Important drugs used in glaucoma

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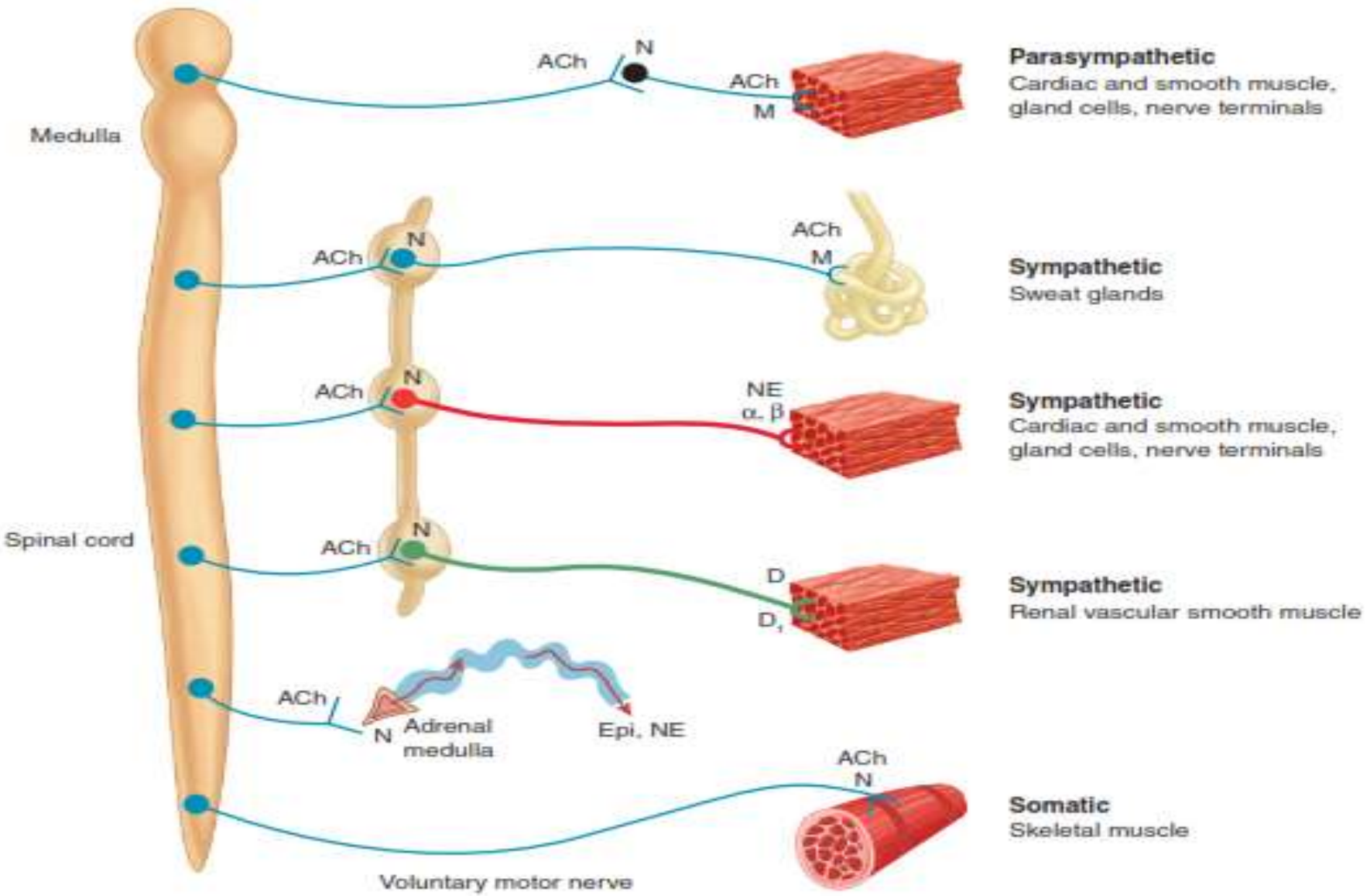
Sources

Lippincott Illustrated Reviews: Pharmacology 7th Edition
Katzung ; Basic & Clinical Pharmacology 14th Edition
Bennett & Brown ; Clinical pharmacology 11th edition
Essentials of Medical Pharmacology; Lafi 09

Nicotinic receptors distribution and effects

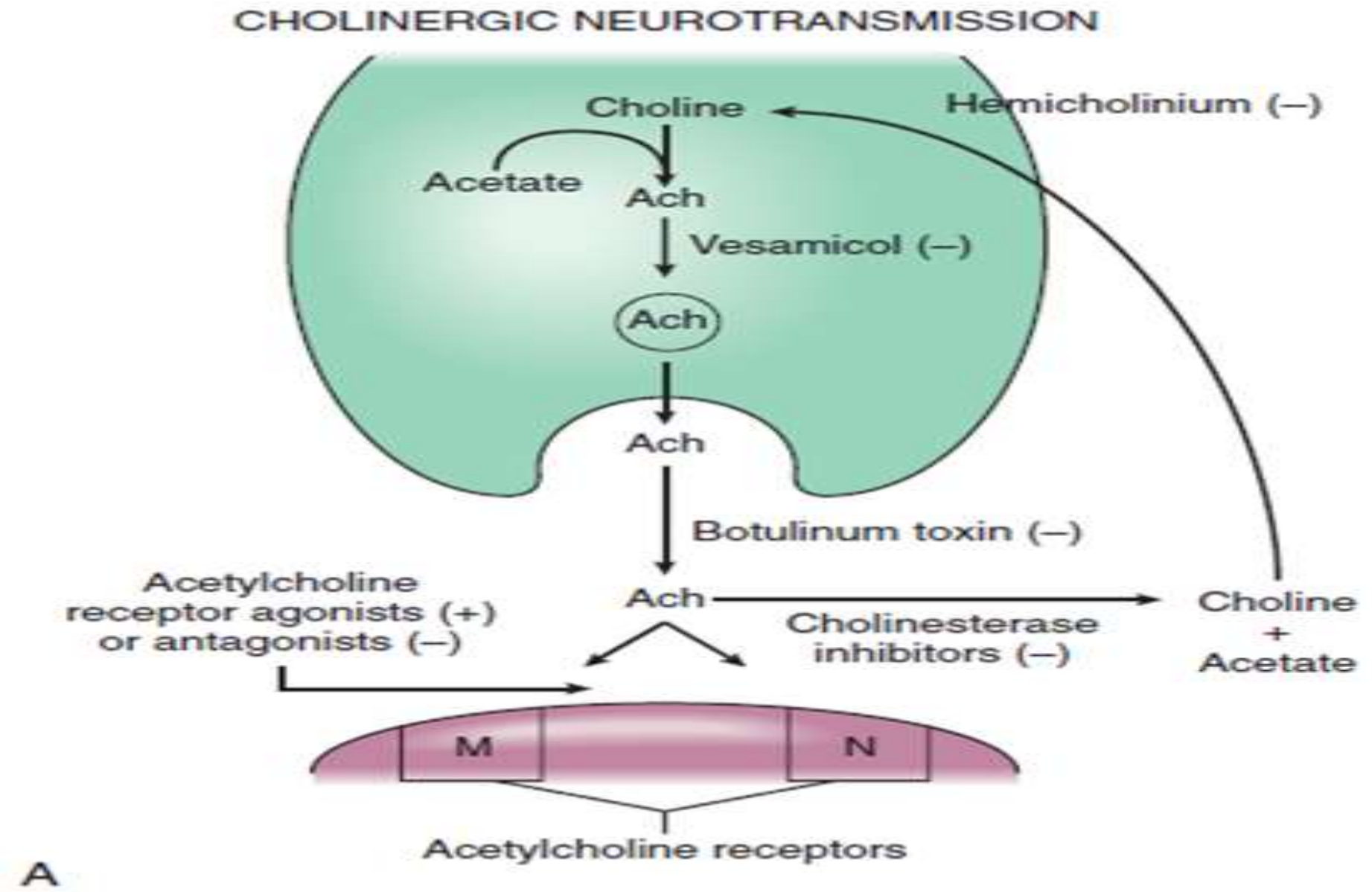


Parasympathetic System

- Cholinergic

- **M1** – CNS/ENS
- **M2** – Heart
- **M3** – **EG MP AC BB**
  - Increases **E**xocrine Gland Secretion
  - Increases **G**ut Motility
  - **M**iosis via **P**upillary sphincter
  - **A**ccommodation via **C**iliary
  - **B**ronchoconstriction
  - **B**ladder constriction

Muscarinic	**All parasympathetic target organ & Sweat glands**	
	Eye	Contraction of the ciliary muscle focuses for near vision
		Contraction of the iris sphincter causes miosis (decreased pupil diameter)

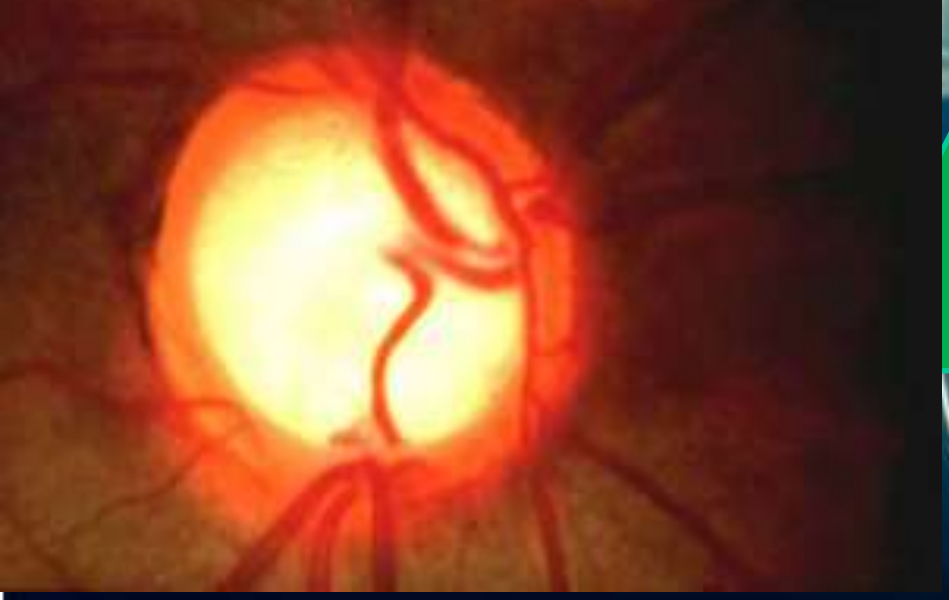

CHOLINERGIC NEUROTRANSMISSION
Choline
Hemicholinium (–)
Acetate
Ach
Vesamicol (–)
Ach
Ach
Botulinum toxin (–)
Acetylcholine
receptor agonists (+)
or antagonists (–)
Ach
Cholinesterase
inhibitors (–)
Choline
+
Acetate
M
N
Acetylcholine receptors
A

Drug	Action	Selected therapeutic uses and important remarks
Directly Acting Agents Ach like		
Bethane**chol**	**Muscarinic receptors (activation)**	Atonic bladder (in postpartum or postoperative non-obstructive urinary retention generalised cholinergic stimulation*
Pilocarpine	**Muscarinic receptors (activation)**	Narrow (closed) and wide (open) angle glaucoma; enter the brain - CNS-disturbances
Carba**chol**	**Muscarinic & nicotinic N_N-receptors (activation)**	glaucoma, when used topically shows little or no adverse-effects Rarely used (high potency and long duration)

* Generalised cholinergic stimulation: salivation, flushing, decreased blood pressure, nausea, abdominal pain, diarrhoea, and bronchospasm; if the drug enters the CNS (e.g. physostigmine), it would show CNS disturbances which may lead to convulsion.

Drug	Action	Selected therapeutic uses and important remarks
Indirectly Acting (Reversible) Agents Inhibits AChE		
Physostigmine Atropine& TCA antidote		• Atony of bladder and intestine, • **glaucoma,** • overdose with anticholinergics (e.g. atropine, phenothiazines and TCA) **enters - brain**, **-generalised cholinergic stimulation***; (0.5-2 hr)
Demecarium		• **Glaucoma**; (4-6 hr) *CDPPIE
2- Neostigmine		• Atony of bladder and intestine, • overdose with competitive neuromuscular blocking agents (e.g. tubocurarine), • **myasthenia gravis** poorly CNS , generalised cholinergic stimulation ; (0.5-2 hr)
3- Pyridostigmine		• chronic management of myasthenia gravis; (3-6 hr)
4-Ambenonium		• chronic management of myasthenia gravis; (4-8 hr)
1-Edrophonium		• diagnosis of myasthenia gravis, * ENPA • postoperative paralytic ileus

Drug	Action	Selected therapeutic uses and important remarks
Indirectly Acting (Irreversible) Agents (organophosphate, Nerve agent) Covalently binds to AChE (click)		
Isoflurophate (DFP)		chronic management of **open angle glaucoma** (ointment, last for 1 week); enters CNS, generalised cholinergic stimulation* (largely reversed by high dose of atropine); DFP ages in 6-8 hr
Echothiophate		In chronic management of **open angle glaucoma**; (100 hr)



VISUAL
FIELD LOSS

GLAUCOMA

OPTIC
NERVE
DAMAGE

INCREASE
IOP

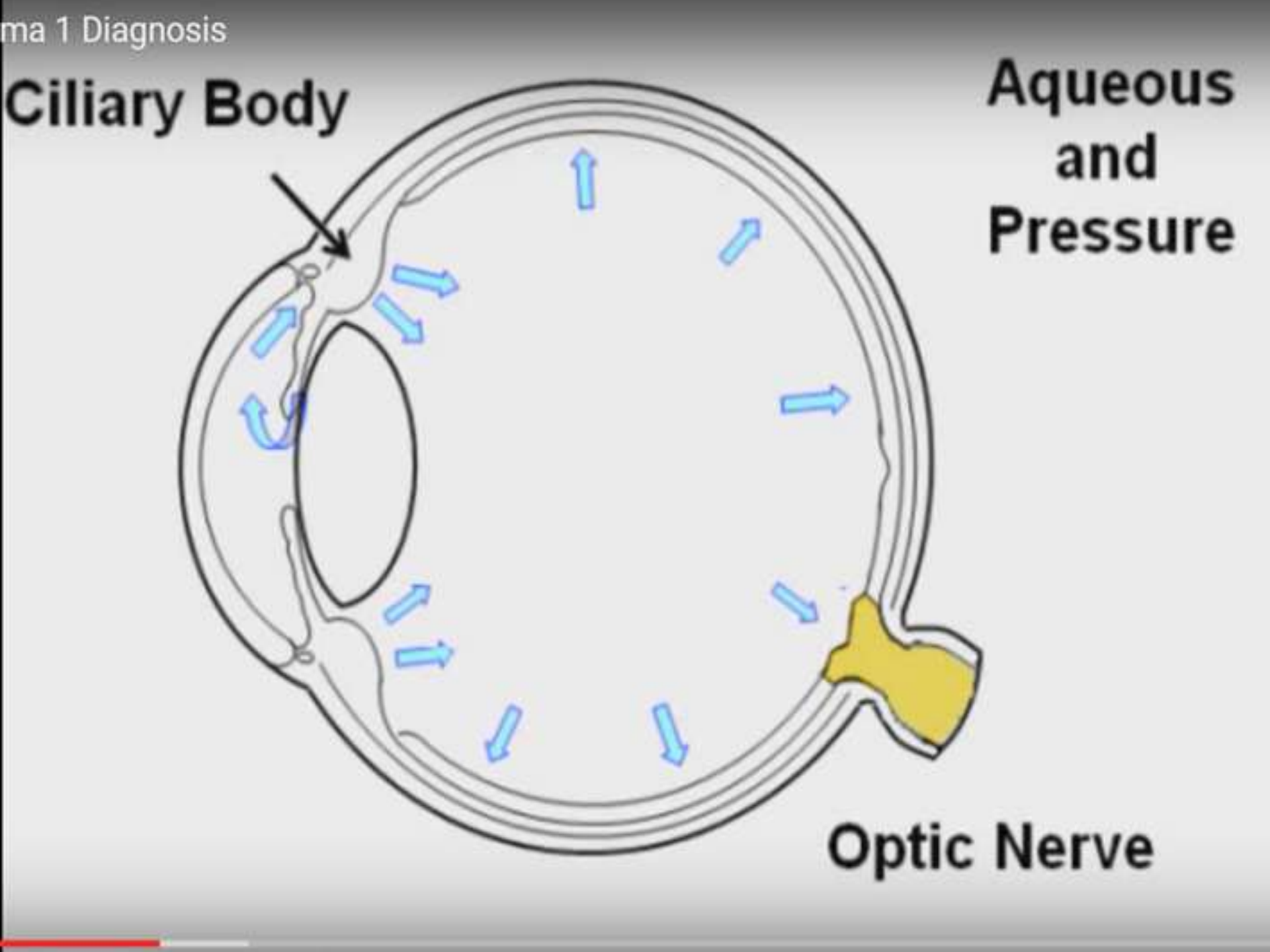
EXTREME GLAUCOMA

ADVANCED GLAUCOMA

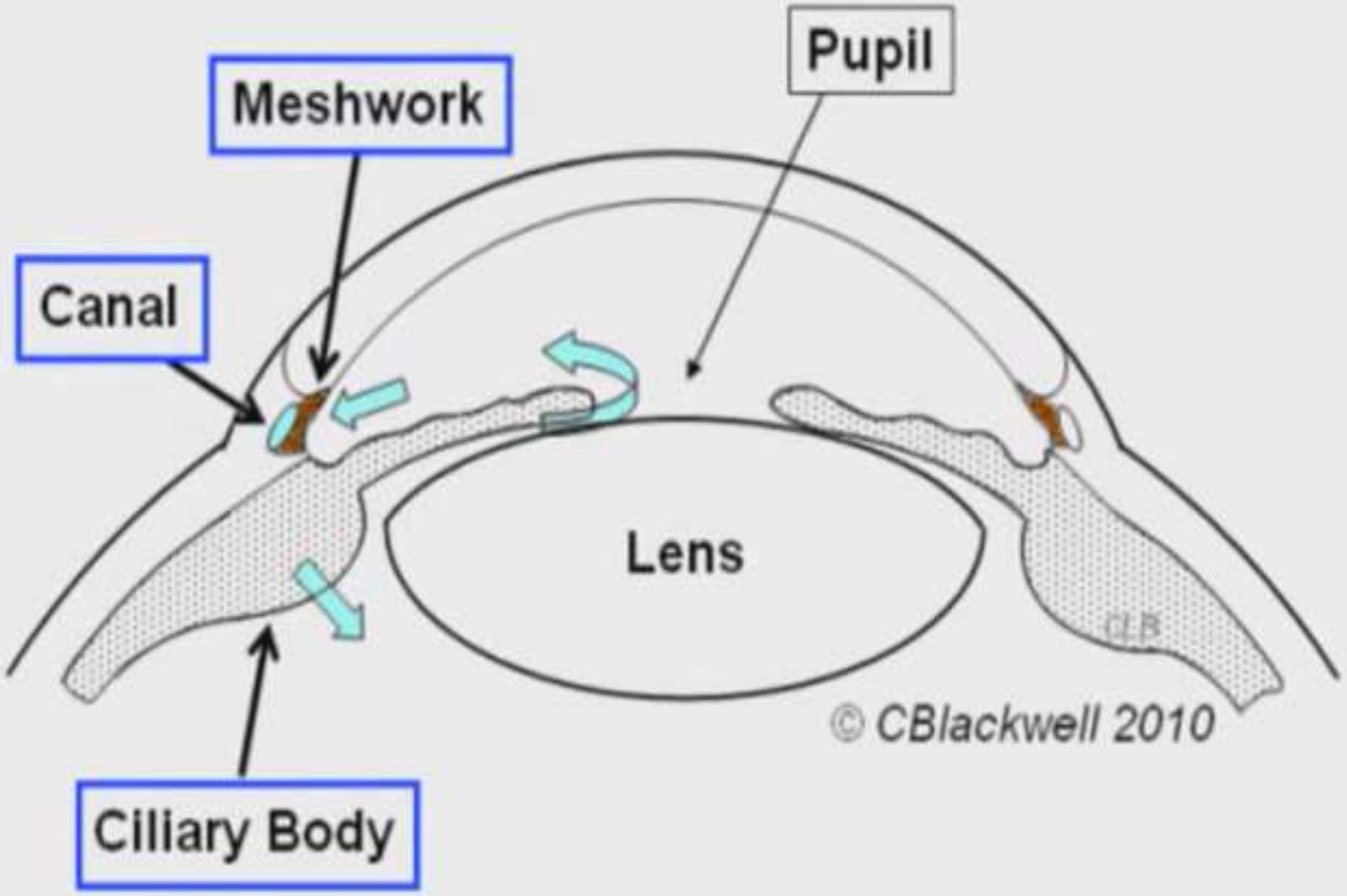
EARLY GLAUCOMA

NORMAL VISION

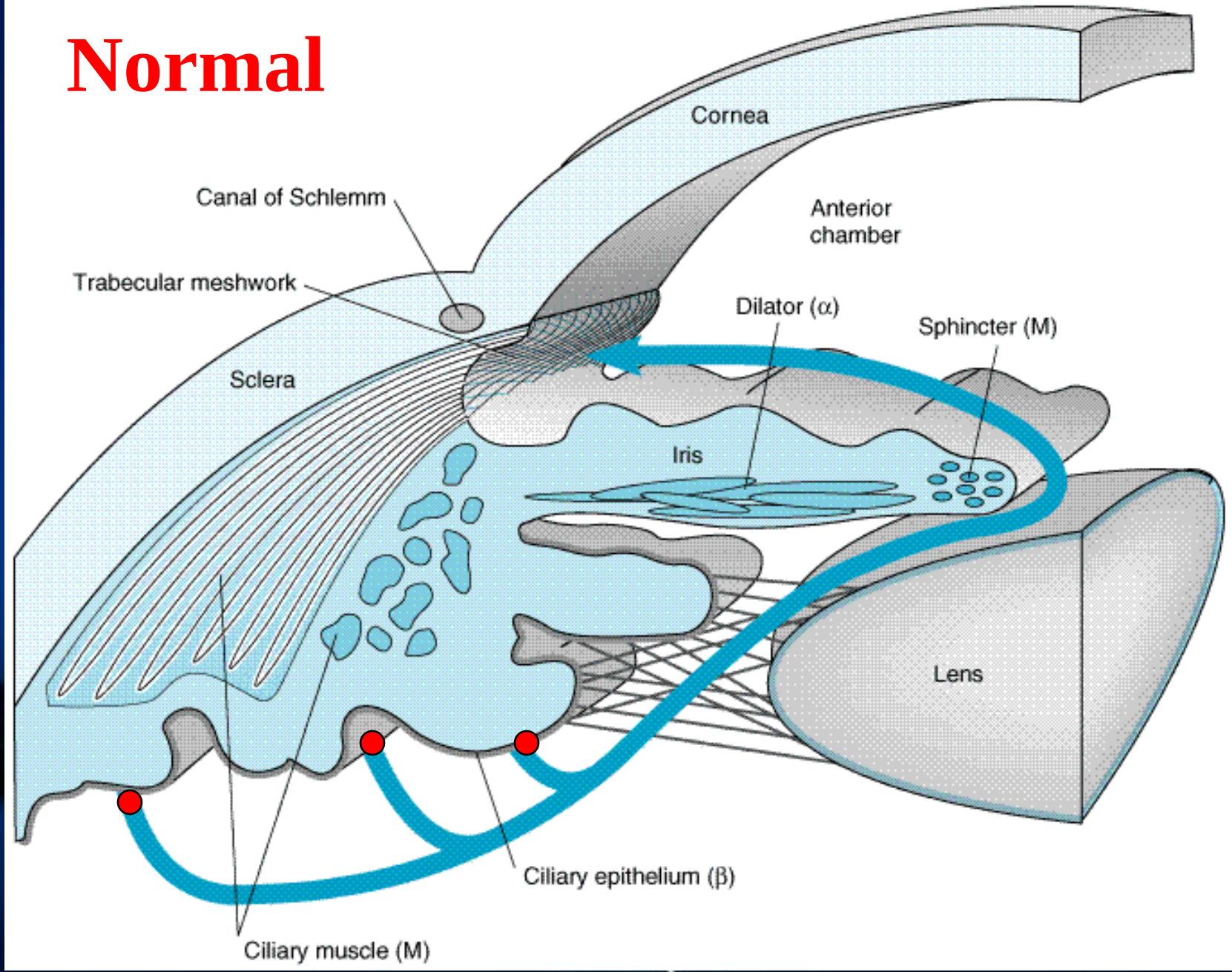
ma 1 Diagnosis

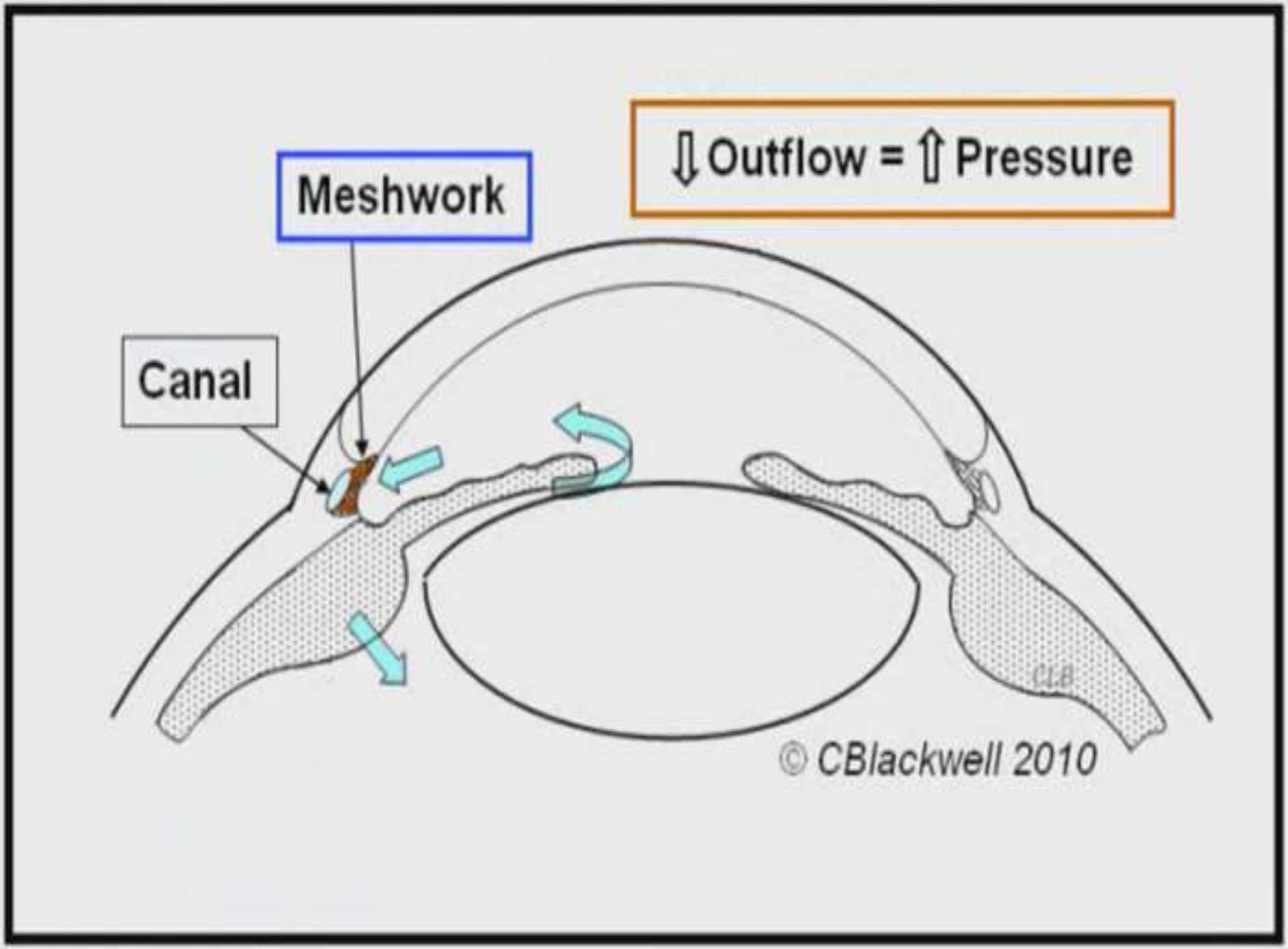


Aqueous Circulation



Normal


Cornea
Canal of Schlemm
Anterior chamber
Trabecular meshwork
Dilator (α)
Sphincter (M)
Sclera
Iris
Lens
Ciliary epithelium (β)
Ciliary muscle (M)


⇩Outflow = ⇧Pressure
Meshwork
Canal
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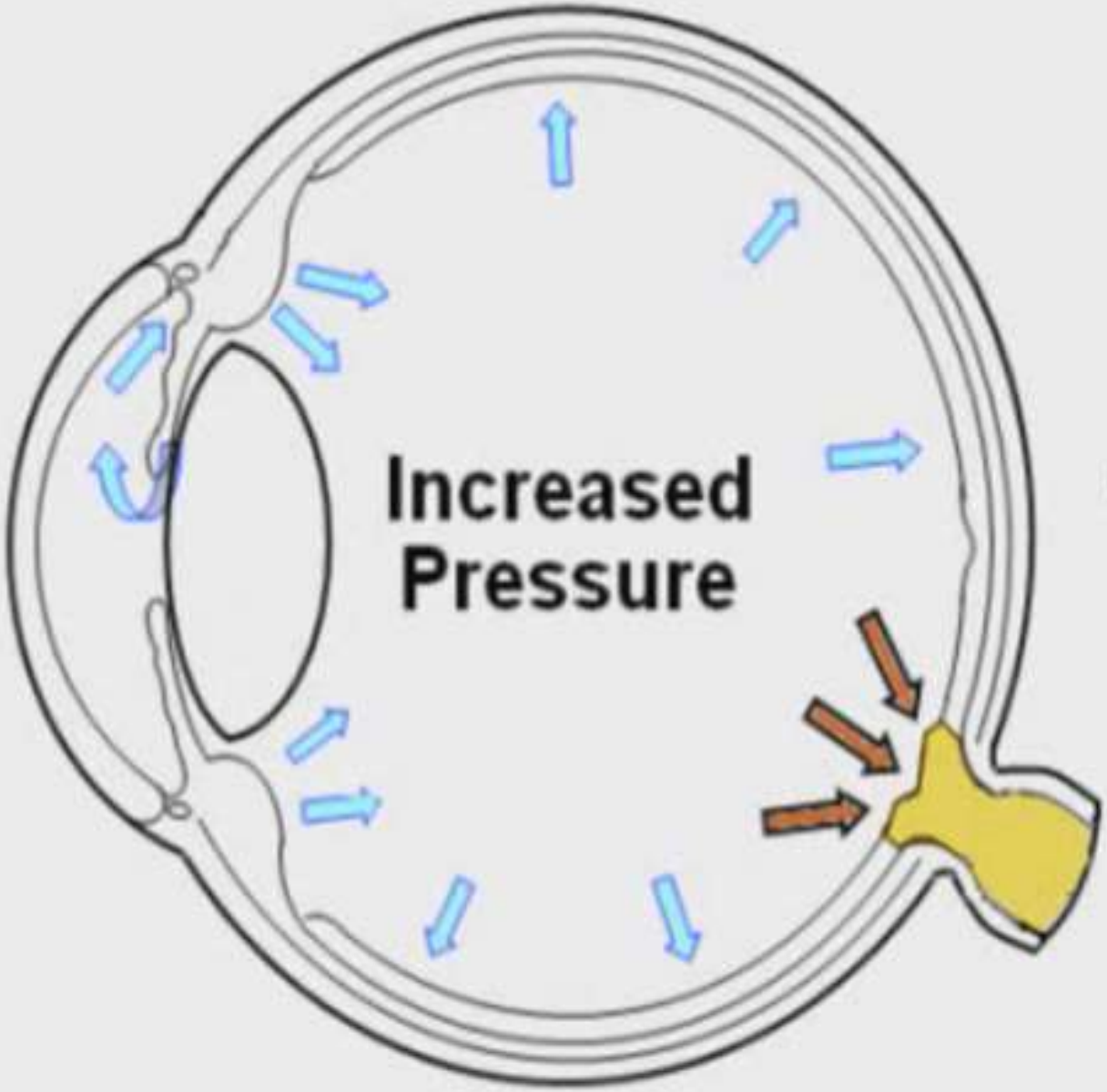
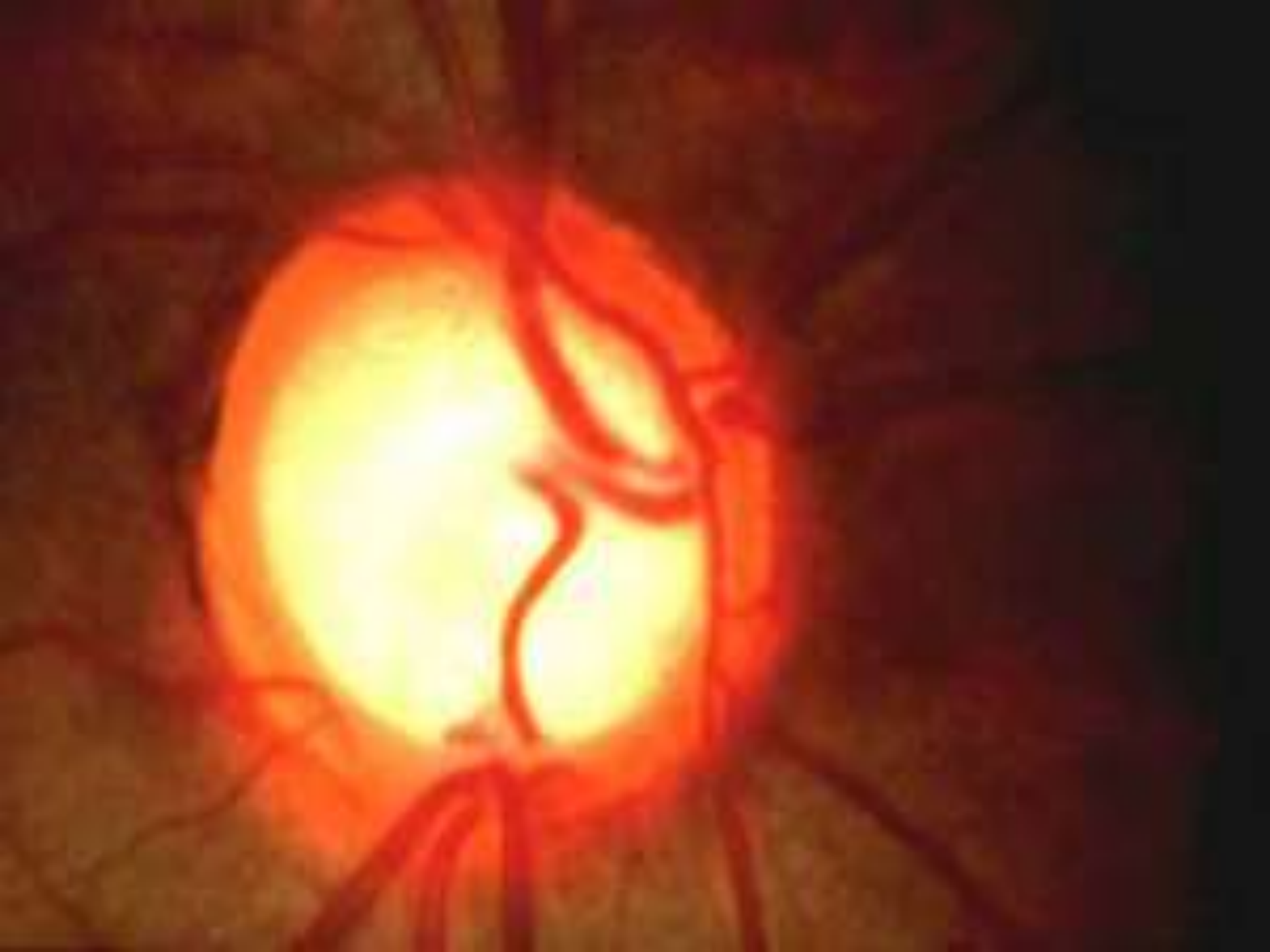
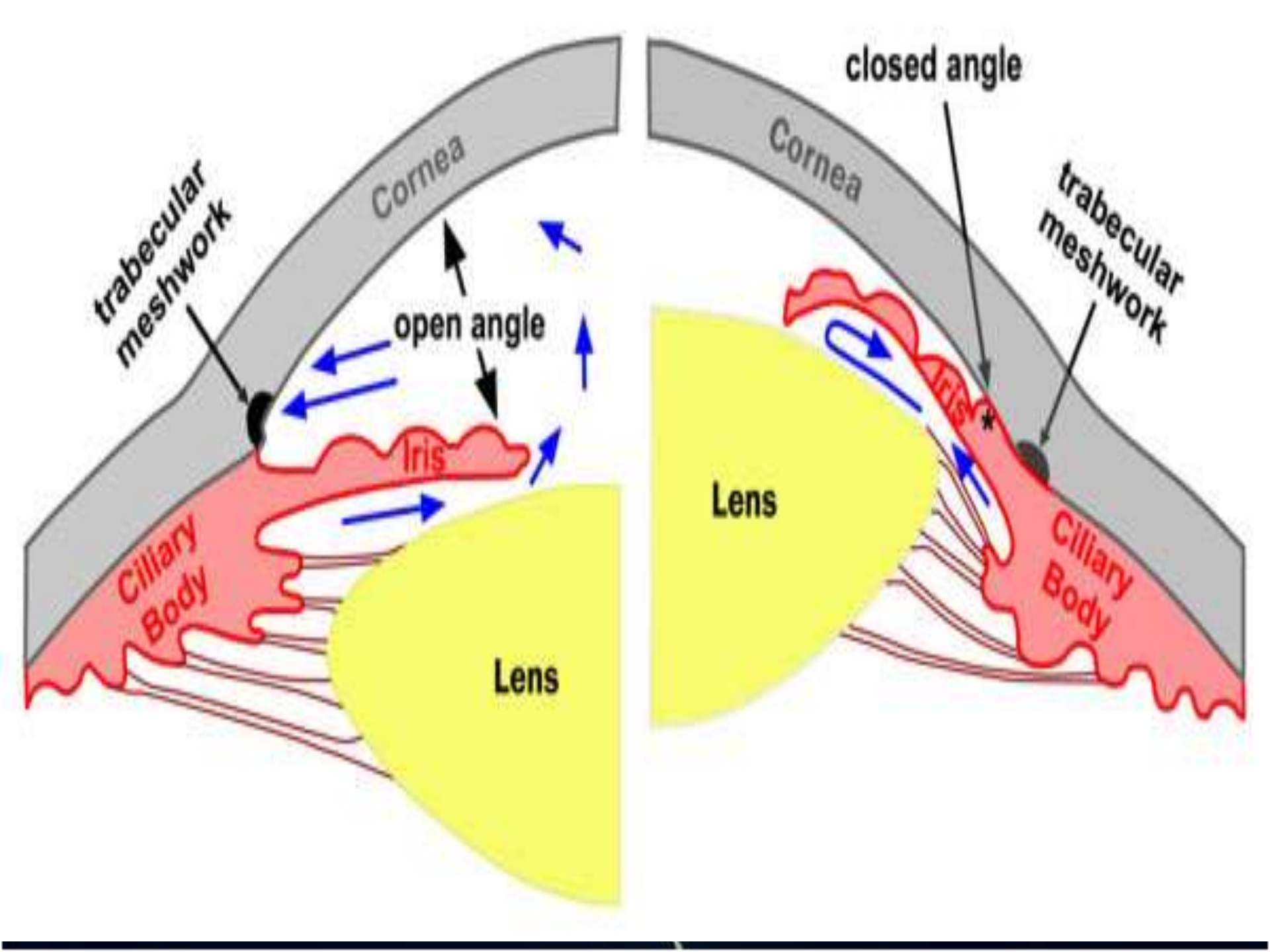
GLAUCOMA



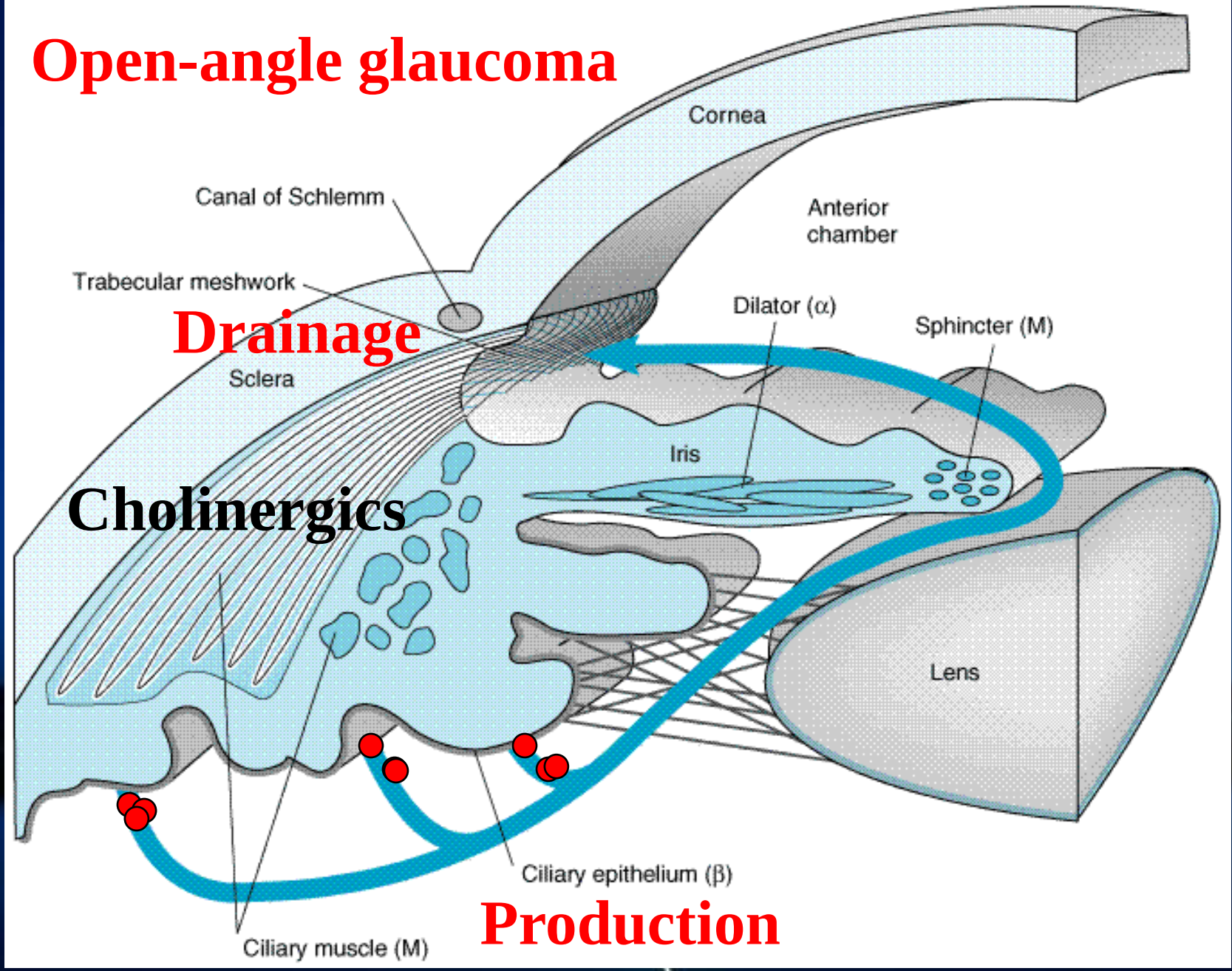


Glaucoma Strategy

Reduce Pressure
to a Level
the Optic Nerve
can Tolerate

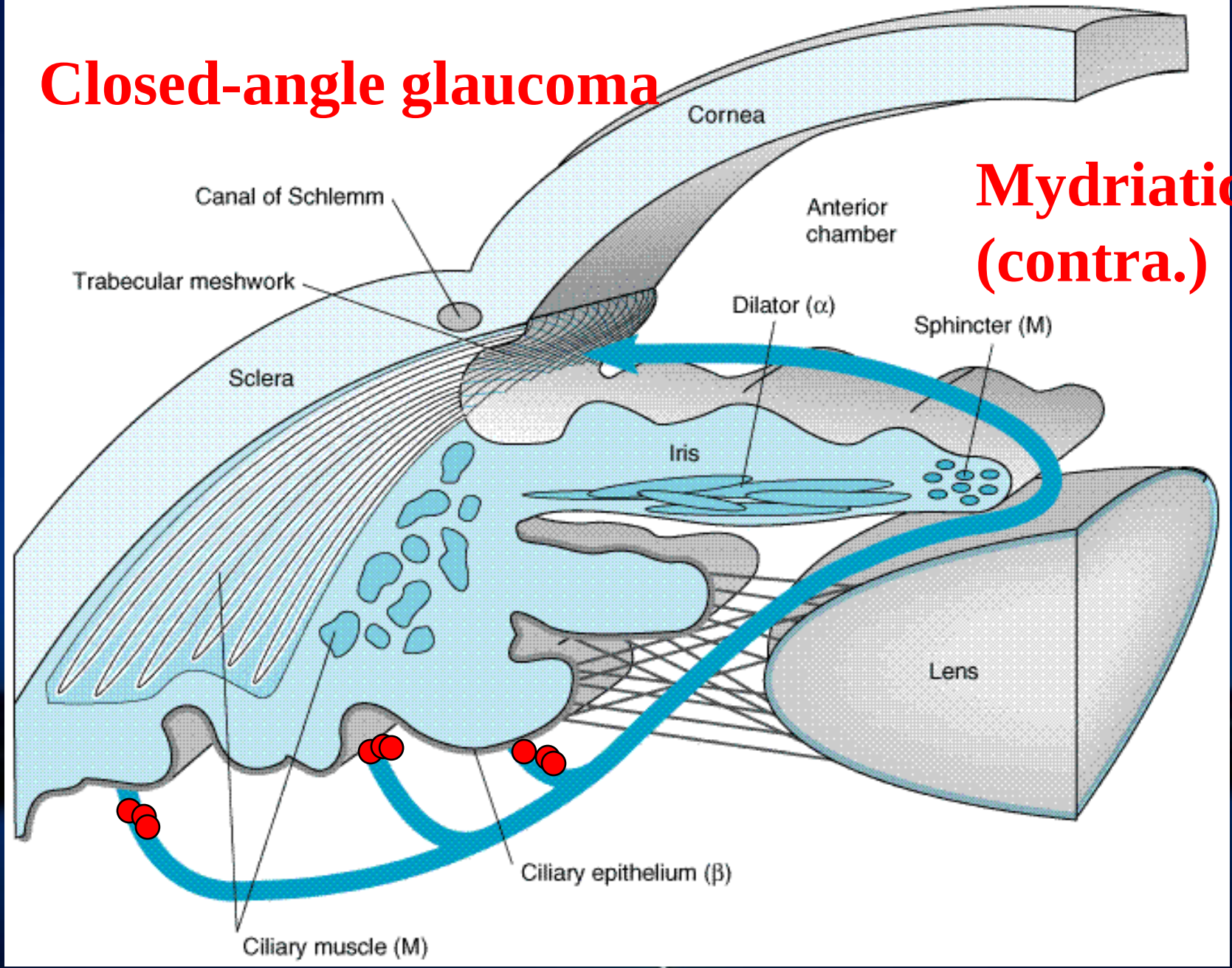

trabecular meshwork
Cornea
open angle
Iris
Ciliary Body
Lens
closed angle
Cornea
trabecular meshwork
Iris
Lens
Ciliary Body

Open-angle glaucoma

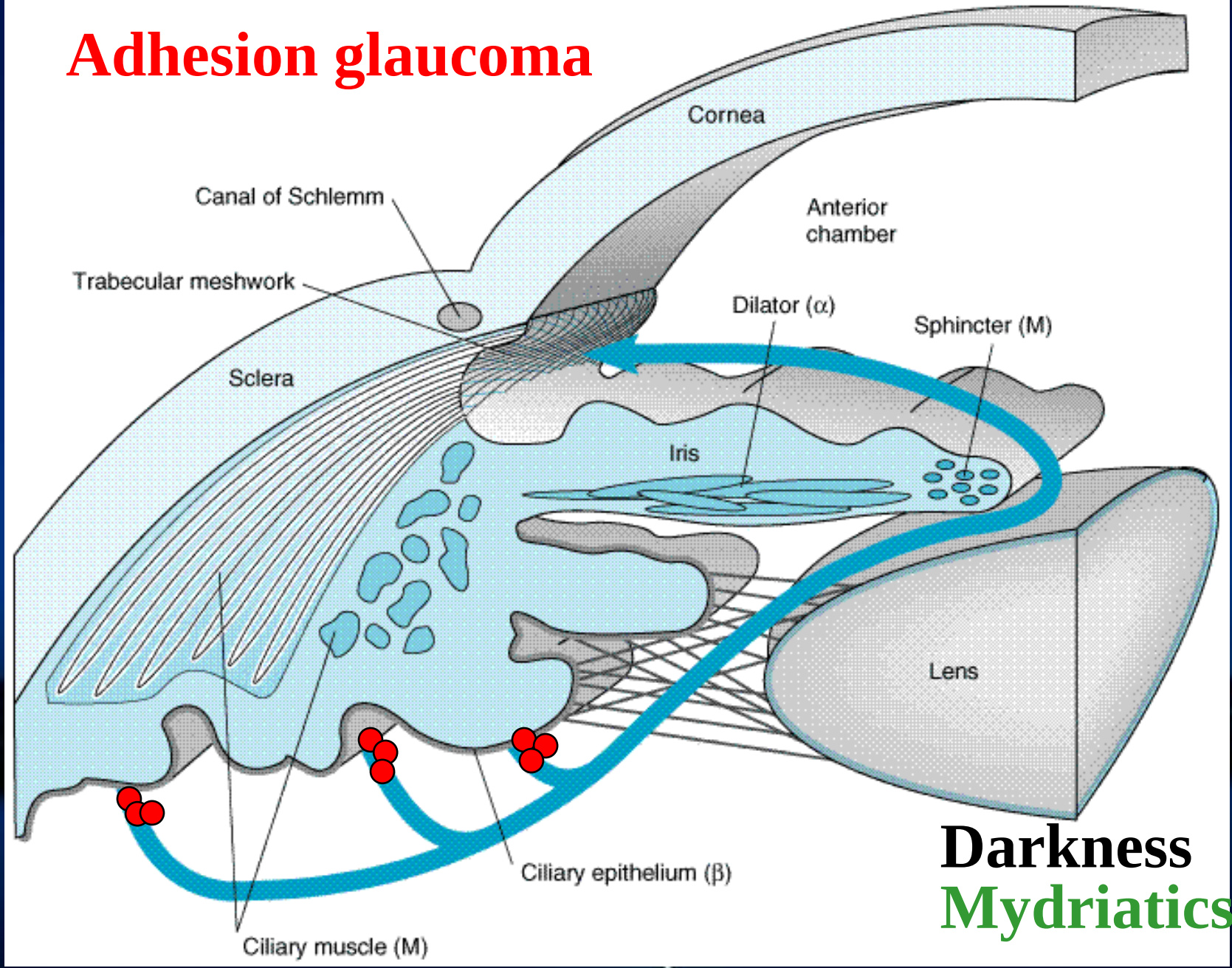


Closed-angle glaucoma

Mydriatics (contra.)



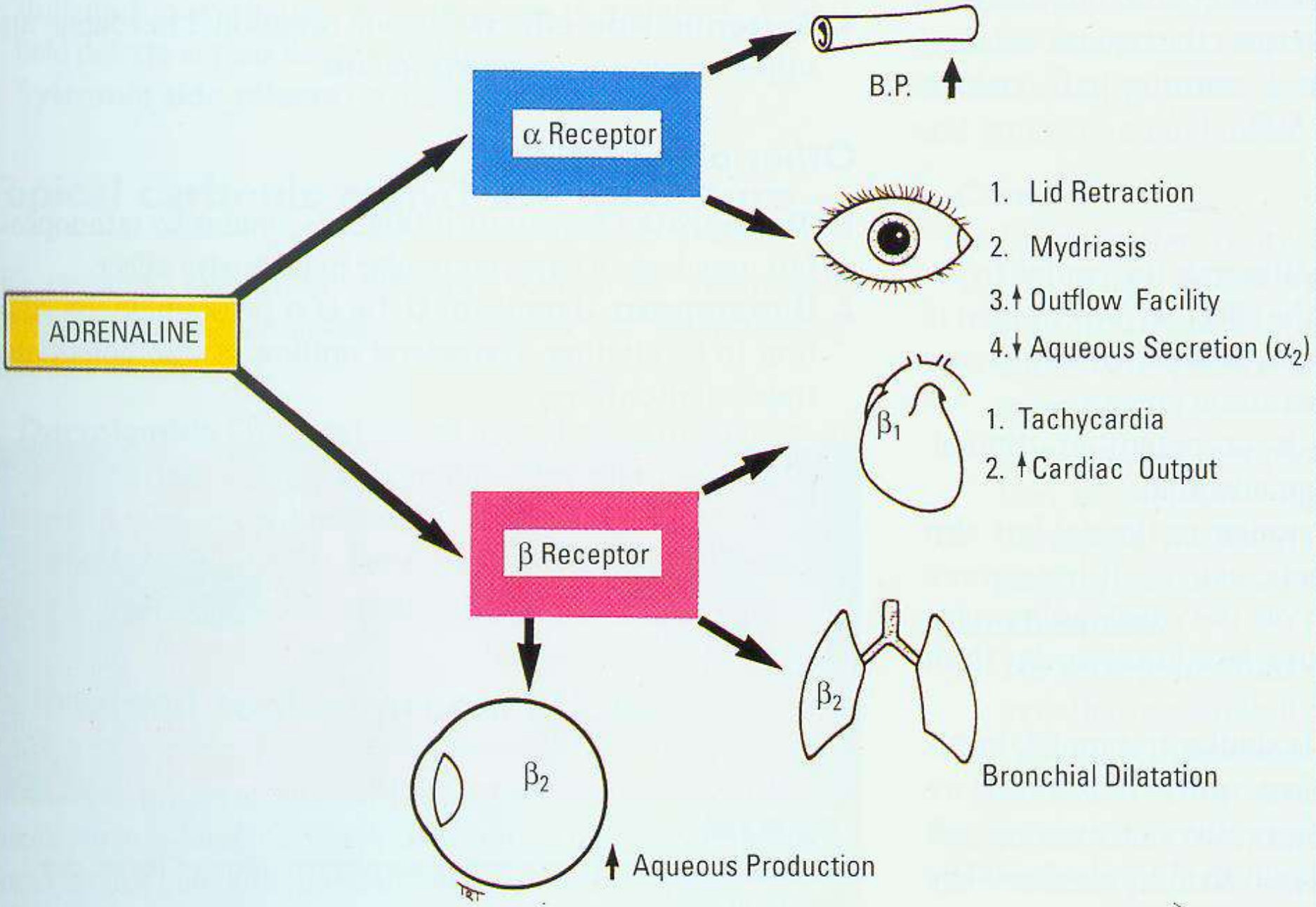
Adhesion glaucoma



Darkness

Mydriatics

Drugs or class	Nature of action and important remarks
Cholinergic agents Muscarinic agonists (pilocarpine) **Anticholinesterases** [physostigmine, DFP (isoflurophate)]	**Improved drainage of aqueous humour (**contracting the longitudinal muscle of the ciliary body leading to **opening the trabecular meshwork around Schlemm's canal** (drainage channels), ⟹ immediate drop (IOP). •acute glaucoma •chronic open-angle glaucoma.


ADRENALINE
α Receptor
β Receptor
B.P.
1. Lid Retraction
2. Mydriasis
3. ↑ Outflow Facility
4. ↓ Aqueous Secretion (α_2)
β_1
1. Tachycardia
2. ↑ Cardiac Output
β_2
Bronchial Dilatation
β_2
↑ Aqueous Production

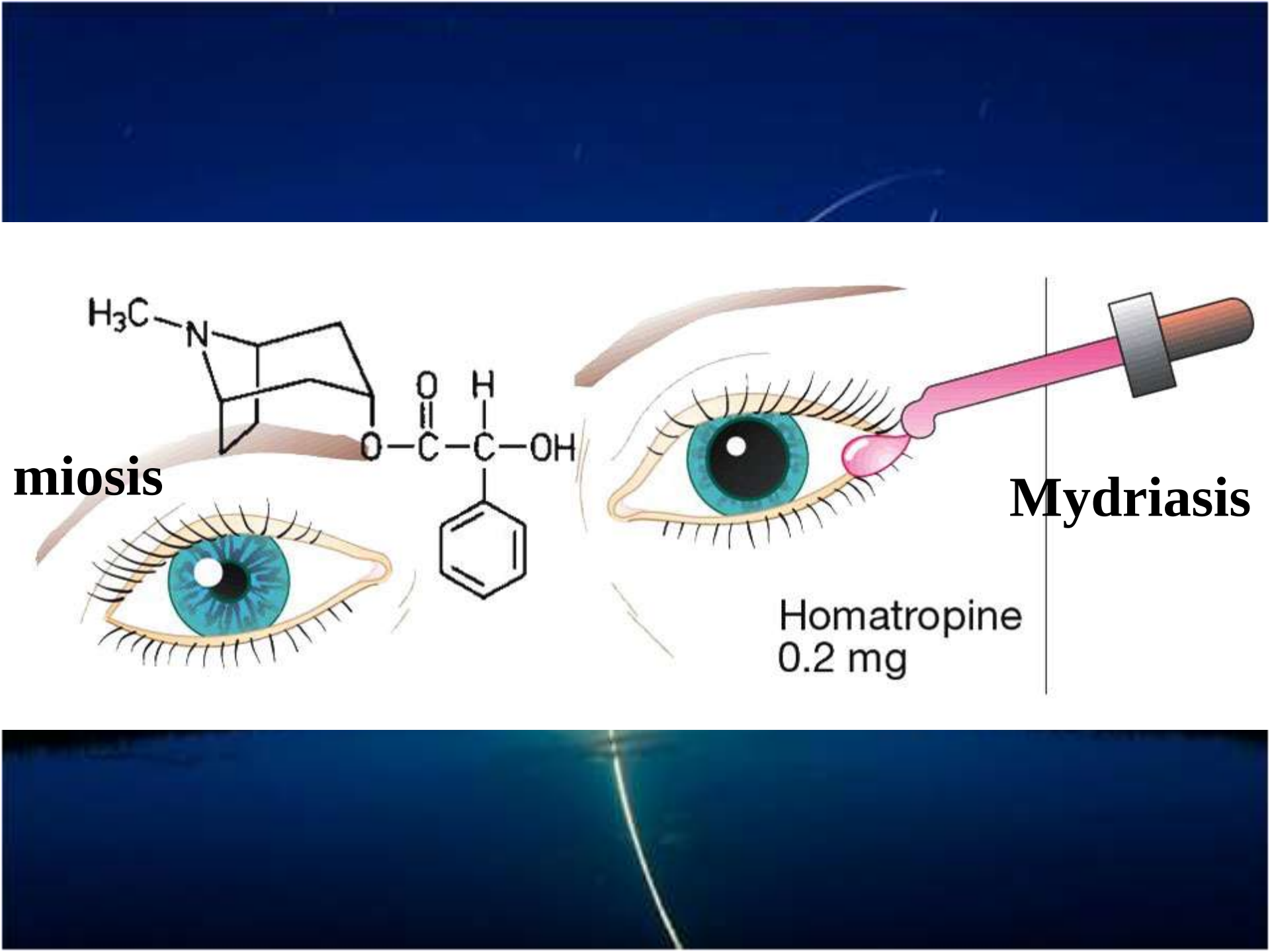
Drugs or class	Nature of action and important remarks
β-blockers Timolol Betaxolol **Cartelol** **Metipranolol**	**Decrease production of AH** -to reduced IOP. No effect on focusing for near vision or pupil size; (used in chronic open-angle glaucoma, narrow and acute glaucoma.

Drugs or class	Nature of action and important remarks
α-agonists Non-selective Adrenaline **α_2**-selective Praclonidine **Brimonidine**	**Enhances AH outflow** (drainage, α-receptors) by increasing PG production that enhance uveoscleral drainage **decreases production of AH** by vasoconstriction of the ciliary body blood vessels leading to reduced IOP. **Topical 2% adrenaline solution used in chronic open-angle glaucoma.** **C/I** •closed-angle •acute glaucomas as they dilate the pupil, dilated iris can occlude the outflow drainage pathway at the angle between the cornea and the ciliary body.

Drugs or class	Nature of action and important remarks
Prostaglandins (PGF2α derivatives: latanoprost, unoprostone)	**Increase outflow** by acting at the FP receptor -stimulates collagenase and metalloproteinase to degrade the extracellular matrix between ciliary muscle bundles, which in turn leads to the reduction of hydraulic resistance to uveoscleral flow SE •irreversible brown pigmentation of the iris and eyelashes, •Eyelash : lengthening, thickening •drying of the eyes, and conjunctivitis.

Drugs or class	Nature of action and important remarks
Diuretics	
Carbonic anhydrase inhibitors Acetazolamide	Decreases production of AH by blocking carbonic anhydrase in the ciliary body leading to reduced IOP. •chronic glaucoma •acute closed-angle glaucoma.
Osmotic agents Mannitol	Reduces IOP in acute closed-angle glaucoma.

Summary of selected mydriatic and cycloplegics


miosis
Mydriasis
Homatropine
0.2 mg

Drug	Duration	Use
Tropicamide	3-6 hr	Fundus examination
Homatropine	1-3 days	Cycloplegic for refraction* in children
Atropine	7-10 days	For refraction as above; also iridocyclitis** (+ phenylephrine♠)
		They may precipitate acute glaucoma in the elderly and predisposed patients

* Refraction: determination of the refractive errors of the eye and their correction by glasses

♠ In iritis, phenylephrine dilates the pupil, therefore, reducing the possibility of adhesion of the iris to the lens (i.e. pupilary block glaucoma).


Thank You