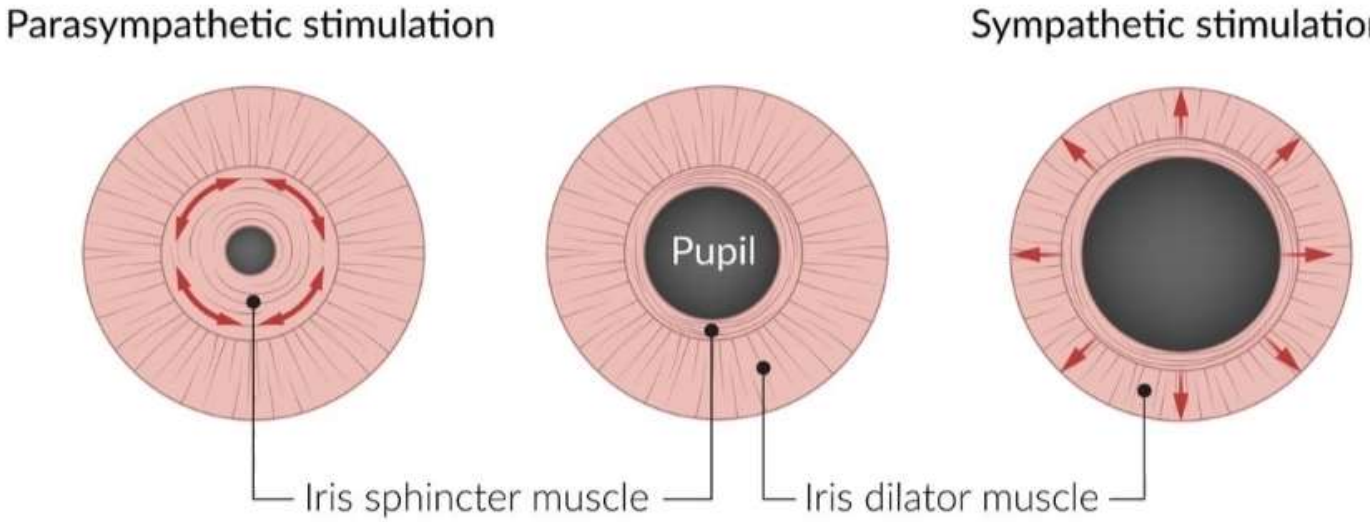
Ciliary Muscle
(Muscarinic receptors)

- Ciliary muscle contraction → Increases flow → Decreases IOP.
- Ciliary muscle Relaxation → Decreases flow → Increases IOP (Glaucoma).

Also

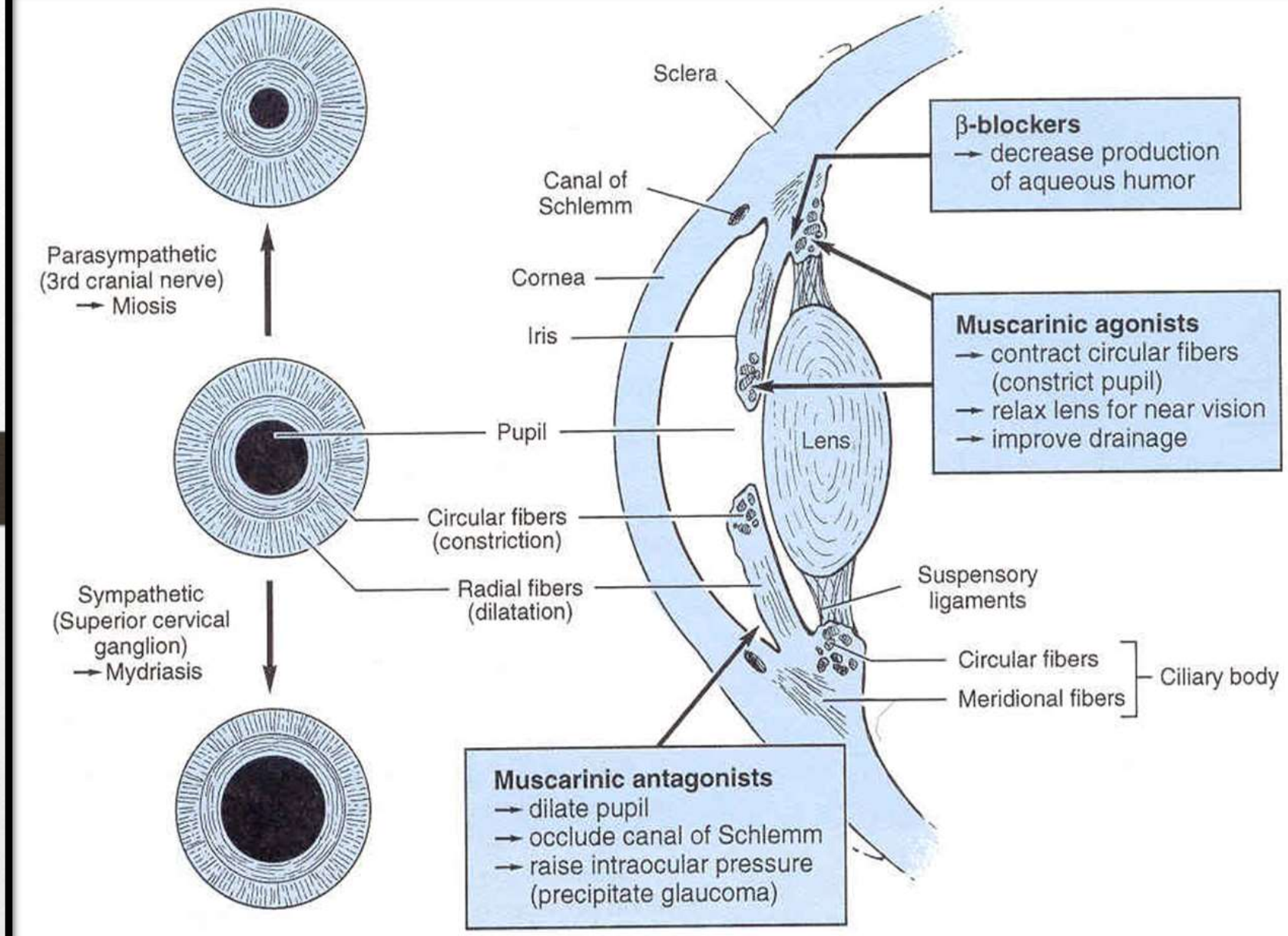
- **Muscarinic agonist** → Ciliary Muscle Contraction → Lens contraction → near vision
- **Anti-Muscarinic agent** → Ciliary Muscle Relaxation → Lens relaxation → far vision




Parasympathetic stimulation
Sympathetic stimulation
Pupil
Iris sphincter muscle
Iris dilator muscle

Ciliary Epithelium
(B2-Receptors)

- Responsible for secretion of aqueous humor.
- Contraction of ciliary muscle presses trabecular meshwork → enhancing the flow of aqueous humor through canal of Schlemm.


Parasympathetic
(3rd cranial nerve)
→ Miosis
Sympathetic
(Superior cervical
ganglion)
→ Mydriasis
Sclera
Canal of
Schlemm
Cornea
Iris
Pupil
Circular fibers
(constriction)
Radial fibers
(dilatation)
Lens
Suspensory
ligaments
Circular fibers
Meridional fibers
Ciliary body
β-blockers
→ decrease production
of aqueous humor
Muscarinic agonists
→ contract circular fibers
(constrict pupil)
→ relax lens for near vision
→ improve drainage
Muscarinic antagonists
→ dilate pupil
→ occlude canal of Schlemm
→ raise intraocular pressure
(precipitate glaucoma)

CILIARY BODY AND AUTONOMIC NERVOUS SYSTEM

- Sympathetic system increases aqueous production
  - Through stimulation of ß receptors
  - ß blockade decreases aqueous production
- Sympathetic system decrease aqueous production
  - Through activation of α2 receptors
  - α2 agonists decrease aqueous production

Drug induced miosis vs mydriasis

CONSTRICTED PUPILS (MIOSIS)

Sympatholytic agents
- Clonidine
- Opioids
- Phenothiazines
- Tetrahydrozoline and oxymetazoline
- Valproic acid

Cholinergic agents
- Carbamate insecticides
- Nicotine[b]
- Organophosphates
- Physostigmine
- Pilocarpine

Others
- Heatstroke
- Pontine infarct
- Subarachnoid hemorrhage

DILATED PUPILS (MYDRIASIS)

Sympathomimetic agents
- Amphetamines and derivatives
- Cocaine
- Dopamine
- LSD (lysergic acid diethylamide)
- Monoamine oxidase inhibitors
- Nicotine[b]

Anticholinergic agents
- Antihistamines
- Atropine and other anticholinergics
- Carbamazepine
- Glutethimide
- Tricyclic antidepressants

Methods

- Place few drops of the agents in the following table into the eyes of rabbits and check for the parameters mentioned in the same table, and the results are as follows:

Table of eye results

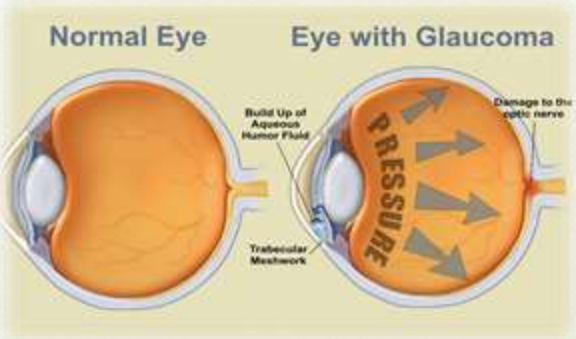
parameter / Agent	Pupil Size	Light Reflex	Accommodation	Conjunctival Blood vessels	Corneal sensation	IOP
Adrenaline	↔	+ve	↔	Pale	+ve	↔
Phenylphrine	Mydriasis	+ve	↔	Pale	+ve	Inc.
Pilocarpine	Miosis	+ve	Near Vision	Congestion	+ve	Dec.
Atropin	Mydriasis	-ve	Far Vision	Pale (Congested in High Dose)	+ve	Inc.
Xylocaine	↔	+ve	↔	↔	-ve	↔
procaine	↔	+ve	↔	↔	+ve	↔

(+ve) indicates the presence of the reflex
(-ve) indicates the absence of the reflex
(↔) indicates that there is no change

Results

- **Adrenaline** acts on alpha-receptors causing vasoconstriction of the epithelium of conjunctiva, but it does not cause mydriasis as it cannot be absorbed by the iris.
- **Phenylephrine** is alpha-receptor agonist → mydriasis
- **Atropine** is antimuscarinic agent, **scopolamine** & **tropicamide** → mydriasis
- **pilocarpine** → Muscarinic agent → miosis
- **Procaine, Xylocaine** (local anesthetic) as the cornea does not absorb it, so it cannot cause loss of corneal reflex.

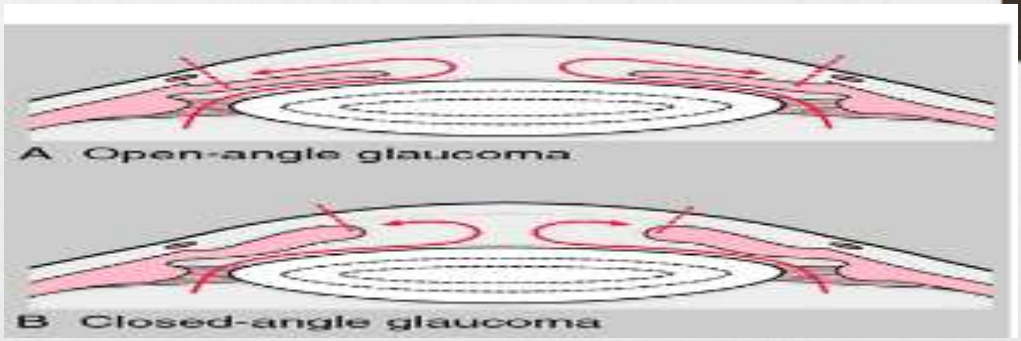
Glaucoma



- A group of eye conditions that damage the optic nerve, often due to high intraocular pressure (**IOP**).
- Leading cause of irreversible blindness.
- Characterized chiefly by **an increase in IOP above 21 mmHg & may be as high as 70 or 80 mmHg during the attack**

Types of Glaucoma

- **1. Open-Angle Glaucoma (POAG):** Gradual increase in IOP, asymptomatic until advanced.



- **2. Angle-Closure Glaucoma:** Sudden increase in IOP, emergency condition.

Phathophysiology

- **1. Increased Intraocular Pressure (IOP):** Imbalance between aqueous humor production and drainage.
- **2. Damage to the Optic Nerve:** Reduced blood flow and nutrient supply to the optic nerve.

Symptoms and signs

- **1. Open-Angle Glaucoma:** No early symptoms, slow peripheral vision loss.
- **2. Angle-Closure Glaucoma:** Severe eye pain, headache, blurred vision, nausea.
- **3. Advanced Signs:** Tunnel vision, optic disc cupping.

Treatment Options

- **1. Medications:**
- **- Prostaglandin analogs (increase fluid drainage).**
- **- Beta-blockers (reduce fluid production).**
- **- Carbonic anhydrase inhibitors.**
- **2. Laser Therapy: Trabeculoplasty (enhances drainage).**
- **3. Surgical Interventions: Trabeculectomy or drainage implants.**

CLASS OF DRUG	DRUG NAMES	MECHANISM OF ACTION	SIDE EFFECTS
β-Adrenergic antagonists (topical)	*Betaxolol, carteolol, levobunolol, metipranolol, timolol*	Decrease of aqueous humor production	Ocular irritation; contraindicated in patients with asthma, obstructive airway disease, bradycardia, and congestive heart failure.
α-Adrenergic agonists (topical)	*Apraclonidine, brimonidine*	Decrease of aqueous humor production and increase of aqueous outflow	Red eye and ocular irritation, allergic reactions, malaise, and headache.
Cholinergic agonists (topical)	*Pilocarpine, carbachol*	Increase of aqueous outflow	Eye or brow pain, increased myopia, and decreased vision.
Prostaglandin-like analogues (topical)	*Latanoprost, travoprost, bimatoprost*	Increase of aqueous humor outflow	Red eye and ocular irritation, increased iris pigmentation, and excessive hair growth of eye lashes.
Carbonic anhydrase inhibitors (topical and systemic)	*Dorzolamide* and *brinzolamide* (topical), *acetazolamide*, and *methazolamide* (oral)	Decrease of aqueous humor production	Transient myopia, nausea, diarrhea, loss of appetite and taste, and renal stones (oral drugs).


Thank
you!!