Glaucoma

Last updated: May 9, 2019

INCIDENCE
- Chronic progressive optic nerve damage (glaucomatous optic neuropathy):
  a) due to IOP (at least partly).
  b) that can be arrested / diminished by IOP lowering.

PATHOGENESIS
- Increased IOP leads to loss of retinal ganglion cells.
- Major theories:
  a) Vascular dysfunction causing ischemia to optic nerve.
  b) Mechanical dysfunction (cribriform plate compression of axons).
- Precise mechanisms 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):
- Located in anterior chamber angle— trabecular meshwork → canal of Schlemm → intrascleral channels → episcleral and conjunctival veins.

Secondary (alternative, uveoscleral) outflow system (5.15% aqueous outflow):
- Aqueous exits through anterior surface 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 gonioscopy (i.e. decreased permeability through trabecular meshwork).
2. CLOSED-ANGLE (ANGLE-CLOSURE) glaucoma (10%) - physical obstruction by forward movement of peripheral iris.

According to etiology

I. CHRONIC TONOPATHY / OPEN-ANGLE glaucomas
1. High-pressure glaucomas
   - 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) iridocyclitis
   3) plateau iris
3. Disorders of lens
   1) exfoliation syndrome
   2) lens-induced open-angle glaucoma
   3) lens immunsence and dislocation
4. Disorders of retina, choroid, vitreous
   1) retinal detachment and vitreoretinal abnormalities
   2) neovascular glaucoma
   3) 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, pseudophakia
3. Epithelial, fibrous, endothelial proliferation
4. Corneal surgery
5. Vitreoretinal surgery

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1) elevated IOP (ocular hypertension) - main clinically treatable risk factor!
   - patients with IOP 28 mmHg is 13 times more likely to develop field loss than patients 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 (STERIOD 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 applation is criterion standard.
- difference between eyes ≥ 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).

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.
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 predominately in inferotemporal / superotemporal regions → enlargement of vertical cup):
Moderate glaucoma - localized loss of neuroretinal rim superiorly (notching) with correspondent nerve fiber layer defect (arrow); another localized NFL defect inferiorly (arrow).

Advanced glaucoma - marked loss of neuroretinal rim in all sectors; α-zone parapapillary atrophy; vertical excavation. Elschnig's scleral ring.
**Advanced glaucoma** - deeply cupped optic nerve head; retina is detached artificially.

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

<table>
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<tr>
<th>At Risk</th>
<th>Narrowest rim width (rim/disc ratio)</th>
<th>Example</th>
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<tr>
<td>1</td>
<td>0.4 or more</td>
<td></td>
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<tr>
<td>2</td>
<td>0.3 to 0.39</td>
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<tr>
<td>3</td>
<td>0.2 to 0.29</td>
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<tr>
<td>4</td>
<td>0.1 to 0.19</td>
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<td>5</td>
<td>less than 0.1</td>
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<td>6</td>
<td>0 (extension: less than 45°)</td>
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<td>7</td>
<td>0 (extension: 45° to 90°)</td>
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<td>8</td>
<td>0 (extension: 91° to 180°)</td>
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<td>9</td>
<td>0 (extension: 181° to 270°)</td>
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<tr>
<td>10</td>
<td>0 (extension: more than 270°)</td>
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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:
  1) African Americans
  2) individuals > 40 yrs.

- screening consists of IOP measurements + optic nerve status assessment (funduscopy + visual field examinations).

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.
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 prevent 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) – PHOSPHOSTIGMINE, ISOFLURAN.
- indirect-acting (topical cholinesterase inhibitors):
  a) reversible – TROPICLAMINE, NEOSTIGMINE.
  b) irreversible (increased risk of retinal detachment) – DIEMECALANE, ECHOTHIOPHATE, ISOFLURAN.

II. Carbonic anhydrase inhibitors – ACETAZOLAMIDE (oral, i/v), DICHLORPHENAMIDE (oral), METILAZOLAMIDE (oral), ETIOXAZOLAMIDE (oral), DORZOLAMIDE (topical), BRINZOLAMIDE (topical).
- decrease aqueous production (by inhibiting carbonic anhydrase in ciliary body).

III. Adrenocortical agonists (topical) –
 a) nonselective (rarely used, cause mydriasis - contraindicated in angle-closure) – EPINEPHRINE, DOPAMIN.
 b) α2-selective – APRACLONIDINE, BRIMONIDINE; do not cause mydriasis (mediated by α1).
- decrease aqueous production, increase uveoscleral aqueous outflow.

IV. β-Blockers (topical) – TIMOLOL, BETAXOLOL, LENSENBLOK, CARTOPROST, BIMATOPROST.
- decrease aqueous production.

V. Prostaglandin analogs (topical) – LATANOPROST, TRAVOPROST, VIVOROPROST, UNIPROSTONE.
- 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 irises & lids and thicken lashes.

VI. Osmotic diuretics – GLUCERIN (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 – NETARUSIL, 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 (GL. 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 (i.e. increased risk for endophthalmitis).
C) GLAUCOMA ENSUING IMPLANT (selective outflow 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 ABBLATION (CYCLODESTRUCTION) – freezing or laser - last resort procedure.

FOLLOW-UPS
- frequency varies from weeks to years.
- perform – IOP check, visual field testing, optic disc 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 pupal dilatation.
  b) secondary - due to something pulling / pushing irises 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.

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

Central retinal vein occlusion with rubious iris, hyphema, secondary angle closure glaucoma; peripheral infections.
Inflammatory uveitis precipitates (i.e. synechiae between peripheral iris and angle structures) pulling iris up into angle. Fluid exudate (fibrin strands in pupil) and precipitates on inferior corneal endothelium - mixed injection and distorted pupil. Cornea is hazy due to high IOP:

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 synchiae / 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 problems).
- 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
- 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 goniplasty** (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**, **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 (goniometry, gonipuncture, trabeculotomy, trabeculectomy) is mainstay of treatment.

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