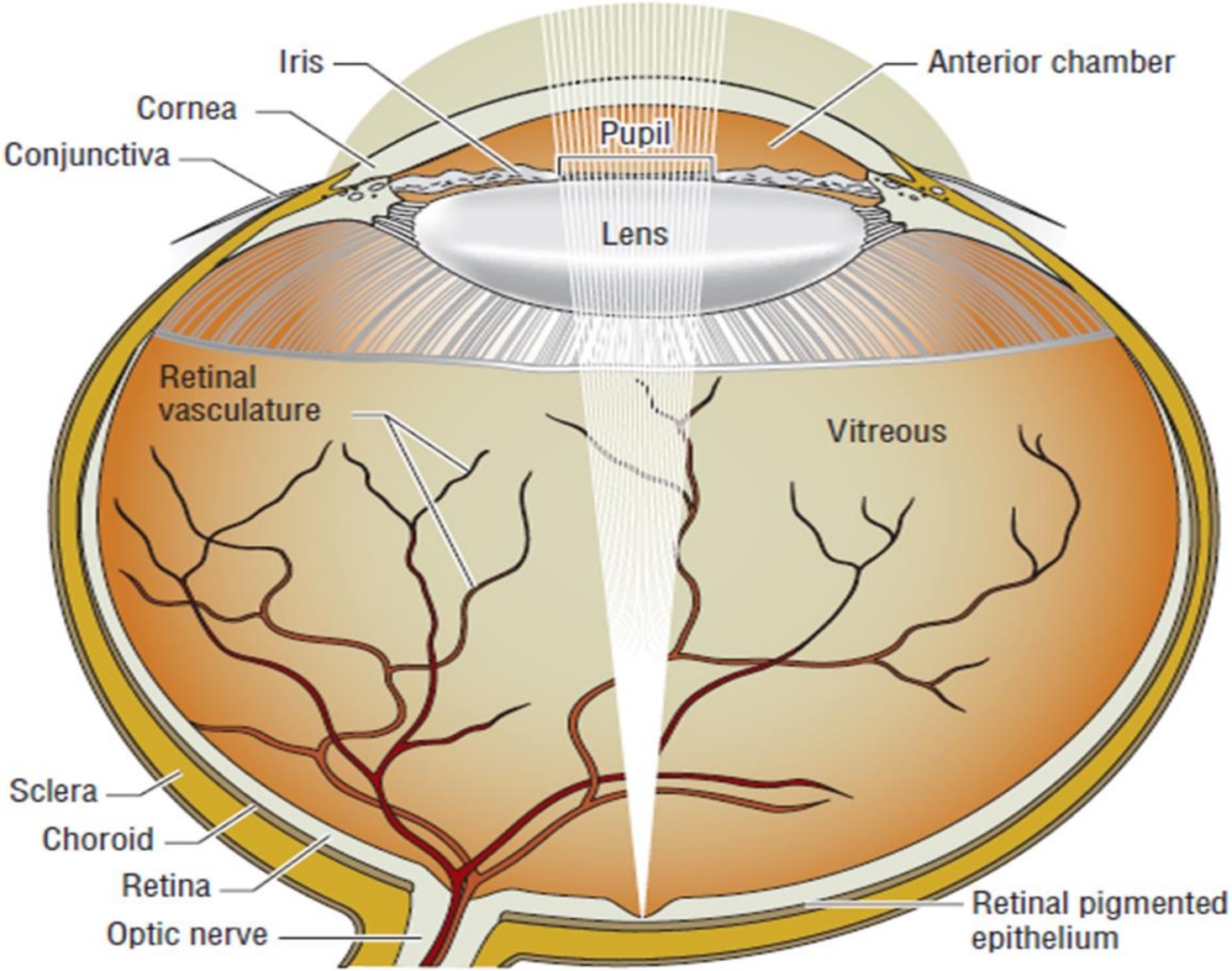
Glaucoma

- Glaucomas are ocular disorders characterized by changes in the optic nerve head (optic disk) and by loss of visual sensitivity and field.

- There are two major types of glaucoma: open-angle glaucoma, which accounts for most cases, and closed-angle glaucoma.

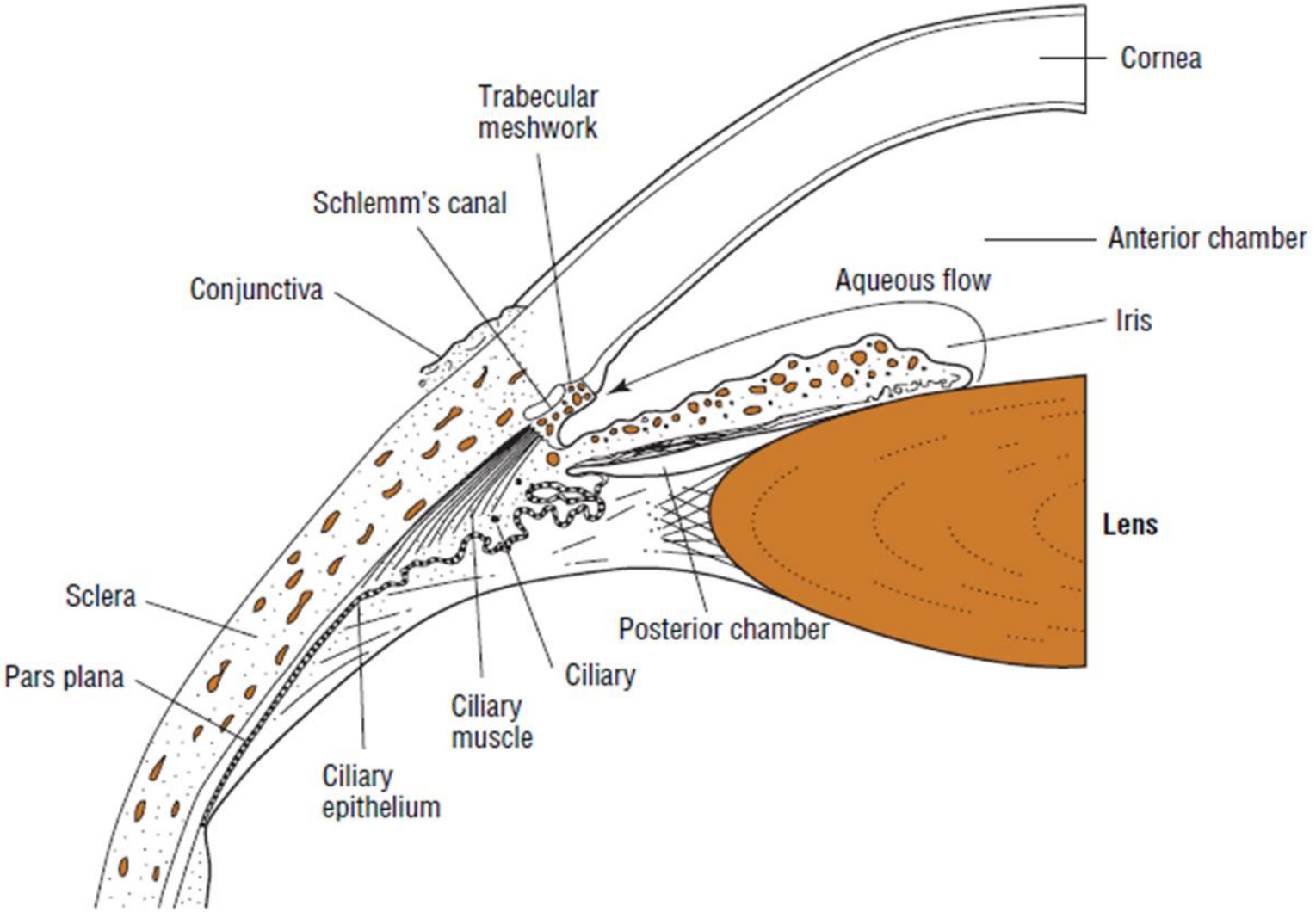
- In open-angle glaucoma, the specific cause of optic neuropathy is unknown. Increased intraocular pressure (IOP) was historically considered to be the sole cause.

- Additional contributing factors include increased susceptibility of the optic nerve to ischemia, reduced or dysregulated blood flow, excitotoxicity, autoimmune reactions, and other abnormal physiologic processes.



Anatomy of the eye

Anterior chambour of the eye and aqeous humor flow



- The balance between the inflow and outflow of aqueous humor determines IOP.

- Inflow is increased by β-adrenergic agents and decreased by α2 and β-adrenergic blockers; dopamine blockers; carbonic anhydrase inhibitors (CAIs); and adenylate cyclase stimulators.

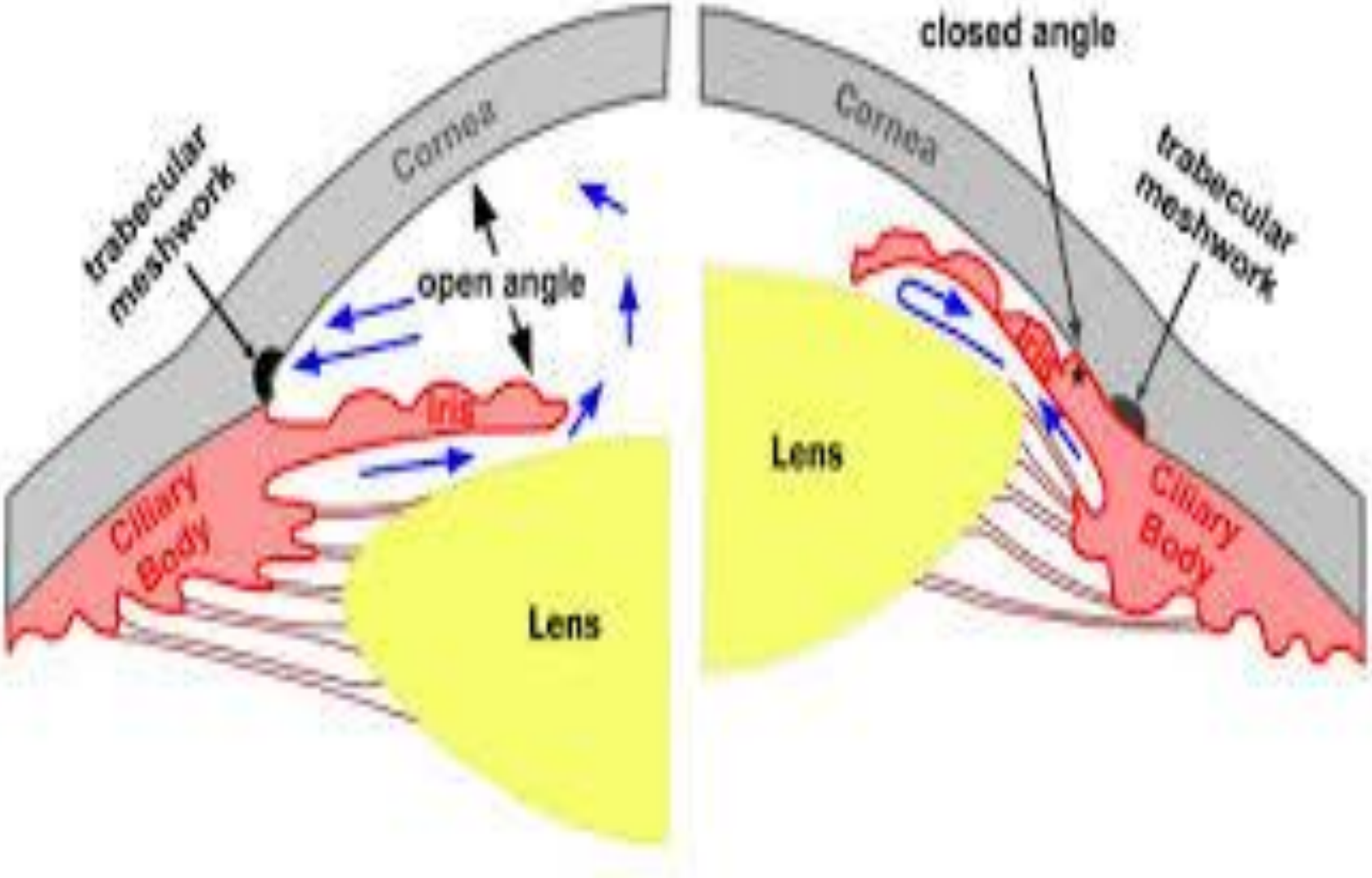
- Outflow is increased by cholinergic agents, which contract the ciliary muscle and open the trabecular meshwork, and by prostaglandin analogs and β- and α2-adrenergic agonists, which affect uveoscleral outflow.

- Secondary open-angle glaucoma has many causes including exfoliation syndrome, pigmentary glaucoma, systemic diseases, trauma, surgery, lens changes, ocular inflammatory diseases, and drugs.

- Secondary glaucoma can be classified as pretrabecular (normal meshwork is covered and prevents outflow of aqueous humor), trabecular (meshwork is altered or material accumulates in the intertrabecular spaces), or posttrabecular (episcleral venous blood pressure is increased).

- Many drugs can increase IOP. The potential to induce or worsen glaucoma depends on the type of glaucoma and on whether it is adequately controlled.

- Closed-angle glaucoma occurs when there is a physical blockage of the trabecular meshwork, resulting in increased IOP.


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

Drugs That May Induce or Potentiate Increased Intraocular Pressure

Open-angle glaucoma
- Ophthalmic corticosteroids (high risk)
- Systemic corticosteroids
- Nasal/inhaled corticosteroids
- Fenoldopam
- Ophthalmic anticholinergics
- Succinylcholine
- Vasodilators (low risk)
- Cimetidine (low risk)

Closed-angle glaucoma
- Topical anticholinergics
- Topical sympathomimetics
- Systemic anticholinergics
- Heterocyclic antidepressants
- Low-potency phenothiazines
- Antihistamines
- Ipratropium
- Benzodiazepines (low risk)
- Theophylline (low risk)
- Vasodilators (low risk)
- Systemic sympathomimetics (low risk)
- Central nervous system stimulants (low risk)
- Selective serotonin reuptake inhibitors
- Imipramine
- Venlafaxine
- Topiramate
- Tetracyclines (low risk)
- Carbonic anhydrase inhibitors (low risk)
- Monoamine oxidase inhibitors (low risk)
- Topical cholinergics (low risk)

CLINICAL PRESENTATION:

- Open-angle glaucoma is slowly progressive and is usually asymptomatic until the onset of substantial visual field loss. Central visual acuity is maintained, even in late stages.

- In closed-angle glaucoma, patients typically experience intermittent prodromal symptoms (e.g., blurred or hazy vision with halos around lights and occasionally, headache).

- Acute episodes produce symptoms associated with a cloudy, edematous cornea; ocular pain; nausea, vomiting, and abdominal pain; and diaphoresis.

DIAGNOSIS:

- The diagnosis of *open-angle glaucoma* is confirmed by the presence of characteristic optic disk changes and visual field loss, with or without increased IOP.

- *Normal tension glaucoma* refers to disk changes, visual field loss, and IOP of less than 21 mm Hg.

- *Ocular hypertension* refers to IOP of more than 21 mm Hg without disk changes or visual field loss.

- For *closed-angle glaucoma, the presence of a narrow angle is usually* visualized by gonioscopy.

- IOP is generally markedly elevated (e.g., 40 to 90 mm Hg) when symptoms are present.

- Additional signs include hyperemic conjunctiva, cloudy cornea, shallow anterior chamber, and occasionally edematous and hyperemic optic disk.

- The goal of drug therapy in patients with glaucoma is to preserve visual function by reducing the IOP to a level at which no further optic nerve damage occurs.

TREATMENT OF OCULAR HYPERTENSION AND OPEN-ANGLE GLAUCOMA:

- Treatment is indicated for ocular hypertension if the patient has a significant risk factor such as IOP greater than 25 mm Hg, vertical cup-disk ratio (CDR) greater than 0.5, or central corneal thickness less than 555 micrometers.

- Additional risk factors to be considered include family history of glaucoma, black race, severe myopia, and presence of only one eye.

- Treatment is indicated for all patients with elevated IOP and characteristic optic disk changes or visual field defects.

- Drug therapy is the most common initial treatment and is initiated in a stepwise manner, starting with a single well tolerated topical agent.

- Historically, β-blockers (e.g., **timolol) were the treatment of choice** and continue to be used if there are no contraindications to potential β- blockade caused by systemic absorption.

- β-Blockers have the advantage of low cost owing to generic formulations.

- Newer agents are also suitable for first-line therapy. Prostaglandin analogs (e.g., **latanoprost, bimatoprost and travoprost) have the advantage of** strong potency, unique mechanism suitable for combination therapy, good safety profile, and once-a-day dosing.

- **Brimonidine has the theoretical** advantage of neuroprotection, which has not yet been demonstrated in humans. Topical CAIs are also suitable for first-line therapy.

- **Pilocarpine and dipivefrin, a prodrug of epinephrine, are used as thirdline** therapies because of adverse events or reduced efficacy as compared with newer agents.

- **Carbachol, topical cholinesterase inhibitors, and oral CAIs (e.g., acetazolamide)** are used as last-resort options after failure of less toxic options.

- The optimal timing of laser or surgical trabeculectomy is controversial, ranging from initial therapy to after failure of third- or fourth-line drug therapy.

- Antiproliferative agents such as **fluorouracil and mitomycin C** are used to modify the healing process and maintain patency.

Topical Drugs Used in the Treatment of Open-Angle Glaucoma

Drug	Pharmacologic Properties	Common Brand Names	Dose Form	Strength (%)	Usual Dose[a]	Mechanism of Action
β-Adrenergic blocking agents						
Betaxolol	Relative β_1-selective	Generic	Solution	0.5	1 drop twice a day	All reduce aqueous production of ciliary body
		Betoptic-S	Suspension	0.25	1 drop twice a day	
Carteolol	Nonselective, intrinsic sympathomimetic activity	Generic	Solution	1	1 drop twice a day	
Levobunolol	Nonselective	Betagan	Solution	0.25, 0.5	1 drop twice a day	
Metipranolol	Nonselective	OptiPranolol	Solution	0.3	1 drop twice a day	
Timolol	Nonselective	Timoptic, Betimol, Istalol	Solution	0.25, 0.5	1 drop one to two times a day	
		Timoptic-XE	Gelling solution	0.25, 0.5	1 drop every day[a]	
Nonspecific adrenergic agonists						
Dipivefrin	Prodrug	Propine	Solution	0.1	1 drop twice a day	Increased aqueous humor outflow
α_2-Adrenergic agonists						
Apraclonidine	Specific α_2-agonists	Iopidine	Solution	0.5, 1	1 drop two to three times a day	Both reduce aqueous humor production; brimonidine known to also increase uveoscleral outflow
Brimonidine		Alphagan P	Solution	0.15, 0.1	1 drop two to three times a day	
Cholinergic agonists direct acting						
Carbachol	Irreversible	Carboptic, Isopto Carbachol	Solution	1.5, 3	1 drop two to three times a day	All increase aqueous humor outflow through trabecular meshwork
Pilocarpine	Irreversible	Isopto Carpine, Pilocar	Solution	0.25, 0.5, 1, 2, 4, 6, 8, 10	1 drop two to three times a day 1 drop four times a day	
		Pilopine HS	Gel	4	Every 24 hours at bedtime	

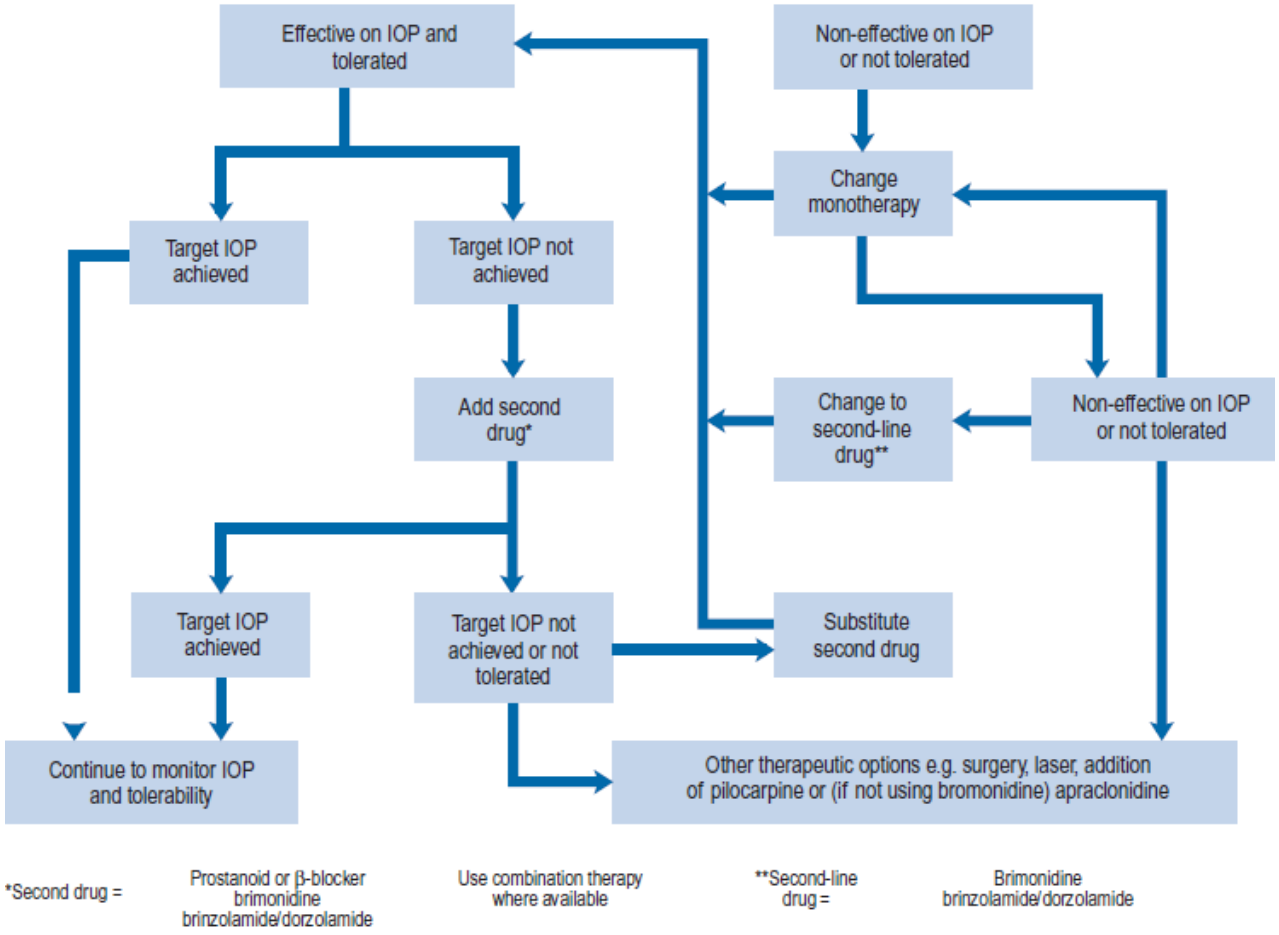
Topical Drugs Used in the Treatment of Open-Angle Glaucoma

Cholinesterase inhibitors						
Echothiophate		Phospholine Iodide	Solution	0.125	Once or twice a day	
Carbonic anhydrase inhibitors						
Topical						
Brinzolamide	Carbonic anhydrase type II inhibition	Azopt	Suspension	1	Two to three times a day	All reduce aqueous humor production of ciliary body
Dorzolamide		Trusopt	Solution	2	Two to three times a day	
Systemic						
Acetazolamide		Generic	Tablet	125 mg, 250 mg	125–250 mg two to four times a day	
			Injection	500 mg/vial	250–500 mg	
		Diamox Sequels	Capsule	500 mg	500 mg twice a day	
Methazolamide		Generic	Tablet	25 mg, 50 mg	25–50 mg two to three times a day	
Prostaglandin analogs						
Latanoprost	Prostaglandin $F_{2\alpha}$ analog	Xalatan	Solution	0.005	1 drop every night	Increases aqueous uveoscleral outflow and to a lesser extent trabecular outflow
Bimatoprost	Prostamide analog	Lumigan	Solution	0.03	1 drop every night	
Travoprost		Travatan, Travatan Z	Solution	0.004	1 drop every night	
Combinations						
Timolol-dorzolamide		Cosopt	Solution	Timolol 0.5% dorzolamide 2%	1 drop twice daily	
Timolol-brimonidine		Combigan	Solution	Timolol 0.5% brimonide 0.2%	1 drop twice daily	

Table 55.1 Drugs used in the treatment of chronic open-angle glaucoma

Therapeutic category	Primary mechanism
Topical prostaglandins	Increase aqueous outflow
Topical prostamides	Increase aqueous outflow
Topical β-blocking agents	Decrease aqueous formation
Topical miotics	Increase aqueous outflow
Topical adrenergic agonists	Increase aqueous outflow and decrease aqueous formation
Topical carbonic anhydrase inhibitors	Decrease aqueous formation
Oral carbonic anhydrase inhibitors	Decrease aqueous formation

Topical therapy for chronic open-angle glaucoma (COAG) based on recommendations of European Glaucoma Society (2008).



TREATMENT OF CLOSED-ANGLE GLAUCOMA:

- Acute closed-angle glaucoma with high IOP requires rapid reduction of IOP.

- Iridectomy is the definitive treatment, which produces a hole in the iris that permits aqueous flow to move directly from the posterior to the anterior chamber.

- Drug therapy of an acute attack typically consists of an osmotic agent and secretory inhibitor (e.g., β-blocker, α2 agonist, **latanoprost, or CAI), with** or without pilocarpine.

- Osmotic agents are used because they rapidly decrease IOP. Examples include **glycerin, 1 to 2 g/kg orally, and mannitol, 1 to 2 g/kg IV.**

- Although traditionally the drug of choice, pilocarpine use is controversial as initial therapy. Once IOP is controlled, pilocarpine should be given every 6 hours until iridectomy is performed.

- Topical corticosteroids can be used to reduce ocular inflammation and synechiae. Epinephrine should be used with caution because it can precipitate acute closed-angle glaucoma, especially when used with a β-blocker.

Algorithm for the treatment of primary angle-closure glaucoma (PACG).