

# Glaucoma

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## INCIDENCE

- in USA - *second most common cause of blindness!!!*  
*leading cause of blindness in African Americans!!!*
- $\approx 2$  million Americans have glaucoma, but  $\approx \frac{1}{2}$  *are unaware of it.*
- generally considered **disorder of elderly**, but it can occur in any age.

## PATHOGENESIS

- *chronic progressive optic nerve damage (glaucomatous optic neuropathy):*

- a) **due to IOP** (at least partly).
- b) that can be arrested / diminished by **IOP lowering**.

- increased IOP leads to loss of retinal ganglia cells.
- major theories:
  - a) **vascular dysfunction** causing ischemia to optic nerve.
  - b) **mechanical dysfunction** (cribriform plate compression of axons).

Precise mechanism is still hot topic of discussion!

Glaucoma is not just disease of IOP but rather *multifactorial optic neuropathy!*

**Primary (conventional, trabecular) outflow system** (83-96% aqueous outflow) is located in anterior chamber angle: trabecular meshwork  $\rightarrow$  canal of Schlemm  $\rightarrow$  intrascleral channels  $\rightarrow$  episcleral and conjunctival veins.

**Secondary (alternative, uveoscleral) outflow system** (5-15% aqueous outflow): aqueous exits through anterior face of ciliary body, percolates through ciliary muscles to suprachoroidal space, exits via scleral channels.

According to MECHANISM OF OUTFLOW OBSTRUCTION:

1. **OPEN-ANGLE glaucoma** (60-70%) - inadequate outflow despite angle that appears open and relatively normal on gonioscopy (i.e. decreased permeability through trabeculae)
2. **CLOSED-ANGLE (ANGLE-CLOSURE) glaucoma** (10%) - physical obstruction by forward movement of peripheral iris.

According to ETIOLOGY:

### I. CHRONIC (IDIOPATHIC) OPEN-ANGLE glaucomas

1. High-pressure glaucomas
2. Normal-pressure glaucomas

### II. PUPILLARY BLOCK glaucomas

1. Acute angle-closure glaucoma
2. Subacute angle-closure glaucoma
3. Chronic angle-closure glaucoma
4. Combined-mechanism glaucoma

### III. DEVELOPMENTAL glaucomas

1. Congenital (infantile) glaucoma
2. Juvenile glaucoma
3. Axenfeld-Rieger syndrome
4. Peters' anomaly
5. Aniridia
6. Other developmental anomalies

### IV. Glaucomas associated with OTHER OCULAR DISORDERS

1. Disorders of corneal endothelium
  - 1) iridocorneal endothelial syndrome
  - 2) posterior polymorphous dystrophy
  - 3) Fuchs' endothelial dystrophy
2. Disorders of iris & ciliary body
  - 1) pigmentary glaucoma
  - 2) iridoschisis
  - 3) plateau iris
3. Disorders of lens
  - 1) exfoliation syndrome
  - 2) lens-induced open-angle glaucoma
  - 3) lens intumescence and dislocation
4. Disorders of retina, choroid, vitreous
  - 1) retinal detachment and vitreoretinal abnormalities
  - 2) neovascular glaucoma
5. Intraocular tumors

### V. Glaucomas associated with ELEVATED EPISCLERAL VENOUS PRESSURE

1. Systemic diseases with associated elevated IOP and glaucoma
2. Corticosteroid-induced glaucoma

### VI. Glaucomas associated with INFLAMMATION /TRAUMA

1. Keratitis, episcleritis, scleritis
2. Uveitis
3. Ocular Trauma
4. Hemorrhage

### VII. Glaucomas following INTRAOCULAR SURGERY

1. Ciliary block (malignant) glaucoma
2. Aphakia, pseudoaphakia
3. Epithelial, fibrous, endothelial proliferation
4. Corneal surgery
5. Vitreoretinal surgery

RISK FACTORS for primary glaucoma:

- 1) **elevated IOP** (ocular hypertension) - main clinically treatable risk factor!  
patient with IOP 28 mmHg is 15 times more likely to develop field loss than patient with IOP 22 mmHg
- 2) **age > 40 yrs** (glaucoma is 6 times more common in persons > 60 yrs; 15% people have glaucoma by seventh decade of life)
- 3) **family history** (risk increased 15 times)
- 4) **black race** (risk increased 3-4 times; glaucoma is earlier and more aggressive; 6-8 times more likely to go blind)
- 5) **diabetes**
- 6) **hypertension**
- 7) **myopia**
- 8) **corticosteroid (systemic or topical) use** – corticosteroids elevate IOP in 5% of general population (*STEROID RESPONDERS*)

## DIAGNOSIS

### IOP measurement (tonometry)

Normal IOP is **11-21 mmHg**; it is arbitrary:

- 1/6 patients have **normal IOP** (**NORMAL- / LOW-PRESSURE GLAUCOMA**).
  - treatment is directed at lowering IOP, even though IOP is "normal";
  - pathogenesis varies; e.g.:
    - a) inadequate blood supply to optic nerve.
    - b) vasospasm (patients have higher incidence of migraines than general population).

90% people with **IOP > 21 mmHg** never develop glaucoma (**OCULAR HYPERTENSION**).

- **GOLDMANN applanation** is criterion standard.
- difference between eyes  $\geq 3$  mmHg indicates suspicion of glaucoma.
- normal diurnal IOP variation 3-4 mmHg (often highest in early morning hours); glaucomatous eyes have higher variation (> 10 mmHg).

N.B. multiple readings should be taken over time.

**Gonioscopy** - angle visualization by special prism or contact lens - differentiation of angle-closure from open-angle glaucoma.

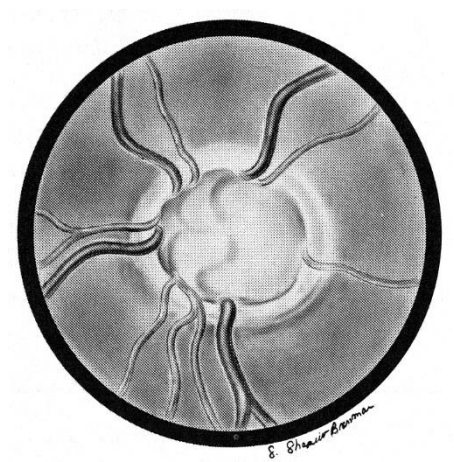
**Normal angle** - darkly pigmented ciliary body (CB), white scleral spur (SS), trabecular meshwork, which looks red due to blood reflux into underlying Schlemm canal (SC):



Source of picture: "Online Journal of Ophthalmology" >>

**Ophthalmoscopy** - examination of optic disks:

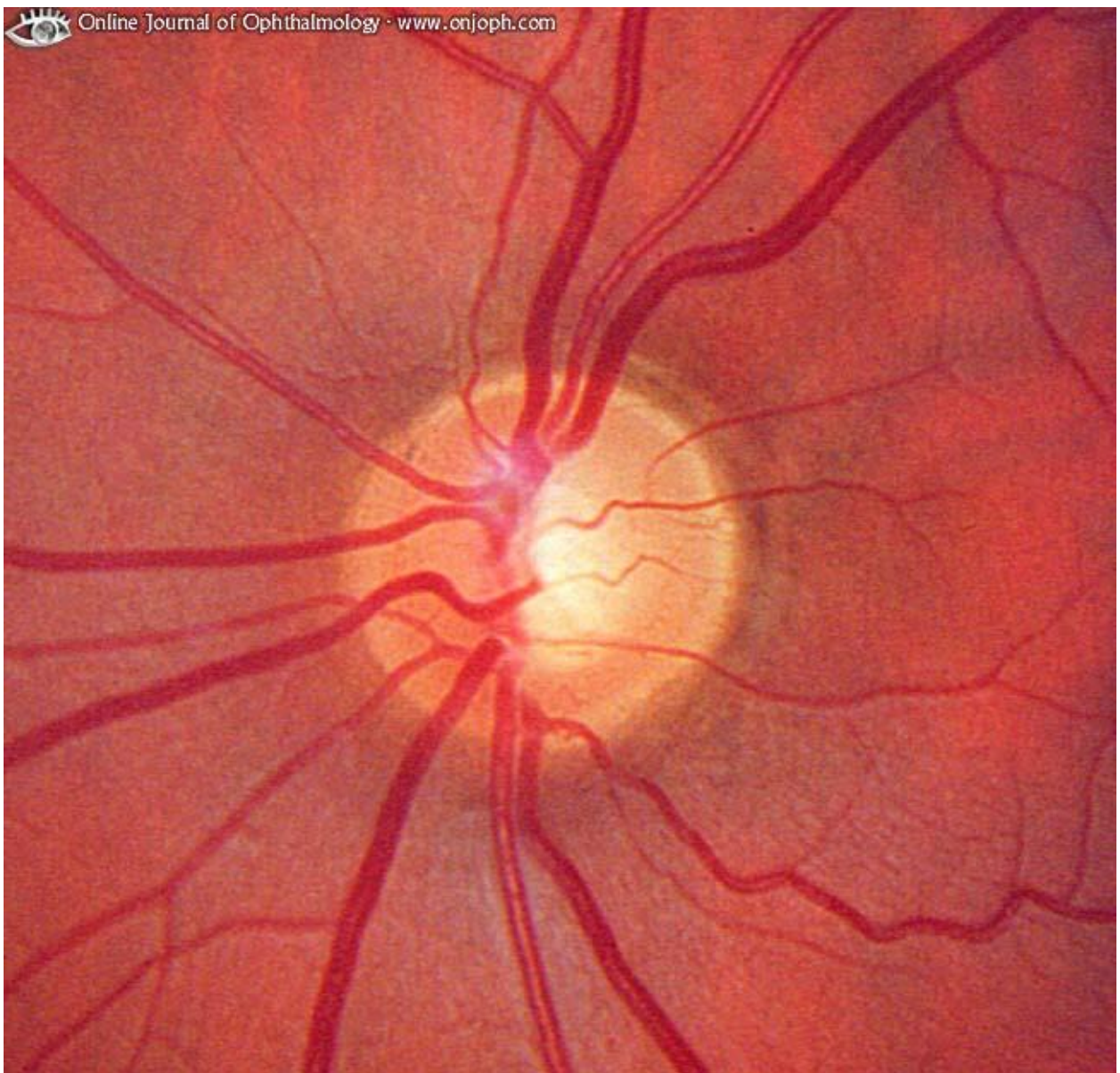
- 1) increased pressure leads to increased cupping (**glaucomatous cupping**) – backward disc depression, enlarged cup (> ½ disc diameter, sometimes cup extends to disc edge), notching or thinning of disc rim, retinal vessels sink in and under cup and may be displaced nasally. glaucomatous disc has normal overall color (disc pallor disproportionate to cupping suggests against glaucoma).
- 2) **nerve fiber layer damage** (seen with red-free filter).
- 3) **disc atrophy**.



- if IOP is normal but glaucomatous optic discs / visual fields exist - NORMAL-TENSION GLAUCOMA (diagnosis of exclusion).
- optic disk stereophotography is extremely helpful for future comparisons; if unavailable, make detailed optic disk drawing.

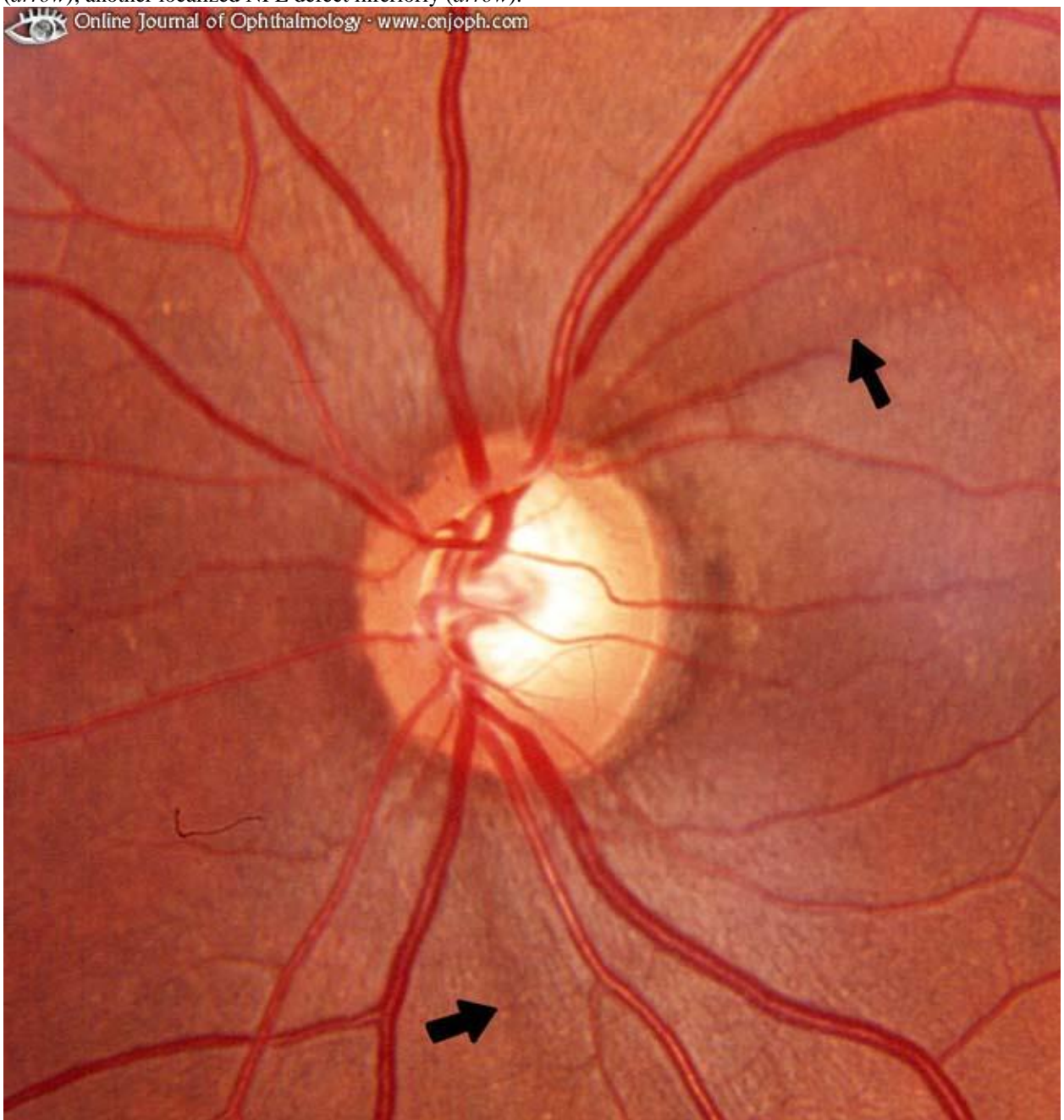
**Early glaucoma** (rim loss predominantly in inferotemporal / superotemporal regions → enlargement of vertical cup):





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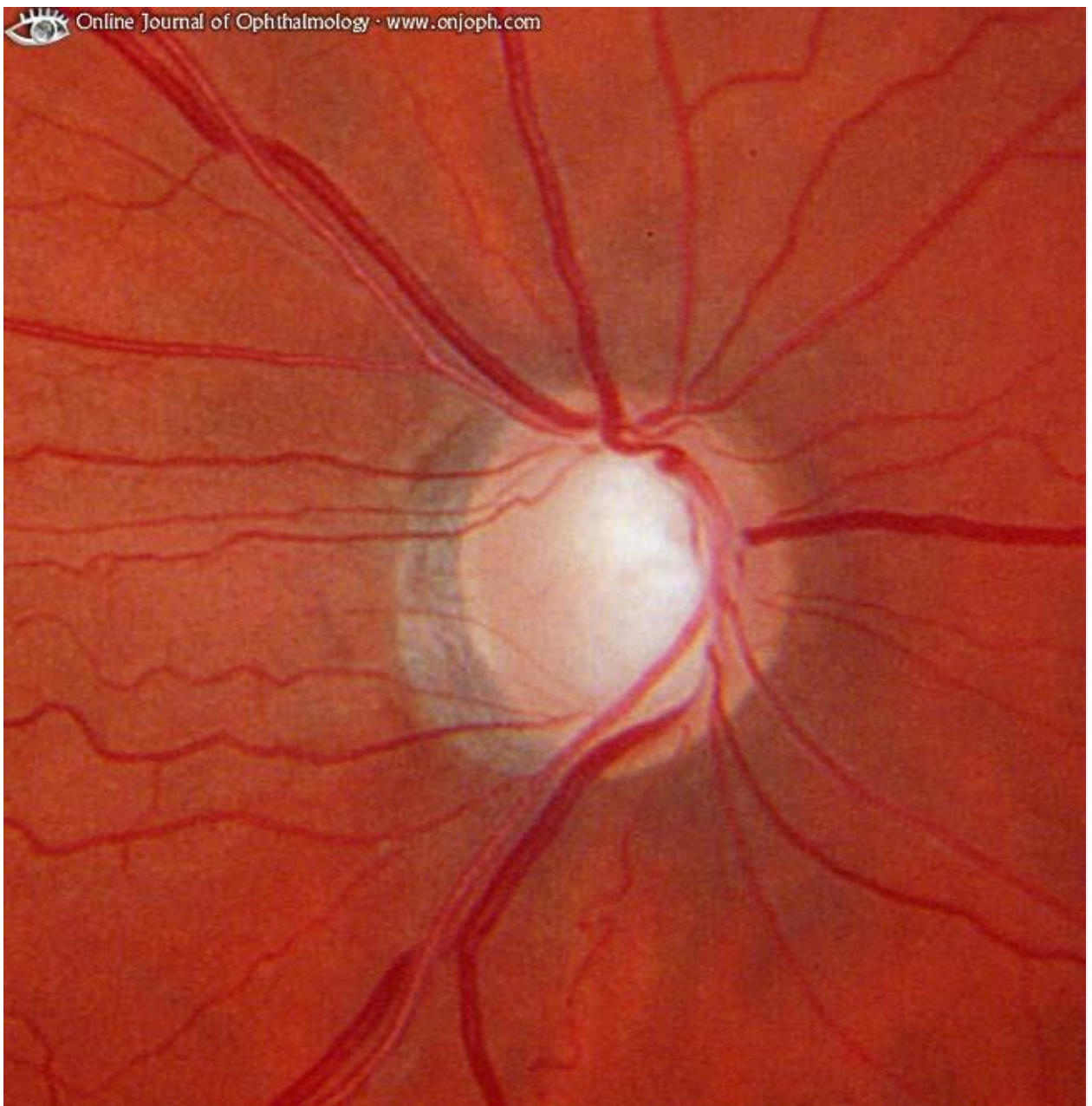
**Moderate glaucoma** - localized loss of neuroretinal rim superiorly (notching) with correspondent nerve fiber layer defect (*arrow*); another localized NFL defect inferiorly (*arrow*):



Source of picture: "Online Journal of Ophthalmology" >>

**Advanced glaucoma** - marked loss of neuroretinal rim in all sectors;  $\alpha$ -zone parapapillary atrophy, vertical excavation, Elschnig's scleral ring:





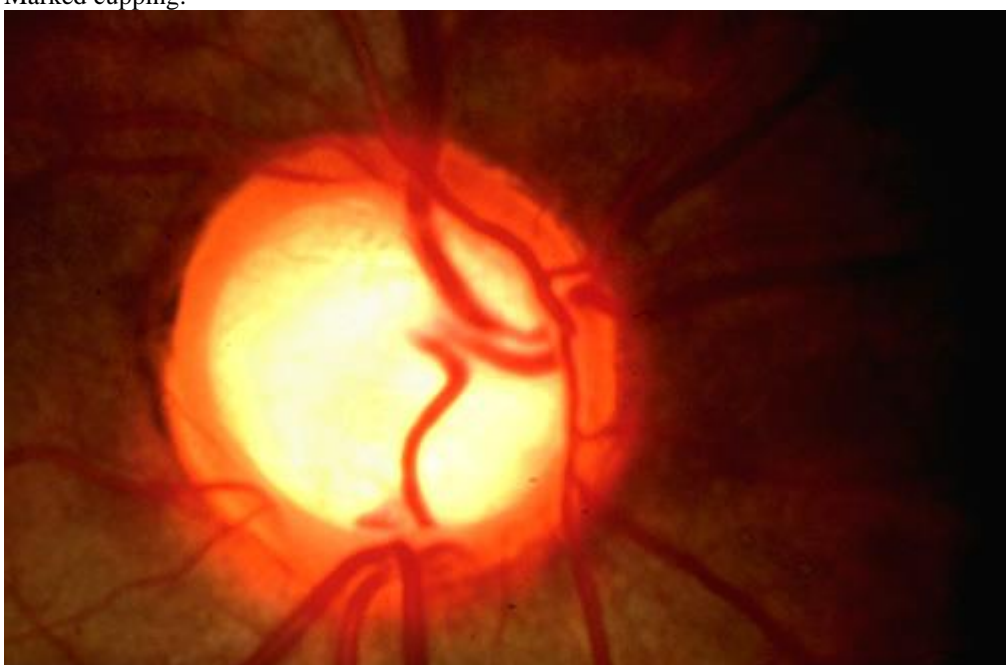
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**Advanced glaucoma** - deeply cupped optic nerve head; retina is detached artificially:

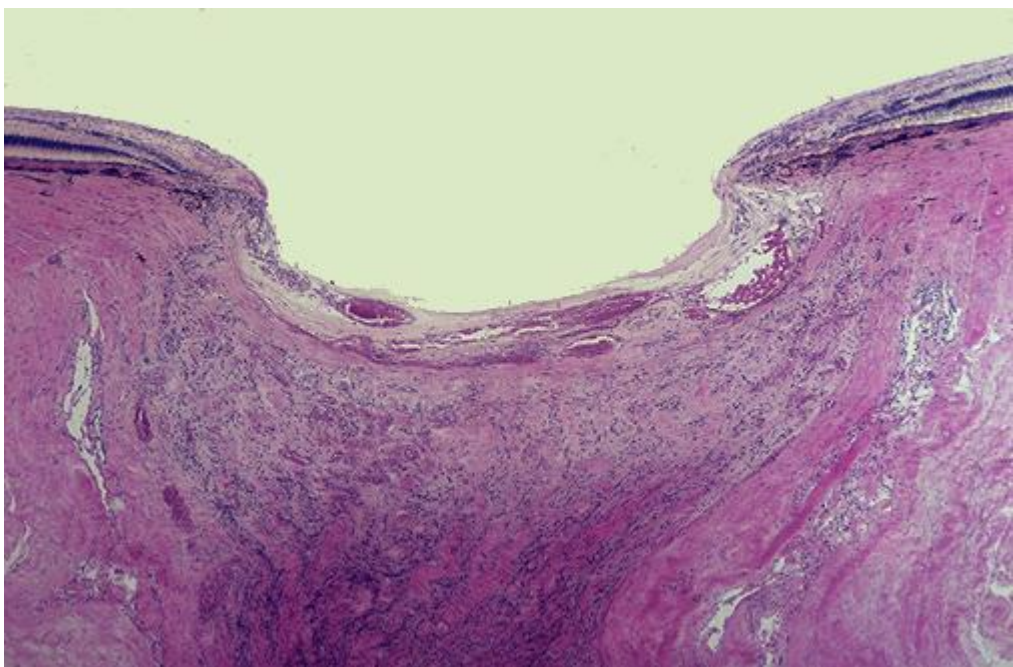


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**Marked cupping:**







Optic nerve cupping and **Disc Damage Likelihood Scale:**

	DDLS Stage	Narrowest rim width (rim/disc ratio) [average disc size: 1.50 - 2.00 mm]	Example
At Risk	1	0.4 or more	
	2	0.3 to 0.39	
	3	0.2 to 0.29	
	4	0.1 to 0.19	
Glaucoma Damage	5	less than 0.1	
	6	0 (extension: less than 45°)	
	7	0 (extension: 46° to 90°)	
Glaucoma Disability	8	0 (extension: 91° to 180°)	
	9	0 (extension: 181° to 270°)	
	10	0 (extension: more than 270°)	

**Visual field examination** - typical visual field loss:

- new-onset **glaucomatous defects** - early nasal step, temporal wedge, paracentral scotoma (more frequent superiorly); generalized depression also can be found.
- typical scotomata – arcuate, around blind spot;
- peripheral fields – **nasal and superior fields** are lost first; last vision remains in temporal field.
- disc cupping & nerve fiber layer losses may occur before actual visual field loss - visual field examination cannot be sole tool used to determine glaucomatous damage.  
N.B. progressive cupping, even without visual field loss, is glaucoma and should be treated!
- SWAP (short wavelength automated perimetry or blue on yellow) - more sensitive method (may detect visual loss up to 3-5 years earlier than conventional perimetry).

**Slit lamp examination**

- microcystic corneal edema (found only with acute IOP elevation).

## SCREENING

- long asymptomatic course (with silent damage) – need for screening!
- at least **every 3-5 years** in asymptomatic patients; **more often** in high risk groups:
  - African Americans
  - individuals > 40 yrs.
- screening consists of **IOP measurements** + **optic nerve status assessment** (funduscopy + visual fields).

N.B. screening based only on IOP has low sensitivity, specificity, and positive predictive value.

## PRIMARY OPEN-ANGLE GLAUCOMA

*Most common form (60-70%) of glaucoma!*

Cause of elevated IOP is **decreased aqueous outflow** through trabecular meshwork.

## SYMPTOMS & SIGNS

No early symptoms (**silent, progressive nature**)!!!

One of leading preventable causes of blindness in world!!!

**VISION LOSS:**

- generally **bilateral** (but almost always asymmetric).
- PERIPHERAL vision** is **lost first and is usually asymptomatic**;  
some patients may have complaints (e.g. missing stairs if inferior visual field has been lost, noticing portions of words missing when reading, difficulty with driving).
- CENTRAL vision** is last to be affected.
- when patient is aware of visual field loss, degree of optic nerve atrophy is generally quite marked.

## DIAGNOSIS

General glaucoma findings + **normal open angle** on gonioscopy.

- IOP** is *normal* or *high* and almost always asymmetric (IOP is higher in eye with more optic nerve damage).

## TREATMENT

*Vision lost by glaucoma cannot be recovered!!!*

**Treatment goal** - to prevent optic nerve / visual field damage by stabilizing IOP.

- goal IOP is 30-40% below level thought to damage optic nerve.

## OCULAR HYPERTENSION

- treat only if risk factors for glaucoma exist (e.g. > 40 yrs, black race, family history, etc.)
- if IOP routinely reaches 27-30 mmHg, therapy should also be initiated.

## DRUGS

- treatment is started with **MONOCULAR TRIAL** – to assess efficacy (difference > 4 mmHg between eyes is strongly suggestive of clinical effect).
- some patients will be nonresponders to some therapies → initiate new drug.
- patients taking topical drugs are taught to perform passive lid closure with punctal occlusion to reduce systemic absorption and associated side effects.

I. **Miotics** (used less commonly today; very effective in emergencies) - **increase aqueous outflow** via traditional pathway:

**direct-acting** (topical cholinergics) - **PILOCARPINE, CARBACHOL**

**indirect-acting** (topical cholinesterase inhibitors):

a) **reversible** – **PHYSOSTIGMINE, NEOSTIGMINE**

b) **irreversible** (increased risk of retinal detachment) – **DEMECARIUM, ECHOTHIOPHATE, ISOFLUROPHATE**

II. **Carbonic anhydrase inhibitors** – **ACETAZOLAMIDE** (oral, i/v), **DICHLORPHENAMIDE** (oral), **METHAZOLAMIDE** (oral), **ETHOXZOLAMIDE** (oral), **DORZOLAMIDE** (topical), **BRINZOLAMIDE** (topical).

- **decrease aqueous production** (by inhibiting carbonic anhydrase in ciliary body).

III. **Adrenergic agonists** (topical):

a) **nonselective** (rarely used, cause mydriasis - contraindicated in angle-closure) – **EPINEPHRINE, DIPIVEFRIN**

b)  **$\alpha_2$ -selective** – **APRACLONIDINE, BRIMONIDINE**; do not cause mydriasis (mediated by  $\alpha_1$ ).

- **decrease aqueous production, increase uveoscleral aqueous outflow.**

IV.  **$\beta$ -Blockers** (topical) – **TIMOLOL, BETAXOLOL, LEVOBUNOLOL, CARTEOLOL, METIPRANOLOL**

- **decrease aqueous production.**

V. **Prostaglandin analogs** (topical) - **LATANOPROST, BIMATOPROST, TRAVOPROST, UNOPROSTONE.**

- **increase uveoscleral aqueous outflow.**
- one mechanism of action may be induction of metalloproteinases in ciliary body → break down extracellular matrix → reduced resistance to outflow through ciliary body.
- effectively lowers IOP for 24 hours after single daily application.
- long-term use can darken iris & lids and thicken lashes.

VI. **Osmotic diuretics** – **GLYCERIN** (oral), **MANNITOL** (i/v), **ISOSORBIDE** (oral).

- hypertonic plasma **draws fluid from eye.**
- most commonly used to reduce extremely elevated IOP in **acute situations** of angle-closure or certain secondary glaucomas.

VII. **ROCK inhibitor** – **NETARSUDIL** ophthalmic solution 0.02%.

## SURGERY

- indicated when glaucomatous optic neuropathy worsens and patient is on maximum tolerated medical therapy; in order of choice:

A) **Argon laser TRABECULOPLASTY** - laser energy is applied to trabecular meshwork for either 180° or 360° - to improve trabecular meshwork functioning

- IOP decrease is not permanent (10% patients will return to pretreatment IOP for each year following treatment).

B) **TRABECULECTOMY (s. GUARDED FILTRATION PROCEDURE)** (most commonly used filtration procedure) – superficial sclera flap is dissected anteriorly to trabecular meshwork, and section of trabecular meshwork is removed underneath flap - allows aqueous fluid to exit eye and to collect under conjunctiva (forming filtration bleb); **increased risk for endophthalmitis** (instruct to immediately report any signs of bleb infection (BLEBITIS) or endophthalmitis).

C) **DRAINAGE IMPLANT** (seton/tube/shunt) surgery - tube (e.g. Molteno valve) is placed in anterior chamber to shunt aqueous to equatorial reservoir, and then posteriorly to be absorbed in subconjunctival space.

D) **CILIARY BODY ABLATION (CYCLODESTRUCTION)** - freezing or laser - last resort procedure.

## FOLLOW-UPS

- frequency varies from weeks to years.
- perform – IOP check, visual field testing, optic disk photography.
- if optic nerve damage is progressing, patient's IOP goal is lowered and additional therapy is initiated.

## ANGLE-CLOSURE GLAUCOMA

- 10% of all glaucomas in **USA**, but more common (than open-angle glaucoma) in **Asia**.
- increased risk for angle closure - **hyperopes** (relatively shallow anterior chamber angles), **elderly** (enlarged lens).

Iris is apposed to trabecular meshwork at angle of anterior chamber:

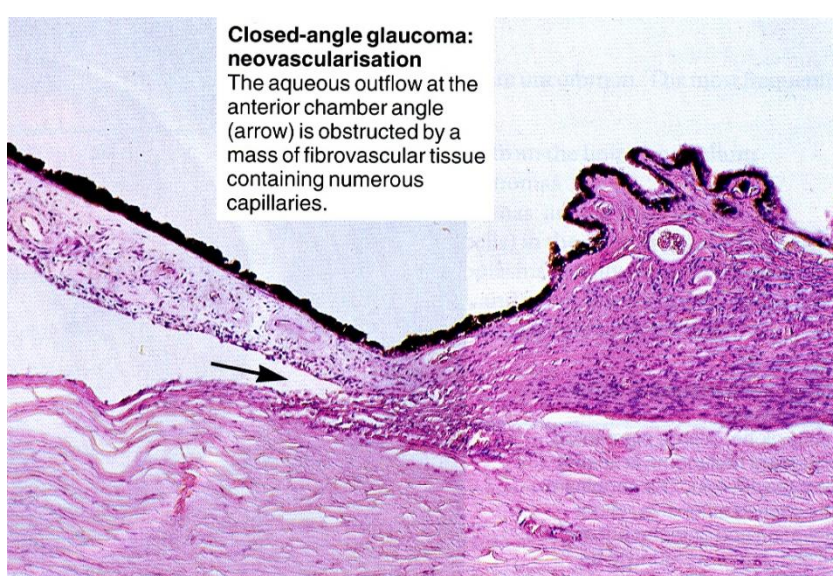
a) **primary** - due to **pupillary block** (contact between lens and iris).

- during **normal aging**, lens becomes thicker → increased apposition between pupillary margin and lens - can impede aqueous fluid flow from posterior chamber to anterior chamber; higher pressure in posterior chamber causes peripheral iris to balloon anteriorly, obstructing angle.
- **plateau iris** (anterior iris insertion to ciliary body) - occludes anterior chamber angle during pupil dilation.

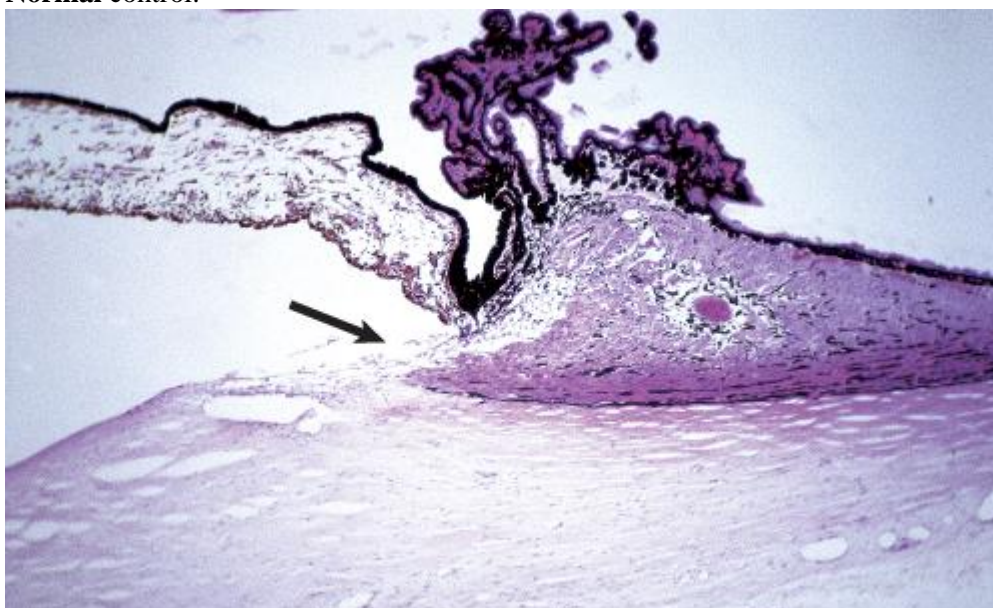
b) **secondary** - due to something **pulling / pushing iris up into angle:**

- posterior pressure from ciliary body / vitreous / lens.
- **contraction of neovascular membrane** (e.g. diabetes, central retinal vein occlusion):
- prolonged apposition or repeated subacute attacks lead to gradual **peripheral anterior synechiae** formation.





Normal control:

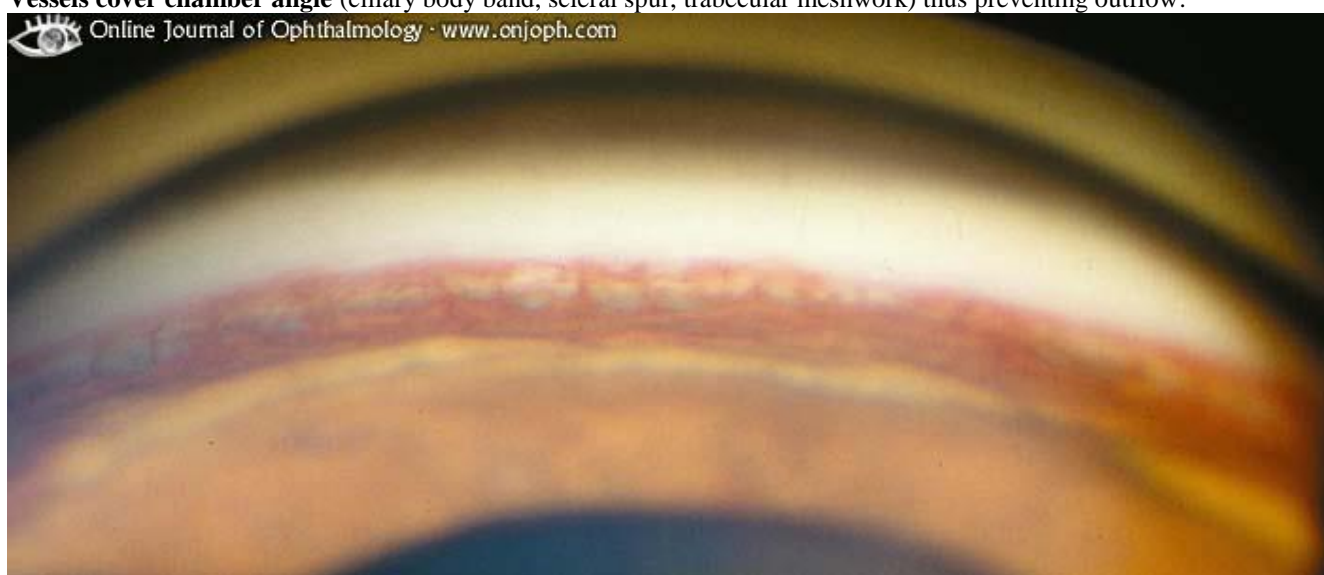


**Proliferative diabetic retinopathy** - active neovascularization over iris surface (esp. in sphincter area); flare in anterior chamber; posterior synechiae:



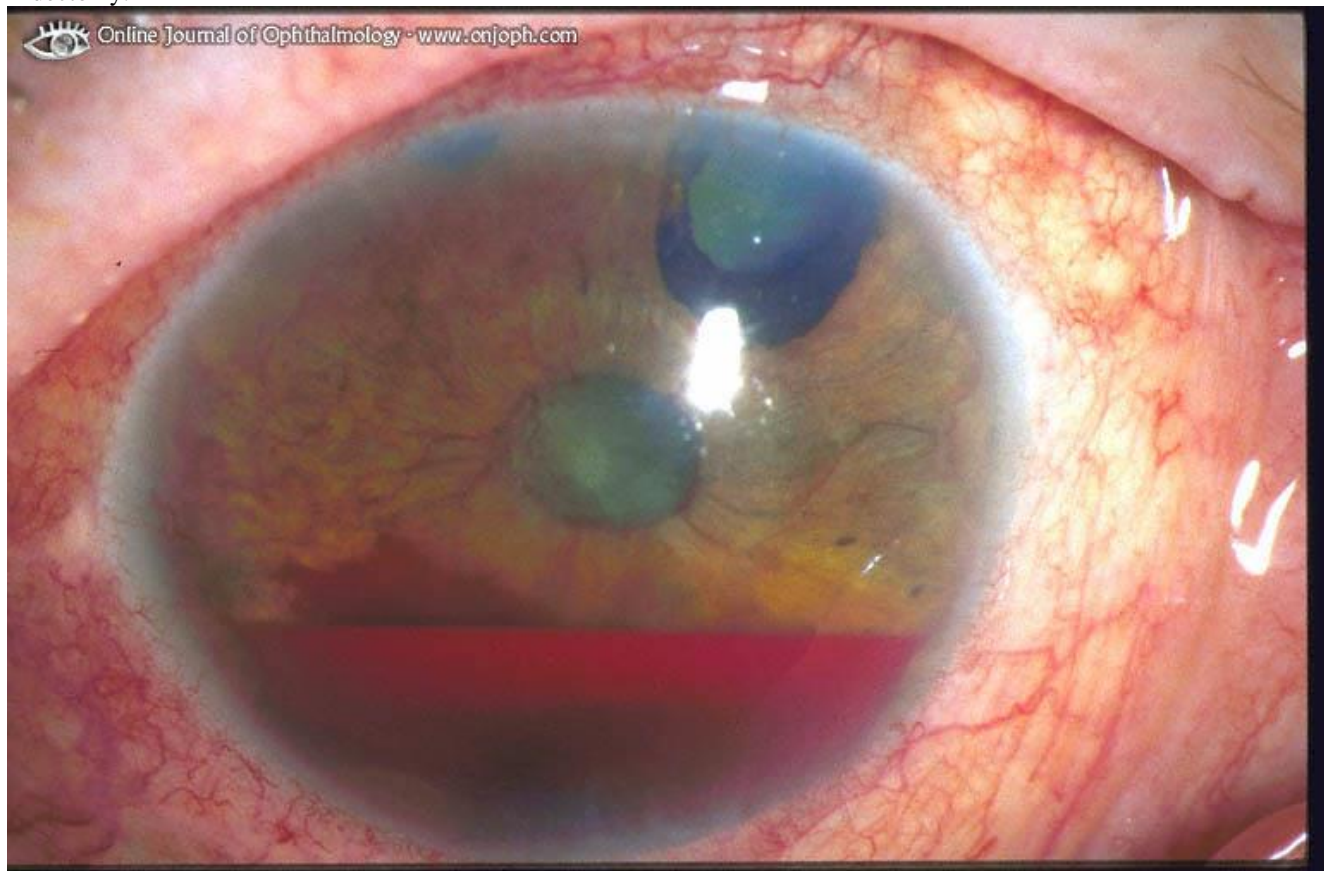
Source of picture: "Online Journal of Ophthalmology" >>

**Vessels cover chamber angle** (ciliary body band, scleral spur, trabecular meshwork) thus preventing outflow:



Source of picture: "Online Journal of Ophthalmology" >>

**Central retinal vein occlusion** with rubeosis iridis, hyphema, secondary angle closure glaucoma; peripheral iridectomy:



Source of picture: "Online Journal of Ophthalmology" >>



**Inflammatory uveitis precipitates** (i.e. synechiae between peripheral iris and angle structures) pulling iris up into angle. Florid uveitis (fibrin strands in pupil and precipitates on inferior corneal endothelium) - mixed injection and distorted pupil; cornea is hazy due to high IOP:



Source of picture: "Online Journal of Ophthalmology" >>

## SYMPTOMS & SIGNS, DIAGNOSIS

**Chronic, subacute, intermittent angle-closure glaucoma** – asymptomatic!

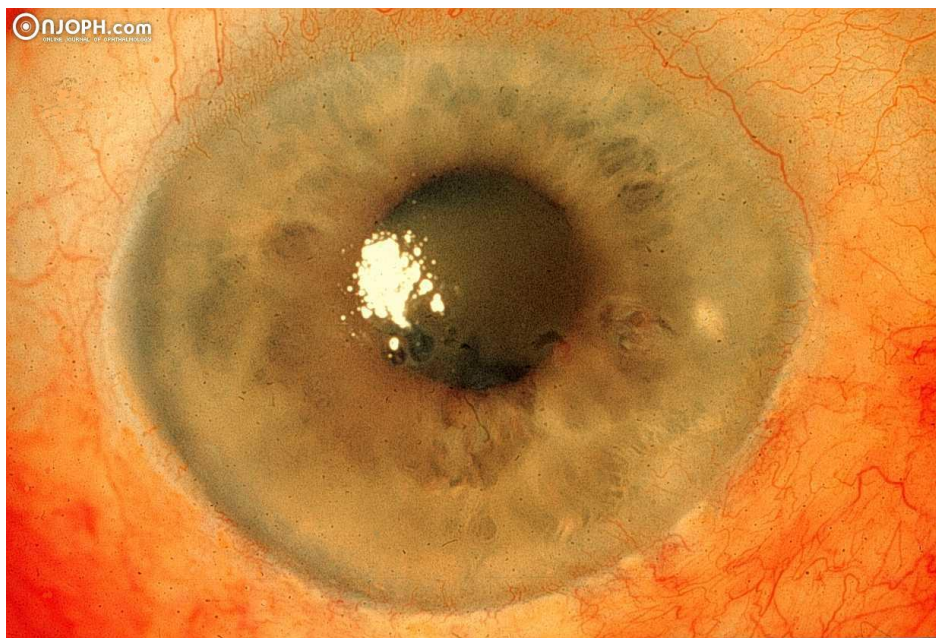
- some may have subtle signs: ocular redness, mild pain, slightly blurred vision, headaches, seeing haloes around lights.
- ocular discomfort improves with sleep (due to sleep-induced miosis).
- **peripheral anterior synechiae / adhesions** may be visible between cornea and iris.

**Acute angle-closure glaucoma attack:**

- commonly **unilateral**.
- **symptoms** - **severe ocular pain & redness**, blurred vision & multicolored halos (due to corneal edema), headache, nausea & vomiting (sometimes have been misdiagnosed as neurologic or GI problem).
- **signs** – diffuse lacrimation, lid edema, ciliary (circumcorneal) and episcleral hyperemia, steamy cornea (edematous and irregular epithelium as indicated by irregular light reflex, bulla formation), fixed irregular mid-dilated pupil, fair amount of anterior chamber inflammation (cells and flare), shallow anterior chamber:



Source of picture: "Online Journal of Ophthalmology" >>



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- patients are extremely uncomfortable and distressed.
- attack may have been *precipitated by pupillary dilation* (peripheral iris relaxes → may bow anteriorly).
- **ophthalmoscopy** - swollen optic disc (vs. excavation in chronic cases).
- **gonioscopy is difficult** (cloudy cornea with friable epithelium); gonioscopy of contralateral eye reveals narrow / occludable angle.  
N.B. if contralateral eye has completely open angle, then other diagnosis must be considered!
- **ultrasonographic biomicroscopy** - gives cross-sections at near-microscopic resolution!

## TREATMENT

**Acute glaucoma attack** (N.B. vision can be lost quickly!!!) – give immediately:

- 1) IV / oral **carbonic anhydrase inhibitor** (vs. in open-angle – administered topically)
  - 2) topical **β-blocker**
  - 3) topical **α2-selective adrenergic agonists**.
- **analgesics** and **antiemetics**.
  - if response inadequate → add **osmotic drug** + **PILOCARPINE** 1-2% twice (15 min apart).  
N.B. miotics are not effective when IOP is > 40-50 mmHg (anoxic pupillary sphincter).



DEFINITIVE TREATMENT of **any angle-closure glaucoma** is **laser peripheral iridotomy** (or **surgical peripheral iridectomy** if laser cannot access) - creates opening in iris (at 12 o'clock) through which humor trapped in posterior chamber can reach anterior chamber and trabecular meshwork.

- in **acute attack**, perform as soon as eye condition permits;
  - before iridotomy, *cornea should be cleared* (with osmotic agents), *pupil should be constricted, IOP should be lowered*.
  - must be performed *bilaterally* (contralateral eye has 80% chance of developing acute attack!);
  - after 1 day postop, may discontinue antiglaucoma medications (that were used in acute attack), but should remain on corticosteroids for 1 week.
- even **asymptomatic patient with occludable angle** (upon gonioscopic examination) must promptly undergo peripheral iridotomy!
- **laser gonioplasty** (creates stromal burns in peripheral iris) is used as:
  - a) *temporary* measure
  - b) *definitive* treatment for PLATEAU IRIS.

## CONGENITAL GLAUCOMA

- *congenital defect in iridocorneal angle*.

- rare disorder; usually bilateral.
- *eyeball becomes considerably enlarged* (**BUPHTHALMOS**, s. **HYDROPTHALMOS**).
- large-diameter cornea is thinned (sometimes cloudy) and bulging; anterior chamber is deep.
- pupil may be large and fixed.
- optic nerve becomes damaged and blindness ensues.
- early surgical intervention (goniotomy, goniotomy, trabeculotomy, trabeculectomy) is mainstay of treatment.

BIBLIOGRAPHY for ch. "Ophthalmology" → follow this [LINK >>](#)