Pharmacology of eye

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Sympathetic Innervation:

quantity not quality ← through α-Receptor.

1- to dilator pupali muscle radial muscles of the iris, leading to pupil dilation (mydriasis)

2- to blood vessels within the eye, influencing ocular blood flow and intraocular pressure

3- to Müller's muscle leading to eyelid retraction

5- Relaxation of ciliary muscle → Accomdation of Far vision

↳protrusion of eye → hyperthyrodism

4- Beta-2 adrenoceptors in the ciliary body increase the secretion of aqueous humor but Alpha-2 adrenoceptors in the ciliary body suppress it.

→ quality not quantity

miosis due to M_3 Receptor.

Parasympathetic innervation:

1-To constrictor pupillae muscle, narrowing the pupil in response to bright light (light reflex).

2-To the ciliary muscle, causing it to contract, leading to lens accommodation.

Drainage of aqueous humor:

Aqueous humor flows from the posterior chamber → anterior chamber → exits via two routes:

1- Conventional Pathway (90% of outflow):

space of Fontan

Fluid traverses the trabecular meshwork → Schlemm's canal → episcleral veins.

2-Unconventional Pathway (10% of outflow):

Fluid drains through the ciliary muscle, suprachoroidal space, and sclera (uveoscleral route).

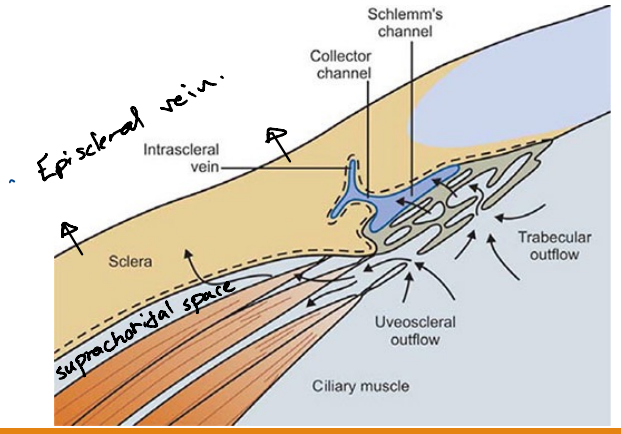
Drugs

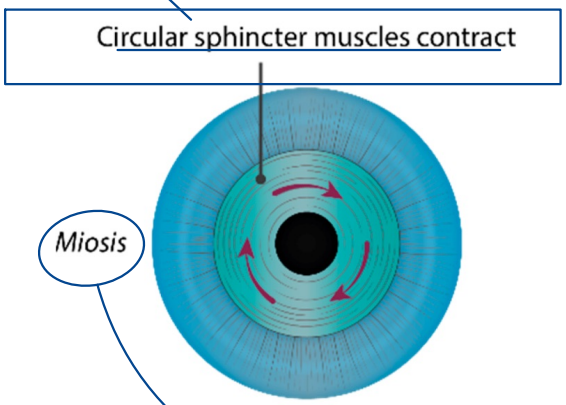
1- Drugs affecting pupil size

2-Treatment of Glaucoma

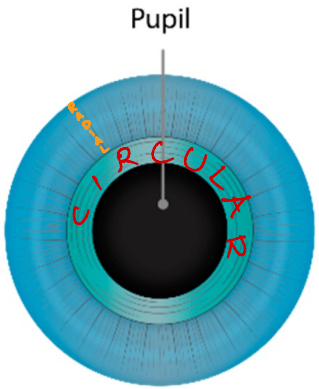
3-Drugs that ↑↑ IOP

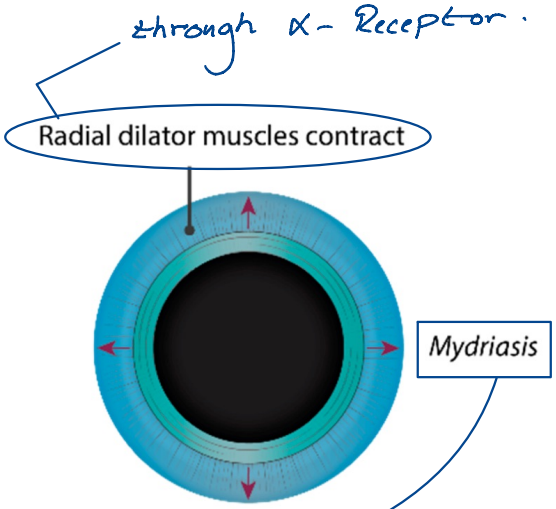
contraindicated with patient of glucoma.





through M_3 Receptor.





through α- Receptor.

① To Reduce Amount of Light enter the pupil

→ through Parasympathetic stimulation. ← Active miosis

→ Or sympathetic inhibtion ← passive miosis

① to increase the Amount of Light Enter the pupil

→ through sympathetic stimulation. ← active mydriasis

→ or Parasympathetic inhibtion ← Passive mydriasis.

A- Drugs affecting pupil size

1- Miotics drugs

Drug Class	Examples	Effect on Pupil	Mechanism
Opioids (systemic) → pin-point-Pupil. ⊛active misos	Morphine, Heroin, Fentanyl	Miosis	Activates μ-opioid receptors, inhibiting sympathetic tone.
Cholinergic Agonists (local)	Pilocarpine, Carbachol	Miosis	Stimulates parasympathetic system (muscarinic receptors).
Acetylcholinesterase Inhibitors (local)	Physostigmine, Neostigmine,	Miosis	Increases acetylcholine levels, activating muscarinic receptors
Guanthiden ↳passive miosis	↳treat prostatic hyperplasia	Miosis	Reduces Release of NE in the eye:
α1-Adrenergic Blockers Passive miosis	Prazosin, Tamsulosin	Miosis	Blocks sympathetic stimulation of the dilator muscle
Sedatives / Barbiturates	Benzodiazepines (high doses)	Miosis	CNS depression reduces sympathetic tone.

Locally acting miotics

(parasympathomimetics): stimulate M3 receptors in

N. B:-

constrictor pupilae muscle

1- CPM → miosis + wide angle of filtration & space of Fontana.

used in treatment of glucoma.

2- Cilliary muscle → accommodation to near vision + open canal of Schlemm.

3- Some stimulate Nm receptors in upper eye lid → upper eyelid twitches.

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1- Direct parasympathomimetics:

-Choline esters: bethanichol(M only) &carbachol (M+N).

- Alkaloid:pilocarpine(M only).

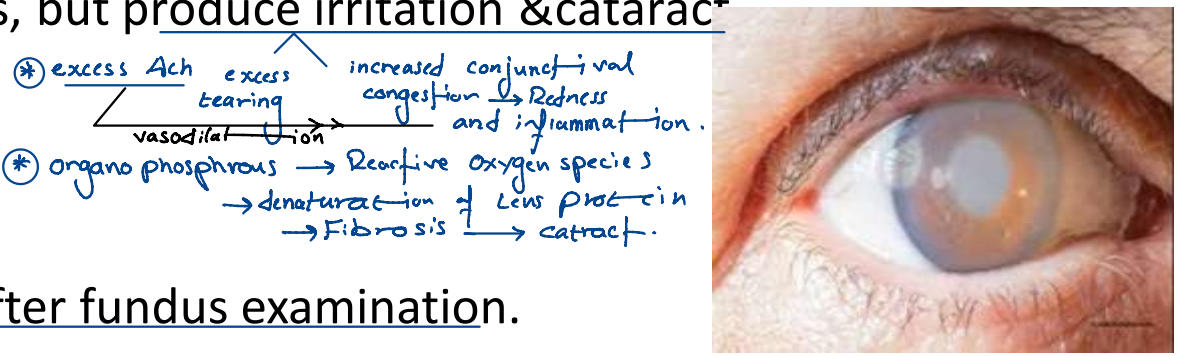
2- Indirect parasympathomimetics:

-Reversible:physostigmine(eserine) &demecarium.

-Irreversible :organophosphorus→ecothiophate&isoflurophate: Long-lasting strong effect with extreme miosis, but produce irritation &cataract

Therapeutic uses:

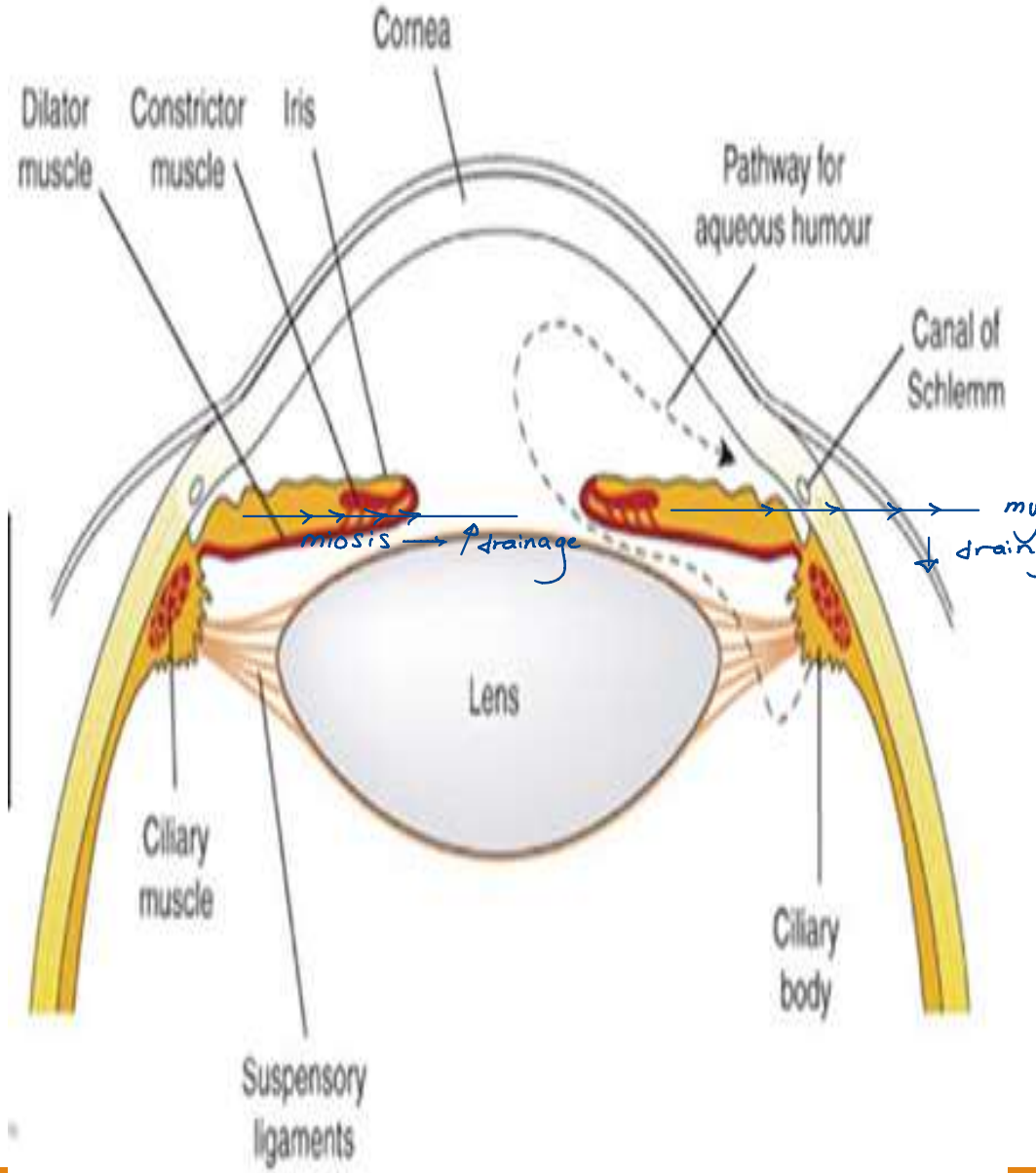
1-Glaucoma.



2-Counteract mydriatics after fundus examination.

3-Alternatively with mydriatics to cut adhesion between iris & lens.

during inflammatory Reaction.


Cornea
Dilator muscle
Constrictor muscle
Iris
Pathway for aqueous humour
Canal of Schlemm
miosis → ↑drainage
mydriasis
↓ drainge
Lens
Ciliary muscle
Ciliary body
Suspensory ligaments


Opiate use or overdose is one of the most common causes of pinpoint pupils.

Guanthidine:

Paralysis of Dilator Pupillae Muscle → miosis + ↓↓ IOP (passively.)

Relaxation of levator palpebrae superiosis → ↓↓ exophthalmos of hyperthyroidism. (and Muller muscle.)

Morphine stimulates **opiate receptor** (μ) in **3rd cranial nerve nucleus** → stimulates oculomotor nerve → **ciliary ganglia (Nn)** → eye → ACh → stimulates **M3** receptors of **CPM** → marked **miosis** (pin point pupil).

Pin-point pupil of morphine can be antagonized by:

1) **Systemic naloxone** → block opiate μ receptors in CNS.
2) **Systemic ganglion blocker** → block Nn of ciliary ganglia.
3) **Topical or systemic atropine** → block M3 receptors on CPM (Atropine.)

2- Mydriatics drugs

contra-indicated in cases of glaucoma.

Drug Class	Examples	Effect on Pupil	Mechanism
Sympathomimetics (indirect).	Epinephrine, Cocaine, Amphetamines	Mydriasis	Stimulates adrenergic receptors, enhancing sympathetic activity
Anticholinergics	Atropine, Tropicamide, Scopolamine	Passive Mydriasis	Blocks parasympathetic innervation to the constrictor pupille muscle.
α1-Adrenergic Agonist	Phenylephrine	Mydriasis	Stimulates dilator muscle via α1 receptors.
SSRIs & SNRIs	Fluoxetine, Venlafaxine	Mydriasis	Increased serotonin activity affects autonomic control
Tricyclic Antidepressants → Atropine-like action	Amitriptyline, Imipramine	Mydriasis	Strong anticholinergic effects block pupil constriction.
Hallucinogens	LSD, MDMA	Mydriasis	Serotonin and dopamine effects increase sympathetic tone
Dopaminergic Drugs	Levodopa, Bromocriptine	Mydriasis	Enhances dopamine signaling, indirectly increasing sympathetic effects

A- Sympathomemetic:

N.B ; ciliary muscle is predominantly supplied by parasympathetic system , to lesser extent with sympathetic supply. if Muscuranic Receptor is Blocked; most of ciliary muscle will be cut → cycloplegia → Atropine

mechanism: Stimulate **α1 receptors** leading to:

→ paralysis of ciliary muscles

Contraction of **DPM** → **Active mydriasis** (intact light reflex) & no cycloplegia , BV → VC → decongestion & ↓ IOP.

- **Examples:** Direct: phenylephrine., Indirect: amphetamine, Mixed: ephedrine.
- **Therapeutic uses:** fundus examination especially in elderly patients liable for glaucoma.

Block Na^+ channel → adrenergic properties.

B- Cocaine:

- **Surface anesthesia** → loss of sensory reflex (corneal & conjunctival reflex)

cocaine overdose Lead to death ; arrythmia

- **Indirect sympathomimetic**: ↓ neuronal uptake (1) + MAO inhibitor → ↑ endogenous NA → stimulates **α1** receptors → **active mydriasis & decongestion.**

No cycloplegia.

C)Parasympatholytics:

Mechanism: Block M3 receptors in:

1) **CPM** → passive mydriasis → lost light reflex & narrow angle of filtration.

2) **Ciliary muscle** → cycloplegia (loss of accommodation) + closing canal of Schlemm.

- Result is **lost light reflex + cycloplegia + ↑↑ IOP.** (blurred vision.) **Examples:**

1) **Natural belladona alkaloids: atropine & hyoscine.**

2) **Synthetic:** homatropine, cyclopentolate , tropicamide & eucatropine.

- **Therapeutic uses:**

1) **Atropine** is used in iritis and corneal ulcer (to prevent adhesions), and measurement of refraction in children. (alternavily with miotic drug. → to examine without the effect of ciliary muscle.)

2) **Synthetic substitutes:** in fundus examination.

All are contraindicated in glaucoma

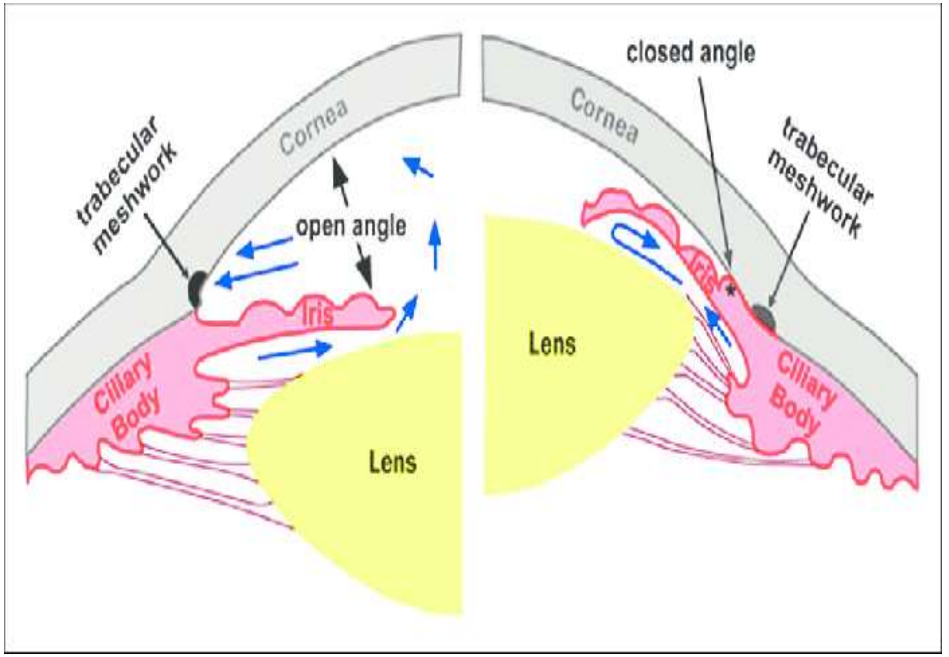
Treatment of Glaucoma

Normal Intra-Ocular Pressure (IOP) = 15-25 mmHg.

Glucoma may be :

1) **Closed angle** (narrow-angle) glaucoma

2) **Open-angle glaucoma** (Chronic glaucoma)



I- Closed angle (narrow-angle) glaucoma:

Acute congestive glaucoma

- Needs **surgical intervention** (iridectomy).
- Due to **occlusion of angle of filtration** by iris root coming in contact with periphery of the cornea (Acute congestive glaucoma).

Drugs used to decrease I.O.P before surgery are:

1) **Miotic eye drops:** a)**Pilocarpine** (of choice) with low concentration.
   b)**Physostigmine** (not perfered due to congestion & extreme miosis).
2) **Carbonic anhydrase inhibitors:** acetazolamide (↓↓ aqueous secretion)
3) 3- Osmotic agents (dehydrating agent): mannitol (20%) IV, MgSO4 rectallly & Glycerine (50%) orally: they produce rapid reduction of IOP.
4) 4- Brimonidine & apraclonidine (α2 agonists). ∴ Reduce Acqueus Humor.
5) 5- Recently β-Blockers can be used with pilocarpine

∴ Reduce Acqueus Humor

II- Open-angle glaucoma (Chronic glaucoma):

- **Drugs used are:**

1) **Miotic eye drops**

(Pilocarpine & Physostigmine).

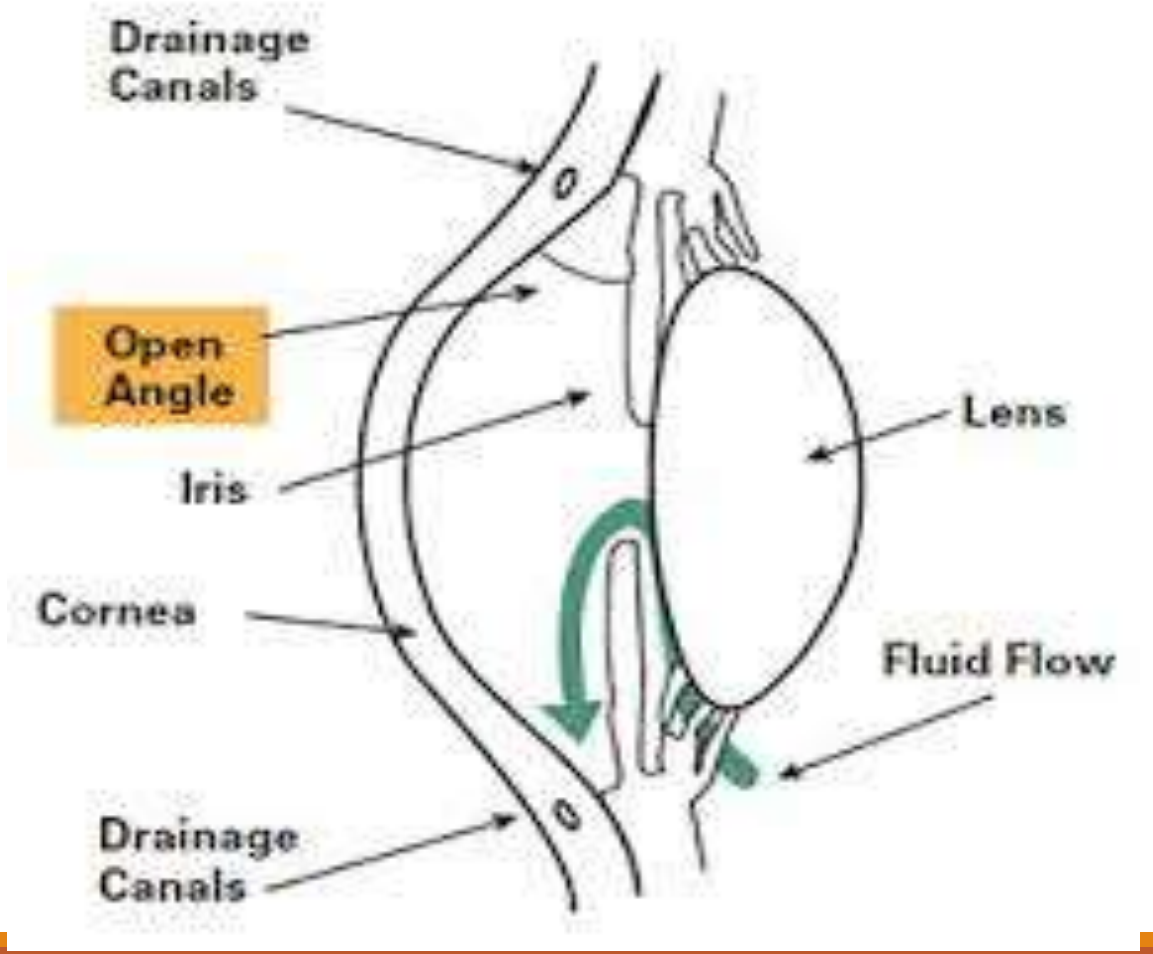
1) **Carbonic anhydrase inhibitors:**

(inhibit aqueous formation):

a- Acetazolamide orally

b- Dorzolamide & Brinzolamide

(locally)



selective to B.V of ciliary Body "Locally"

3- Sympathomimetic eye drops: (Adrenaline & Dipivefrin) → VC → decrease synthesis of aqueous humor.

4- B-blockers: decrease cAMP → decrease aqueous humor e.g. timolol & betaxolol.Side effects: tolerance, systemic absorption.

SUDDEN DECREASE of DRUG effectiveness.

5)α2 agonists: a-Apraclonidine: used only for short time due to tachyphylaxis. b-Brimonidine: decrease aqueous secretion & ↑ uveoscleral outflow.

Side effects: allergic conjuncitivitis, dry mouth & fatigue.

6)PGF2α analogues e.g. Latanoprost, trovaprost & bimatoprost:

They decrease IOP by ↑↑ uveoscleral outflow.

The most potent ocular hypotensives.

Side effects: conjunctival hyperpigmentation & hyperemia, and headache.

causes VD

7)Guanethidine

Drugs that ↑↑ IOP:

1. **Parasympatholytics** (atropine). — mydriatic drug

2. **Drugs with atropine-like effect**:

a) Some H1 blockers (Diphenhydramine).

b) Some antiarrhythmics (Disopyramide). — substitute of quinidine with more Atropine Like Reaction.

1. **Ganglion blockers.**

2. **Corticosteroids.** — mostly with topical use. Steroid induced glucoma due to ↑ Resistance of Acqueus Humor secretion.

3. **Nitrates.** — Vasodilation of Blood vessele → ↓ ciliary secretion.

Thank you