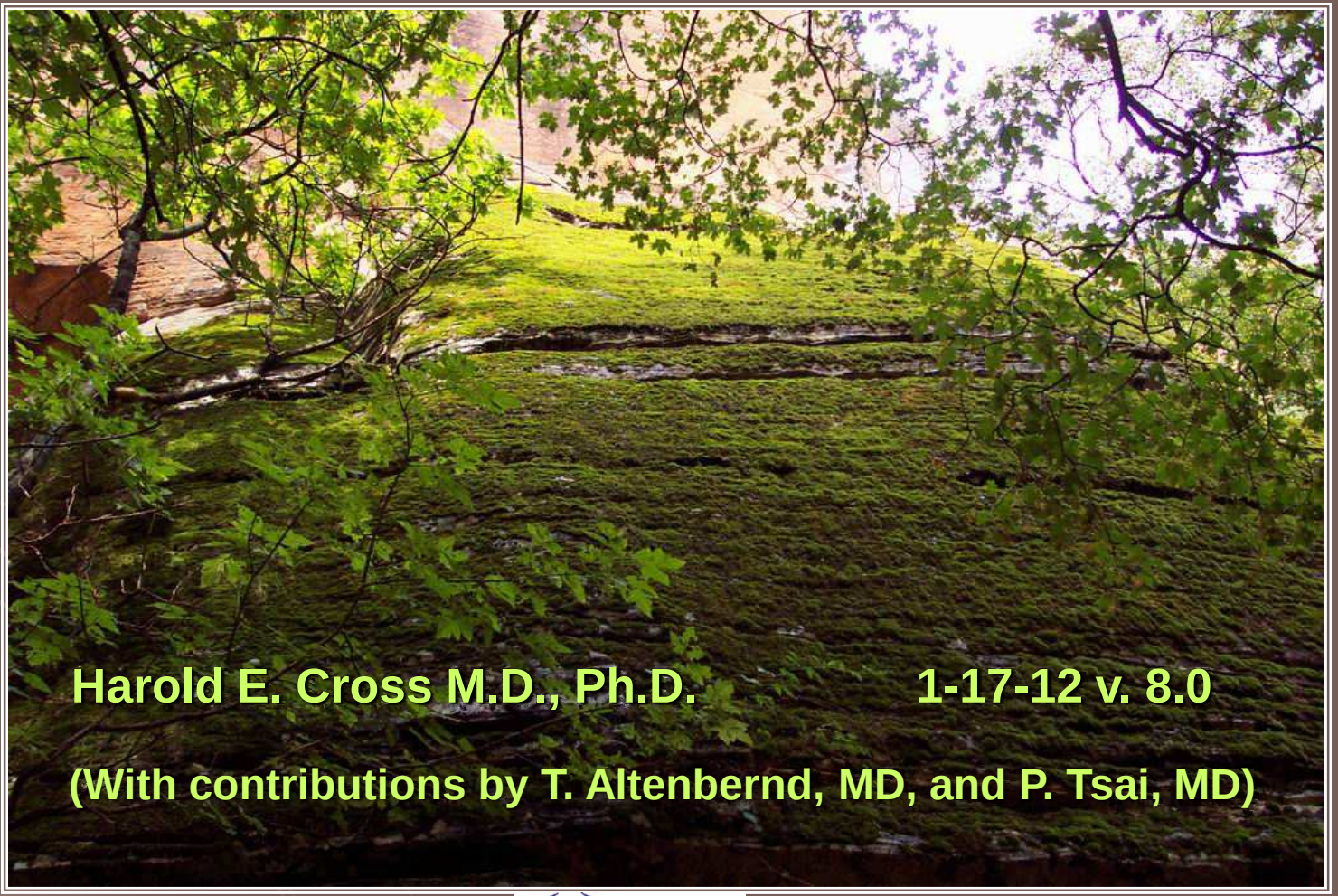
GLAUCOMA



Harold E. Cross M.D., Ph.D. 1-17-12 v. 8.0

(With contributions by T. Altenbernd, MD, and P. Tsai, MD)

OPHTHALMOLOGY

GLAUCOMA

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

"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."

Libby, RT, et al: Annu Rev Genomics Hum Genet 6: 15, 2005

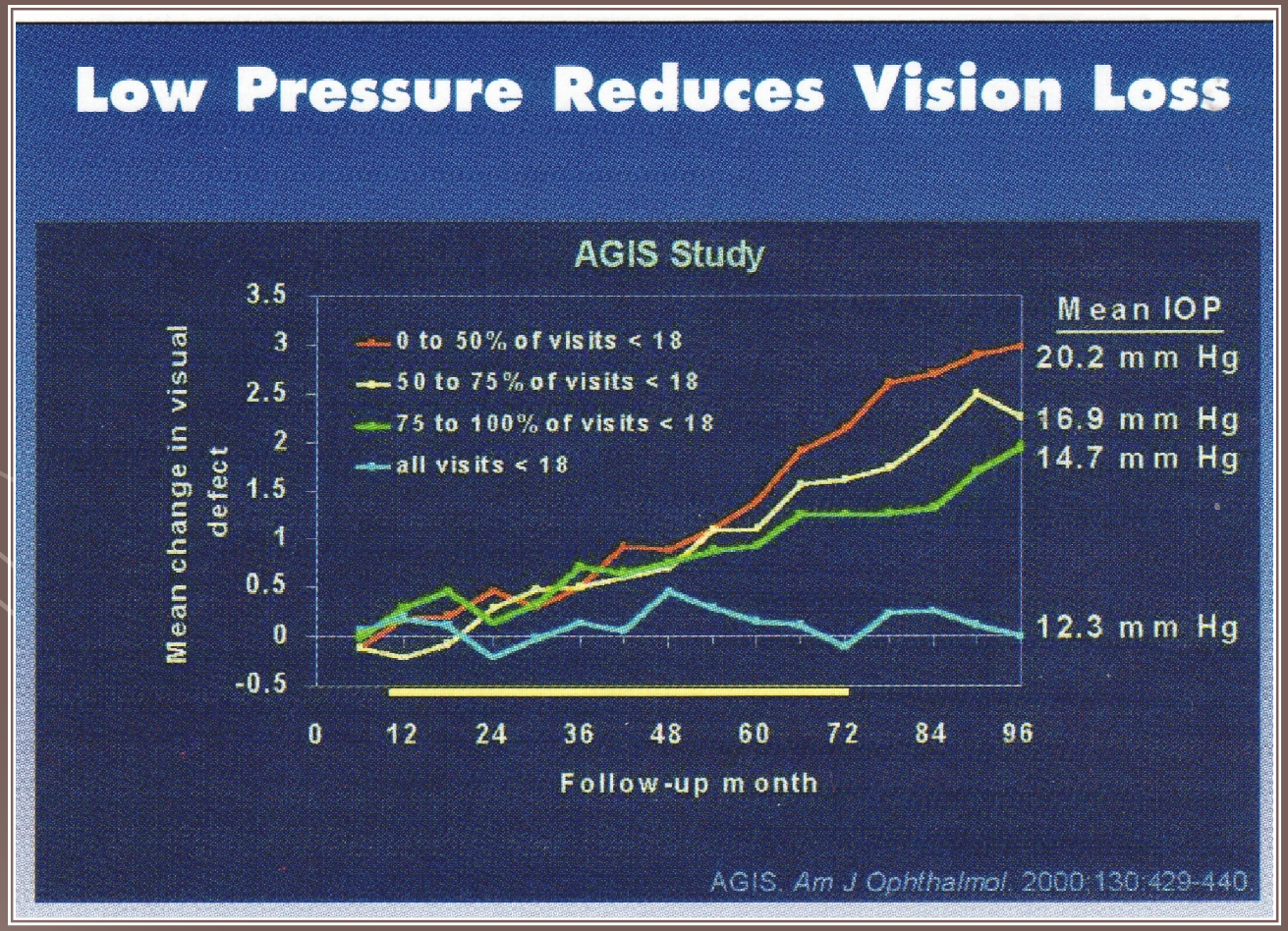
GLAUCOMA

What causes it?

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

GLAUCOMA

ADVANCED GLAUCOMA INTERVENTION STUDY



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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!

GLAUCOMA

Intraocular pressure is not the only factor responsible for glaucoma!

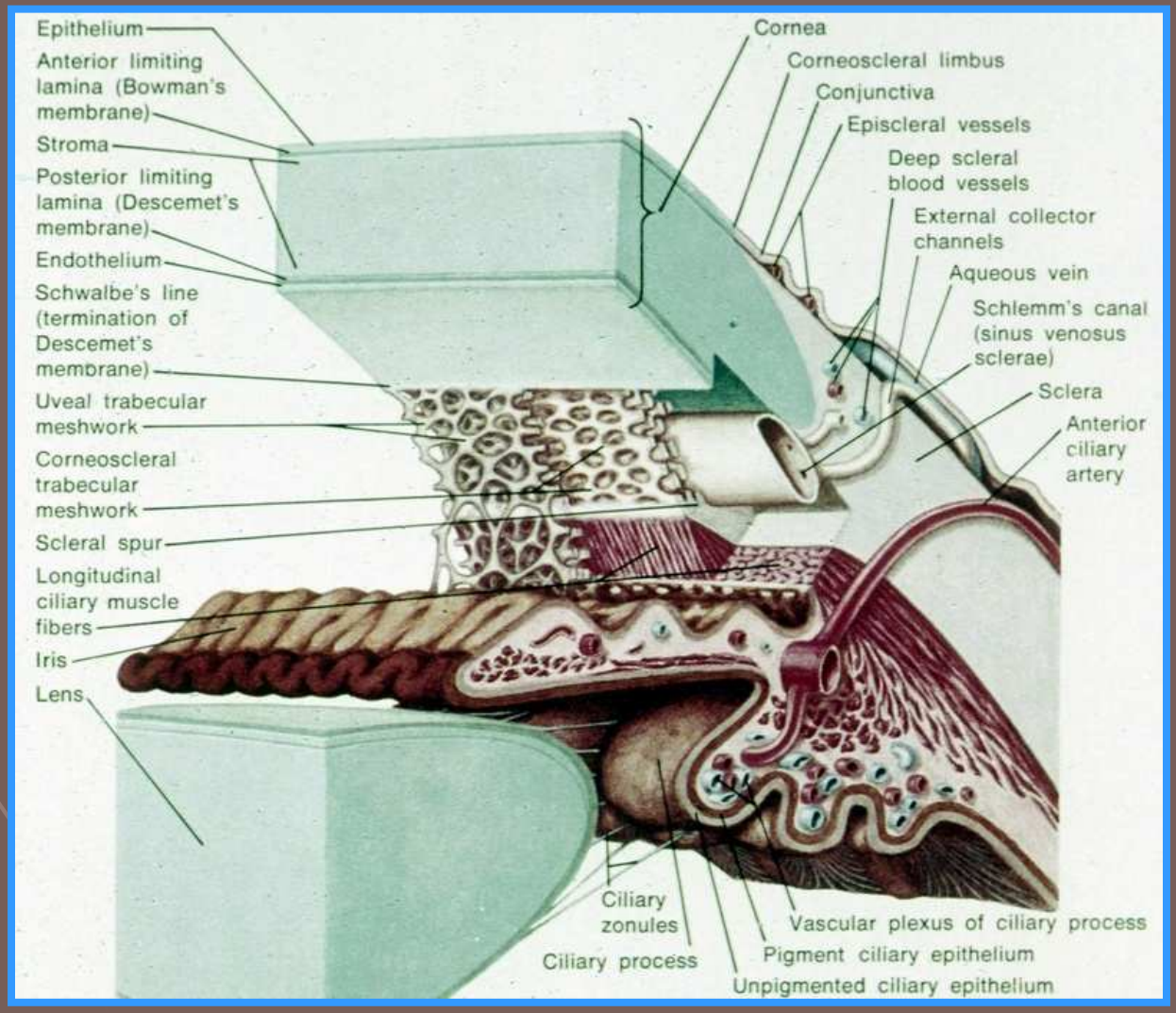
- **95% of people with elevated IOP will never have the damage associated with glaucoma.**
- **One-third of patients with glaucoma do not have elevated IOP.**
- **Most of the ocular findings that occur in people with glaucoma also occur in people without glaucoma.**

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 flucuation normally < 6 mmHg
- Women have slightly higher pressures

GLAUCOMA

Anatomy of anterior chamber angle



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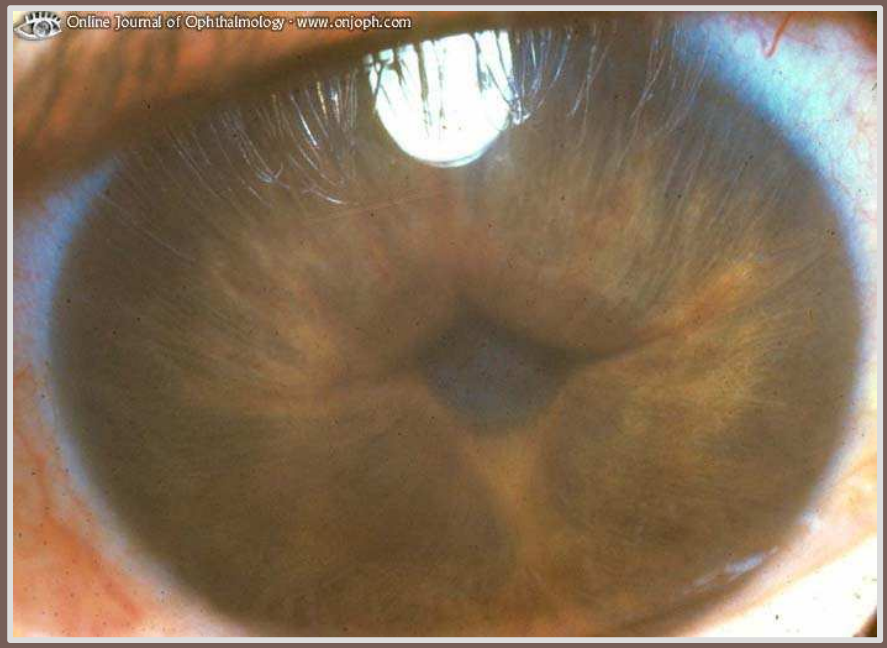
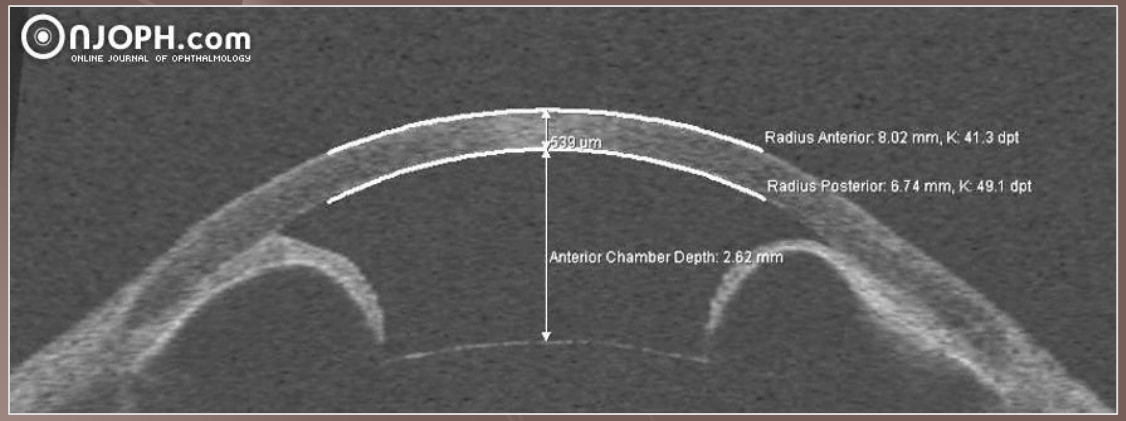
Iris bombé





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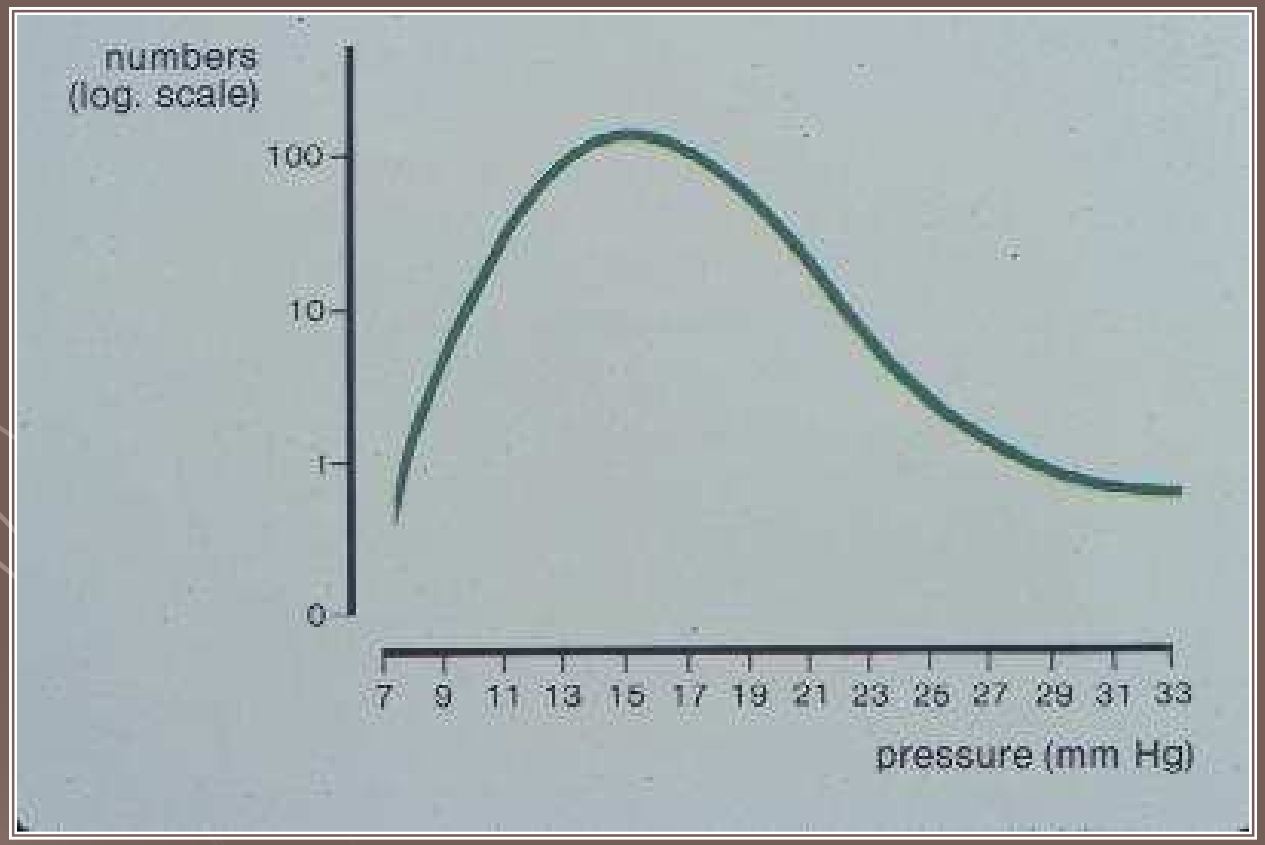
Population distribution of IOP



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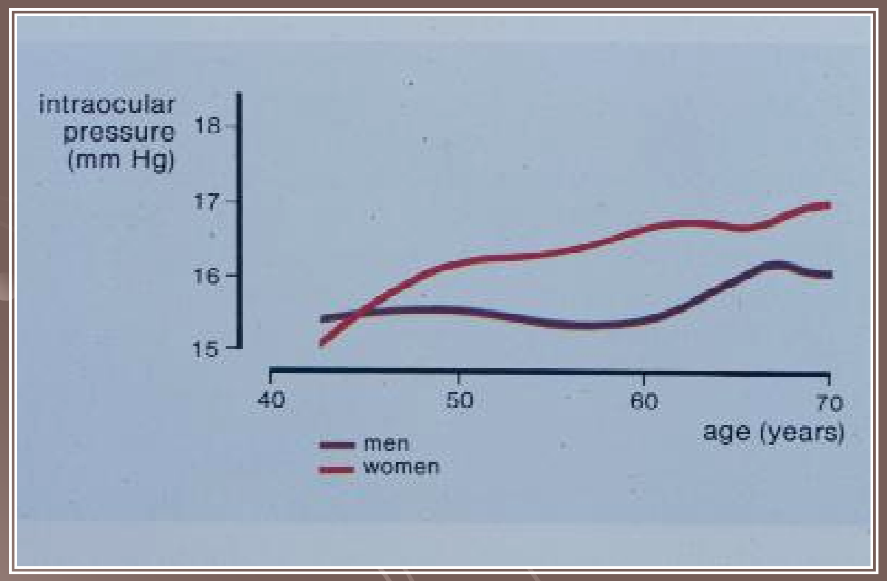
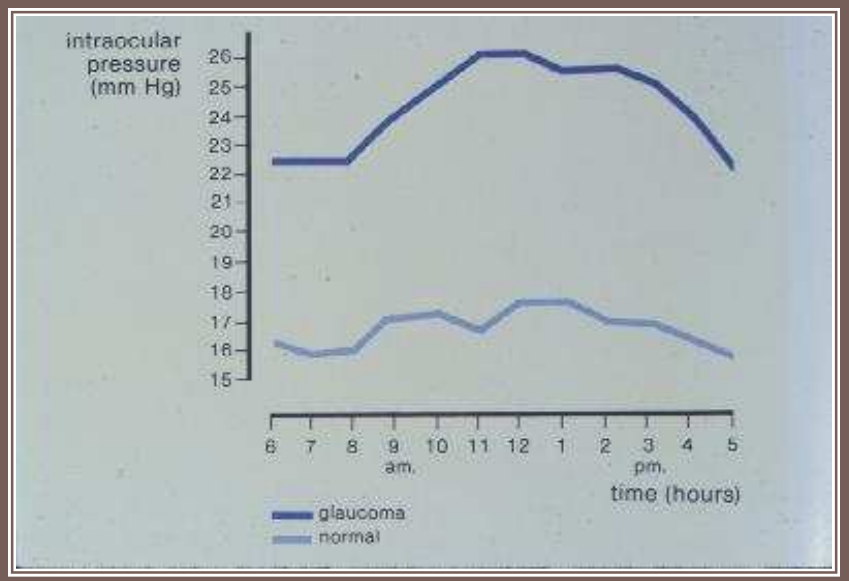
IOP Variables

Gender influences:



Normal vs glaucoma:



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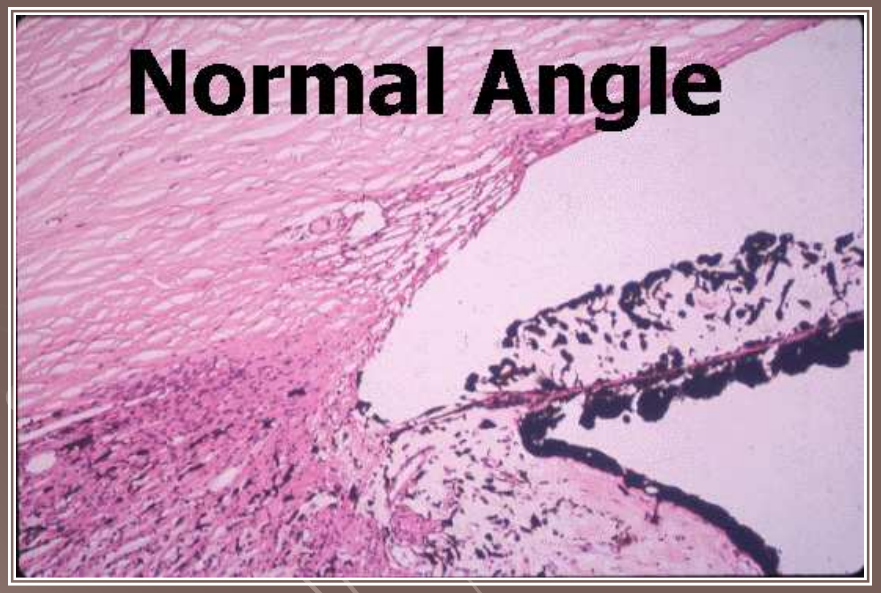
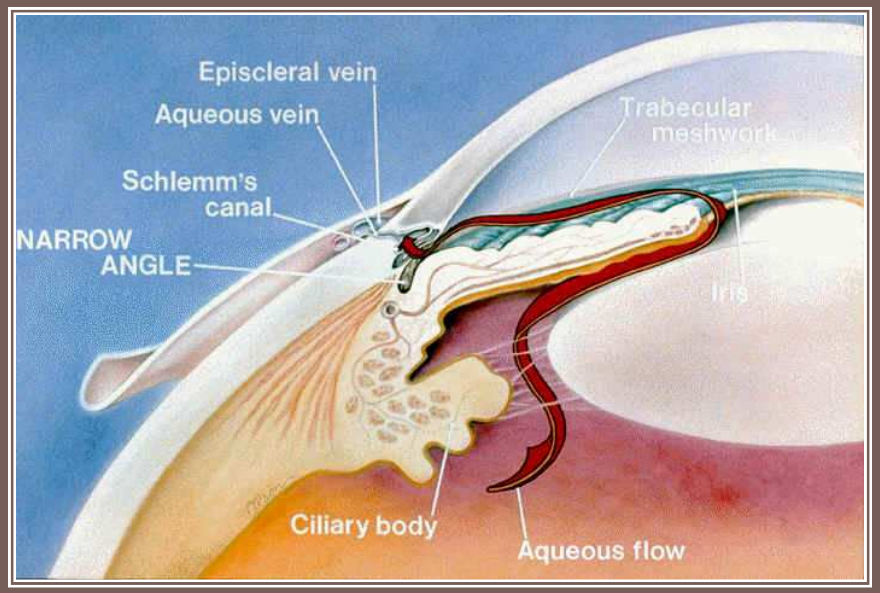
Angle Anatomy





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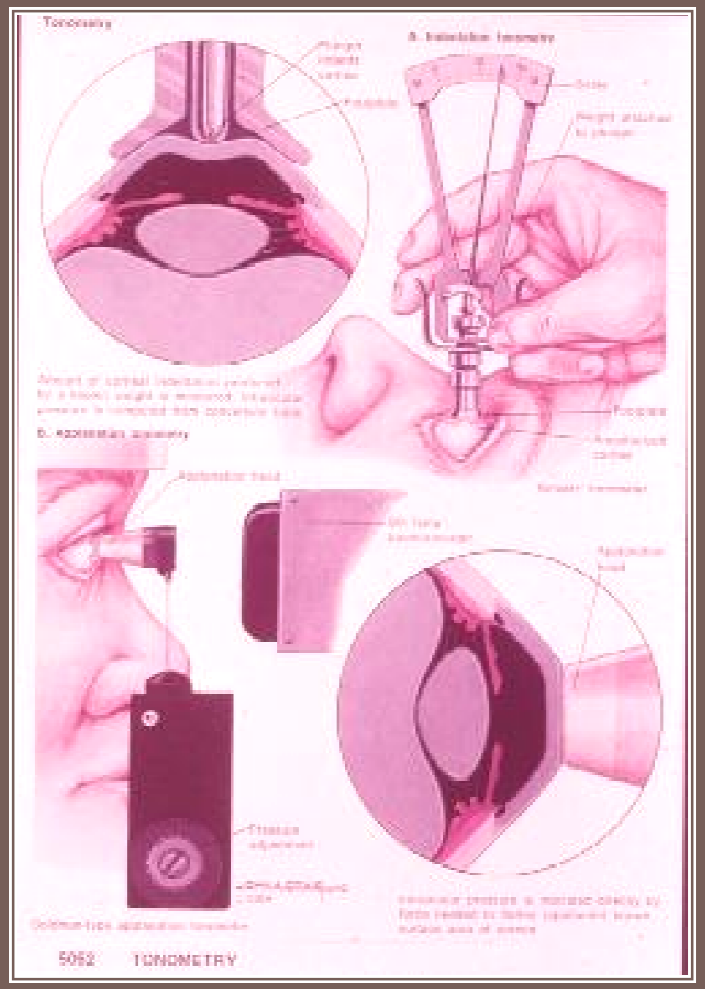
How do we measure IOP?

- **Applanation**
- **Tonopen**
- **Schiotz**
- **Air**
- **Non-contact**



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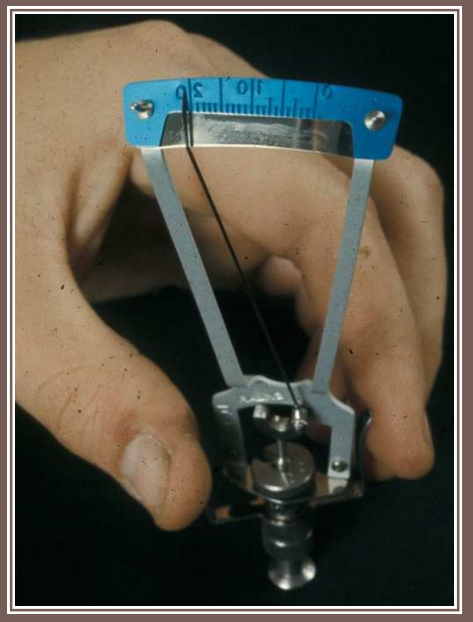
Tonometry

Applanation

Schiotz



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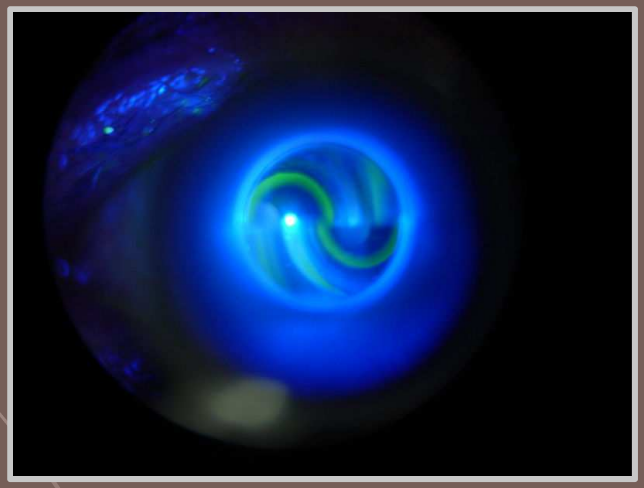
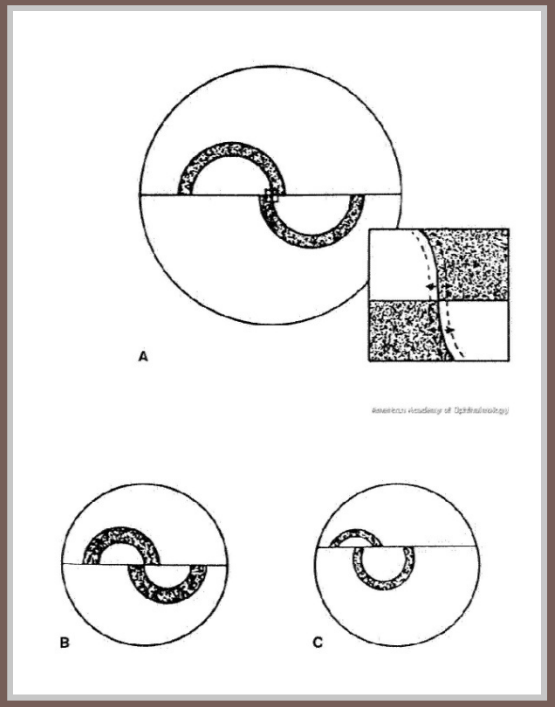
Goldmann applanation tonometer





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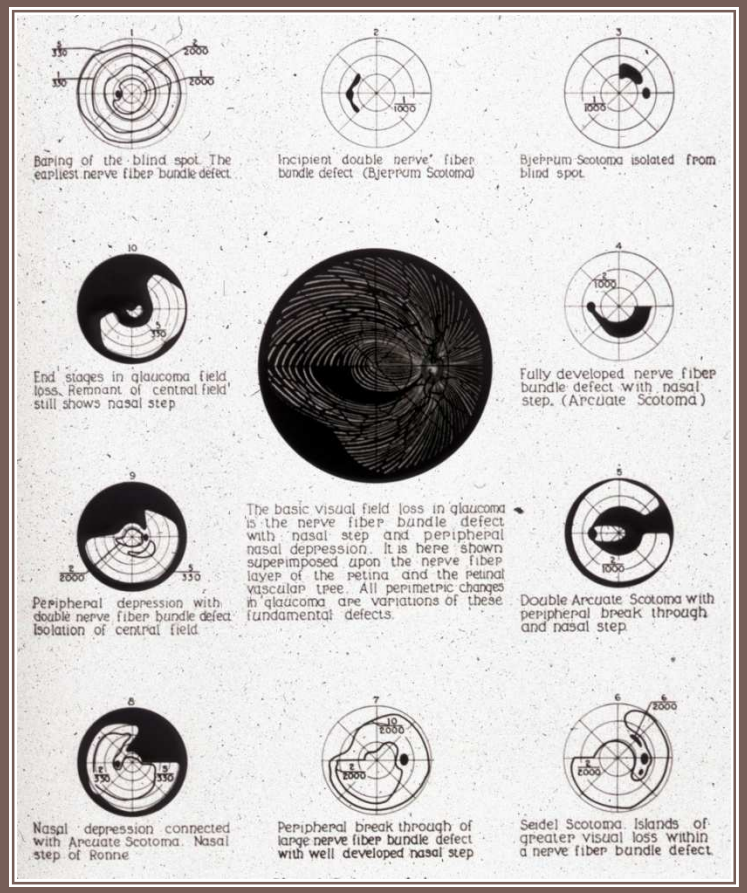
Tonopen

GLAUCOMA

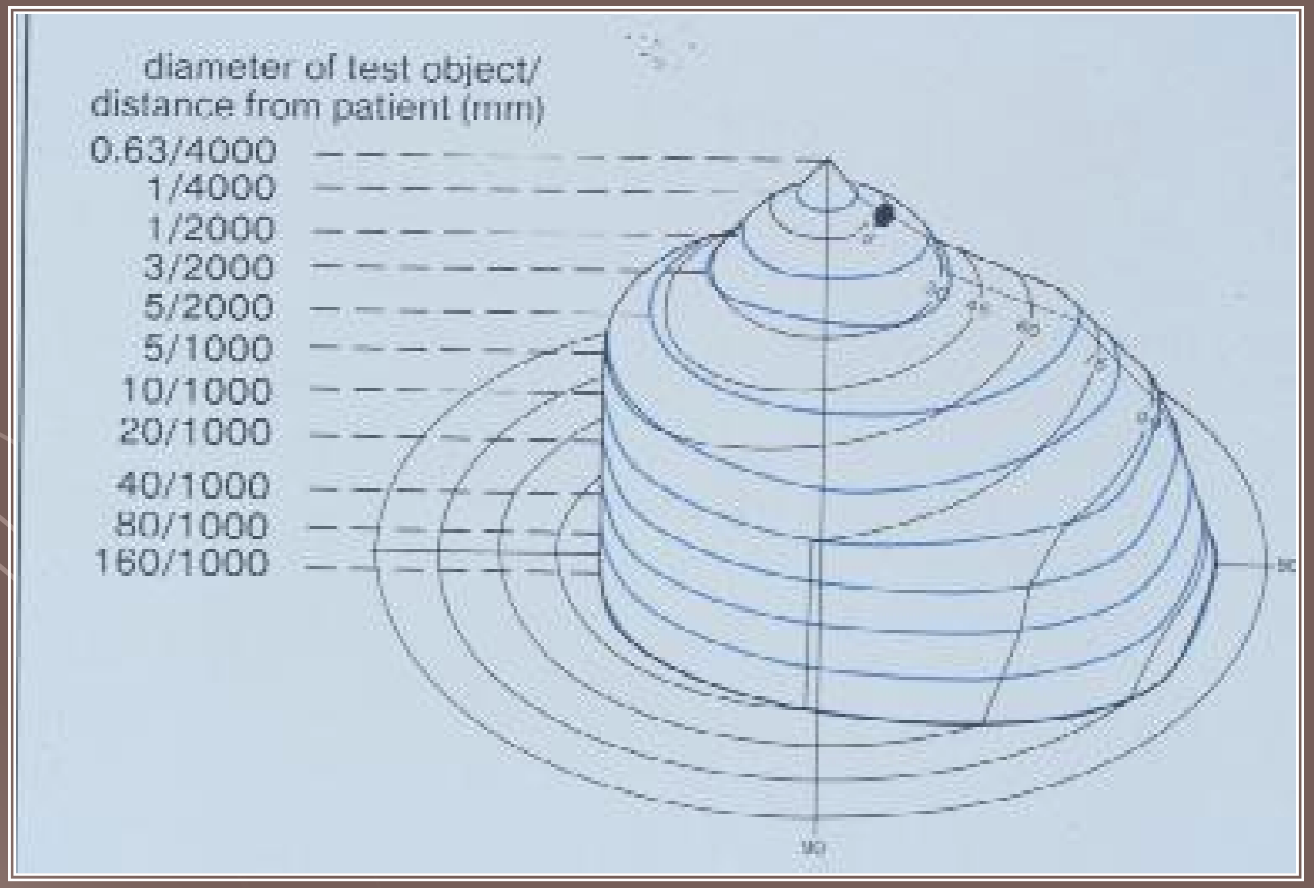
Goldmann perimeter

Glaucoma visual fields



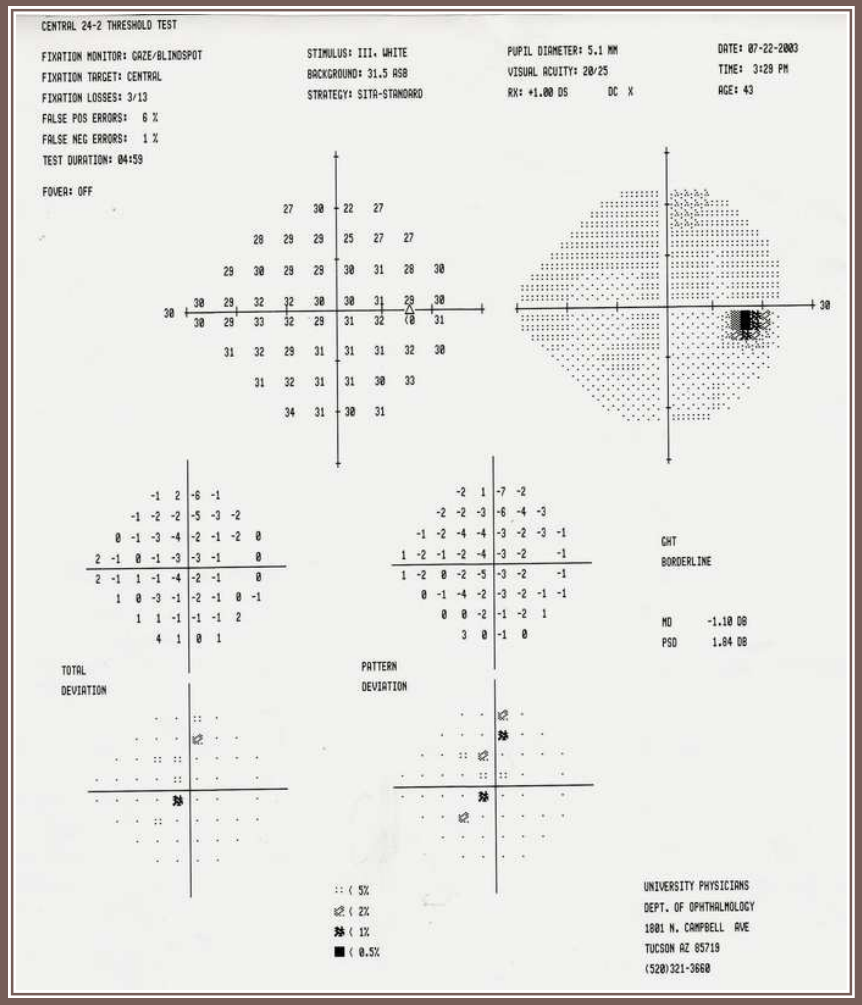
GLAUCOMA

The normal visual field: an island of vision in a sea of darkness:



THE VISUAL FIELD

Humphrey automated perimetry



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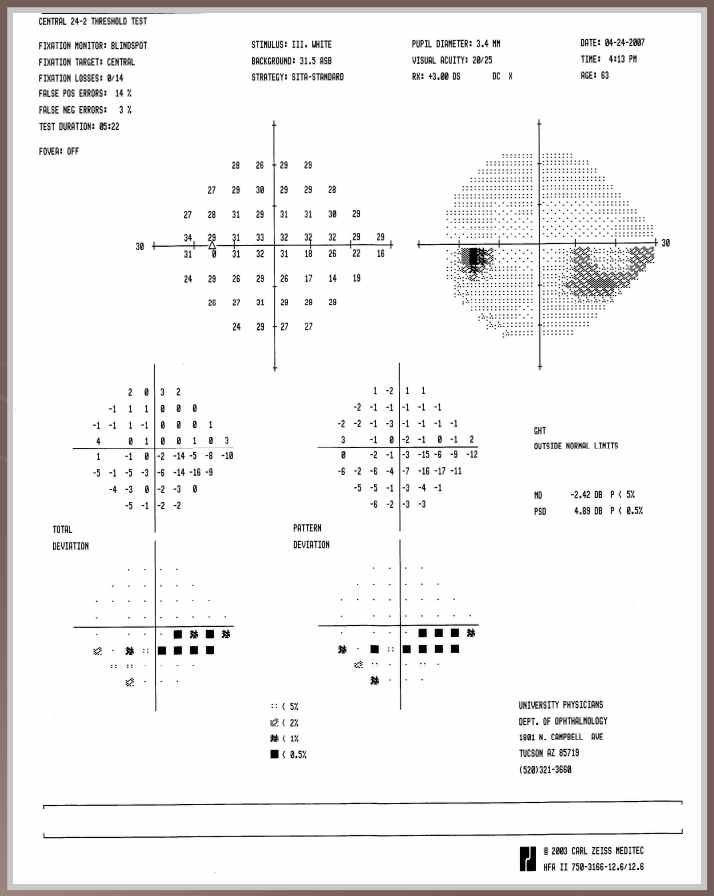
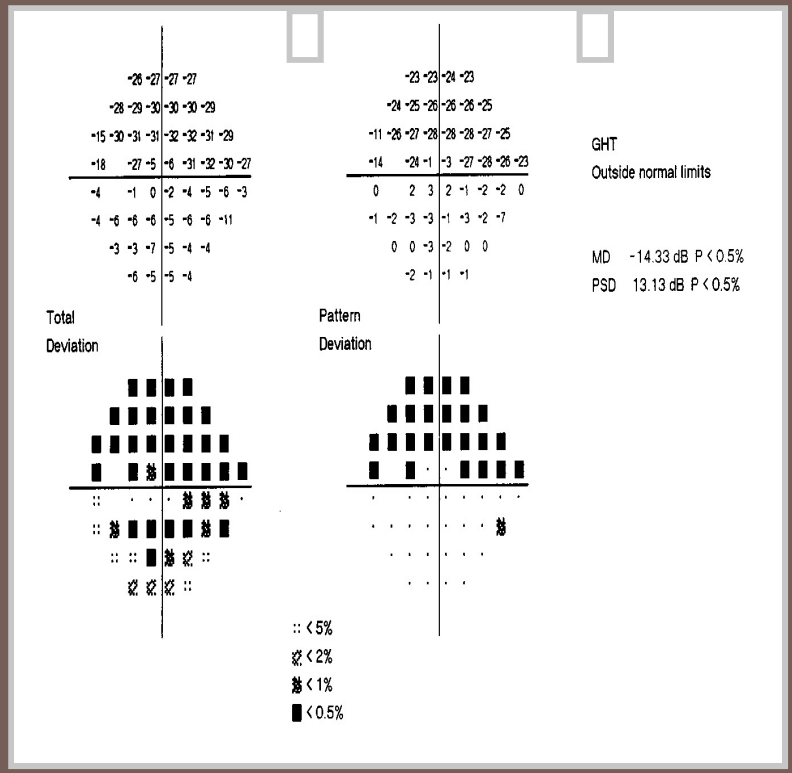
Visual fields in glaucoma

Early



Late



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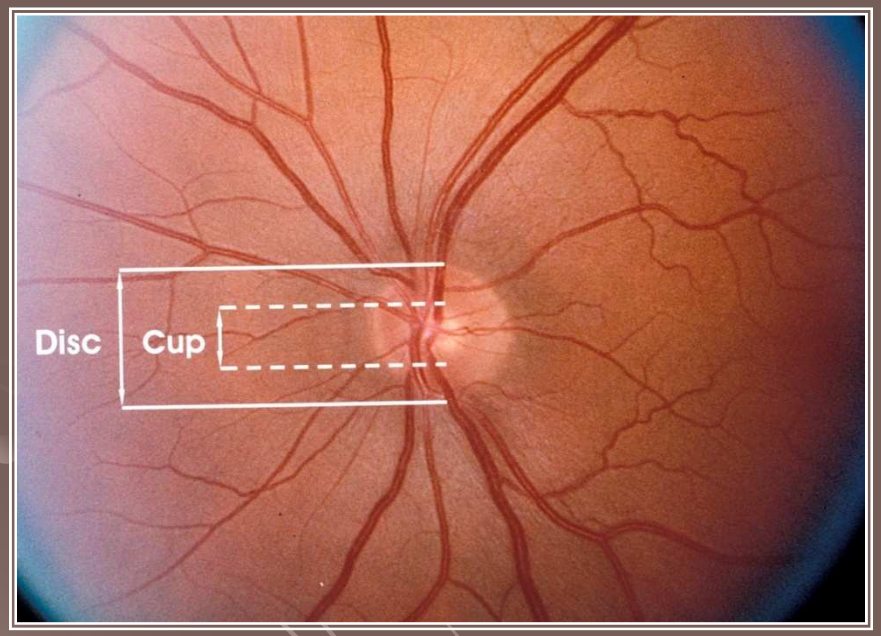
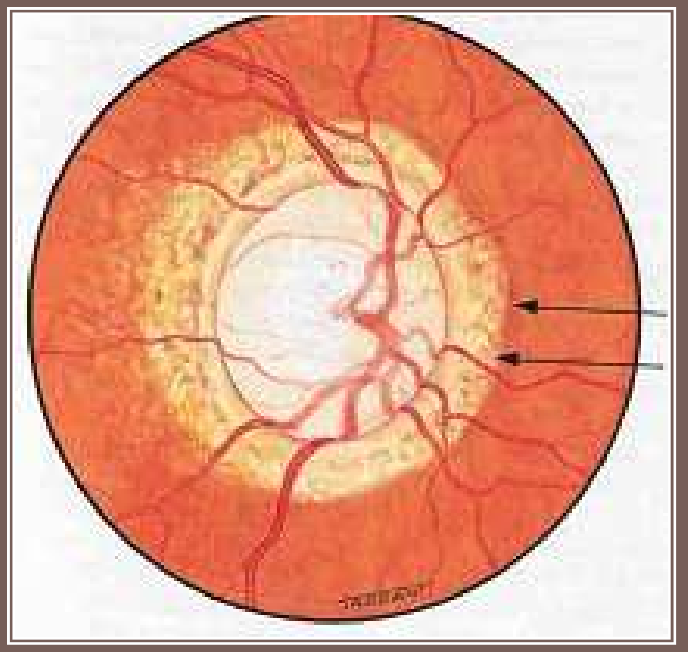
Cup-to-disk ratio

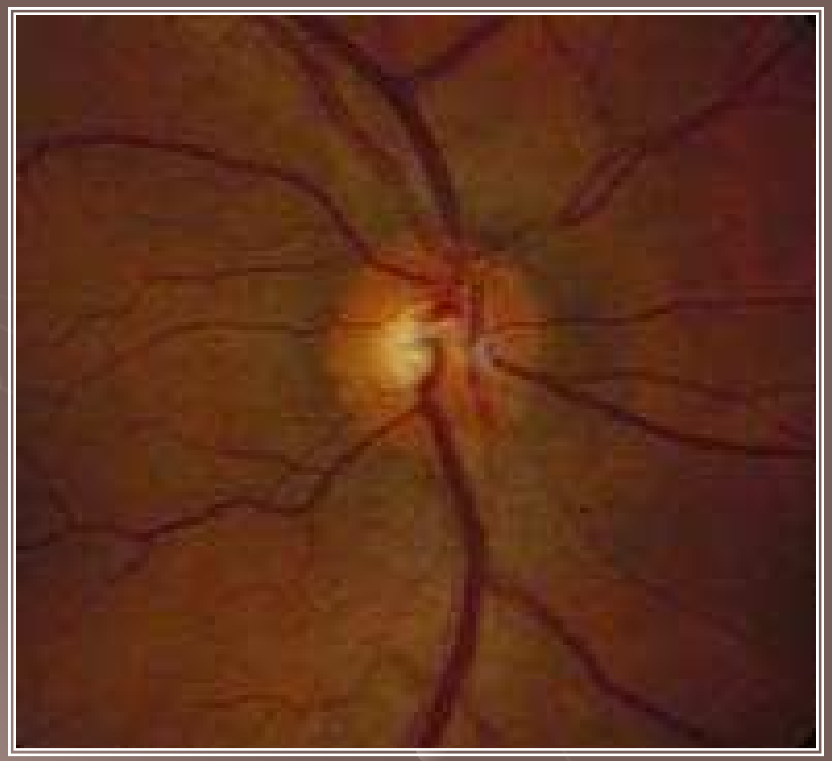




GLAUCOMA

DISK CUPPING

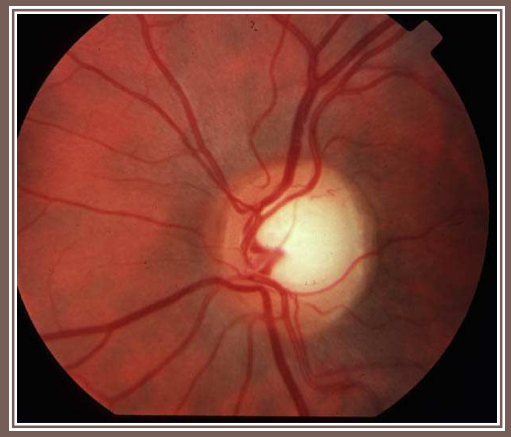
Normal

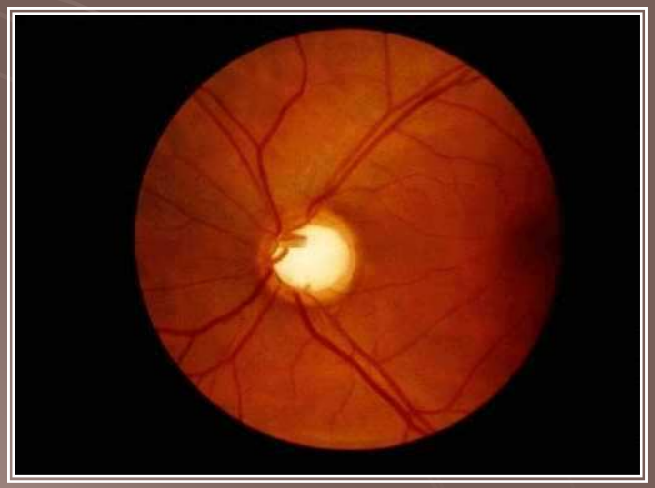


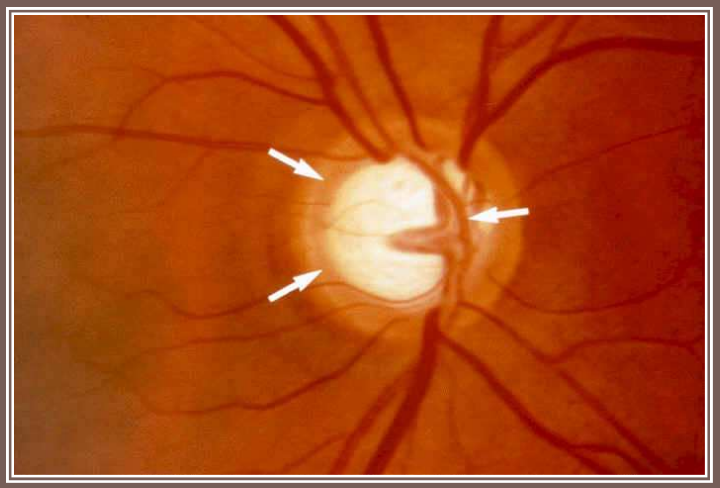
Glaucoma

GLAUCOMA

Glaucomatous cupping







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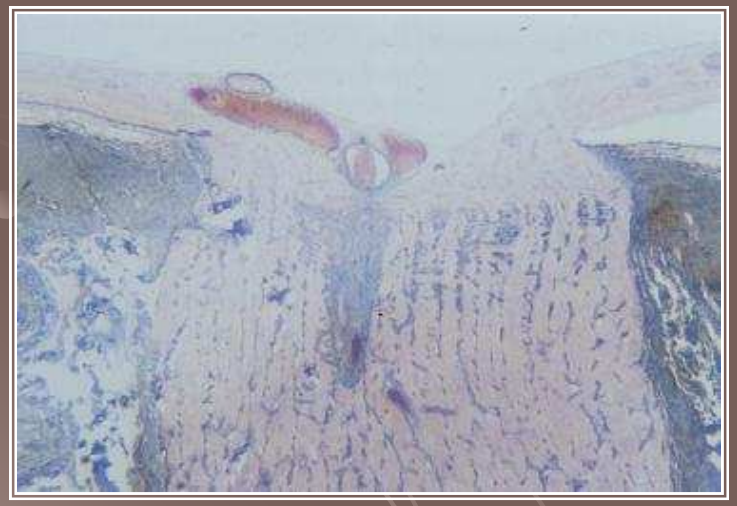
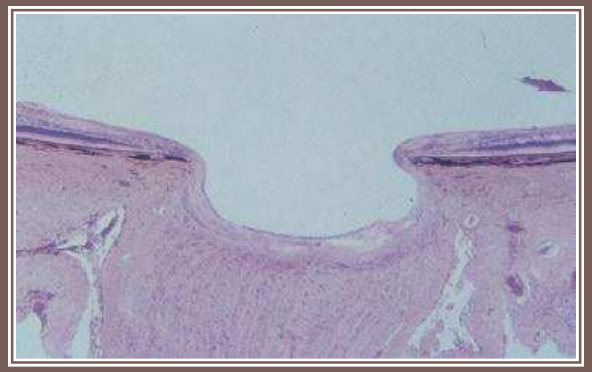
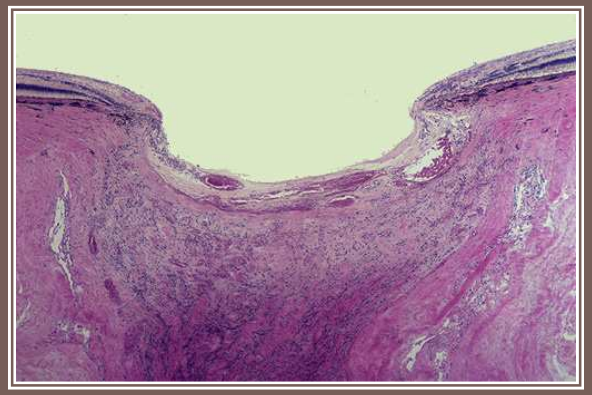
The histology of glaucomatous optic nerve cupping:

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.

GLAUCOMA

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.

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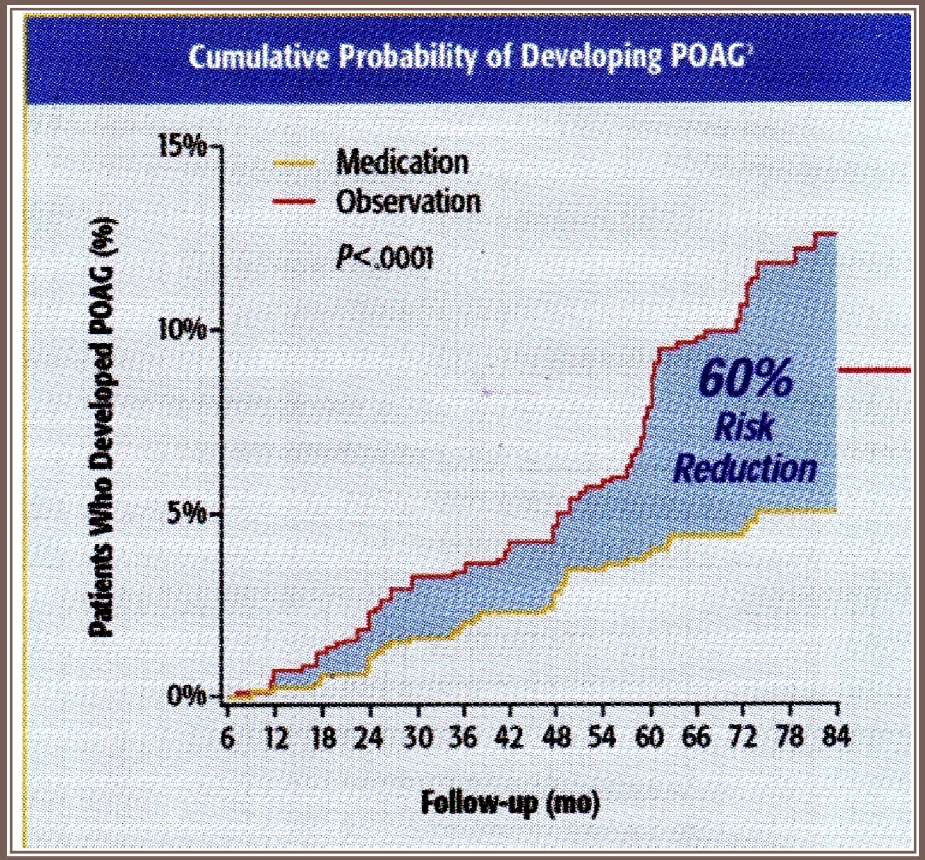
OHTS Conclusions

At 60 months, the probability of developing glaucoma was:

9.5% in observation group

4.4% in treatment group



GLAUCOMA

OHTS parameters that influence the risk of developing POAG

IOP

Age

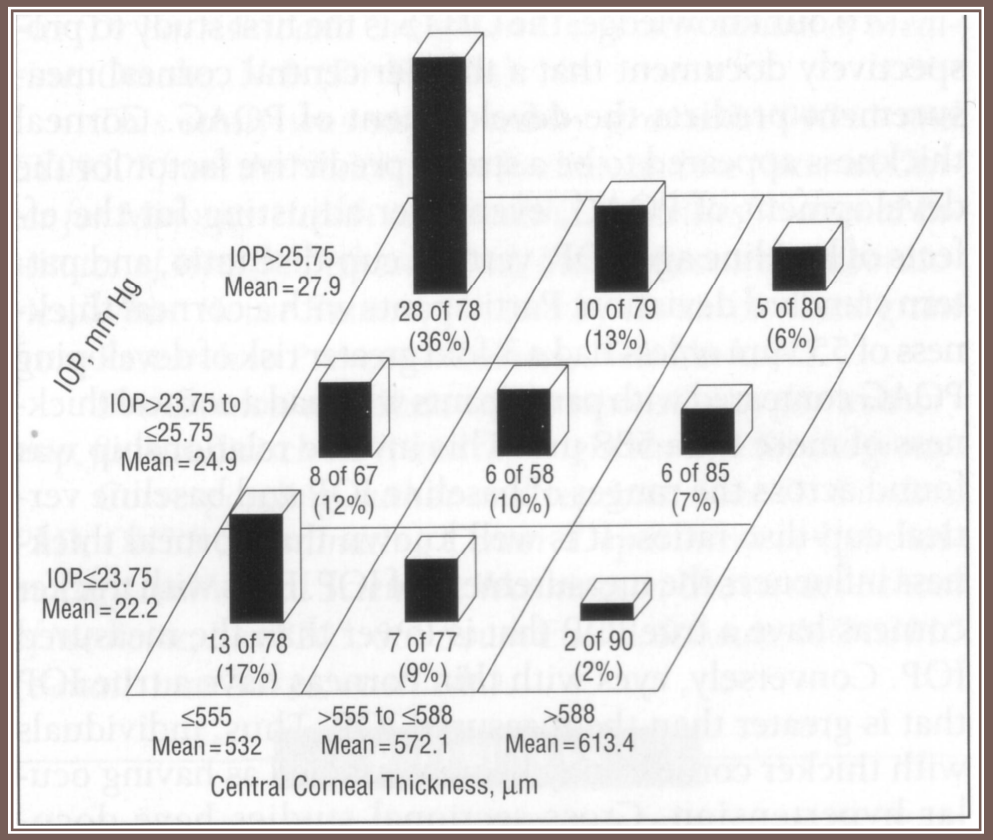
Cup-disk ratio

Central corneal thickness

GLAUCOMA

Percentage of OHTS participants in observation group who developed POAG (mean follow-up = 72 mo)

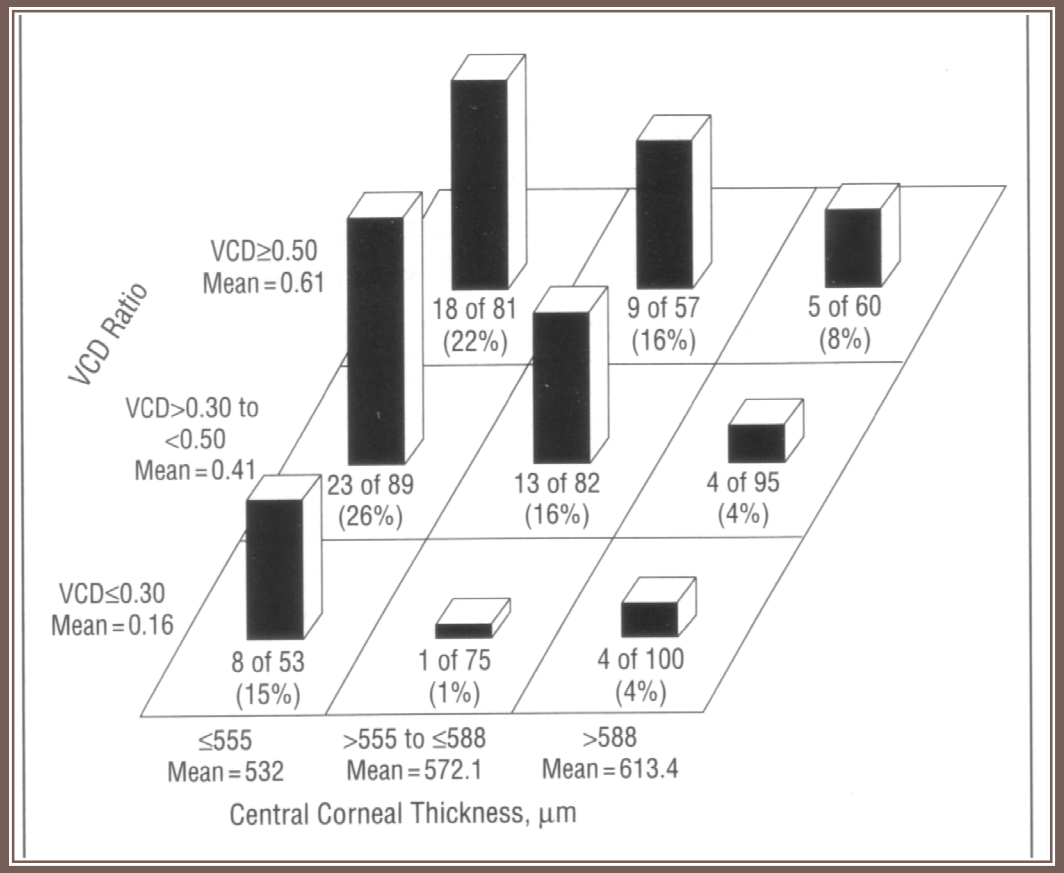
IOP vs central corneal thickness



GLAUCOMA

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 u

Add or subtract 2.5 mmHg for each 50 u 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

Symptoms

- Irritability
- Photophobia
- Epiphora
- Poor vision

Signs

- Elevated IOP
- Buphthalmos
- Haab's striae
- Corneal clouding
- Glaucomatous cupping
- Field loss

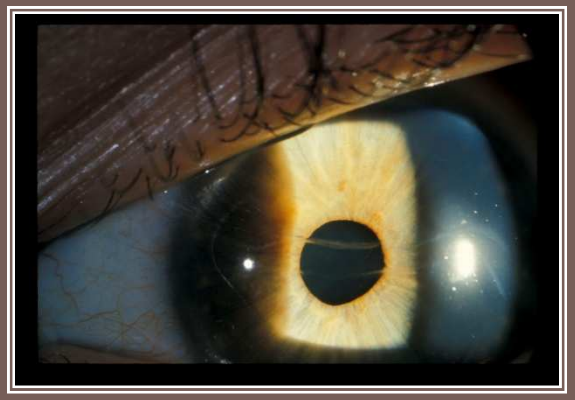
Congenital Glaucoma

Buphthalmos and cloudy corneas

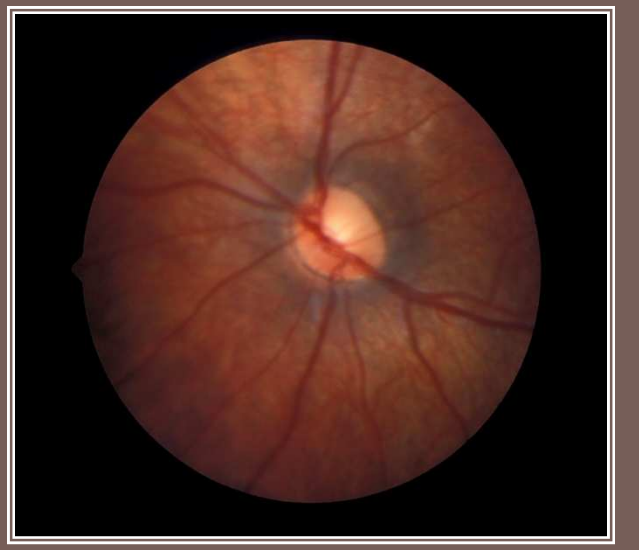
Congenital Glaucoma

Buphthalmos, glaucomatous cupping, and cloudy cornea OD

Normal OS



Haab's striae



Narrow Angle Glaucoma

Onset: 50+ years of age

Symptoms

- Severe eye/headache pain
- Blurred vision
- Red eye
- Nausea and vomiting
- Halos around lights
- Intermittent eye ache at night

Signs

- Red, teary eye
- Corneal edema
- Closed angle
- Shallow AC
- Mid-dilated, fixed pupil
- "Glaucomflecken"
- Iris atrophy
- AC inflammation

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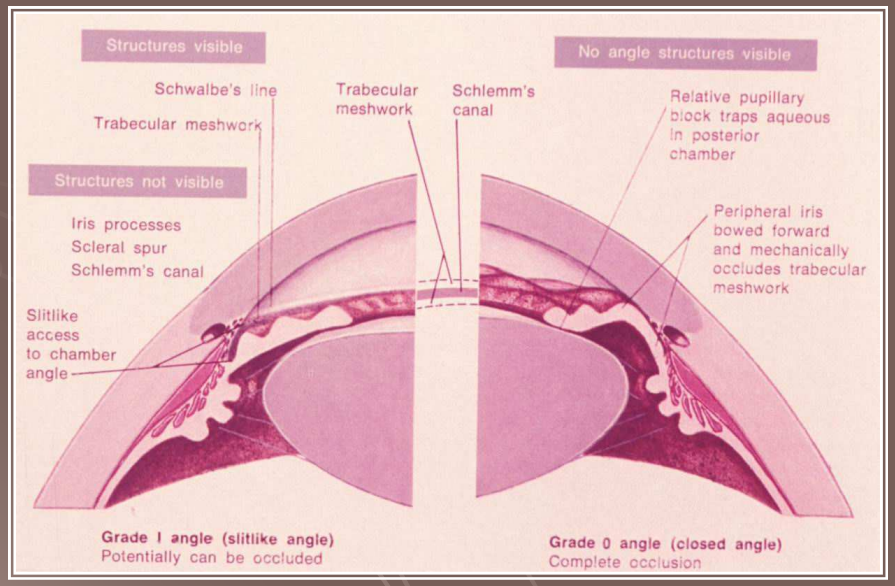
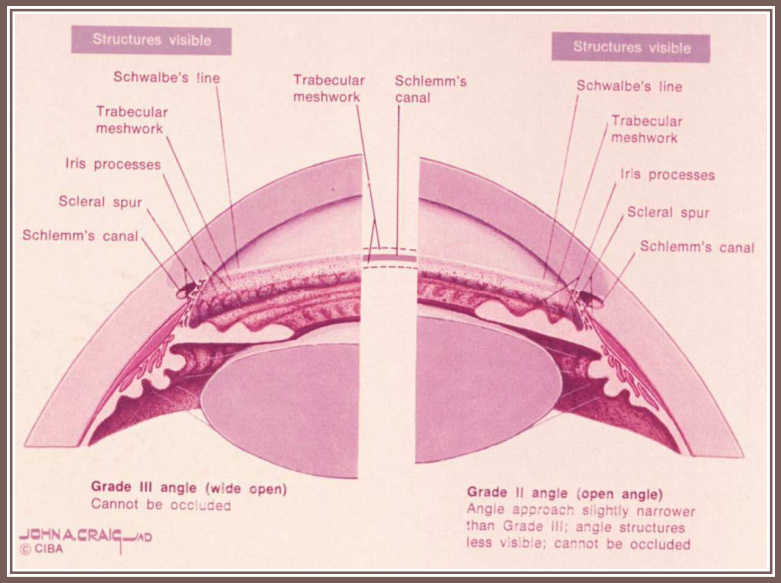
Angle anatomy

Grade I **Grade 0** **Grade III** **Grade II**





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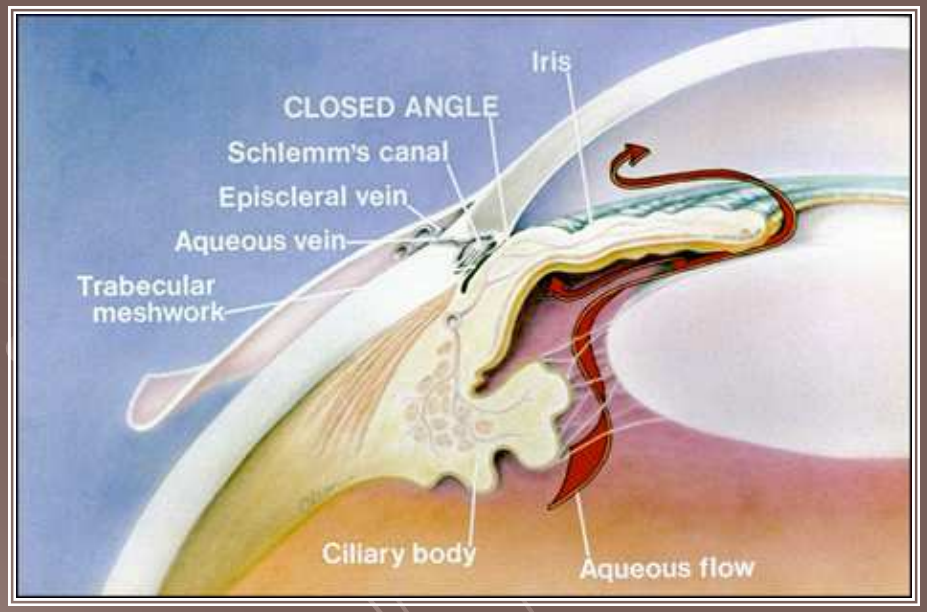
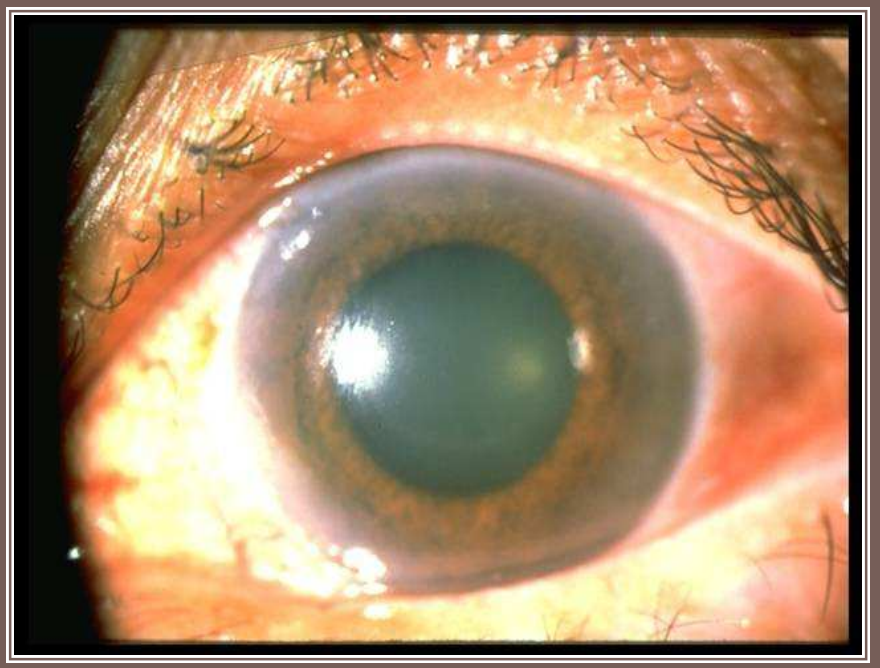
Anatomy of Angle Closure Glaucoma



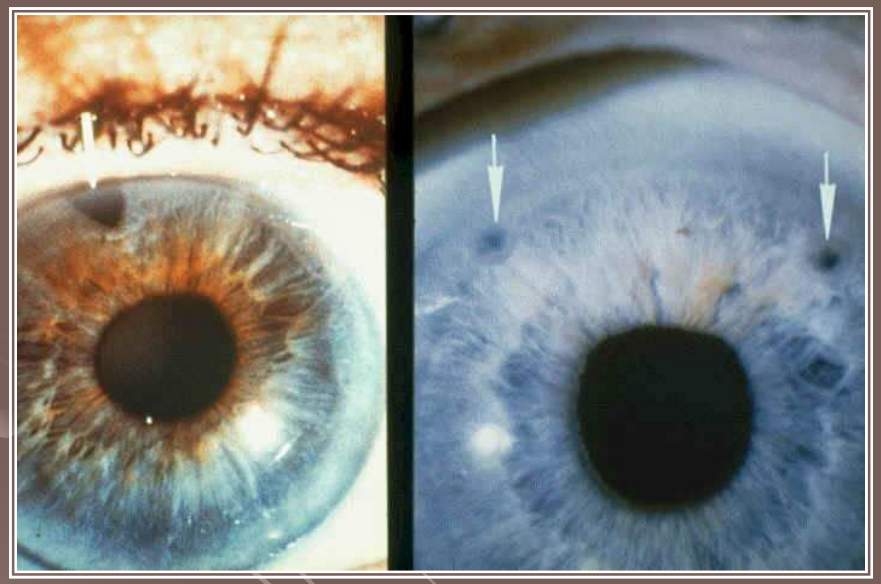
Narrow Angle Glaucoma

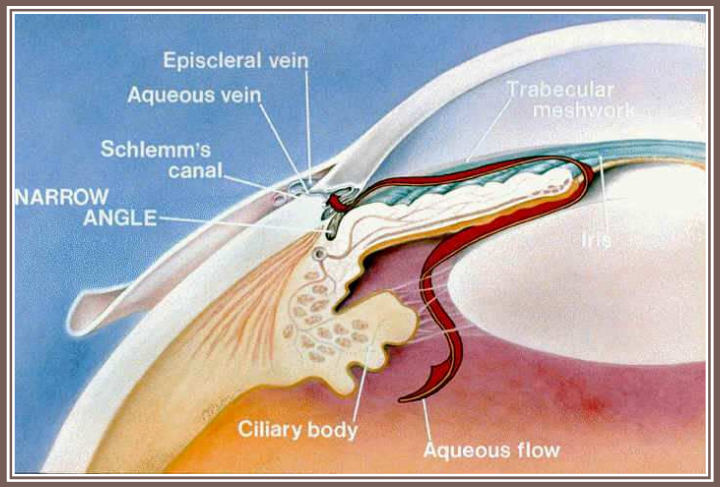
Mid-dilated, fixed pupil

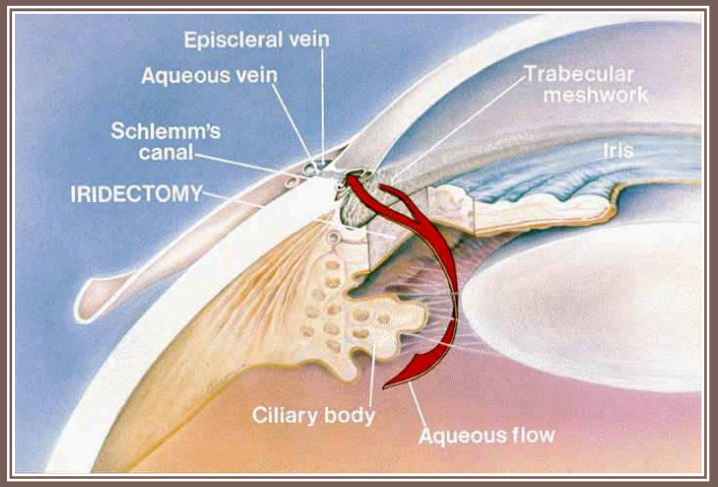


Narrow Angle Glaucoma

Treatment: Peripheral Iridotomy







Open Angle Glaucoma

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

Risk Factors

- IOP
- Age
- Race
- Family history
- Central corneal thickness
- Diabetes
- Myopia
- Gender
- Cardiovascular disease
- Hormones

Open Angle Glaucoma

Onset: 50+ years of age

Symptoms	Signs
Usually none May have loss of central and peripheral vision late	Elevated IOP Visual field loss Glaucomatous disk changes

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

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Treatment

Mechanisms of Action of Glaucoma Medication

	Increase outflow facility?	Increase uveoscleral outflow?	Decrease aqueous flow?
Bimatoprost	YES	YES	NO
Pilocarpine	YES	NO	NO
Latanoprost	???	YES	NO
Travoprost	???	YES	NO
Brimonidine	NO	YES	YES
Timolol	NO	NO	YES
Dorzolamide	NO	NO	YES

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

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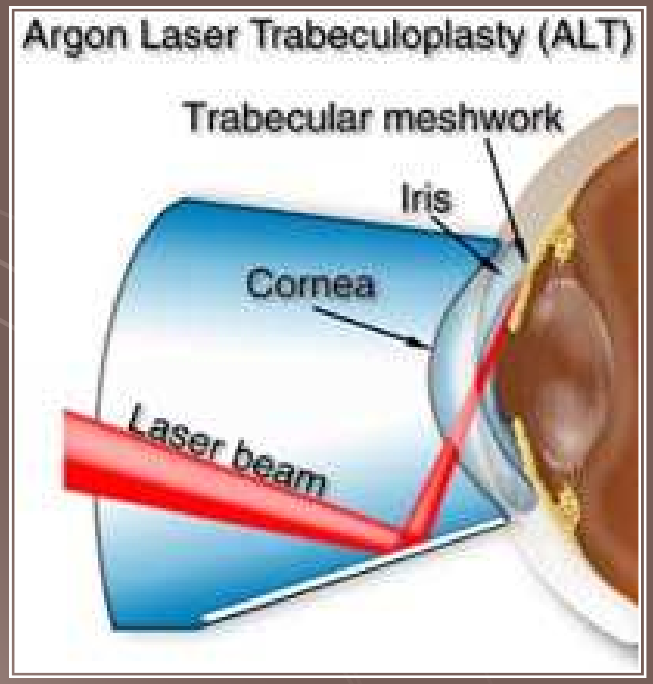
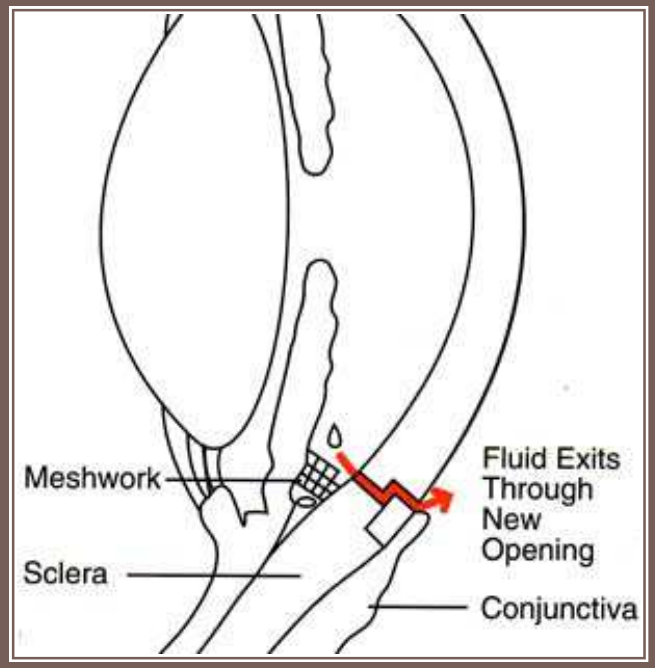
Surgical treatment of glaucoma

Argon laser trabeculoplasty



Filtration procedures



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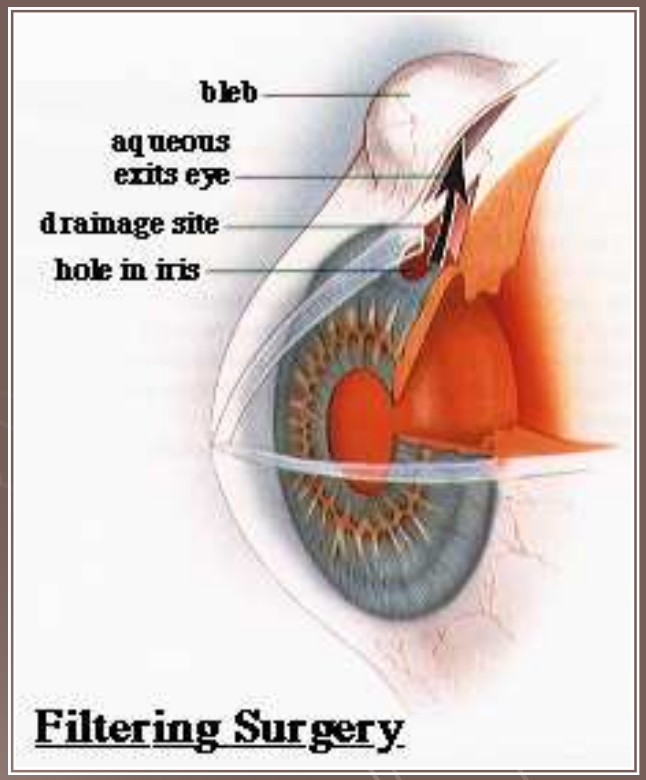
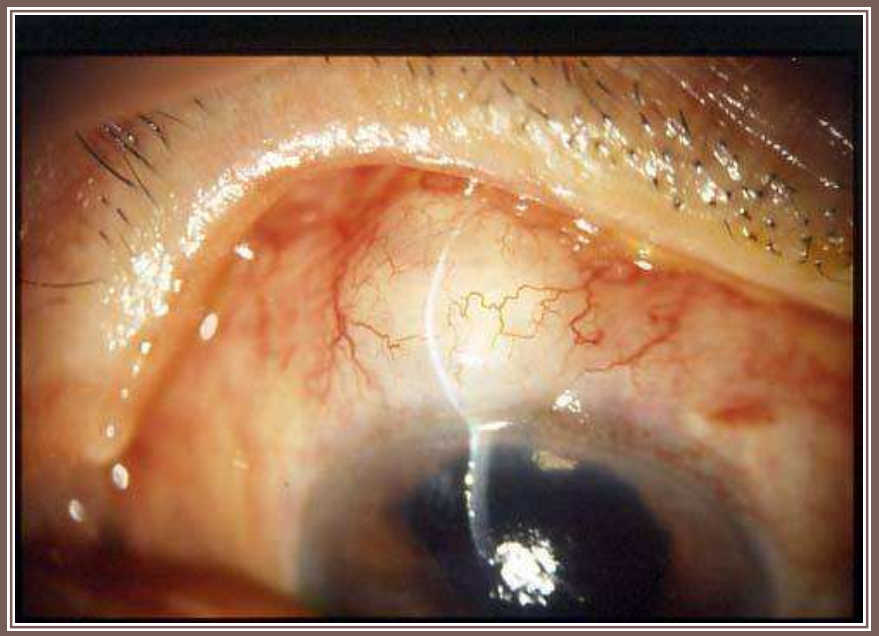
Filtration blebs





GLAUCOMA

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 concentratons in trabeculer meshwork
- Myocilin found intra- and extracellularly but not in nucleus
- Prolonged and dramatic induction by steriods
- Mutations in MYOC inhibits extracellular appearanc of MYOC exosomes in TM cells


THANK YOU ALL FOR LISTENING!