

Glaucoma

By

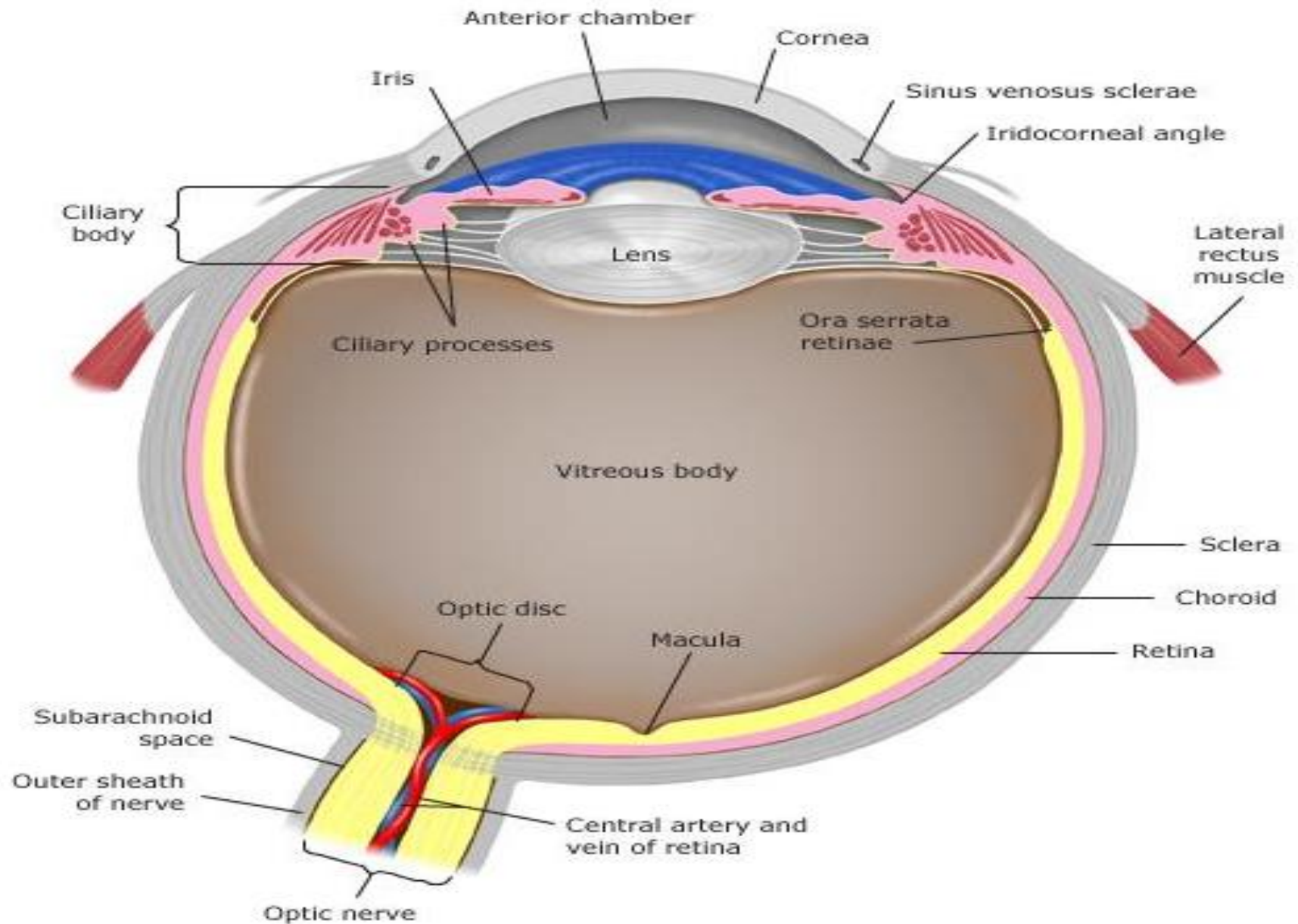
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2020

Glaucoma

- A group of ocular diseases characterized by **optic neuropathy**.
- Optic nerve damage results in **visual field loss** and may lead to irreversible blindness if left untreated.
- Elevated intra-ocular pressure(IOP) is one of the primary risk factors.
- Normal IOP is 10-21mm Hg.

Anatomy of the eye



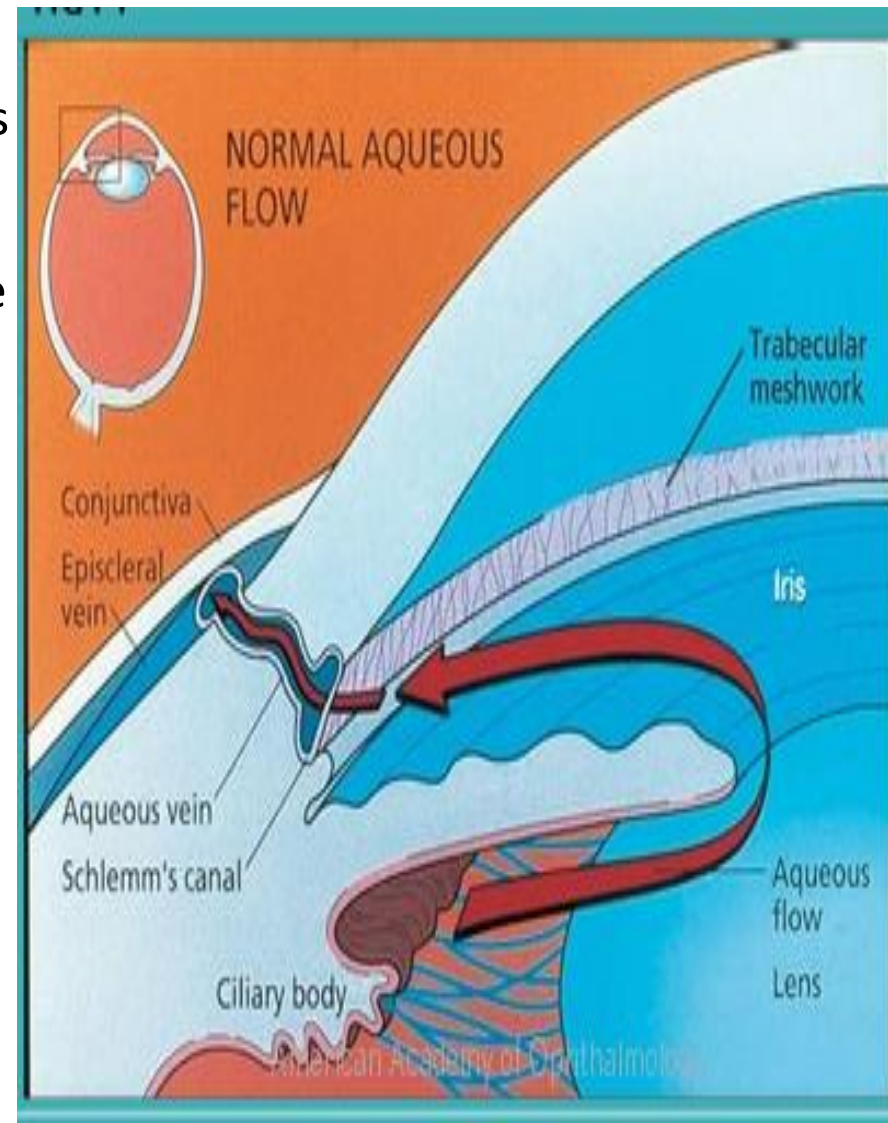
Aqueous humor dynamics & IOP

Aqueous humor is produced by epithelial cells of the ciliary body.

- Then it passes b/n the iris and the lens to anterior chamber(AC)
- absorbed from the angle of AC through trabecular meshwork by active transport
- goes to 'canal of Schlemm'
- passes to small episcleral veins to enter ocular venous system.

■ IOP is controlled by the balance b/n production & drainage of aqueous.

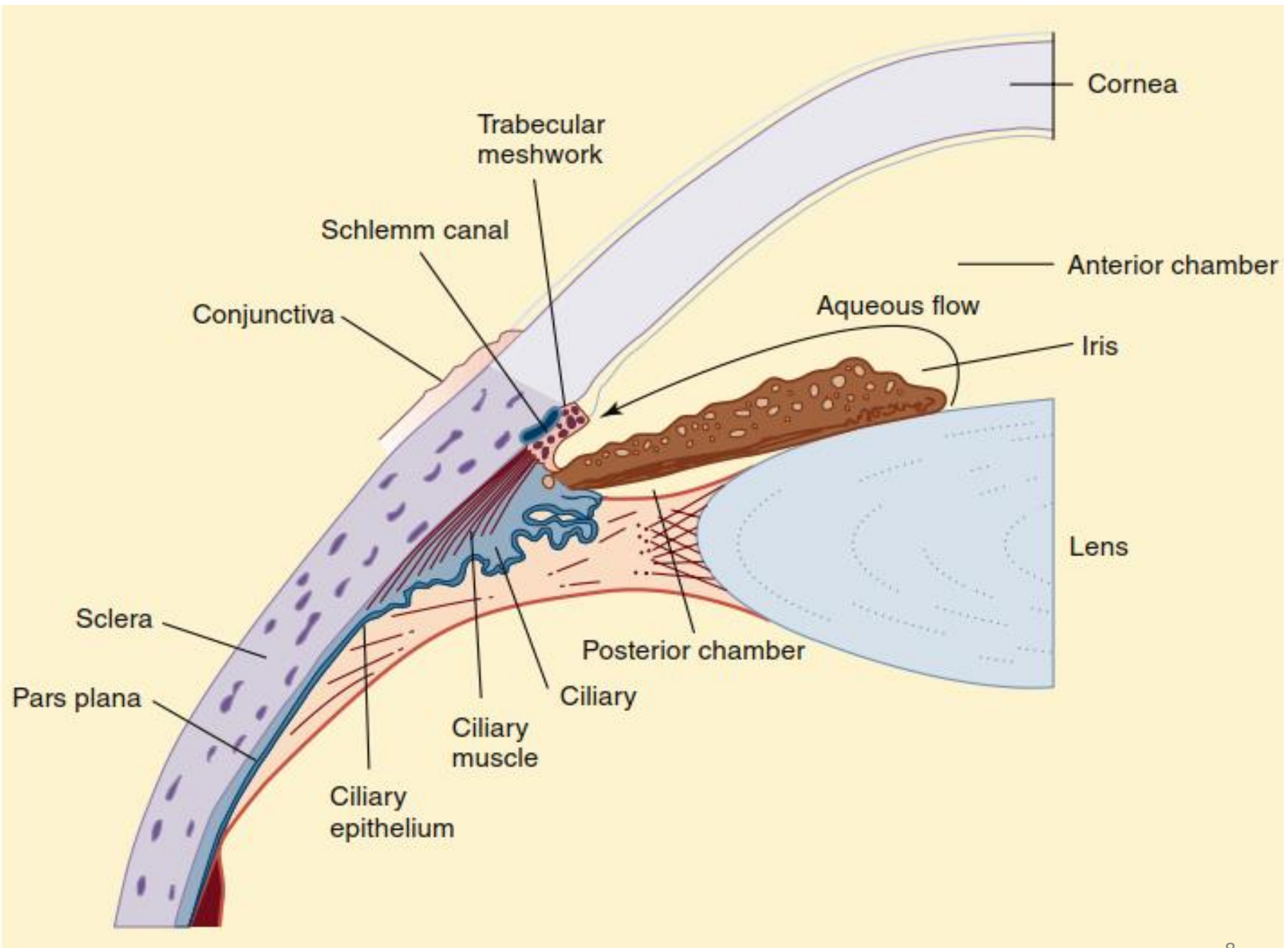
■ Impaired drainage \Rightarrow high IOP \Rightarrow glaucoma



- Aqueous humor provides oxygen and nutrition to the avascular lens and cornea.
- IOP is dependent on the balance between aqueous humor production and outflow from the anterior segment.
- The anterior segment of the eye is separated by the iris into the posterior and anterior chambers.
- The ciliary body, a ring-like structure that surrounds and supports the lens.
- It produces aqueous humor through the diffusion and ultrafiltration of plasma.
- The nonpigmented epithelium of the ciliary body secretes aqueous humor into the posterior chamber.

- Aqueous humor formation can be modified pharmacologically through the α - and β -adrenoceptors, carbonic anhydrase, and sodium and potassium adenosine triphosphatase of the nonpigmented ciliary epithelium.
- After secretion, aqueous humor flows from the posterior chamber through the pupil into the anterior chamber.
- From the anterior chamber, approximately 80% of aqueous humor then exits through the **trabecular meshwork** while the remaining 20% exits through the **uveoscleral pathway**.
- The trabecular meshwork is a lattice of connective tissue that surrounds edge of the anterior chamber located in the inside intersection of the edge of the cornea and the iris insertion.

- The size of the trabecular meshwork can be altered by the contraction or the relaxation of the ciliary muscle.
- Stimulation of muscarinic receptors on the ciliary muscle causes contraction, which in turn causes the pores of the trabecular meshwork to open, increasing aqueous humor outflow into Schlemm canal and the episcleral venous system.
- In the uveoscleral pathway, aqueous humor exits the anterior chamber through the iris root and through spaces in the ciliary muscles, which then drain into the suprachoroidal space.
- Uveoscleral outflow can be pharmacologically modulated by adrenoceptors, prostanoïd receptors, and prostamide receptors.



✓ Aqueous humor in the anterior chamber leaves the eye by two routes:

- ✓ filtration through the **trabecular meshwork** (conventional outflow) to the Schlemm canal (80% to 85%)
- ✓ through the ciliary body and the **suprachoroidal space** (uveoscleral outflow or unconventional outflow)

Classifications of glaucoma

- Two major types; **open angle & closed angle**
 - **Primary glaucoma**
 - open angle
 - closed angle
 - **Secondary glaucoma**
 - open angle
 - closed angle
- OAG accounts for the great majority of cases.

Primary open angle glaucoma(POAG)

- POAG is a bilateral, genetically determined disorder constituting 60% to 70% of all glaucomas and 90% to 95% of primary glaucomas
- World-wide prevalence ~ 1%
- The aqueous humor is produced and circulates normally, but it does not drain properly through the trabecular meshwork and Schlemm's canal.
- **Risk factors:** elevated IOP, advanced age, black race, FHx, T2DM, double among females, corticosteroids use

Symptoms

- None until substantial visual field loss occurs
- No pain or inflammation
- Gradual loss of vision

Signs

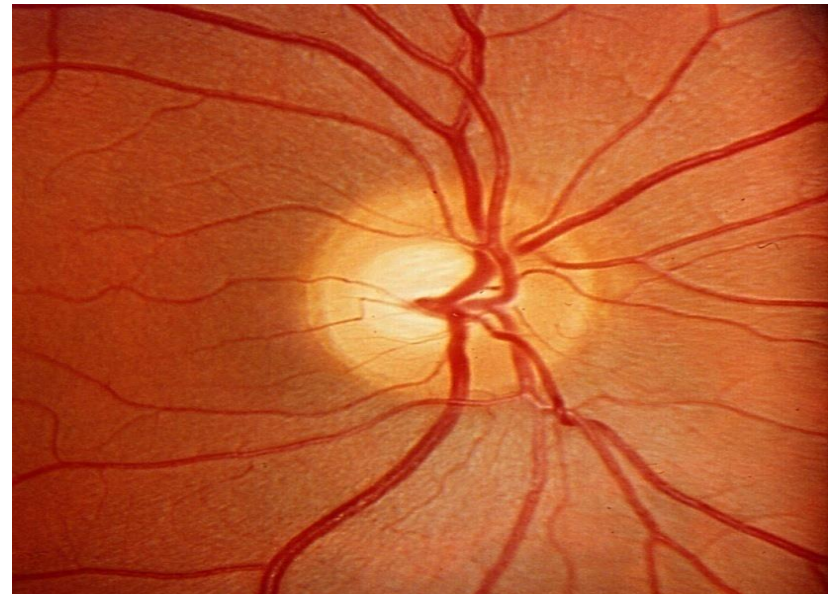
- Changes in the optic disc appearance
- IOP can be normal or elevated (>21 mm Hg)

- The optic disk is the portion of the optic nerve that leaves the eye.
- The optic nerve head (optic disc) is the 1st tissue to be damaged by high IOP

=> due to impairment of blood supply to the optic nerve head

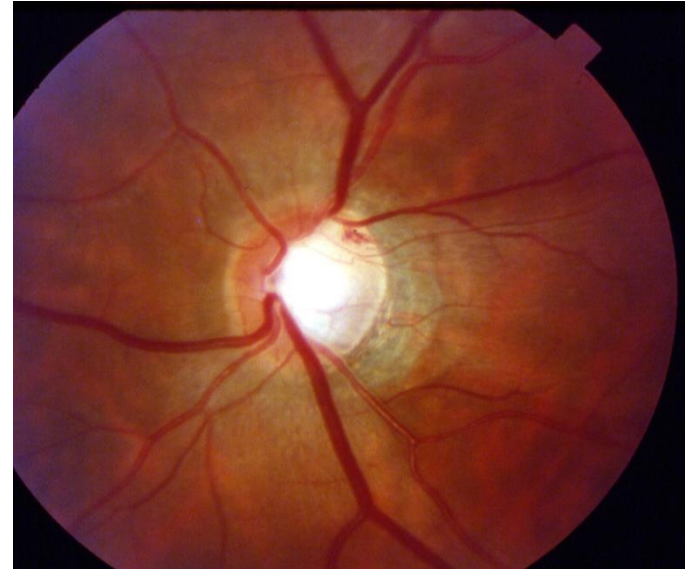
The optic disc has two parts

1. the outer part (neural rim)
 - orange-pink color
2. the central part (cup)
 - white color
 - has no nerve fibers



- As the nerve axons die, the cup becomes larger in relation to the whole disk

- Cup-to-disk ratio >0.5
- *asymmetry of CDR in the 2 eyes*
- Progressive increase in cup size
- Vertical elongation of the cup
- Pallor of the cup
- Splinter hemorrhages



- the VF defects are not noticed by pts until they are quite advanced!

POAG; intraocular pressure (IOP)

- The normal IOP = 10 to 21 mm Hg
- The higher the IOP, the more likely that the optic nerve will be damaged.
- However, sensitivity to higher IOP varies among eyes of different people.
 - IOP > 30mmHg= pt will develop glaucoma
 - IOP 20-30mmHg= may or may not have glaucoma
 - ocular hypertension =raised IOP but no sign of glaucoma
 - normal tension glaucoma =IOP< 20mmHg but definite glaucomatous signs

Angle closure glaucoma

- ACG is a form of glaucoma characterized by narrowing or closure of the anterior chamber angle.
 - **Primary angle closure**
 - **Secondary angle closure**

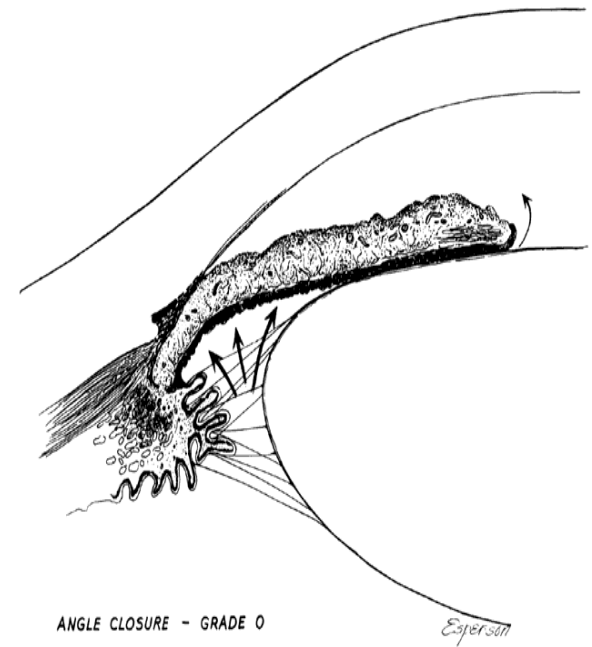
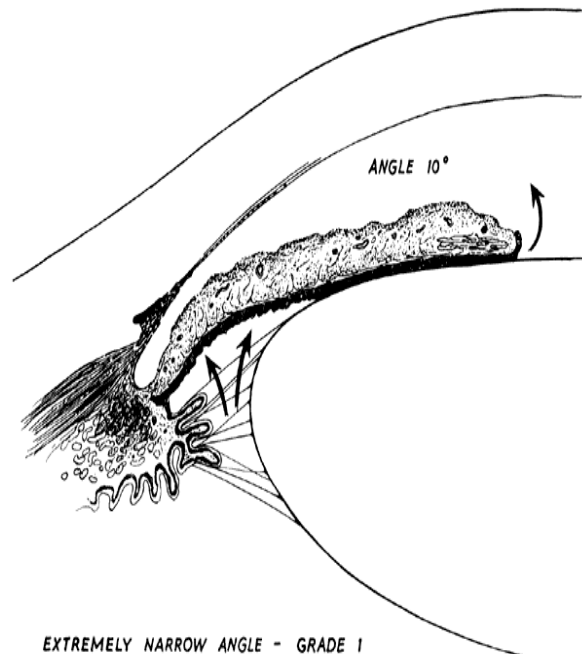
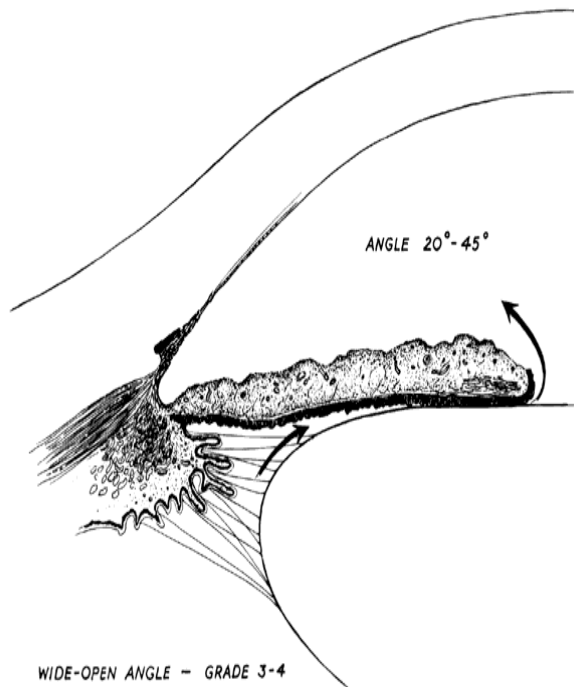
Primary angle closure glaucoma (PACG)

- The lens rests against the iris.
 - This results in pupillary block, a condition in which aqueous humor can no longer flow normally through the pupil.
 - Pressure builds up behind the iris, causing the peripheral iris to bow forward and cover all or part of the anterior chamber angle.
 - Prolonged or repeated contact b/n the iris and the angle can lead to scarring and functional damage to the trabecular meshwork

- **Acute angle closure**
 - the entire angle is blocked suddenly, as occurs in complete pupillary block, =>rapid IOP rises => acute symptoms
- **Chronic angle closure**
 - only a portion of the angle is blocked at a time and develops scarring.
 - Over time, the angle may become progressively more closed.
- **Risk Factors**
 - Advancing age
 - Asian or Eskimo ethnicity
 - Female gender
 - Shallow anterior chamber
 - Family history of angle-closure glaucoma

Pathophysiology

- Functional block b/n the iris and the lens
- Increase resistance to aqueous flow from P/C to A/C



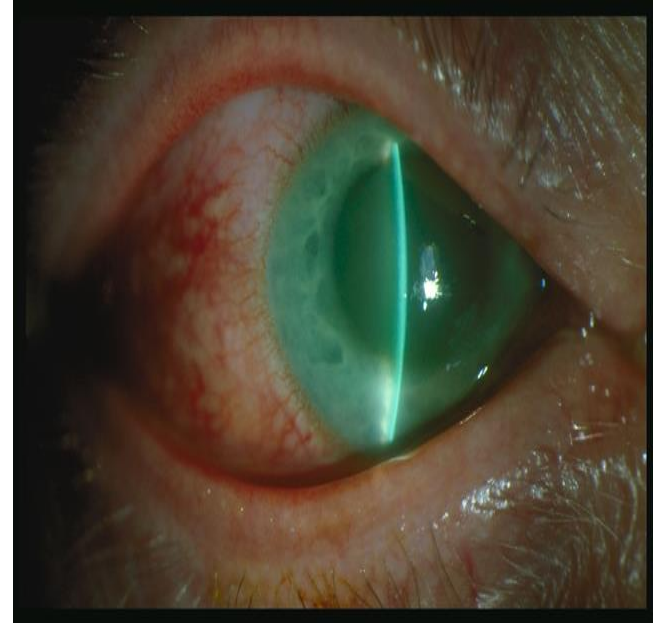
Acute ACG: clinical presentation

symptoms:

- ✓ Sudden onset of severe eye pain
- ✓ Ocular pain
- ✓ Headache
- ✓ Blurring of vision
- ✓ Red eye
- ✓ Nausea, vomiting
- ✓ Diaphoresis (profuse sweating)

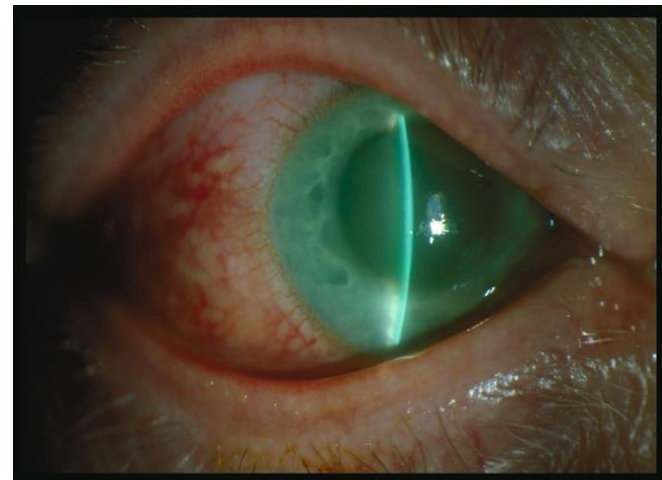
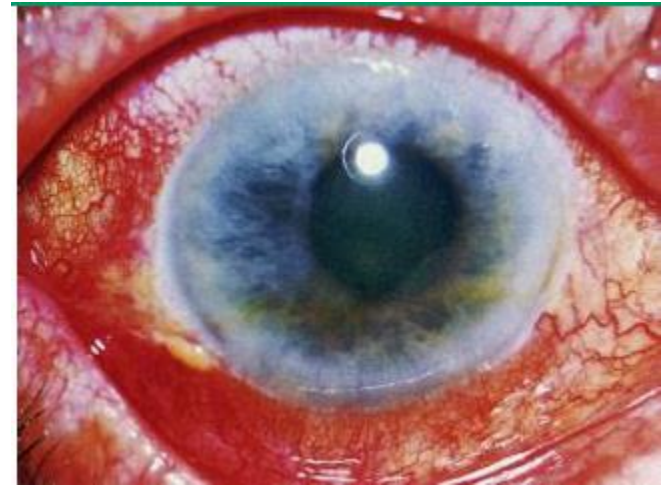
• **precipitating factors:**

- Dim light or evening
- Emotional stress



Signs

- Very high IOP, 40-60mmHg
- Decreased visual acuity
- marked conjunctival hyperemia
- Cloudy cornea caused by corneal edema
- A shallow anterior chamber
- A mid-dilated pupil (4 to 6 mm) that reacts poorly to light



Treatment

- The goals of therapy are to
 - prevent further loss of visual function
 - minimize adverse effects of therapy
 - maintain IOP at or below a pressure at which further optic nerve damage is unlikely to occur
- Current therapy is directed at altering the flow and production of aqueous humor, which is the major determinant of IOP.

Anti-glaucoma drugs

1. Beta blockers

- Reduce aqueous humor production
- Lower IOP by 20% to 30%
- Ophthalmic β -blockers are presently available:
 - **Betaxolol** (0.25–0.5% ophthalmic solution 1 gtt BID)
 - **Timolol** (0.25–0.5% ophthalmic solution 1 gtt BID)
 - Levobunolol (0.25–0.5% ophthalmic solution 1 gtt BID)
 - Metipranolol (0.3 % ophthalmic solution 1 gtt BID)
 - Carteolol (1 % ophthalmic solution 1 gtt BID)
- C/I : hypersensitivity rxn, cardiac and obstructive pulmonary diseases

2. α_2 - Adrenergic agonist

- Decrease the rate of aqueous humor production
- Increase in uveoscleral outflow
- The drugs reduce IOP by 18% to 27% at peak
 - **Brimonidine** (0.15–0.2% ophthalmic solution, 1 gtt BID to TID)- first-line or adjuvant therapy
 - **Apraclonidine (0.5% solution 1-2 gtt TID)** short term use due to allergic rxn and tachycardia. Second line or adjuvant therapy

3. Cholinergic

- Reduce IOP by increasing aqueous humor trabecular outflow.
 - CB contraction => stretching and spreading of trabecular meshwork = facilitates drainage
- May reduce uveoscleral outflow.
- Pilocarpine (2-6% ophthalmic drops, instill 1 drop QID)

4. Carbonic Anhydrase Inhibitors(CAIs)

- Decrease aqueous formation by direct antagonistic activity on the ciliary epithelial **carbonic anhydrase**
- Inhibit aqueous production by blocking active secretion of Na^+ and HCO_3^- ions from the ciliary body
- Over 90% of the ciliary epithelial carbonic anhydrase must be abolished to decrease aqueous production and decrease IOP.

Topical CAIs

- Dorzolamide(2% ophthalmic solution): 1 gtt TID
- Brinzolamide(1% ophthalmic suspension): 1 gtt TID
 - Equally effective & reduce IOP by 15% to 26% as monotherapy
 - No advantage of concomitant use with systemic CAIs
- Adverse effects: transient burning and stinging, ocular discomfort and transient blurred vision, tearing, conjunctivitis, photophobia
- Main contraindication is sulfur allergy

CAI's - Oral

- If not respond or tolerance to maximum topical therapy
- **Acetazolamide**
 - Sustained released has longer action and is often better tolerated than conventional tablets
 - It is not metabolized and is excreted in urine.
- **Methazolamide**
 - Longer duration of action
 - Less bound to serum protein
 - Metabolized by the liver and has less systemic S/Es
- CAIs reduce IOP by 25% to 40%.

CAI's Oral; Side effects

- Anorexia & Wt loss
- Abdominal pain and diarrhea
- Decreased libido and impotence
- Unpleasant taste (metallic)
- Severe mental depression
- Increased risk renal stones
- Allergic reaction in pts with sulfur allergy
- Idiosyncratic reaction of aplastic anemia
- Thrombocytopenia and agranulocytosis
- Hypokalemia

5. Prostaglandin analogue

- Significant and sustainable IOP lowering effect
 - Most potent of the topical glaucoma medications
 - Increase uveoscleral outflow by 50%
 - Latanoprost 0.005% ophthalmic solution 1 gtt QD
 - Travoprost 0.004% ophthalmic solution 1 gtt QD
 - Bimatoprost 0.01, 0.03% ophthalmic solution 1 gtt QD
 - Tafluprost 0.0015 % ophthalmic solution 1 gtt QD
 - They are additive to all the other topical medications.
 - Latanoprost and travoprost are pro-drugs – they become biologically active after penetrating the cornea and being hydrolyzed by corneal esterase.
 - Tafluprost is preservative free
- SE: hyperpigmentation, eyelash growth.

6. Hyperosmotic agents

- Used in emergency condition like acute ACG with very high IOP
- **Glycerin** -oral 1 g/kg of 50% solution
Action: onset 30 min, peak 60 min, duration 6 hrs
- **Mannitol**: 1.5–2 g/kg iv as a 20% solution over 30–60 minutes.
Action: peak 30 min, duration 6 hrs

SE: Nausea and vomiting, confusion, headache, backache, intracranial hemorrhage, pulmonary edema, precipitate cardiac and renal failure and urinary retention