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What is it?

A disease of progressive optic neuropathy with loss of retinal neurons and their axons (nerve fiber layer) resulting in blindness if left untreated.
“Glaucoma describes a group of diseases that kill retinal ganglion cells.”

“High IOP is the strongest known risk factor for glaucoma but it is neither necessary nor sufficient to induce the neuropathy.”

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What causes it?

There is a dose-response relationship between intraocular pressure and the risk of damage to the visual field.
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ADVANCED GLAUCOMA INTERVENTION STUDY

Low Pressure Reduces Vision Loss

AGIS Study

Mean IOP

- 20.2 mm Hg
- 16.9 mm Hg
- 14.7 mm Hg
- 12.3 mm Hg

Follow-up month

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How do we diagnose it?

- IOP is not helpful diagnostically until it reaches approximately 40 mm Hg at which level the likelihood of damage is significant.
- Visual fields are also not helpful in the early stages of diagnosis because a considerable number of neurons must be lost before VF changes can be detected.
- Optic nerve damage in the early stages is difficult or impossible to recognize.
- 50% of people with glaucoma do not know it!
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Intraocular pressure is not the only factor responsible for glaucoma!

- 95% of people with elevated IOP will never have the damage associated with glaucoma.
- One-third of patients with glaucoma do not have elevated IOP.
- Most of the ocular findings that occur in people with glaucoma also occur in people without glaucoma.
CHARACTERISTICS OF IOP

- Normal range: 10-22 mm Hg
- Follows non-Gaussian curve with right skewed tail
- 30-50% of open angle glaucoma patients have IOP <22 mmHg
- Diurnal fluctuation normally < 6 mmHg
- Women have slightly higher pressures
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Anatomy of anterior chamber angle
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Iris bombé
GLAUCOMA

Population distribution of IOP
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IOP Variables

Gender influences:

Normal vs glaucoma:
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Angle Anatomy

Normal Angle
How do we measure IOP?

- Applanation
- Tonopen
- Schiotz
- Air
- Non-contact
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Tonometry

Applanation

Schiotz
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Goldmann applanation tonometer
GLAUCOMA

Tonopen
GLAUCOMA

Goldmann perimeter

Glaucoma visual fields
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The normal visual field: an island of vision in a sea of darkness:
THE VISUAL FIELD

Humphrey automated perimetry
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Visual fields in glaucoma

Early

Late

<table>
<thead>
<tr>
<th>GHT</th>
<th>Outside normal limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD</td>
<td>-14.33 dB P &lt; 0.5%</td>
</tr>
<tr>
<td>PSD</td>
<td>12.13 dB P &lt; 0.5%</td>
</tr>
</tbody>
</table>

Total Deviation

Pattern Deviation

< 5%

< 2%

< 1%

< 0.5%
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Cup-to-disk ratio
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DISK CUPPING

Normal  Glaucoma
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Glaucomatous cupping
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The histology of glaucomatous optic nerve cupping:

Normal:

Glaucomatous:
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Optic nerve signs of glaucoma progression

- Increasing C:D ratio
- Development of disk pallor
- Disc hemorrhage (60% will show progression of visual field damage)
- Vessel displacement
- Increased visibility of lamina cribosa
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Ocular hypertension treatment study
(OHTS study)

- **GOALS:** To evaluate the effectiveness of topical ocular hypotensive medications in preventing or delaying visual field loss and/or optic nerve damage in subjects with ocular hypertension at moderate risk for developing open-angle glaucoma (POAG).

- **POPULATION:** 1636 participants aged 40-80 years with IOP 24-32 mm HG in one eye, and 21-32 in the other, randomly assigned to observation and treatment groups.
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OHTS parameters

- **TREATMENT GOALS:** Reduce pressure to less than or equal to 24 mm Hg with a minimum pressure reduction of 20% from the baseline.

- **OUTCOME MEASURES:** Development of reproducible visual field abnormality or development of optic disc deterioration.

- **MEDICATIONS USED:** beta-adrenergic antagonists, prostaglandin analogues, topical carbonic anhydrase inhibitors, alpha-2 agonists, parasympathomimetic agents, and epinephrine.
At 60 months, the probability of developing glaucoma was:
9.5% in observation group
4.4% in treatment group
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OHTS parameters that influence the risk of developing POAG

- IOP
- Age
- Cup-disk ratio
- Central corneal thickness
Percentage of OHTS participants in observation group who developed POAG (mean follow-up = 72 mo)

IOP vs central corneal thickness
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Percentage of OHTS participants in observation group who developed POAG (mean follow-up = 72 mo)

Vertical CD ratio vs central corneal thickness
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Normal central corneal thickness: 545 – 550 µ

Add or subtract 2.5 mmHg for each 50 µ change in central corneal thickness
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Types of glaucoma

I. Primary:
   A. Congenital
   B. Hereditary
   C. Adult (common types)
      1. Narrow angle
      2. Open angle
         (Normal tension glaucoma)

II. Secondary
   A. Inflammatory
   B. Traumatic
   C. Rubeotic
   D. Phacolytic
      etc.
# Congenital Glaucoma

**Onset:** antenatally to 2 years old

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritability</td>
<td>Elevated IOP</td>
</tr>
<tr>
<td>Photophobia</td>
<td>Buphthalmos</td>
</tr>
<tr>
<td>Epiphora</td>
<td>Haab’s striae</td>
</tr>
<tr>
<td>Poor vision</td>
<td>Corneal clouding</td>
</tr>
<tr>
<td></td>
<td>Glaucomatous cupping</td>
</tr>
<tr>
<td></td>
<td>Field loss</td>
</tr>
</tbody>
</table>
Congenital Glaucoma

Buphthalmos and cloudy corneas
Congenital Glaucoma

Buphthalmos, glaucomatous cupping, and cloudy cornea OD

Haab’s striae

Normal OS
# Narrow Angle Glaucoma

**Onset:** 50+ years of age

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe eye/headache pain</td>
<td>Red, teary eye</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>Corneal edema</td>
</tr>
<tr>
<td>Red eye</td>
<td>Closed angle</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Shallow AC</td>
</tr>
<tr>
<td>Halos around lights</td>
<td>Mid-dilated, fixed pupil</td>
</tr>
<tr>
<td>Intermittent eye ache at night</td>
<td>“Glaucomflecken”</td>
</tr>
<tr>
<td></td>
<td>Iris atrophy</td>
</tr>
<tr>
<td></td>
<td>AC inflammation</td>
</tr>
</tbody>
</table>
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Angle anatomy

Grade I                       Grade 0     Grade III               Grade II

Grade I angle (slitlike angle) Potentially can be occluded

Grade 0 angle (closed angle) Complete occlusion

Grade III angle (wide open) Cannot be occluded

Grade II angle (open angle) Angle approach slightly narrower than Grade III; angle structures less visible, cannot be occluded
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Anatomy of Angle Closure Glaucoma
Narrow Angle Glaucoma

Mid-dilated, fixed pupil
Narrow Angle Glaucoma

Treatment: Peripheral Iridotomy
# Open Angle Glaucoma

Aka: chronic simple glaucoma (CSG) and primary open angle glaucoma (POAG)

## Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Age</td>
<td>Myopia</td>
</tr>
<tr>
<td>Race</td>
<td>Gender</td>
</tr>
<tr>
<td>Family history</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Central corneal thickness</td>
<td>Hormones</td>
</tr>
</tbody>
</table>
# Open Angle Glaucoma

**Onset:** 50+ years of age

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usually none</td>
<td>Elevated IOP</td>
</tr>
<tr>
<td>May have loss of central and peripheral vision</td>
<td>Visual field loss</td>
</tr>
<tr>
<td>late</td>
<td>Glaucomatous disk changes</td>
</tr>
</tbody>
</table>
Normal Tension Glaucoma
(NPG, LTG, LPB, NTG)

- Similar to OAG but IOP always < 21 mmHg
- Higher prevalence of vasospastic disorders, blood dyscrasias, autoimmune diseases
- May be related to episodic hypotension, hyopthyroidism
- A diagnosis of exclusion!!!
Open Angle Glaucoma

Risk factors

**HISTORY:**
- Positive family history
- African American and Hispanic background
- History of trauma
- History of steroid use

**EXAMINATION:**
- C/D 0.6 or greater
- Vertical elongation of disc
- Inf. rim thinner than sup.
- C/D asymmetry > 0.2
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Treatment

Medical
- Miotics
- Beta-blockers
- Carbonic anhydrase inhibitors
- Prostaglandin analogues
- Alpha-2 agonists

Surgical
- Argon laser trabeculoplasty
- Trabeculectomy
- Filtering procedure
- Cyclocryotherapy
- Cyclolaser ablation
- Iridotomy
# GLAUCOMA

## Treatment

### Mechanisms of Action of Glaucoma Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Increase outflow facility?</th>
<th>Increase uveoscleral outflow?</th>
<th>Decrease aqueous flow?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bimatoprost</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Latanoprost</td>
<td>???</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Travoprost</td>
<td>???</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Brimonidine</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Timolol</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Dorzolamide</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
</tr>
</tbody>
</table>

**Table 1.** When selecting an adjunctive medication, consider agents with complementary mechanisms of action. (Figure taken from 3 Targets series)
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Surgical treatment of glaucoma

Argon laser trabeculoplasty

Filtration procedures
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Filtration blebs

Filtering Surgery
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Genetics

- Three causative genes found: MYOC (myocilin); OPTN (optineurin); and WDR36 (WD repeat domain 36)
- So far, 20 loci involving myocilin (MYOC) have been found in humans
- Myocilin levels are ubiquitous and uniform
- Outflow facility decreased in mutants
- Myocilin not found in aqueous humor of mutants but higher concentrations in trabecular meshwork
- Myocilin found intra- and extracellularly but not in nucleus
- Prolonged and dramatic induction by steroids
- Mutations in MYOC inhibits extracellular appearance of MYOC exosomes in TM cells
THANK YOU ALL FOR LISTENING!