



**TOURO**  
UNIVERSITY

## Management of Glaucoma:

Reading: Katzung's Chapter 10 page 151, and table 10-3, Dr. Gayer's Autonomic Handout. Lecture PPT. **Uptodate** sections on Primary open-angle glaucoma and Angle-closure glaucoma



Normal optic nerve head      Glaucomatous cupping



treatment is to get pressure down even if it's not the cause  
when to tx is very subjective

pressure comes from vitreous humor production - comes from ciliary epithelium (lining of ciliary body)  
is continually made but also have to be continually drained

stimulate production of aqueous humor is mixed beta 1 and beta 2 - mixed blockers  
aqueous humor involved carbonic anhydrase shuttling - carbonic anhydrase inhibitor  
outflow in canal of schlemm with trabecular meshwork 60%  
uveal sclera pathway 40%

way to increase outflow either through uveal-scleral (side of eye) or canal of schlemm

more flow when ciliary body moves tissue away from canal of schlemm - M3R (pilocarpine): pupil will decrease in diameter  
problem is blurry vision bc can no longer accommodate  
use corrective lenses to counter

what is the best thing to use that causes the least damage?  
glaucoma is one of leading preventable causes of blindness

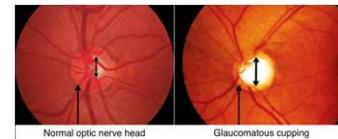
other outflow is uveal-sclera will not affect ciliary muscles - prostaglandins work on extracellular matrix to soften and make it n

elevated IOP is not diagnostic for glaucoma but if it reaches a certain point will become emergent ~40

daily meds, laser, surgery to insert a tube

## Glaucoma

representation over years



### Pathogenesis:

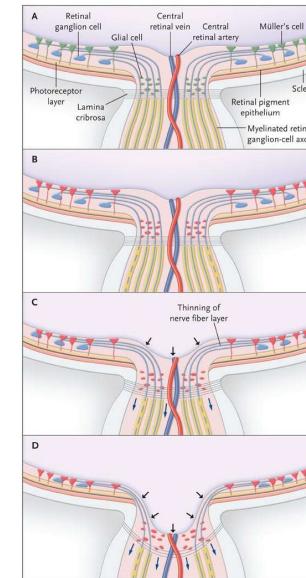
Optic nerve axon loss  
ganglion cell susceptibility  
microcirculatory deficiency at the optic nerve head  
extracellular matrix factors  
Sometimes elevated IOP (not always causal or required)  
Progressive loss leads to decreased visual field over time

widened c/d = indicative of neural damage  
pharm is to stop widening bc is irreversible



Published online 2021 Sep 16. doi: [10.1016/j.survophthal.2021.09.001](https://doi.org/10.1016/j.survophthal.2021.09.001)

Published online 2020 Nov 24. doi: [10.7759/cureus.11686](https://doi.org/10.7759/cureus.11686)



Kwon Y et al. N Engl J Med 2009;360:1113-1124

# Know the clinical presentations of open angle and closed angle glaucoma.

"The word glaucoma comes from Greek word for blue-green hue or opacity that was used to describe both cataracts and glaucoma."

From UPTODATE:

### EPIDEMOIOLOGY

After cataracts, glaucoma is the second leading cause of blindness in the world [2]. It is a leading cause of

irreversible blindness and the leading cause of blindness among Black Americans [3,4]. Open-angle glaucoma is the most common type of glaucoma among White and Black populations, whereas angle-closure glaucoma is more common among Asian populations [2,3]. Worldwide in 2015, there were an estimated 57.5 million people with open-angle glaucoma, and this number is projected to increase to 65.5 million by 2020 [5]. It is estimated that there are 2.8 million people with open-angle glaucoma in the United States in 2010 [6] and that the number will increase to 3.4 million in 2020 [7].

Patients with open-angle glaucoma report decreased quality-of-life and difficulties with daily functioning, including driving [8,9]. Patients with glaucoma are also more likely to report falls and motor vehicle collisions [10]. However, one meta-analysis found no association between open-angle glaucoma and all-cause mortality [11].

Risk factors — The major risk factors for developing open-angle glaucoma include age, being a Black person, family history, and elevated intraocular pressure (IOP) [12-14]. These and other risk factors are discussed below:

- **Age** – The incidence of open-angle glaucoma increases with age, particularly in White and Black persons [15-17]. The prevalence of open-angle glaucoma is <1 percent in individuals under 55 years of age, approaches 2 percent at age 65, and reaches approximately 4 percent at age 80 [7]. The rate of blindness from open-angle glaucoma also increases with age [4].
- **Race** – Race is an important risk factor for development and progression of open-angle glaucoma [18]. The estimated prevalence of open-angle glaucoma is approximately three times higher in Black compared with White persons [7]. The age-adjusted rate of blindness from glaucoma among Black persons was 6.6 times that among White persons, with blindness beginning 10 years earlier in Black persons [4]. The incidence of open-angle glaucoma in Hispanic persons is higher than in non-Hispanic White persons, though lower than in African Caribbean individuals [19]. Non-Hispanic White females comprise the largest group with open-angle glaucoma in the United States in 2011, but it is anticipated that this will shift to Hispanic males over the next several decades [20].
- **Family history** – Family history is a significant risk factor for open-angle glaucoma in several population studies [21-24]. The Baltimore Eye Survey found that the relative risk of open-angle glaucoma increased 3.7- and 2.2-fold for individuals with an affected sibling or parent, respectively [21]. Several early-onset glaucoma syndromes are inherited as Mendelian dominant or recessive traits; open-angle glaucoma, however, has a complex inheritance pattern, with the likelihood that multiple genes interact with environmental factors [22]. A report of genetic variants in Japanese primary open-angle glaucoma patients found that non-IOP-related risk (optic nerve vulnerability) was associated with family history of glaucoma, and that IOP-related risk (IOP elevation) was

associated with age at the diagnosis [25].

● **Diabetes** – Observational studies also suggest an association between diabetes and primary open-angle glaucoma. A 2014 systematic review and meta-analysis of 47 observational studies found that the risk for primary open-angle glaucoma was increased for patients with diabetes compared with those without (RR 1.48, 95% CI 1.29-1.71) [26]. The risk increased 5 percent each year after the diagnosis of diabetes.

● **Hypertension** – Observational studies suggest an association between hypertension and primary open-angle glaucoma. A 2014 systematic review and meta-analysis of 60 observational studies found that the risk for primary open-angle glaucoma was increased in patients with hypertension compared with those without (relative risk [RR] 1.16, 95% CI 1.05-1.28); nearly all studies noted an association between hypertension and increased intraocular pressure [27].

● **Elevated intraocular pressure** – There is a large body of literature illustrating the association between elevated IOP and both development and progression of open-angle glaucoma [24,28-32].

As an example, the Early Manifest Glaucoma Trial followed 255 patients with a diagnosis of open-angle glaucoma over a mean of eight years; mean IOP was a significant risk factor for progression of glaucoma (hazard ratio [HR] 1.11, 95% CI 1.06-1.17), even when IOP was within the "normal" range of 8 to 22 mmHg [33].

However, nearly 40 percent of patients with otherwise characteristic open-angle glaucoma will not have an elevated IOP [14]. These patients constitute a subgroup commonly referred to as low-tension or normal-tension glaucoma. While a small proportion of open-angle glaucoma in the United States may be classified as normal tension, the majority of patients with open-angle glaucoma in Asia have normal tension glaucoma [34]. By contrast, many patients with elevated pressures never develop the optic nerve and field changes characteristic of glaucoma [28,29]. Thus, although high pressure is clearly associated with open-angle glaucoma, it is neither necessary nor sufficient for the diagnosis and is therefore termed a "risk factor" for the condition.

● **Other factors** – Other possible risk factors for developing open-angle glaucoma include myopia, pseudoexfoliation, low diastolic perfusion pressure, cardiovascular disease, a history of prior vitreoretinal surgery, hypothyroidism, and high coffee consumption [35-42].

Although risk factors for the development of open-angle glaucoma have been well documented, risk factors for progression of open-angle glaucoma are less certain [43-45]. Results conflict whether fluctuation in IOP is predictive of glaucoma progression [31,32]. Even in patients with documented findings of glaucoma on comprehensive eye examination (eg, visual field deficits, optic disc changes), it is unclear which patients go on to

develop loss of visual acuity and blindness [46].

glucose is a fuel - high energy if in the blood will attach to things and throw out electrons considered a vasculopathic toxic if elevated too much will attach to endothelial cells and get glycation products and start causing damage microcapillary issues - distal issue with fingers and toes, kidneys, an eyes

glucocorticoids cause elevated IOP

## Glaucoma

### Epidemiology

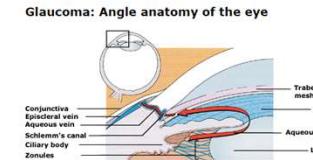
- Age: Increases with age, <1% under 55, approaches 2% at age 65, 4% age 80
  - Myopia **depending on eye shape**
  - Family history/ethnic concentrations/genetics (3-4 times higher)
    - Myocilin (MYOC)
    - Cytochrome P450 Family 1 Subfamily B Member 1 (CYP1B1)
    - Latent transforming growth factor-beta-binding protein 2 (LTBP2)
    - Optineurin (OPTN) and TANK-binding kinase 1 (TBK1)
  - Diabetes: increased risk 5% per year.
  - Smoking
  - Systemic hypotension or hypertension
- Secondary:
- Uveitis
  - Trauma,
  - Glucocorticoid therapy,
  - Vasoproliferative retinopathy

acute angle -  
anatomy, progression  
or thickening with age



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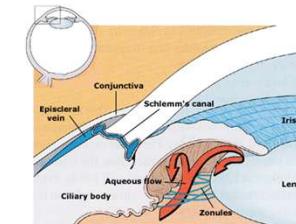


The angle is the recess formed by the irido-corneal juncture. The scleral spur, trabecular meshwork, and Schwalbe's line lie within this angle. The trabecular meshwork is a fenestrated structure that transmits aqueous fluid to Schlemm's canal, from which it drains into the venous system. The normal flow of aqueous is demonstrated here.

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UpToDate®

### Acute angle-closure glaucoma



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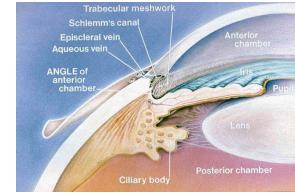
develop loss of visual acuity and blindness [46].

can be acute, painful, red eyes, something preventing drainage

tx depending on pressure is similar to open angle but may have to add more to get IOP down

>25 will treat anyway

## Glaucoma Categories



### Open Angle

Open-angle glaucoma: Optic neuropathy with progressive peripheral → central visual field loss; often (not always) elevated IOP.

Mechanisms for increase IOP: Increased aqueous production and/or decreased outflow;

ganglion cell axon loss.

Ganglion cell susceptibility (genetic/extracellular matrix component?)

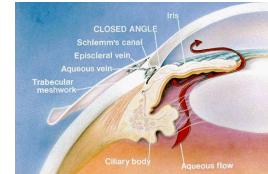
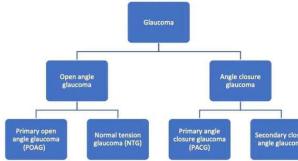
Note not all patients with elevated IOP have damage

Microcirculatory deficiencies

Elevated IOP

½ to 2/3 have this issue

Attachment A: Types of Glaucoma



### Closed Angle

Angle-closure glaucoma: Narrowing/closure of anterior chamber angle → inadequate drainage → elevated IOP → optic nerve damage.

Acute angle-closure: Painful red eye; ophthalmic emergency—treat within 24 hours to prevent permanent vision loss.

Anatomic = poor drainage  
Prolonged contact of iris and trabecular network can lead to scarring/fibrosis  
Surgery of iris  
Age related thickening  
Occlusion of anterior chamber  
Inflammation  
Abnormal corneal endothelial cell proliferation or fibroblast invasion of the angle

<http://www.avclinic.com/Glaucoma.htm>

# Testable Objectives: Know the clinical presentations of open angle and closed angle glaucoma.

This is an introductory slide. The two types of glaucoma discussed in this lecture will be Primary open-angle glaucoma (POAG) and Acute Angle Closure Glaucoma. There are secondary causes of glaucoma and congenital glaucoma. These later forms will be discussed elsewhere.

canal of schlemm and trabecular meshwork

Demographic statistics on the prevalence of glaucoma are typically available from several trusted sources, including:

**1. Centers for Disease Control and Prevention (CDC)**

The CDC provides statistics and information on the prevalence of glaucoma in the U.S., including demographic data such as age, gender, and ethnicity. This data is often gathered through large-scale health surveys and studies like the National Health and Nutrition Examination Survey (NHANES).

- 1. CDC Glaucoma Page:** <https://www.cdc.gov/glaucoma/>

**2. National Eye Institute (NEI)**

The NEI offers detailed reports and statistics about the prevalence of eye diseases, including glaucoma, across various demographic groups such as age, race, and gender. They publish research-based data, including trends in eye health.

- 1. NEI Glaucoma Facts and Statistics:** <https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/glaucoma/glaucoma-facts-and-statistics>

**3. World Health Organization (WHO)**

For global statistics on glaucoma, the WHO offers data on the worldwide prevalence of eye conditions, including glaucoma, with breakdowns by region, gender, and other demographics.

- 1. WHO Vision Health Data:** <https://www.who.int/health-topics/blindness-and-vision-loss>

**4. Research Publications and Journals**

Many demographic studies related to glaucoma are published in peer-reviewed journals. You can find specific studies on glaucoma prevalence in various populations through medical databases such as PubMed or through specialized ophthalmology journals.

- 1. PubMed (National Library of Medicine):** <https://pubmed.ncbi.nlm.nih.gov/>

dilating drops to do a fundus exam  
tropicamide (only lasts for hours)

bigger c/d the more damage and is irreversible

slit lamp tell if open/closed

worried >25  
30-40 worried about optic nerve death  
>40 emergency room

## Diagnosis

### Open Angle

Optic nerve damage

Fundus examination:

Thinning or notching of the disc rim (fundus examination)

Cup > 50%

Visual field abnormalities (visual field testing, damage)

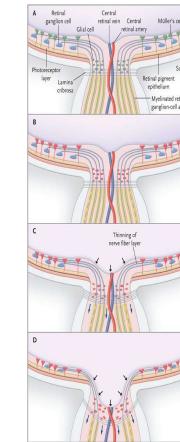
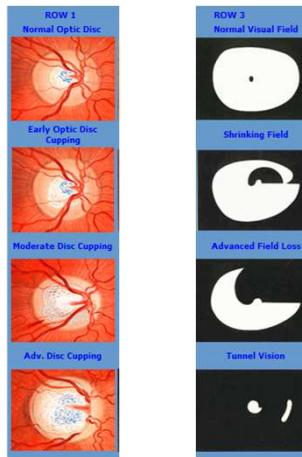
Adult onset

Open anterior chambers (slit lamp test)

Absence of secondary causes

Tonometry--Elevated intraocular pressure (> 21 mmHg)

only 1/3 to 1/2 have observable increase in IP



The following represent indications for ophthalmologic referral based on clinical practice experience:  
•IOP >40 mmHg – Emergency referral  
•IOP 30 to 40 mmHg – Urgent referral (within 24 hours) if no symptoms suggesting acute glaucoma  
•IOP 25 to 29 mmHg – Evaluation within one week  
•IOP 23 to 24 mmHg – Repeat measurement to confirm and/or referral for comprehensive eye examination

# Testable objectives: Know the clinical presentations of open angle and closed angle glaucoma.

## DIAGNOSIS

Diagnostic criteria — Glaucoma is diagnosed in patients with characteristic nerve damage on fundus examination ([picture 1A-B](#)) and visual field testing, typically in the presence of elevated intraocular pressure (IOP). Some authorities consider either characteristic optic nerve change OR visual field defects as sufficient

criteria for diagnosis of open-angle glaucoma [62,63].

The American Academy of Ophthalmology (AAO) Preferred Practice Pattern defines primary open-angle glaucoma as a chronic, generally bilateral, and often asymmetrical disease, which is characterized (in at least one eye) by all of the following [14]:

- Evidence of optic nerve damage from either or both of the following:
- Optic disc or retinal nerve fiber layer structural abnormalities (eg, thinning, cupping, or notching of the disc rim, progressive change, nerve fiber layer defects)
- Reliable and reproducible visual field abnormalities (eg, arcuate defect, nasal step paracentral scotoma, generalized depression) in the absence of other causes or explanations for a field defect.
- Adult onset.
- Open, normal appearing anterior chamber angles.
- Absence of known (eg, secondary) causes of open-angle glaucoma.

Who should be referred for comprehensive eye examination? — Patients with abnormal cupping on funduscopic examination or risk factors (eg, age >40) should be referred to an ophthalmologist or optometrist for a comprehensive eye examination. Any patient with high IOP detected during community-based screening or spectacle/contact lens evaluation should also be referred for a comprehensive eye examination. The best available data support examination by an ophthalmologist as the most accurate way to detect glaucoma [64]. (See '[Risk factors](#)' above.)

#### Diagnostic tests

**Fundus examination** — The primary care clinician should be attentive to the presence of cupping seen in the fundus. Cupping describes a hollowed-out appearance of the optic nerve or "disc" on fundus examination. A cup whose diameter is greater than 50 percent of the vertical disc diameter is suspicious for glaucoma.

Although cupping has the highest sensitivity and specificity of any other finding on eye examination, there is no single cutoff criteria that yields sufficiently high sensitivity and specificity to make cupping a useful diagnostic test [65]. One study found that ophthalmologists, using direct ophthalmoscopy, detected less than one-half of cases of glaucoma [54]. Combining cupping with other criteria increased diagnostic yield.

Other findings on fundus examination indicative of glaucoma include thinning or notching of the disc rim, progressive change of the size or shape of the cup, and asymmetry of the cup-to-disc ratio between the eyes [65,66].

**Visual field testing** — Open-angle glaucoma ideally should be diagnosed before there is significant visual field loss.

However, confrontational field testing, using the examiner's fingers, is not useful in the detection of glaucoma.

Automated perimetry is an important diagnostic tool that is much more reliable at detecting visual field loss in glaucoma compared with confrontational field testing ([figure 4](#)) [67].

There are several types of automated perimetry technologies, including standard threshold automated perimetry, frequency-doubling technology perimetry, and short-wavelength automated perimetry [55]. Automated perimetry has become the standard of care for optometric and ophthalmic practice in the detection and monitoring of glaucoma, although there is a role for careful manual perimetry in some cases, particularly in patients with advanced field loss or dementia. Reliable field testing requires comprehension and cooperation on the part of the patient. Dementia and other mental or physical problems may preclude testing in certain individuals, forcing the clinician to rely upon other variables in diagnostic and therapeutic decision-making.

Visual field testing can be time consuming and of variable specificity and sensitivity, depending on user characteristics and the type of test being used. Newer technologies to measure visual fields with greater reliability are in development. (See '[Newer technologies](#)' below.)

Intraocular pressure — Elevated IOP alone does not establish the diagnosis of open-angle glaucoma [14,68]. One-third to one-half of individuals with glaucoma field defects have intraocular pressures  $\leq 21$  mmHg when first detected (normal IOP 8 to 21 mmHg) [69]. In addition, over 90 percent of adults with pressures  $>21$  mmHg have no optic nerve damage. However, patients with elevated IOP should be referred to an ophthalmologist given their higher risk of open-angle glaucoma. (See '[Risk factors](#)' above and '[Management of isolated ocular hypertension](#)' below.)

A prospective population study of risk factors associated with glaucomatous field loss found that, during a period of five years, 99 percent of eyes with an initial pressure  $<20$  mmHg continued to be free of glaucomatous field defects, compared with 93 percent of eyes with an initial pressure  $\geq 20$  mmHg [70]. The sensitivity for the diagnosis of open-angle glaucoma by IOP measurement was 47.1 percent and the specificity over 90 percent at an IOP cutoff point of  $>21$  mmHg [56]. The presence of either increased IOP ( $>21$  mmHg) or increased vertical cup/disc ratio ( $\geq 0.5$ ) increased the sensitivity to 61 percent but decreased the specificity to 84 percent. There was no cutoff value for IOP that had reasonable sensitivity and specificity as a screening tool for the diagnosis of open-angle glaucoma.

Ophthalmologists and optometrists can measure IOP by applanation tonometry, pneumotonometry, or air-puff tonometry. Applanation tonometry is a method that determines the IOP from the force required to flatten (applanate) a constant area of the cornea ([picture 2](#)). Applanation tonometry is most accurate and less subject to artifact. All tonometry methods require specialized equipment and skill and thus fall out of the realm of the

primary care clinician. Due to the effects of central corneal thickness on the mechanics of applanation tonometry, falsely higher measurements occur in patients with thicker corneas and falsely lower measurements occur in those with thinner corneas [71]. This can be partially corrected with pachymetry. (See '[Pachymetry](#)' below.)

Schiotz tonometry is a handheld device that is relatively inexpensive but requires frequent use for reliable results.

Generalists who practice in populations that do not have access to optometric or ophthalmic care can learn Schiotz tonometry and use it in conjunction with the optic disc examination in deciding whom to treat or refer. In resource-abundant countries, it is less common for primary care providers to measure IOP.

There is some evidence that wearing a tight necktie may temporarily increase IOP [72]. The clinical implications of these findings require further study. Regardless, it is prudent to ask patients to loosen collars and ties prior to measuring IOP.

Pressure parameters for referral — There are no standard criteria for referral to an ophthalmologist for patients with elevated pressures. Primary open-angle glaucoma rarely presents with IOP >30 mmHg, which is more common among patients with angle-closure glaucoma or secondary (rather than primary) open-angle glaucoma. (See '[Angle-closure glaucoma](#)' and '[The red eye: Evaluation and management](#)'.)

The following represent indications for ophthalmologic referral based on clinical practice experience:

- IOP >40 mmHg – Emergency referral
- IOP 30 to 40 mmHg – Urgent referral (within 24 hours) if no symptoms suggesting acute glaucoma
- IOP 25 to 29 mmHg – Evaluation within one week
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These indications are not absolute and should be interpreted in the context of patient history and examination findings. As an example, a patient with an IOP of 28 and advanced open-angle glaucoma including field loss and cupping may represent an emergency because of risk of imminent field loss, while a patient with a healthy nerve could withstand an IOP at that level for weeks with little risk of further nerve damage.

Pachymetry — Pachymetry is the measurement of corneal thickness; it can be performed by ultrasound or other methods. Patients with thin corneas are at higher risk for the development of open-angle glaucoma [73,74]. Ophthalmologists may perform pachymetry in patients with suspected or diagnosed open-angle glaucoma to further evaluate their risk for development or progression of open-angle glaucoma [75]. Additionally, corneal thickness affects the results of applanation tonometry, and pachymetry may adjust for this effect. (See '[Intraocular pressure](#)' above.)

Newer technologies — Several newer technologies have been developed to evaluate the optic disc, retinal nerve fiber layer, and visual field. These may aid in the early detection of glaucoma, as well as other eye diseases.

- **Optical coherence tomography** – Optical coherence tomography (OCT), Heidelberg retinal tomography (HRT), and scanning laser polarimetry are noninvasive imaging techniques that analyze light reflected off the fundus [76,77]. The need for pupil dilation varies with the particular device and the part of the fundus being studied. These tests are well-tolerated by patients. The devices generate a digital image and quantification of specific features of optic nerve head anatomy.

One study comparing OCT, HRT, and scanning laser polarimetry with conventional qualitative assessment of stereoscopic photographs of the optic disc showed that the three newer technologies performed as well as, but not better than, stereoscopic photographs [78]. Accuracy of results from stereoscopic images is, however, dependent on the experience and skill of the interpreter, whereas the newer technologies provide more quantitative data that is less user-dependent. A study from Finland found that screening capabilities of newer technologies including OCT, scanning laser polarimetry (GDx), and HRT were similar, with only moderate accuracy, and concluded that screening with these parameters alone is not reliable [79].

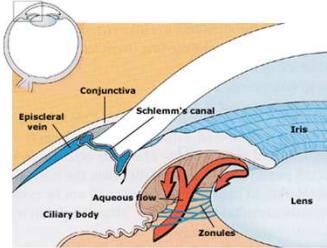
Additionally, in highly myopic but otherwise healthy eyes where there may be visual field defects and the optic nerve may have an abnormal appearance, OCT may provide the clinician an additional tool to help distinguish these findings from true glaucomatous changes [80].

- **Visual field testing with brain computer interface** – A portable brain-computer interface (wearable, wireless, dry electroencephalogram and electrooculogram systems) that assesses electrical brain responses to visual field stimulation has shown promise as an alternative and potentially more reliable means of diagnosing glaucoma compared with standard visual field testing [81].

blocking drainage

## Diagnosis

### Acute angle-closure glaucoma



The pupillary margin blocks the passage of aqueous from the posterior chamber to the anterior chamber (pupillary block), ballooning the iris forward (iris bombe), causing the iris root to occlude the trabecular meshwork and completely obstruct drainage of aqueous fluid from the anterior chamber (angle closure). The resulting rapid elevation of intraocular pressure requires urgent intervention to prevent permanent visual loss.

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### Acute closed angle

- Decreased vision
- Halos around lights
- Headache
- Severe eye pain
- Nausea and vomiting
- Elevated intraocular pressure
- Conjunctival redness
- Corneal edema or cloudiness
- A mid-dilated pupil (4-6 mm) that reacts poorly to light
- A shallow anterior chamber (slit lamp or gonioscopy)

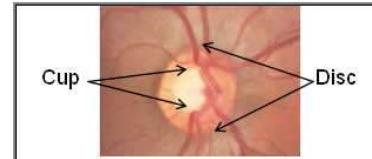
Testable objectives: Know the clinical presentations of open angle and closed angle glaucoma.

juvenile onset  
probably matrix  
issues

cue on exam:  
if slit lamp is normal  
think open angle  
prob juvenile onset

#### Glaucoma (" a silent disease")

- 34 year old molecular biology professor presents with chief Complaint: "My left eye is foggy, and I get blurred vision that progresses to tunnel vision and Headaches"
- History of advanced open-angle-glaucoma
- Eye Examination
  - Visual acuity--OD (rt.: oculus dexter)--hand motion at 3 inches with correction spectacles: OS (lft.:oculus sinister)--20/30
  - Slit lamp" normal (no inflammation, tumors, cataracts, closed angle, or adhesions)
  - Intraocular --OD-- 14 mm Hg; OS--20 mm Hg (norm 10-21.5mm Hg)
  - Vitreous examination: clear ou (oculus uterque (each eye)
  - Disk: OD--whitish with marked pallor, cup-to-disk ratio (1.0), OS-- CD ration 0.99 with only a narrow rim present (normal C/D =< 0.33



C:D of 0.5 means that the Cup to Disc ratio is 0.5 i.e. cupping is about 50% of total disc area. The 'orange/pink' rim of disc contains nerve fibers. The 'white' cup is a pit with no nerve fibers. As glaucoma advances, the cup (white pit) occupies most of the disc area.

Pharmacotherapy Casebook, A patient-Focused Approach, 2nd ed. Schwinghammer, Appleton and Lange



This slide provides clinical context to this lecture regarding POAG. Students should use this slide as contextual reference only.

doesn't always have to be associated with elevated IOP just associated with susceptibility for increased pressure

## Case Study Cont'd

- Color vision
  - OD--unable to see; OS--WNL
- Visual Fields:
  - OD unable to see the Amsler grid (macular degeneration) can only see hand motion at 3 inches away; OS--several paracentral scotomata (blind spots) with the Amsler grid 20/30. Diurnal curve of IOP revealed pressures between 10 and 21 mm HG
- Assessment
  - High myopia with advanced chronic juvenile open-angle glaucoma
  - Depression associated with chronic open-angle glaucoma

This slide provides clinical context to this lecture regarding POAG. Students should use this slide as contextual reference only.

## Case Study Cont'd

- Past medications
  - pilocarpine (muscarinic agonist)
  - Timoptic (Timolol,  $\beta$  antagonist)
  - Diamox (Acetazolamide, diuretic)
  - Pred-Forte (Prednisolone Acetate glucocorticoid)
- Did not work : switch in medication
  - Betoptic 0.5% ou BID: Betaxolol ( $\beta$ 1 antagonist)
  - Iopidine 0.5% os TID: Aprocyclidine ( $\alpha$ 2 agonist)
  - Trusopt 2% os TID: Dorzolamide (diuretic) **carbonic anhydrase inhibitor**
  - FML 0.1% ou TID: Fluorometholone (glucocorticoid) **can cause elevate IOP - shouldn't be using it here**
  - Bion Tears ou BID
  - Paxil 20 mg po QD: Paroxetine (SSRI antidepressant) **for depression**

1. pull tissue away from canal of schlemm increase outflow
2. decrease production
3. too weak in PCT so main use is to reduce production aq. humor and elevation/altitude sickness

**presynaptic decrease NE so beta receptors not activated**  
**carbonic anhydrase inhibitor**  
**can cause elevate IOP - shouldn't be using it here**  
**for depression**



Which drug/s listed is least likely to help this patient?

tricyclic - also causes muscarinic activity

antipsychotics also do

SSRIs are cleaner

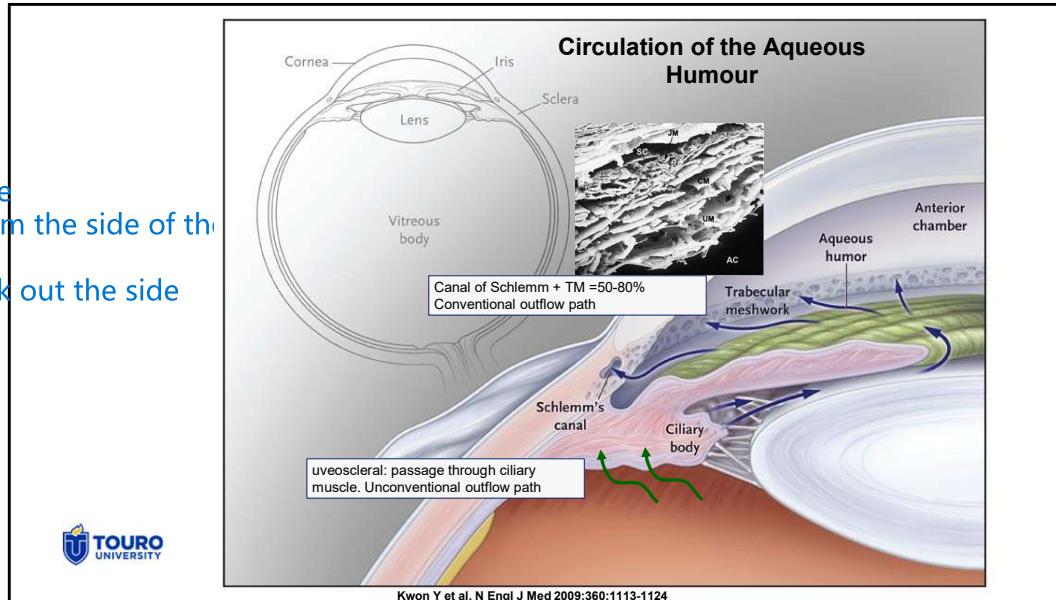


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## Control of Eye Function



trabecular meshwork is a cytoskeletal structure  
keep patency open want tissue to be away from the side of the eye  
uveal-sclera = unconventional (40-50%), a leak out the side

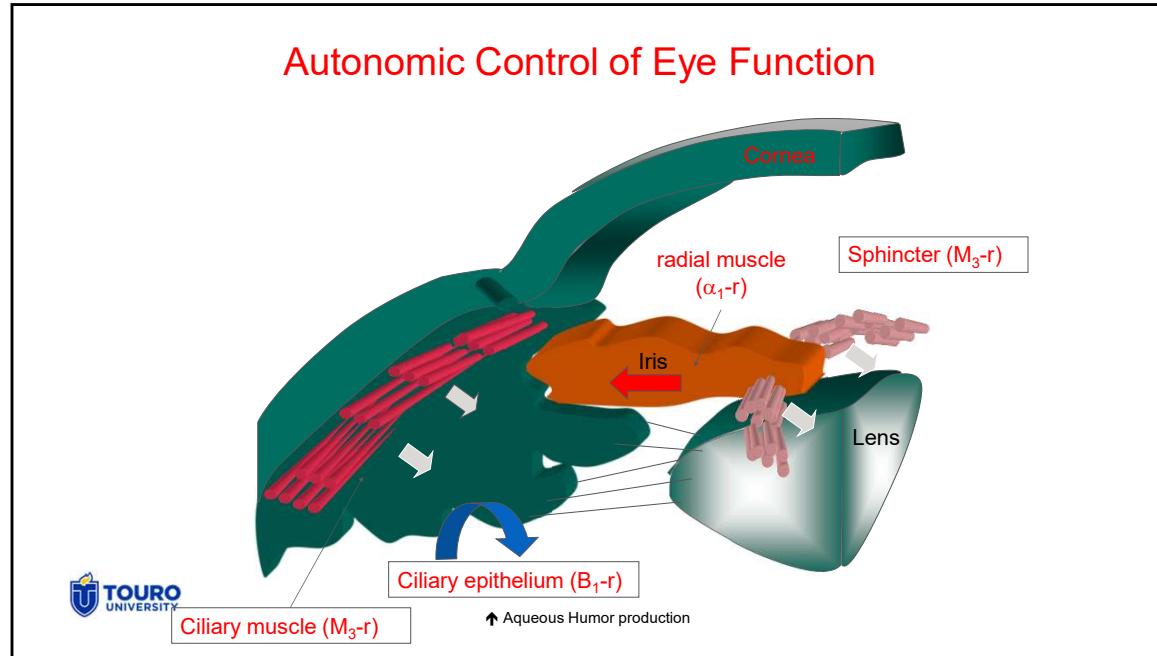


## Testable Objective: Know the “normal regulation” of eye function

Students should review this slide and use as a visual reference for the following slides.

Scanning electron microscope image of the trabecular meshwork, showing multiple stacked collagen and elastin sheets. (AC) Anterior Chamber, (UM) uveal meshwork, (P) large-size pores of the uveal meshwork, (CM) corneoscleral meshwork, (JM) juxtacanalicular meshwork, (SC) Schlemm's canal. Source: Johnson DH and Lutjen-Drecoll E. Glaucomatous Changes in the Trabecular Meshwork. In: Tombran-Tink J, Barnstable KJ, and Shields MB. Mechanisms of Glaucoma: Disease Processes and Therapeutic Modalities. Totowa, New Jersey: Humana Press, 2008:101

high yield board review



Testable Objective: Know the “normal regulation” of eye function: ciliary, circular, radial muscle control; the physiologic factors that influence outflow through the canal of Schlemm; and the regulation of aqueous humor production.

Students should review this slide and note the types and location of the various autonomic receptors.

The **radial muscle** contracts to open pupil when alpha-1 adrenoceptors activates the G-protein (Gq) that in turn activates phospholipase C. When activated phospholipase C cleaves the membrane lipid phosphoinositide-bis-

phosphate liberating the sugar IP3. IP3 results in the release of intracellular calcium in the iris smooth muscle and causes contraction.

The **ciliary** and **sphincter** muscles contract in response to activation of the cholinergic M3 receptors located on their respective membranes. M3 like alpha-1 is coupled to Gq and when activated increases intracellular Ca++ and smooth muscle contraction. The **ciliary muscle** is responsible for accommodation (adjusting lens diameter to view close objects) and the **sphincter muscle** controls pupillary constriction.

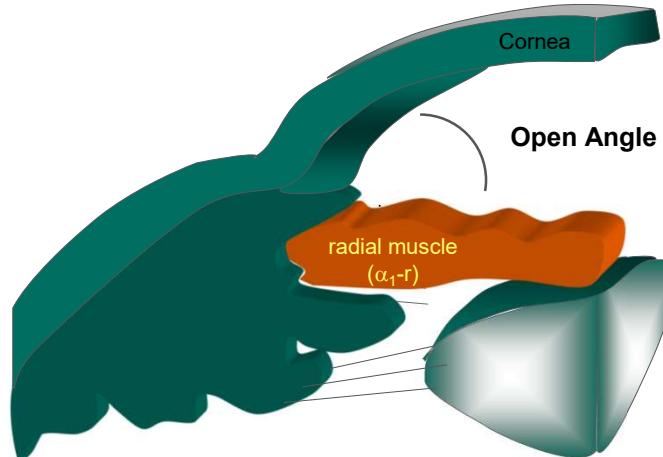
Beta-1 receptors located on the ciliary epithelium when activated increase aqueous humor production.

pull tissue open will go toward side of eye

get more symptoms with closed angle glaucoma at night bc tissue pulls in and will press up against canal of schlemm

avoid alpha 1 agonist (amphetamine), any drug that causes iris contraction

NE- $\alpha_1$  ↑ pupillary diameter



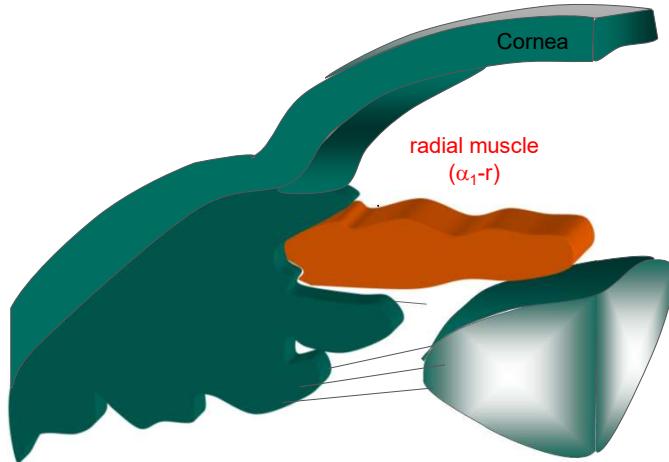
Testable Objective: Know the “normal regulation” of eye function: ciliary, circular, radial muscle control; the physiologic factors that influence outflow through the canal of Schlemm; and the regulation of aqueous humor production.

Students should review this slide and note the role of alpha-1 receptors in increasing pupillary diameter.

The **radial muscle** contracts to open pupil when alpha-1 adrenoceptors activates the G-protein (Gq) that in turn activates phospholipase C. When activated phospholipase C cleaves the membrane lipid phosphoinositide-bis-

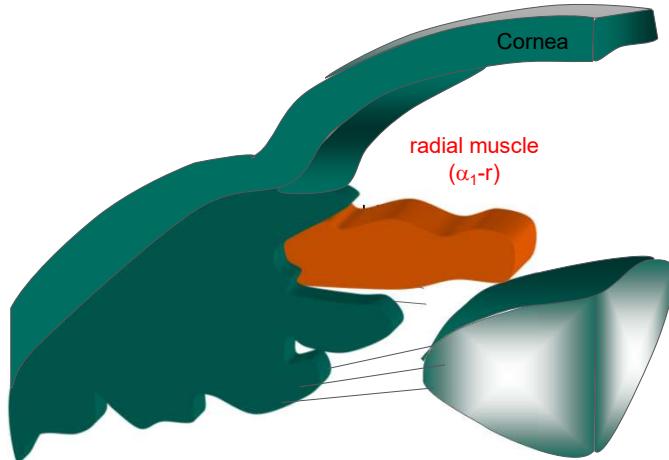
phosphate liberating the sugar IP<sub>3</sub>. IP<sub>3</sub> results in the release of intracellular calcium in the iris smooth muscle and causes contraction.

NE- $\alpha_1$  ↑ pupillary diameter



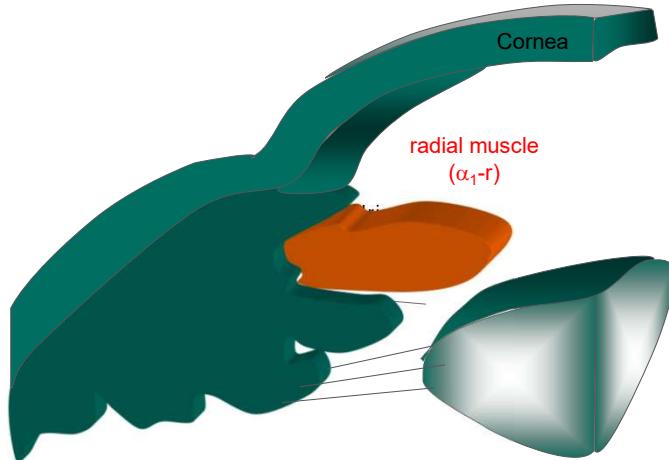
Animation to previous slide

NE- $\alpha_1$  ↑ pupillary diameter



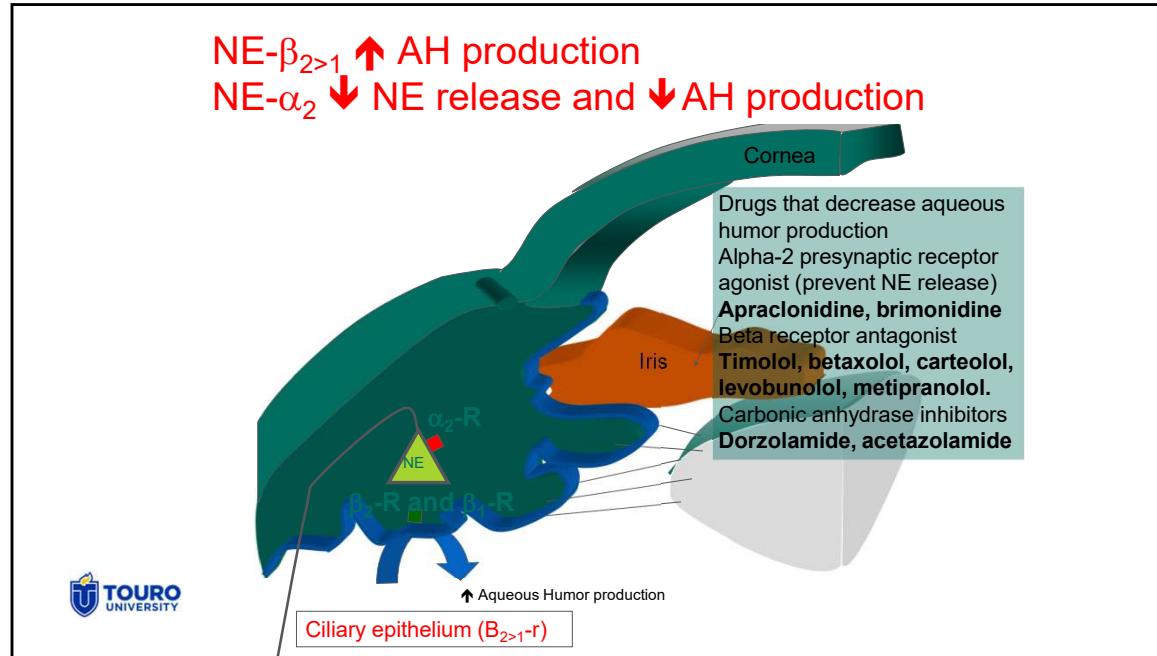
Animation to previous slide

NE- $\alpha_1$  ↑ pupillary diameter



Animation to previous slide

timolol and betaxolol only bc beta blockers  
some can engage with Na channels or  
have anesthetic properties and don't work  
that



Testable Objectives:

Know the treatments for both.

Know the mechanism of action and toxicities of the drugs used to treat glaucoma

Students should review this slide for detail. The central principle shown here is that drugs that

prevent decrease aqueous humor production . This can result in a decrease in intraocular pressure.

There are three general methods to pharmacologically decrease aqueous humor production.

- 1) Beta-blockers have been a first line therapy in the past. These drugs decrease beta-1 receptor-mediated aqueous humor production.
- 2) Alpha-2 receptor activation decrease the release of endogenous norepinephrine and the

subsequent activation of beta-1 receptors.

- 2) Carbonic anhydrase inhibitors can directly decrease the production of aqueous humor

alpha 2 used for tourette's too much activation  
decreases NE  
used for HTN

don't like to use HTN bc of excitatory pathways - causes sedation

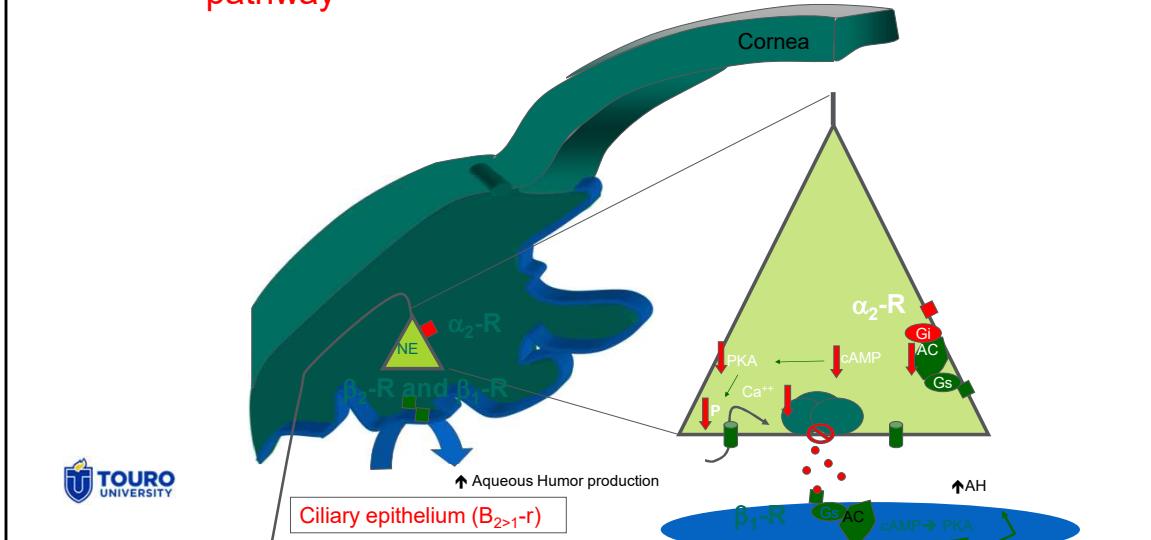
signal to be a signal needs to be on and off

why have specific reuptake mechanisms  
and can be destroyed by MAO or repackaged

MAOI - limit diet cannot have cured meat  
bc of cured meats, cheese, red wine

also breaks down 5-HT and can cause serotonin syndrome

### Board relevant review of signal transduction pathway

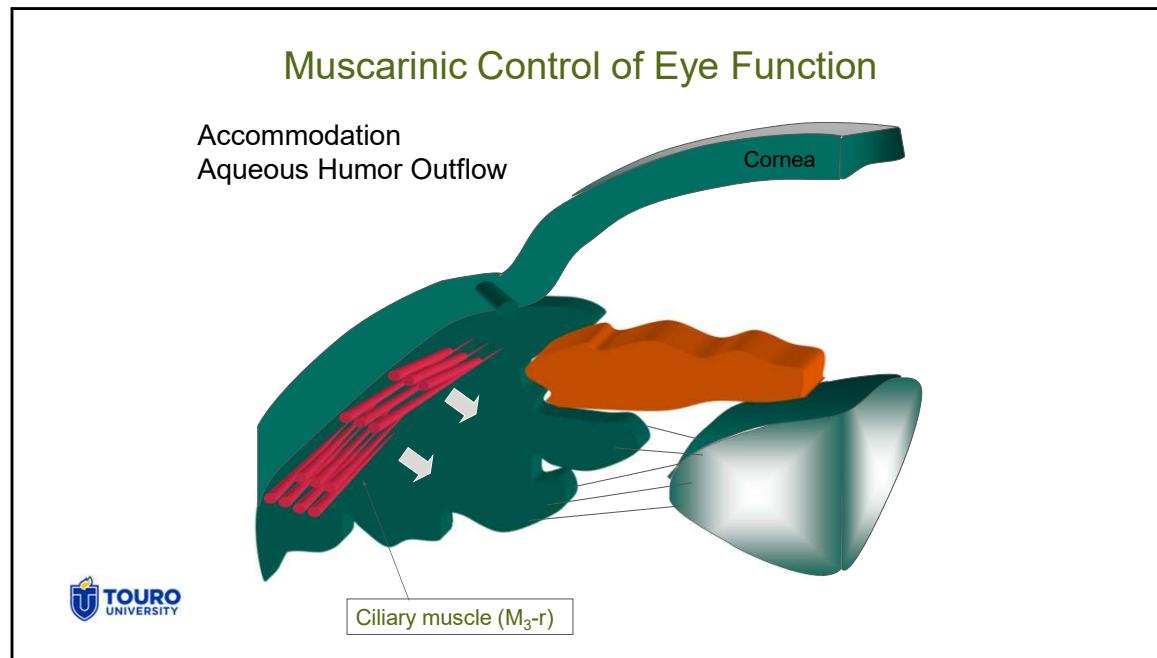


Testable Objectives:

Know the treatments for both.  
Know the mechanism of action and toxicities of the drugs used to treat glaucoma

Shown is the mechanism of action of drugs that activate alpha-2 receptors. Alpha-2 receptors are located primarily on presynaptic neurons. When these receptors are activated by drugs, like brimonidine and apraclonidine, they activate Gi which reduces the activity of adenylyl cyclase. In neurons and cardiac cells cAMP via activation of PKA and the phosphorylation of voltage-gated-calcium channels increases calcium influx. In neurons the rise in intracellular calcium concentration increases neurotransmitter release. Drugs that activate alpha-2 receptors reduce this process.

ciliary muscle moves in and moves tissue away from canal of Schlemm allows for outflow



Testable Objective: Know the “normal regulation” of eye function: ciliary, circular, radial muscle control; the physiologic factors that influence outflow through the canal of Schlemm; and the regulation of aqueous humor production.

This slide is the first slide in a series of animation slides used to illustrate the function of the ciliary muscle. There are two main consequences of ciliary muscle contraction.

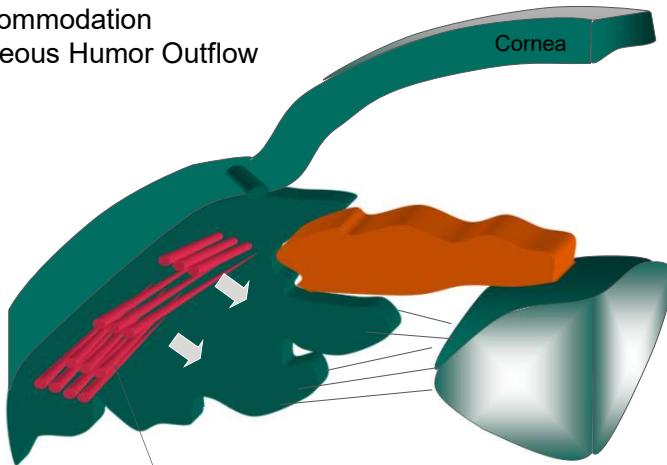
- 1) Contraction causes the lens to become more round when focusing on near objects is required.
- 2) When the ciliary muscle contracts it allows for flow of aqueous humor through the canal of Schlemm.

## Muscarinic Control of Eye Function

Accommodation  
Aqueous Humor Outflow



Ciliary muscle ( $M_3\text{-r}$ )



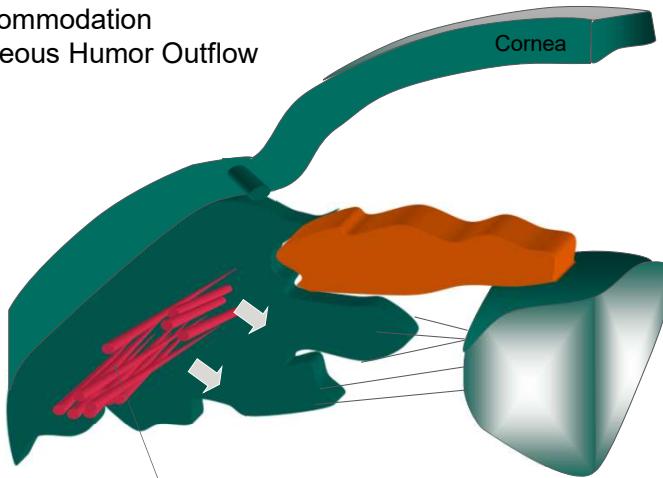
Animation sequence to previous slide

## Muscarinic Control of Eye Function

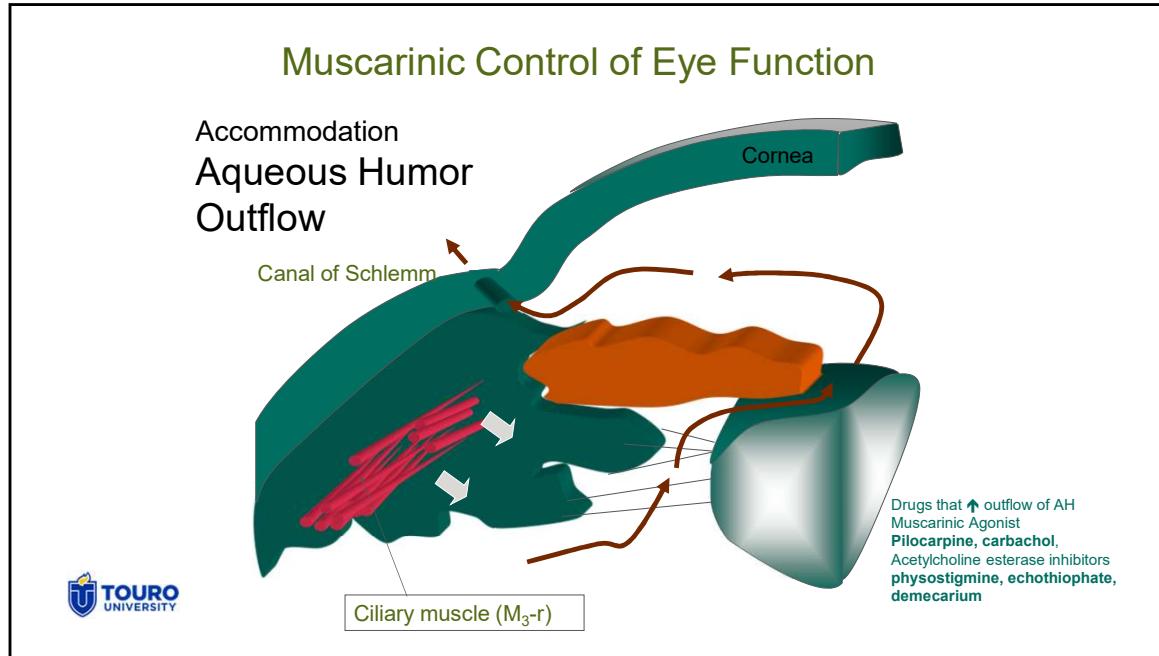
Accommodation  
Aqueous Humor Outflow



Ciliary muscle ( $M_3-r$ )



Animation sequence to previous slide

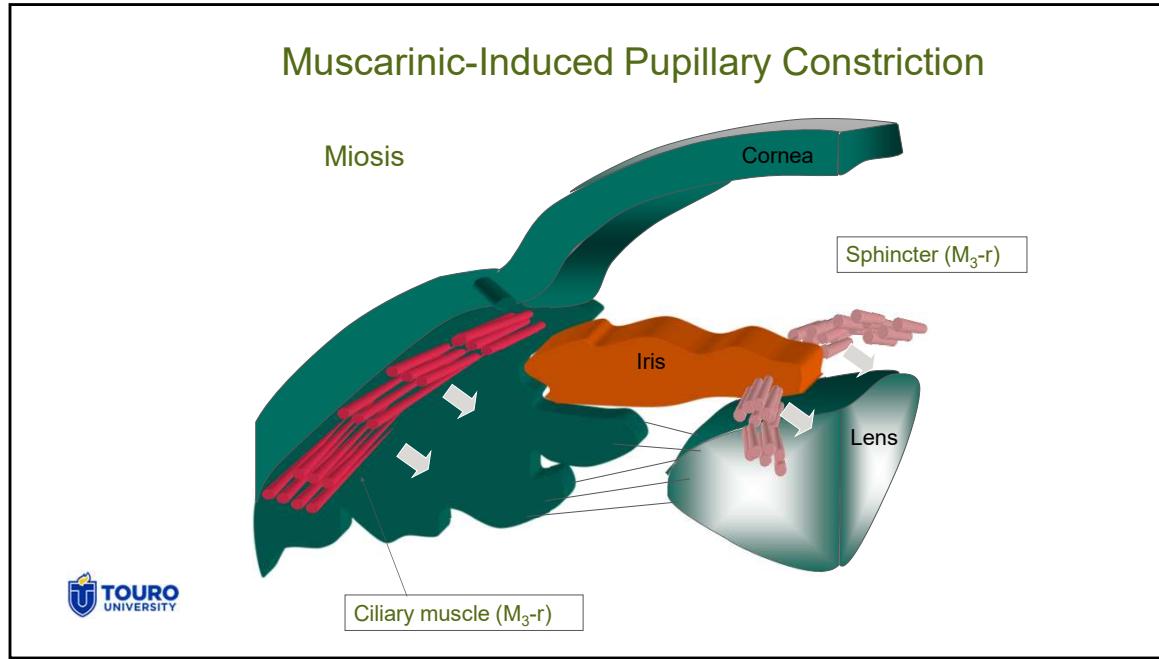


Testable Objectives:

**Know the treatments for both.**  
**Know the mechanism of action and toxicities of the drugs used to treat glaucoma**

Drugs that activate muscarinic receptors can decrease intraocular pressure by optimizing the outflow of aqueous humor through the canal of Schlemm.

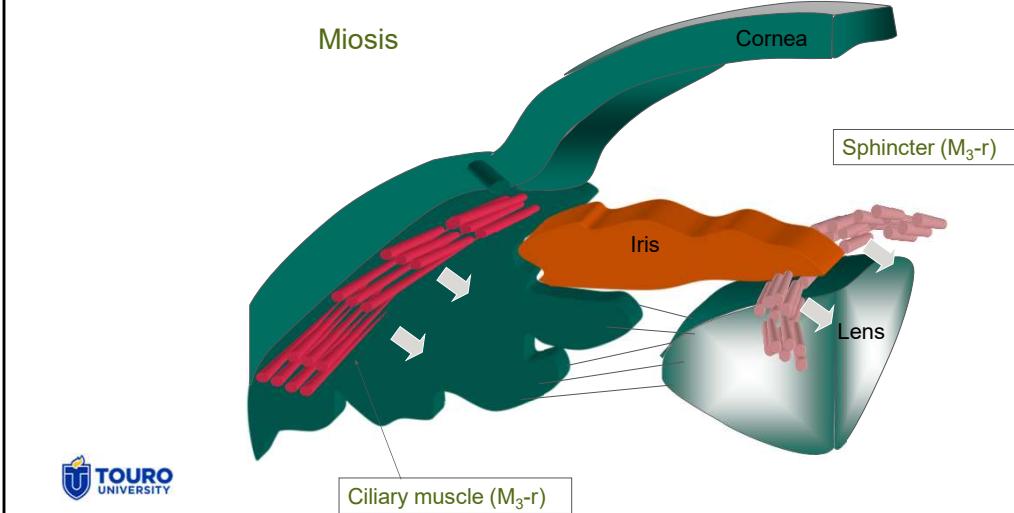
Both indirect and direct acting drugs can be used to activate the muscarinic receptors.



Know the “normal regulation” of eye function: ciliary, circular, radial muscle control; the physiologic factors that influence outflow through the canal of Schlemm; and the regulation of aqueous humor production.

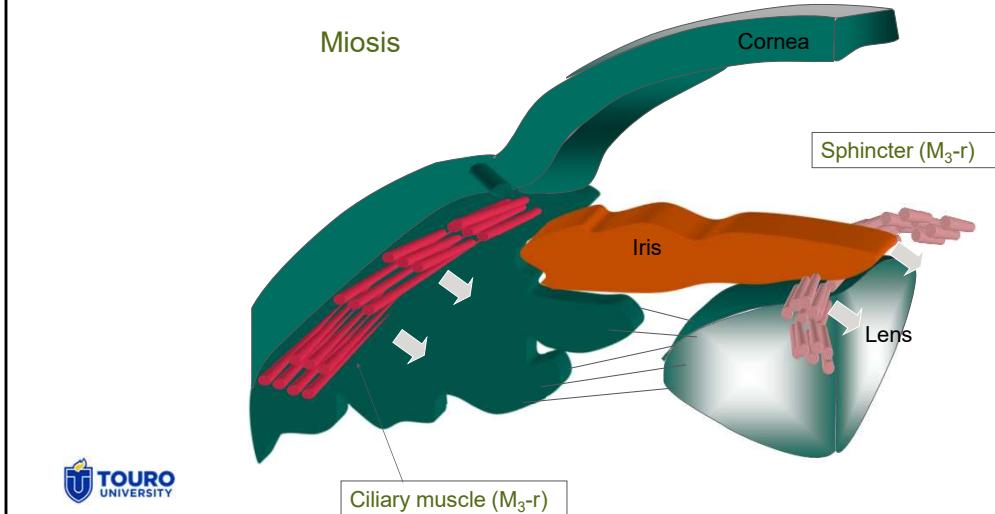
Note what happens to the pupil when the sphincter muscle contracts.

## Muscarinic-Induced Pupillary Constriction



Animation sequence to previous slide.

## Muscarinic-Induced Pupillary Constriction



Animation sequence to previous slide.



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## Clinical Management

Pharmacology

don't want to stop/start bc causes pressure fluxes and is more damaging to optic nerve

## Management

prostaglandins not associated with tha

↑ IOP = both development and progression of OAG

### Initiation of therapy

Presence of optic neuropathy **retinal damage/vision loss**

No threshold IOP (generally started >23-25)

note elevated IOP is not diagnostic (1/6 US patients have normal IOP)

### Target IOP

Therapeutic goal: reduce or prevent further optic nerve damage by ↓ IOP

No standard, graded effect of ↓ in IOP with risk of visual field loss. ↓ IOP target if nerve damage continues. Attempt to reduce initial IOP ≥ 25-30%

Prostaglandins are first line for pharm, combinations if needed

### Therapy

drug → laser ( trabeculoplasty) or surgery =discuss options with patient  
trabeculoplasty vs pharm outcomes at ↓ IOP similar

Surgery if necessary – more complications

**Compliance** (more dosing = less compliance) **need to do daily**

### Lifetime monitoring

More initially

2 X year after establishing therapeutic goals

AAO, Preferred Practice  
Pattern, Primary Open-Angle  
Glaucoma, American Academy  
of Ophthalmology 1996

pilocarpine causes visual things  
beta blockers then to become  
systemic bc drains - heart issues

Testable objectives: **Know the treatments for both.**

**Be aware of treatment goals**

**Know the mechanism of action and toxicities of the drugs used to treat glaucoma**

uveal scleral using prostaglandins

## Pharmacology

- ➔ IOP, ↓progression of visual field loss
- ↑ outflow
  - Conventional (CS +TM)
    - Muscarinic agonist or AChE inhibitors
    - Newest (TM outflow)
      - Netarsudil (rho kinase inhibitor)
  - Unconventional (US)
    - Ciliary muscle relaxation –open pores
      - Beta -2 receptor activation (epinephrine)
      - Alters extracellular matrix increases pores
        - PGF2-a (used commonly, a preferred therapy {once a day dosing)
- ↓ production
  - Alpha-2 agonist
  - Beta-receptor blockers
    - common initial therapy
  - Carbonic anhydrase inhibitors
  - Topical or systemic

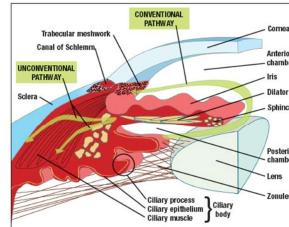


Figure 2. A schematic representation of conventional and unconventional aqueous humor (AH) pathways. As indicated by the arrows, AH is produced in the ciliary process, then flows into the posterior chamber and through the pupil into the anterior chamber, exiting via the conventional pathway (trabecular meshwork and Schlemm canal) or unconventional pathway (unconventional route). Reproduced with permission from Cengage University SPAH.

### An Overview of Glaucoma Management for Pharmacists

Karen K. O'Brien, Alan W. Y. Chock, Catherine A. Opere,

[http://www.uspharmacist.com/continuing\\_education/ceviewtest/lessonid/106698/](http://www.uspharmacist.com/continuing_education/ceviewtest/lessonid/106698/)

Know the treatments for both.  
Be aware of treatment goals  
Know the mechanism of action and toxicities of the drugs used to treat glaucoma

remember what gayer said earlier

M3 agonist  
prostaglandins

don't need administration times

gayer will ask outflow vs  
production

will ask about latanoprost  
(number 1 drug)- increases uveal  
scleral outflow  
associated with vascular  
inflammation, eyelash growth,  
skin/iris pigmentation issues  
depending on preservative can  
cause pain  
but is preferred bc more  
pressure decrease

Drug / Class	Administration	Mechanism (Apt: production vs outflow)	Mechanism of Drug Action (target/pathway)	Effect on IOP	Key Toxicities / Cautions	Most prescribed?	Notes
Latanoprost (PGA)	Topical 1 drop QHS	I Uveoscleral outflow	FP receptor agonist on cilary muscle → I MMPs & ECM remodeling – uveoscleral pathway widened	-25-31% reduction; 24-h efficacy	Conjunctival hyperemia; iris/skin pigmentation; eyelash growth; periorbital fat atrophy; rare CME post-treatment	Yes (most widely used in US)	First-line in POAG/HT; generic
Travoprost (PGA)	Topical 1 drop QHS	I Uveoscleral outflow	FP receptor agonist – cilary muscle relaxation & ECM remodeling	-25-31% reduction	Similar to latanoprost	No (less widely used)	Benzalkonium-free options exist
Bimatoprost (PGA)	Topical 1 drop QHS	I Uveoscleral outflow	Prostamide analog; FP receptor activity → I MMPs; possible trabecular effect	-25-33% reduction	Hyperemia more common; periorcular changes	No	Also used for eyelash growth (off-label)
Talazoprost (PGA)	Topical 1 drop QHS	I Uveoscleral outflow	FP receptor agonist; preservative-free formulation available	-25-30% reduction	Similar to class; preservative-free option	No	Consider for ocular surface disease
Latanoprostene bunod 0.02% (NO-donating PGA)	Topical 1 drop QHS	I Uveoscleral outflow AND I Trabecular outflow	FP receptor agonist (preserves) + NO release → cGMP ↑	> Greater than timolol in RCTs; robust data effect	Hyperemia; similar to PGAs	No	Dual pathway (uveoscleral + trabecular)
Netsarsudil 0.02% (rho-kinase inhibitor)	Topical 1 drop QHS	I Trabecular outflow; I Epicardial blood flow; preservative; modest ↓ production	ROCK II inhibitor → I adenosine concentration & stiffness in epicardial blood vessels; modest ↓ production	-3-5 mmHg (-15-20%)	Conjunctival hyperemia; corneal verticillata; instillation-site discomfort	No	Useful add-on targeting instillation site
Timolol (β-blocker, non-selective)	Topical 1 drop BID (QD gel once/week)	I Aqueous production	β1/β2 antagonist on non-pigmented cilary epithelium → I adenyl cyclase → I cAMP → I Na+ fluid transport	-20-27% daytime reduction; minimal nocturnal effect	Bradycardia; AV block; hypotension; bronchospasm; avoid in asthma/COPD/heart block	No	Common 2nd line or add-on
Betaxolol (β1-selective blocker)	Topical 1 drop BID	I Aqueous production	β1-selective antagonist → I cAMP in cilary epithelium	-15-25% reduction (less than timolol)	Systemic β-blocker effects; relatively safer in reactive airway disease but still caution	No	β1-selective
Brimonidine (α2-agonist)	Topical 1 drop TID (BID in practice)	I Aqueous production; I Uveoscleral outflow	α2-adrenergic agonist on cilary epithelium → GI → I adenylyl cyclase/cAMP; secondary I uveoscleral outflow	-12-29% reduction (study-dependent)	Allergic rhinitis; conjunctival erythema; fatigue; hypertension	No	Allergy risk increases over time
Aprastropine (α2-agonist)	Topical 1 drop TID (short-term)	I Aqueous production	α2-adrenergic agonist → I cAMP & I aqueous inflow (tachyphylaxis common)	Moderate reduction; rapid onset	High rates of allergy and tachyphylaxis	No	Short-term use (e.g., post-laser soaks)
Dorzolamide 2% (topical CAI)	Topical 1 drop TID (BID often)	I Aqueous production	Inhibits carbonic anhydrase II/IV in cilary processes → I HCO3- generation → I Na+ fluid secretion	-15-20% reduction	Ocular irritation; bitter taste; sulfonamide cross-reactivity caution	No	Useful adjunct; watch OSD
Brinzolamide 1% (topical CAI)	Topical 1 drop TID (BID often)	I Aqueous production	Carbonic anhydrase II inhibition in cilary processes → I aqueous secretion	-15-20% reduction	Blur/irritation; sulfonamide caution	No	Suspension (shake)
Pilocarpine (miotic)	Topical 1 drop QID (gel HS)	I Trabecular outflow	Muscarinic M3 agonist on iris sphincter & cilary muscle – miosis & cilary contraction → scleral spur traction = TM outflow ↓	[Effective but less favored chronically]	Brow ache; induced myopia; ↓ night vision; RD risk in predisposed	No	Use limited by tolerability
Dorzolamide/Timolol (fixed combo)	Topical 1 drop BID	I Production (additive)	CAI (I HCO3-) + α1/β-blocker (I cAMP) = I aqueous formation via complementary targets	-27% reduction (greater than either alone)	Component β-blocker/CAV AEs	No	Reduced drop burden; adherence aid
Brinzolamide/Timolol (fixed combo)	Topical 1 drop BID	I Production; modest I outflow	α2 agonist (GI → I cAMP) + β-blocker (I cAMP)	Greater than either alone	Component AEs; brinzolamide allergy risk	No	BID
Brinzolamide/Brimonidine (fixed combo)	Topical 1 drop BID	I Production; some I outflow	CAI (I HCO3-) + α2 agonist (I cAMP); I uveoscleral	Additive to components	Component AEs	No	Single-bottle alternative to triple therapy
Netsarsudil/Latanoprost (fixed combo)	Topical 1 drop QHS	I Trabecular outflow & I EVP + I Uveoscleral outflow	ROCK inhibition + FP receptor agonism; NO/cEVF effect from netsarsudil contribution	Greater than either alone; strong nocturnal/daytime coverage	Hyperemia; corneal verticillata; PGA class effects	No	Dual-pathway feed combi

only used last few years increases  
trabecular outflow and softens/open pores

B1 selective has less lung effects



30

go through toxicities

Drug Class	Toxicity
Cholinomimetics	<u>Miosis</u> , <u>blurred vision</u> , and night blindness are fairly common with topical application. Ciliary spasm may cause <u>headache</u> . Long term cataracts and lens adhesions. Cat C
Alpha agonist	dipivefrin include hyperemia (6.5%) and burning or stinging (6%). Ocular pruritis and ocular pain have also been reported. <u>Photophobia</u> (2%). Mydriasis occurs within 30 minutes with dipivefrin and may persist for several hours, causing transient blurred vision. Caution in patients with cerebral or coronary insufficiency, Raynaud's, postural hypotension, hepatic and renal impairment
A2 agonist	Ocular allergic-like reactions. Upper lid elevation, blepharitis, conjunctivitis, abnormal or blurred vision, xerophthalmia, photophobia, corneal staining, keratitis, conjunctival blanching, and mydriasis, xerostomia (10%), dysgeusia (3%), and nasal dryness (2%). Cat C
Beta blockers	Ocular allergic-like reactions. Upper lid elevation, blepharitis, conjunctivitis, abnormal or blurred vision, xerophthalmia, photophobia, corneal staining, keratitis, conjunctival blanching, and mydriasis, xerostomia (10%), dysgeusia (3%), and nasal dryness (2%). Systemic side effects can occur. <b>Contraindicated in patients with bradycardia, heart block, heart failure, asthma, and COPD</b> 
Diuretics	ocular irritation, bitter taste, superficial punctate keratitis in (10—15% ), blurred vision, excessive lacrimation, photophobia, and xerophthalmia. headache, nausea, asthenia, fatigue, skin rash, and urolithiasis. Sulfonamide allergy can produce severe responses. Cat C
Prostaglandins	<u>Less side effects than B-blockers</u> , However, in some—blurred vision, conjunctival hyperemia, foreign body sensation, iridal discoloration, ocular irritation (itching, burning, stinging), and punctate corneal keratopathy. Cat C

get T3 synergic

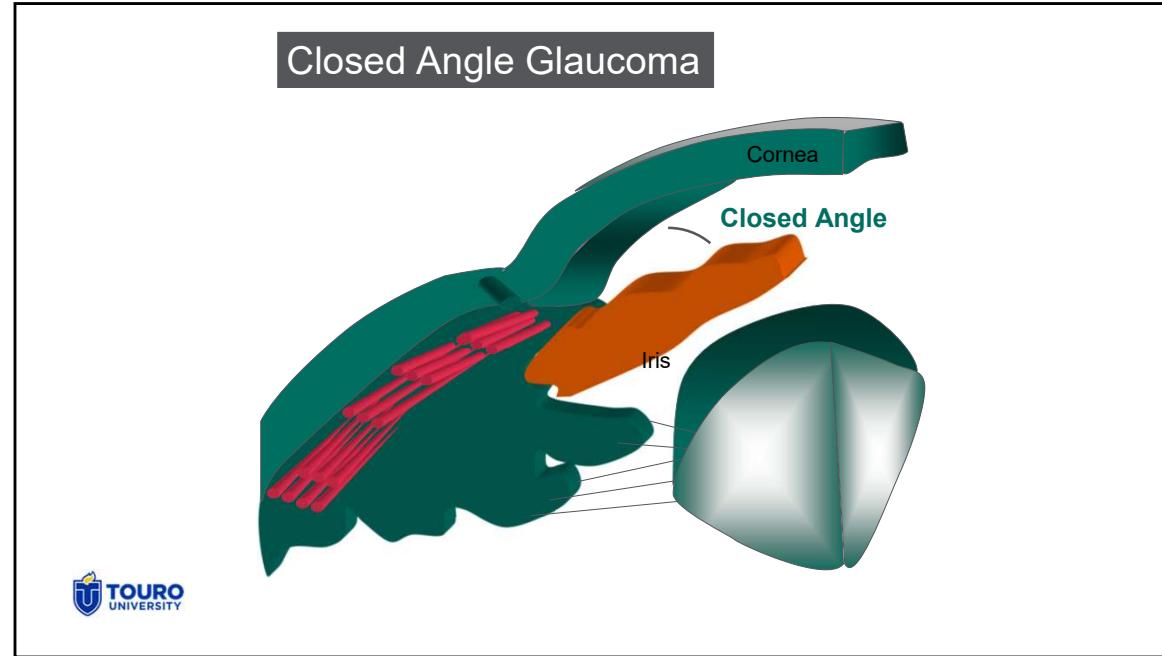
Know the treatments for both.

Be aware of treatment goals

Know the mechanism of action and toxicities of the drugs used to treat glaucoma

Know details of this table. It is a summary table that of material covered.

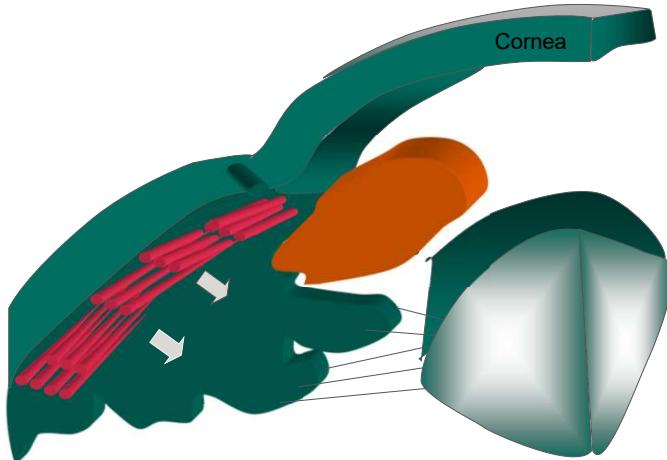
avoid pupillary constriction - Epi,  
methamphetamine bc will block canal c  
schlemm



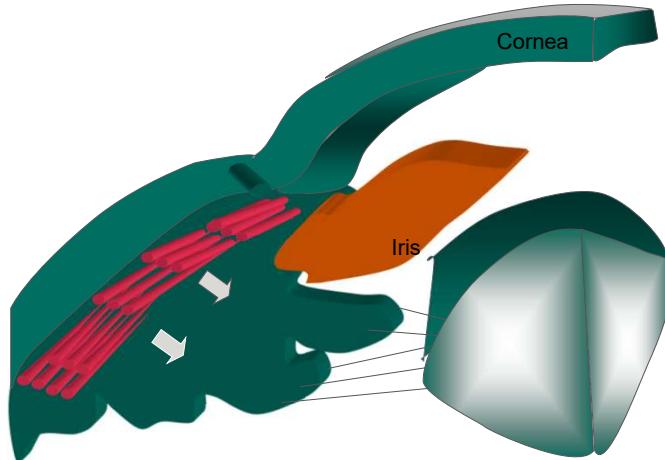
**Testable objectives:** Be prepared to answers questions regarding the pathophysiology of both  
Know the anatomical differences between the two types and how they relate to the diagnosis and management

Students should note that closed angle glaucoma is a disease that reflects the iris angle to cornea. Note: the location of the canal of Schlemm.

## Closed Angle Glaucoma



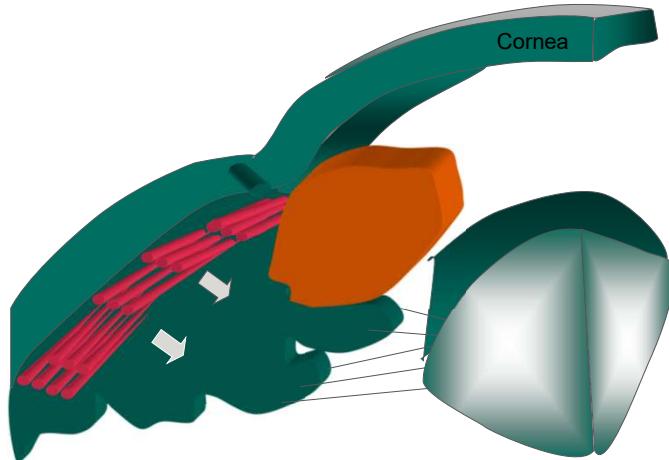
## Closed Angle Glaucoma



Testable objectives: Be prepared to answers questions regarding the pathophysiology of both  
Know the anatomical differences between the two types and how they relate to the diagnosis and management

Animation slide to previous. When the iris contracts it can block the canal of Schlemm.

## Closed Angle Glaucoma

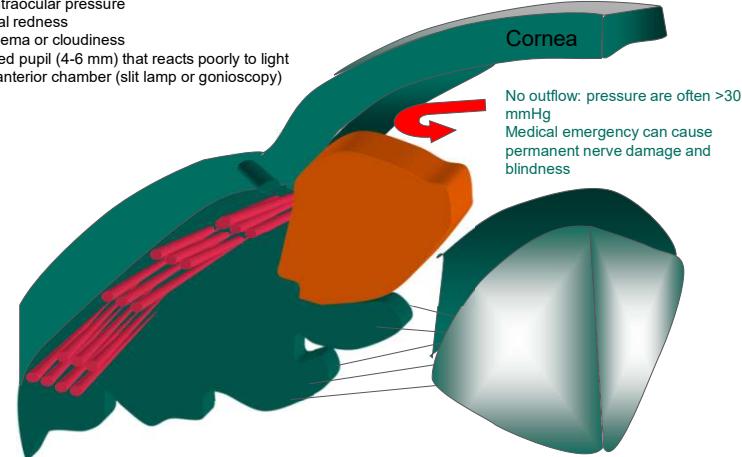


Testable objectives: Be prepared to answers questions regarding the pathophysiology of both  
Know the anatomical differences between the two types and how they relate to the diagnosis and management

Animation slide to previous. When the iris contracts it can block the canal of Schlemm.

## Closed Angle Glaucoma

Elevated intraocular pressure  
Conjunctival redness  
Corneal edema or cloudiness  
A mid-dilated pupil (4-6 mm) that reacts poorly to light  
A shallow anterior chamber (slit lamp or gonioscopy)



No outflow: pressure are often >30 mmHg  
Medical emergency can cause permanent nerve damage and blindness

Symptoms often arise at night with low light levels  
Treatment: avoid drugs that cause the pupil to dilate (alpha-1 adrenoceptor agonist)



## Treatment of Acute Closed Angle Glaucoma

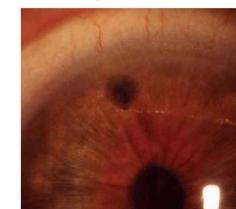
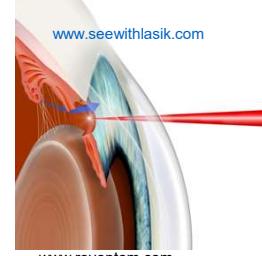
### Surgery

Iridotomy (laser focused on iris tissue leaving cornea intact)

### Medication (until surgery or to maintain IOP)

Topical

Systemic



## Testable Objectives

Know the treatments for both.

Know the mechanism of action and toxicities of the drugs used to treat glaucoma

Acute closed angle glaucoma is a medical emergency and usually requires prompt surgical intervention.

Pharmacologic therapy can be used to reduce IOP until surgery. Drugs that increase aqueous humor outflow or

decrease production can be used. Drugs that constrict the pupil (alpha-agonist) should not be used. Constriction of the pupil can close the canal of Schlemm.

Acute primary angle closure glaucoma — There are no available trials comparing medical options for treatment of acute angle closure, and treatment recommendations are based on clinical experience [14]. When an ophthalmologist is available for consultation within one hour of patient presentation, patients with signs or symptoms suggesting possible acute angle closure should be referred for emergent assessment and treatment.

When there is likely to be an hour or more delay before a patient can be seen by an ophthalmologist, and the suspicion of an acute attack is high, empiric treatment should be initiated. For an acute primary angle closure attack, initial management involves prompt administration of pressure-lowering eye drops. A possible regimen would be one drop each, one minute apart, of [14]:

0.5% [timolol](#) maleate (Timoptic)

1% [apraclonidine](#) (Iopidine), and

2% [pilocarpine](#) (Isopto Carpine)

Systemic medications (oral or IV [acetazolamide](#), IV [mannitol](#), or oral glycerol or isosorbide) to control the intraocular pressure are often given. We suggest giving the patient two 250 mg tablets of acetazolamide in the office. The eye pressure should be checked 30 to 60 minutes after giving pressure-lowering drops and oral acetazolamide. Systemic medications other than oral acetazolamide should be administered under the guidance of an ophthalmologist, since angle closure should be confirmed before they are given

think of this as can be emergent/urgent issue  
present to ER with 40 mm Hg or higher need to give something that gets the pressure down

*suck fluid out*

Medications for Closed Angle Glaucoma						
Drug / Class	Administration	Mechanism (AH: production vs outflow)	Mechanism of Drug Action (target/pathway)	Effect on IOP	Key Toxicities / Cautions	Notes
Acetazolamide (systemic CAI)	IV 500 mg or PO 500 mg load; then 250 mg PO QID or 500 mg SR BID (short-term)	↓ Aqueous production	Systemic inhibition of carbonic anhydrase II in ciliary processes → ↓ HCO <sub>3</sub> <sup>-</sup> formation → ↓ aqueous secretion	Rapid reduction; bridge to definitive therapy	Paresthesias; diuresis; metabolic acidosis; kidney stones; avoid in severe renal/hepatic disease & sulfonamide allergy	First pharmacologic step in APAC
Timolol ( $\beta$ -blocker)	Topical 1 drop once; may repeat per protocol	↓ Aqueous production	$\beta$ 1/ $\beta$ 2 antagonism on ciliary epithelium → ↓ cAMP	Adjunctive reduction	Cardiopulmonary contraindications as above	Given early with systemic CAI
Brimonidine ( $\alpha$ 2-agonist)	Topical 1 drop once; repeat per protocol	↓ Aqueous production; ↑ Uveoscleral outflow	$\alpha$ 2 agonist → Gi → ↓ adenylyl cyclase/cAMP in ciliary epithelium	Adjunctive reduction	Allergic conjunctivitis; systemic sedation/hypotension	Often combined with timolol initially
Prostaglandin analog (e.g., latanoprost)	Topical 1 drop	↑ Uveoscleral outflow	FP receptor agonism → ↑ MMPs/ECM remodeling	Adjunctive; slower onset vs others	Hyperemia; pigmentation changes	May be added in APAC protocols
Mannitol 20% (hyperosmotic)	IV 0.5–2 g/kg over 30–60 min	↓ Ocular volume IOP ↓	↑ Plasma osmolarity → osmotic dehydration of vitreous/aqueous compartments	Rapid fall in very high IOP	Diuresis; electrolyte shifts; caution in HF/renal disease	If IOP remains very high or severe pain/edema
Glycerol (oral hyperosmotic)	PO 1–1.5 g/kg	↓ Ocular volume IOP ↓	draws water out of eye; raises glucose	Rapid adjunctive reduction	Nausea; ↑ glucose—avoid in diabetes	Alternative when IV access delayed
Isosorbide (oral hyperosmotic)	PO 1–3 g/kg	↓ Ocular volume IOP ↓	Non-sugar osmotic agent ↑ serum osmolarity → vitreous dehydration	Rapid adjunctive reduction	GI upset; headache	Preferred over glycerol in diabetes
Pilocarpine (miotic)	Topical 1–2%: 1 drop q15 min × 2 doses AFTER IOP lowered, then QID	↑ Trabecular outflow	M3 receptor agonist → miosis & ciliary contraction → opens TM (after ischemia resolves)	Facilitates resolution of pupillary block	Brow ache; induced myopia; ↓ night initially	Give after pressure drops (ischemic iris unresponsive)

Mannitol, Glycerol, and Isosorbide - sugar and will not go across transporters so will stay on one side wherever you put it - wa will go to (fluid flow out of eye) and eleva IOP will help reduce - suck fluid out of br

## Use of Medications with Glaucoma Warnings

Drug Class	Use results in:
Glucocorticoids	Glucocorticoid preparations (ie, ocular, oral, inhaled, and periocular dermatologic preparations) can raise intraocular pressure (IOP) in open-angle glaucoma patients. May take two weeks to observe therefore short courses are not associated with ophthalmologic issues. Longer courses require should visit their eye doctor Decrease outflow through trabecular meshwork.
Systemic sympathomimetics	This includes over the counter ephedrine and pseudoephedrine, and TCA, antipsychotics. May increase angle closer intraocular pressure but congesting the canal of Schlemm and thus reduce outflow with any drug that has alpha activity potential.
Systemic anticholinergics	This includes anticholinergic inhalers, overactive bladder medications, antihistamines and some drugs for muscle spasm. Antimuscarinic activity will also congest the canal of Schlemm and reduce outflow.

increase IOP, watch out for pts on these for systemic things)

reduced outflow - watch out for esp in closed angle

Know the treatments for both.

Be aware of treatment goals

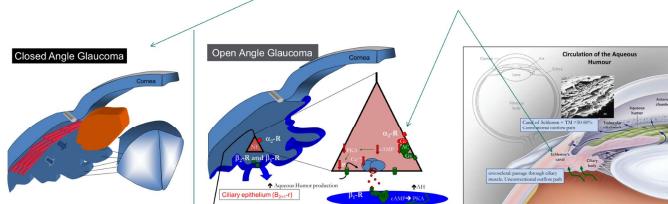
Know the mechanism of action and toxicities of the drugs used to treat glaucoma

Know details of this table. It is a summary table that of material covered.

## Questions?

<http://forums.studentdoctor.net/threads/glaucoma-treatment-question.345069/>

- hey all,  
I don't understand how epinephrine can treat glaucoma.  
Epinephrine would dilate the pupil, which can cause the acute closed angle glaucoma. So...how can it treat glaucoma?



not the alpha 1 that we want it's alpha 2 and DO NOT used for closed angle

## Questions?

<http://forums.studentdoctor.net/threads/>

- If someone can explain the effects of alpha and beta on the eye and its relation to glaucoma that would be great.

(I tried understanding it from First Aid and googling, but I just don't understand it)



B1 - aq humor production

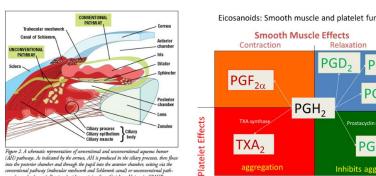
A2 - decrease NE release

## Questions?

<http://forums.studentdoctor.net/threads/>

- Does anyone know why prostaglandin is contraindicated when a pregnant woman has asthma or glaucoma? First aid says prostaglandin can be used to treat glaucoma. And first aid also says it lowers bronchial tone...

Cat C : Risk cannot be ruled out, either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus.



Tissue	Biologic Effect	Comments
GI	Smooth muscle Contractor of longitudinal & circular muscle. Delays emptying	TXA <sub>2</sub> , K <sub>2</sub> O <sub>3</sub> , EP <sub>3</sub> , PGF <sub>2α</sub> , PG <sub>2</sub> , PG <sub>3</sub>
Muscle	General relaxant - relaxes smooth muscle & skeletal muscle	PGI <sub>2</sub> , K <sub>2</sub> O <sub>3</sub>
Lung	Smooth muscle Relaxation	TXA <sub>2</sub> , PG <sub>2</sub> , PGF <sub>2α</sub> , PG <sub>3</sub>
Kidney	Blood vessels Contractor of renal blood flow (especially in glomeruli) stimulates renin secretion; regulates free water excretion	PG <sub>2</sub> , PG <sub>3</sub>
Female Reproductive	Female Role in ovulation, lactation, and fertilization Male Inhibits smooth muscle contraction	TXA <sub>2</sub> , PG <sub>2</sub> , EP <sub>3</sub> , PGF <sub>2α</sub> , PG <sub>3</sub>
Neuronal	Fever (CHSI) Increased body temp ↓ M release sympathetic T axon ↓ M release sensory neurons	PG <sub>2</sub> , EP <sub>3</sub>
Bone/Muscl	↑ bone turnover rate in healing Muscl ↓ tone turnover rate in healing	PG <sub>2</sub> , PG <sub>3</sub>
Ost	Yeast-control Antifungal	PG <sub>2</sub> , PG <sub>3</sub>
Cancer	Prooncokerin breast and skin	TXA <sub>2</sub> , TXB <sub>2</sub> , EP <sub>2</sub> , EP <sub>3</sub>

FA isn't gospel

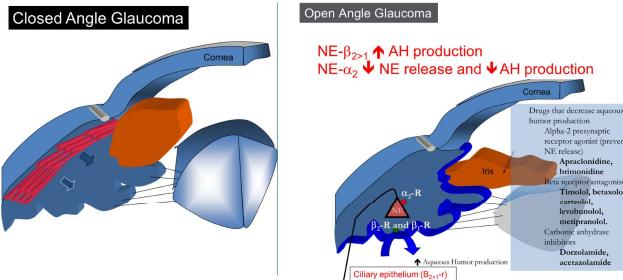
latanoprost is given topically so not getting in systemically (less SE profile)

if did inject PTF2A will cause smooth muscle contraction - can cause abortion bc of uterine cor  
also causes issues in the lungs

## Questions?

<http://forums.studentdoctor.net/threads/>

- Does anyone know if there is any major differences in the treatment of the 2 different types of glaucoma?



major diff is if it becomes emergent/urgent issue - IOP increases too much will start to use systemic to get pressure down will still use topicals  
no alpha 1s bc causes pupillary constriction

## Summary

- Open angle V Closed Angle
- Management
- Good luck—I have my eye on you.



## Management of Glaucoma:

### Objectives:

Be able to describe in detail the “normal regulation” of eye function: ciliary, circular, radial muscle control; the physiologic factors that influence outflow through the canal of Schlemm; and the regulation of aqueous humor production.

Diagnose the difference in clinical presentations of open angle and closed angle glaucoma.

Use the various diagnostic tests for both states to confirm diagnosis

Be prepared to answer questions regarding the pathophysiology of both

Know the anatomical differences between the two types and how they relate to the diagnosis and management

Be able to diagnose and prescribe treatments for both.

Be aware of treatment goals

Describe in detail the mechanism of action and toxicities of the drugs used to treat glaucoma

Know drugs that are to be used with caution and why when a patient is suffering from either type of glaucoma.

Drug / Class
Latanoprost (PGA)
Travoprost (PGA)
Bimatoprost (PGA)
Taluprost (PGA)
Latanoprostene bunod 0.024% (NO-donating PGA)
Netarsudil 0.02% (Rho-kinase inhibitor)
Timolol ( $\beta$ -blocker, non-selective)
Betaxolol ( $\beta_1$ -selective blocker)
Brimonidine ( $\alpha_2$ -agonist)
Apraclonidine ( $\alpha_2$ -agonist)
Dorzolamide 2% (topical CAI)
Brinzolamide 1% (topical CAI)
Pilocarpine (miotic)
Mannitol 20% (hyperosmotic)
Glycerol (oral hyperosmotic)
Isosorbide (oral hyperosmotic)
Pilocarpine (miotic)

Drug / Class

# Drug List

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