Slide 1

The Secondary Glaucomas

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Disclosures and Special Request

Paid consultant for:

- Alcon Pharmaceuticals, Bausch and Lomb, Carl Zeiss Meditec, NiCox

Special Request:

Interactive remotes don't work on your TV, so please don't take them home! ☺

Commitment to change:

- write down three things that you "learned" from this presentation that you can incorporate into your practice to improve patient care

Slide 3

The Secondary Glaucomas

- most basic approach is to separate the various types of glaucoma into two categories:
  - secondary open-angle and
  - secondary narrow or closed-angle glaucoma
- classification may be based on:
  - the etiology of the disease or
  - the mechanism by which the elevation in IOP is produced

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The Secondary Glaucomas

- secondary glaucoma may be:
  - congenital,
  - occur as a result of another ophthalmic disorder,
  - or be induced by or follow trauma or intraocular surgery.

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Agenda

- Secondary glaucoma associated with ophthalmic disorders:
  - Neovascular glaucoma (NVG)
  - Lens induced glaucoma
    - Phacolytic
    - Phacomorphic
- Secondary glaucoma associated with trauma:
  - Angle recession glaucoma
- Secondary glaucoma associated with inflammation:
  - Uveitic glaucoma
  - Fuchs Heterochromia
  - Glaucomatocyclitic crisis

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Neovascular Glaucoma (NVG)

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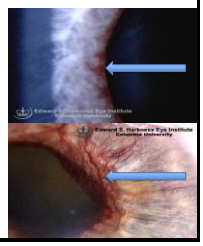
NVG

- NVG is one of the most difficult types of glaucoma to manage
  - once secondary angle closure occurs it is extremely difficult to reverse

Slide 8

Iris Neovascularization

- New vessel growth usually begins at the pupil margin
  - enlarge, and grow in an irregular pattern along the iris surface



http://dro.hs.columbia.edu/nvg.htm

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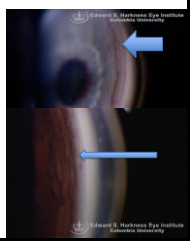
Angle Neovascularization

- New vessels grow to anterior chamber angle
  - new blood vessel growth brings along fibrovascular tissue
  - causes a reduction of aqueous humor outflow



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Peripheral Anterior Synechiae (PAS)

- If the membrane contracts it pulls the peripheral iris into the TM leading to the formation of PAS

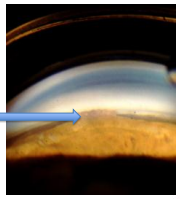

Image courtesy: John McSoley, OD

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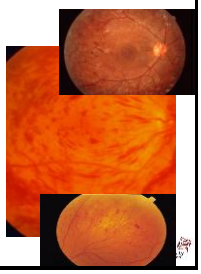
NVG: Etiology

- Ocular ischemic disorders account for 97% of cases with NVG
  - The most common disorders leading to NVG are:
    - diabetes mellitus,
    - CRVO, and
    - ocular ischemic syndrome.



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NVG and VEGF

- There is adequate evidence supporting the role of VEGF-A in the pathogenesis of ocular neovascularization,
  - studies have confirmed the increased levels of VEGF-A in glaucoma and NVG in particular
  - experimental elevation of VEGF-A levels induces typical neovascularization

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NVG: Diagnosis

- Patients typically present with:
  - acute onset of pain,
  - redness, and
  - decreased VA

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Case

- A 68-year-old woman with a history of poorly controlled diabetes presents with poor vision of the left eye for about 2 months.
- She notes an episode of left eye pain 2 months ago that lasted for a week

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Case Presentation

	OD	OS
VA	20/40	20/800
Pupils	No APD	Mild APD
SLE	Cornea clear No NVI Angle Open 2+ NS	Extensive NVI with angle synechiae 20% hyphema 4+ NS
IOP	18 mm Hg	44 mm Hg
Fundus	PDR with NVD and NVE Focal area of subhyaloid hemorrhage	PDR with NVD and NVE Focal area of subhyaloid hemorrhage
C/D	0.4	0.7

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NVG: Management

- Treatment of the underlying disease and control of IOP.
- The key to NVG management lies in elimination of the angiogenic stimulus
- Effective treatments for retinal ischemia include:
  - Panretinal photocoagulation (PRP),
  - cryotherapy, and
  - endolaser treatment combined with vitrectomy.
- Despite the reduction of retinal ischemia and additional antiglaucoma medication
  - NVG frequently exhibits irreversible intraocular pressure (IOP) elevation.

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NVG: Medical Management

- Medical therapy is beneficial in lowering the IOP and include:
  - topical ß-blockers,
  - a-2 agonists, and
  - topical or oral carbonic inhibitors
- Miotics (pilocarpine) and epinephrine drugs are contraindicated:
  - they may increase inflammation (increase permeability of the blood-aqueous barrier),
  - cause miosis, and
  - worsen synechial angle closure

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NVG: Medical Management

- Topical prostaglandins are generally not used because they too can exacerbate inflammation
- Intraocular inflammation may be treated with topical corticosteroids.

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NVG: Anti-VEGF

- New treatment includes the use of anti-VEGF
  - several studies have shown that specific inhibition of VEGF-A inhibits pathologic neovascularization in the iris, choroid, cornea, and retina
- The 3 traditional anti–VEGF-A agents available for clinical use are:
  - Bevacizumab (Avastin),
  - Ranibizumab (Lucentis), and
  - Pegaptanib (Macugen).
- Most recent addition is:
  - **Aflibercept (VEGF-TRAP) (Eyelea)**

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NVG: Anti-VEGF

- Intra-vitreal anti-VEGF has been shown effective in regression of new vessels and reduction of IOP in NVG
  - regression occurs quickly, often within 1 week.
  - however, bevacizumab's duration of action is short-lived, lasting about 4 weeks.
- The mechanism by which IOP may be reduced by bevacizumab or any other anti–VEGF-A agent is a matter of speculation

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NVG: Anti-VEGF

- Recent retrospective studies regarding IVB for iris neovascularization and NVG:
  - shows that the IOP-lowering effect for NVG was transient
    - secondary to the drug's short life and
    - the irreversible elevation of outflow resistance in the angle of NVG patients,
      - requiring subsequent surgery to stabilize IOP levels.

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NVG: Glaucoma Surgery

- Glaucoma filtering surgery is now considered standard for the treatment of the elevated IOP in NVG patients
- Glaucoma surgery is indicated to optimally control IOP if medical therapy has proven to be inadequate. Includes procedures such as:
  - aqueous tube shunt surgery,
  - cyclodestruction, or
  - antimetabolite-enhanced filtration surgery.

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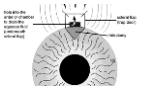
Trabeculectomy

- Trabeculectomy with and without mitomycin-C has been shown to be successful in controlling intraocular pressure
- The use of anti-metabolites improves IOP control and the success of trabeculectomy



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NVG: Trabeculectomy

- Trabeculectomy with intraoperative MMC after an adjunctive treatment with IVB and PRP is a good treatment modality in the management of eyes with NVG.
  - It is effective in reducing NVI and intraoperative complications during trabeculectomy.
  - **Management of Neovascular Glaucoma With Panretinal Photocoagulation, Intravitreal Bevacizumab, and Subsequent Trabeculectomy With Mitomycin C**. (J Glaucoma 2010;19:622–626)
  - **Combined Intravitreal Bevacizumab and Trabeculectomy With Mitomycin C Versus Trabeculectomy With Mitomycin C Alone for Neovascular Glaucoma** (J Glaucoma 2011;20:196–201

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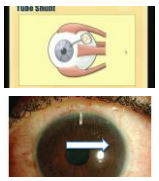
Glaucoma Drainage Implant

- implantation of a tube shunt
- most common treatment for glaucoma when medications have proven to be insufficient



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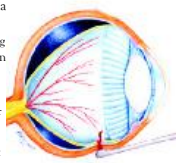
Cyclodestructive Procedures

- Ablating a portion of the cilia body
  - IOP is lowered by decreasing aqueous humour production
- Destruction of the ciliary body by:
  - transscleral application of cryotherapy or
  - transscleral or endoscopic delivery of diode, krypton Nd:YAG laser.



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NVG: End Stage

- For blind painful eyes with uncontrollable IOP, options include:
  - continued medical therapy,
  - cyclodestruction,
  - retrobulbar alcohol injection, or
  - enucleation.

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LEN INDUCED GLAUCOMA

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Clinical Pearl

- In all of these cases:
  - the glaucoma is typically very symptomatic with pain and redness in the involved eye, and cells and flare in the anterior chamber.
  - frequently, an advanced cataract in the involved eye severely reduces vision.

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Len Induced Glaucoma

- Lens-induced glaucoma can be subdivided into two major categories.
  - The first category relates to a blockage of the anterior flow of the aqueous humor from the lens that results in an increase of intraocular pressure (IOP). Conditions included in this category are:
    - (1) pupillary block glaucoma caused by an intumescent cataractous lens (phacomorphic glaucoma),
    - (2) ectopia lentis.

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Len Induced Glaucoma

- The second category is characterized by the blockage of the trabecular meshwork from lens proteins (phacolytic glaucoma), lens material or debris, and rarely by phacoanaphylactic response to lens material.

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Len Induced Glaucoma

- The most important factor is a shallow anterior chamber.
  - the depth of the chamber is dependent on the dimensions of the lens, the cornea, and the axial length of the globe.
  - with aging, the lens assumes greater thickness, a greater curve of its anterior surface, and the zonules loosen.
- These factors cause increasing shallowness of the anterior chamber and iridolenticular contact, which results in a greater amount of pupillary block.
- As a consequence, hyperopic eyes have a propensity for pupillary block.

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Phacomorphic

- A senile cataractous lens that has progressed enough to become intumescent
  - has an increased anteroposterior length,
  - which could lead to pupillary block.
  - this type of glaucoma is named **phacomorphic**

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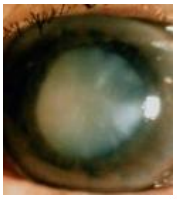
Phacomorphic Glaucoma

- often occurs from a mature cataract
- could present asymptomatically as chronic angle-closure glaucoma,
  - however it more often presents as acute angle closure glaucoma.



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Acute Angle Closure Glaucoma

- Acute angle-closure glaucoma will cause:
  - significant increase in IOP,
  - characterized by ocular pain, headache, blurred vision,
  - perception of halos around lights (due to the corneal edema),
  - and also nausea, vomiting, bradycardia, and diaphoresis due to the vasovagal response.
- Symptoms usually occur at night because mid-dilation predisposes relative pupillary block.

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Treatment

- Treatment focuses on two objectives:
  - lower the IOP as soon as possible and
  - prevent the diseased and fellow eye from another episode.
- Initially, IOP-lowering medications are used.
  - Topical beta blockers,
  - carbonic anhydrase inhibitors, and
  - hyperosmotic agents (mannitol IV) are the mainstay of medical treatment.

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Treatment

- Parasympathomimetic agents (pilocarpine 1% or 2%) tend to increase pupillary block, so they should be used with caution.
- In the case of phacomorphic glaucoma:
  - after IOP control and establishing intraocular inflammation
  - proceed to cataract extraction
    - which erases the major causative factor of angle-closure glaucoma

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Phacomorphic Glaucoma

Clinical Pearl:

In patients with hypermature cataracts and shallow anterior chambers with angle closure, consider phacomorphic glaucoma, especially if the fellow lens has less intumescence and there is a deeper chamber.

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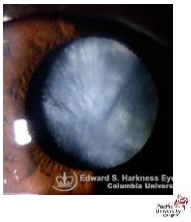
Phacolytic Glaucoma

- This acute open-angle glaucoma is the result of:
  - leakage of lenticular material from senile hypermature or Morgagnian cataract through an intact lens capsule



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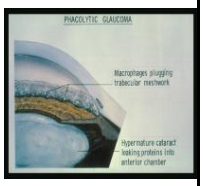
Phacolytic Glaucoma

- The presentation is:
  - red and painful eye,
  - history of gradual decline of visual acuity reflecting the slow maturation of the cataract,
    - Vision is typically 20/400 or worse (LP)
  - corneal edema,
  - high IOP (>35 mm Hg),
  - open-angle in gonioscopy,



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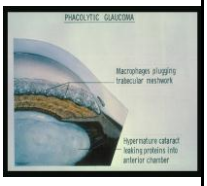
Phacolytic Glaucoma

- heavy flare, and aqueous cells larger than the lymphocytes seen in uveitis
  - these cells are thought to be macrophages swollen with eosinophilic lenticular material which they have engulfed.



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Phacolytic Glaucoma

- Soft white patches on the lens capsule can be observed
  - aggregates of macrophages trying to seal the site of leakage
  - the fellow eye usually has a mature cataract and a deep anterior chamber.

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Phacolytic Glaucoma Treatment

- The majority of patients with phacolytic glaucoma can be managed through:
  - topical cycloplegia,
  - topical steroids, and
  - aqueous suppressants.
- If despite intensive antiglaucomatous therapy, IOP continues to increase,
  - emergency admission may be advocated, and in
  - rare instances urgent cataract or vitreoretinal surgery may be required.

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Clinical Pearl

Phacomorphic and phacolytic glaucoma develop only in eyes with hypermature cataracts. Vision typically ranges from 20/400 to light perception. If vision is better than 20/400, consider another cause for the glaucoma.

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Lens-Particle Glaucoma

- In contrast to phacolytic glaucoma
  - this form of lens-induced glaucoma is associated with a grossly disrupted capsule and the presence of obvious fragments of lens material in the anterior chamber.
  - It may occur after:
    - cataract surgery,
    - trauma to the lens, or
    - YAG posterior capsulotomy.
  - The IOP increase is due to the obstruction of the aqueous outflow by the lens particles

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Lens-Particle Glaucoma

- Trial of medical antiglaucomatous therapy may be attempted,
  - but miotics should be avoided.
  - mild to moderate steroid therapy can help to prevent synechiae, pupillary membranes, cystoid macular edema, etc.
  - if the glaucoma is severe and/or there is a large amount of lens material in the anterior chamber, its surgical removal should be undertaken

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Clinical Pearl

Lens particle glaucoma:

The mechanism of lens particle glaucoma resembles that of phacolytic glaucoma, except that there is a history of surgery or trauma that releases the lens proteins into the anterior chamber and initiates a macrophage-driven inflammatory reaction. The angle remains open.

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Phacoanaphylactic glaucoma

- Phacoanaphylactic glaucoma is an inflammatory reaction directed against lenticular antigens with elevation of the IOP
  - due to involvement of the trabecular meshwork by the inflammation or by obstruction from inflammatory cells

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Phacoanaphylactic Glaucoma

- the patient is sensitized to his own lens antigens and these proteins are kept in an immunologically privileged site within the lens capsule.
- after an eye surgery or other trauma to the lens capsule
  - lens antigens are exposed to the circulation,
  - may be recognized as 'foreign' by the individual's immune system and
  - incite an inflammatory response.

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Phacoanaphylactic Glaucoma

- The time interval between the trauma and the onset of inflammation is 24 hours to 14 days.
- The clinical signs include:
  - lid edema,
  - chemosis,
  - conjuctival injection,
  - corneal edema,
  - heavy anterior chamber reaction,
  - posterior synechiae, and
  - mutton fat keratic precipitates

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Phacoanaphylactic Glaucoma Treatment

- The first step in therapy is the effort to control the IOP and inflammation medically.
- If this proves unsuccessful then the next phase is surgical removal of the remaining lens material

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Phacoanaphylactic Glaucoma

Clinical Pearl:

- **In cases of severe granulomatous uveitis with IOP rise following cataract extraction, consider phacoanaphylactic uveitis/glaucoma.**

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ANGLE RECESSION GLAUCOMA

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Angle Recession

- investigators have reported that more than 60% of eyes with non-penetrating traumatic injuries will have some degree of angle recession.
- although traumatic angle recessions may occur without anterior chamber hemorrhage,
  - a strong correlation between hyphema and angle recession has been established.
- Careful gonioscopy has revealed that between 56% and 100% of patients with traumatic hyphema have some degree of angle recession

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Angle Recession: Causes

- The most frequent cause of injury-inducing angle recession occurred as a result of:
  - sports or other recreational accidents
  - assault
    - Less common causes are:
      - automobile or industrial accidents,
      - projectiles from toy guns or slingshots, and
      - other leisure activities
  - A small percentage of people will deny any previous episode of ocular trauma despite the presence of obvious eyelid scars and pupillary sphincter tears.

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Angle Recession Glaucoma

- Although recession of the iridocorneal angle is common after blunt trauma,
  - only 6% to 7% of these eyes will eventually develop glaucoma
- There appear to be two peak incidences of glaucoma after angle recession.
  - the first peak occurs within the first few weeks to years after the trauma, and
  - the second peak occurs 10 or more years after the injury

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Angle Recession Glaucoma

- There is an association between the extent of angle recession and the development of glaucoma
- It appears that those eyes with less than 180 degrees of recession are unlikely to develop glaucoma
- whereas most investigators agree that patients with 180 to 360 degrees of angle recession will have a greater risk of developing late-occurring glaucoma

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Angle Recession Glaucoma

- In eyes that do develop angle recession glaucoma:
  - the contralateral nontraumatized eye has been reported to have a 50% chance of developing open-angle glaucoma, sometimes years after the pressure rise was noted in the traumatized eye.

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Angle Recession Diagnosis

- The diagnosis of angle recession is made by patient history and clinical examination.
  - In cases of unilateral glaucoma or traumatic hyphema or after blunt trauma, angle recession should always be considered
- With milder injuries
  - the examiner may have to compare the gonioscopic appearance of two parts of the angle of 1 eye to identify subtle changes in the injured angle.

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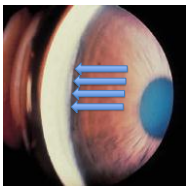
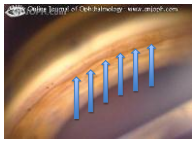
Angle Recession





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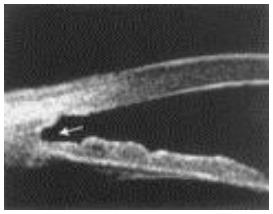
Ultrasound Angle Recession



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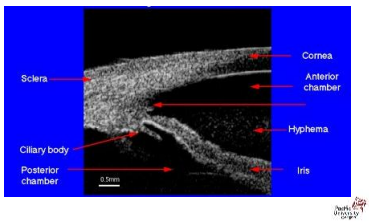
Anterior Segment OCT: Angle Recession



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Treatment

- The IOP rise that occurs immediately after blunt trauma to the eye is usually self-limited and, in the majority of cases, can be controlled with medication alone.
- The late IOP rise that occurs years after the injury is more difficult to treat medically and may require surgical intervention.

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Treatment

- Angle recession glaucoma is initially treated medically with the realization that miotics may be ineffective because of the disruption of the normal ciliary muscle–scleral spur relationship.
- There have been reports that miotics may cause a paradoxical increase in intraocular pressure in patients with angle recession, possibly by decreasing the uveoscleral outflow.

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Treatment

- Glaucoma medications that decrease aqueous formation, such as beta blockers, carbonic anhydrase inhibitors, or alpha2-agonists, may be useful.
- Prostaglandin analogs, which are claimed to increase uveoscleral outflow, may also be of benefit

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Surgical Management

- Surgical management of eyes with angle recession glaucoma is more challenging than that in patients with open-angle glaucoma.
- Argon laser trabeculoplasty is usually unsatisfactory and fails to lower the IOP in this group of patients.
- Trabeculectomy has also been reported to have a lower success rate in eyes with angle recession glaucoma (43%) as compared to eyes in patients with open-angle glaucoma (74%).

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Inflammation Induced Glaucoma

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Case

- 30 BF presents with eye pain in both eyes for the past several days
  - Severe pain (8/10)
  - Never had eye exam before
- PMHx:
  - Has chronic bronchitis
  - Rash on legs
  - Has recently lost weight and has a fever
  - Taking aspirin for pain

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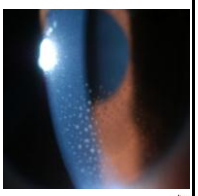
Ocular Health Assessment

- VA: 20/30 OD, OS
- PERRL
- FTFC
- EOM"s: FROM with eye pain in all quadrants
- SLE: 3+ injection, 3+ cells and trace flare, deposits on endo (see photo)
- IOP: 16, 16 mmHg
- DFE: sheathing of posterior pole vasculature, vitreal cells, and white fluffy deposits at ora.



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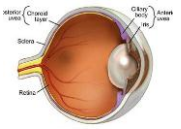
Uveitis

- Uveitis frequently is nonspecific but can be associated with:
  - systemic disease,
  - occur following trauma, or
  - be the result of a primary ocular disorder such as:
    - Fuchs's heterochromic iridocyclitis or
    - glaucomatocyclitic crisis (ie, Possner-Schlossman syndrome)



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Uveitis

- The clinical features of anterior uveitis are readily recognizable
- complaints of:
  - photophobia,
  - pain,
  - blurred or variable vision
- A change in the blood-aqueous barrier results in the liberation of protein and cellular matter into the anterior chamber and the vitreous.

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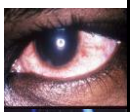
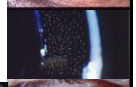
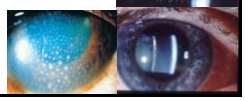
Uveitis

- Clinical findings of:
  - circumlimbal hyperemia,
  - cells and flare in the aqueous and anterior vitreous, and
  - keratitic and trabecular precipitates







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Uveitis

- IOP elevation in uveitis is the end result of a combination of changes in:
  - aqueous composition (increased protein and hence viscosity),
  - aqueous production (reduced),
  - conventional outflow (reduced), and
  - uveoscleral outflow (increased)

Slide 74

Uveitis

- a reduction in the IOP is often seen in the acute uveitis episode
  - paradoxically, an eye with uveitic glaucoma may develop chronic hypotony from ciliary insufficiency in the longer term.
- outflow facility is reduced in the presence of:
  - increased aqueous protein concentration,
  - inflammatory cytokines,
  - pigment deposition, and
  - direct inflammation also influence trabeculocyte function in uveitis.

Slide 75

Uveitis

- The clinician should be alert to the possibility of glaucoma secondary to the inflammation.
- Attention should be given to the possibility that primary acute angle-closure glaucoma may be present, since many of the clinical features are similar.

Slide 76

Uveitis: Treatment

- "Classical treatment":
  - Pred forte: every 1-2 hours, ensure taper
    - Pred forte: prednisolone acetate formulation which allows penetration through cornea to anterior chamber
- Newer treatment option:
  - Durezol

Slide 77

Treatment Options

- Durezol:
  - Difluprednate
    - only difluorinated steroid
  - Steroid emulsion
  - BAK free
  - Increased "potency" so dosing needs to be less than "classical treatment" with Pred Forte
    - rough recommendation is 1/2 dosing of Pred Forte

Slide 78

Cycloplegia

- Cycloplegia/mydriatics:
  - Homatropine 5% qd-bid
- Provides three useful functions in the treatment of uveitis:
  - Prevents synechiae formation
  - Takes ciliary body out of spasm thus reducing pain
  - Reduces inflammation

Slide 79

Common Uveitic Causes

- Uveitis is seen in conditions such as:
  - sarcoidosis,
  - Reiters syndrome (reactive arthritis),
  - ankylosing spondylitis,
  - syphilis and
  - Juvenile idiopathic arthritis,
  - as well as a number of other systemic conditions.

Slide 80

Uveitic Glaucoma

- Any uveitic process is capable of producing secondary angle-closure or open-angle glaucoma.
  - Ocular inflammation that results in secondary anterior uveitis has the potential to produce an elevation in IOP and subsequently, if left unchecked, glaucoma.
    - Common causes include:
      - herpes simplex,
      - herpes zoster ophthalmicus, and
      - rubella

Slide 81

Uveitic Glaucoma

- Chronic inflammation can result in permanent changes to ocular structures, causing anomalies such as:
  - iris atrophy,
  - synechiae, and cataract.
- The established mode of treatment, topical and systemic corticosteroids, can also result in permanent ocular tissue changes.

Slide 82

Uveitic Glaucoma

- overall prevalence of 20% in a clinic-based study of 1099 uveitis sufferers
- Glaucoma is considerably more common than this in a number of specific uveitic syndromes, such as:
  - Fuchs heterochromic cyclitis (27%),
  - Sarcoidosis (34%),
  - herpes simplex keratouveitis (54%) , and
  - zoster uveitis (38%),
- However, the **most common cause is idiopathic acute anterior uveitis,** even though the reported prevalence is lower.

Slide 83

Uveitic Glaucoma

- Glaucoma secondary to juvenile idiopathic arthritis (JIA) is a potentially blinding complication in children and young adults.
  - 35% of affected eyes with secondary glaucoma lost all vision in one large previous study

Slide 84

Uveitic Glaucoma Management

- Despite initial fears, it seems that prostaglandin receptor agonists have a propensity to increase the activity of uveitis in only a very small percentage of patients
- However, prostaglandin agonists should still be used cautiously in uveitics with a history of cystoid macular edema or herpetic keratouveitis

Slide 85

Uveitic Glaucoma Management

- The first step in the management of glaucoma resulting from anterior uveitis is medical control of the inflammation and prevention of complications.
  - topical corticosteroids,
  - mydriatics/cycloplegics should be employed

Slide 86

Uveitic Glaucoma Management

- Homatropine 5% used twice daily in combination with a sympathomimetic such as phenylephrine 2.5% will reduce the discomfort caused by photophobia and ciliary spasm.
- Atropine has also been shown to lower IOP by increasing uveoscleral outflow.
- Cycloplegic agents will help to stabilize the permeability of the iris vasculature.
- Cycloplegics help to prevent synechiae from forming, and in combination with phenylephrine may help to break formed synechiae.

Slide 87

Uveitic Glaucoma Management

- Topical corticosteroids inhibit the inflammatory response and decrease capillary permeability
  - restoring the blood- aqueous homeostasis and reducing the release of cellular exudates and protein.
- Penetration of topical corticosteroids is increased by the inflammatory response
  - if topical agents prove to be ineffective, subconjunctival or systemic steroids may be administered.

Slide 88

Uveitic Glaucoma Management

- Elimination of the anterior uveitis initiates the treatment of the accompanying secondary glaucoma.
- Mydriatic cycloplegics will prevent pupillary block and peripheral anterior synechiae.
- If the IOP remains elevated
  - adrenergic antagonists, carbonic anhydrase inhibitors or B-blockers
- Miotics should be avoided since they may aggravate the inflammation and precipitate pupillary block and iris bombe.

Slide 89

Uveitic Glaucoma Management

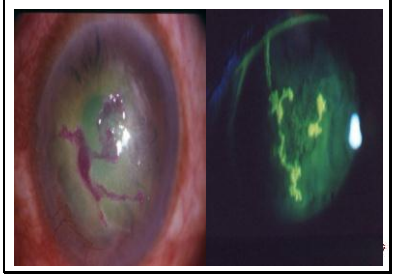
- Intractable uveitic glaucoma that is unresponsive to medical therapy may be treated with laser surgery.
  - LPI may prove to be difficult in inflammatory states, and
  - laser trabeculoplasty has proven to be ineffective
- Surgical iridectomy is the recommended procedure and is considered safer than filtration surgery.

Slide 90

Herpes Simplex Virus Keratitis

- HSV keratitis presents with:
  - varying irritation, pain, photophobia, and
  - generalized injection.
  - branching ulcers which stain with fluorescein and rose bengal
  - patients may report previous bouts of keratitis or cold sores
- Recurrent HSV is most common cause of central infectious keratitis
- Recurrence rate is 25% in first year, 50% during second year

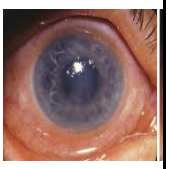
Slide 91



Slide 92

HSV Keratouveitic Glaucoma

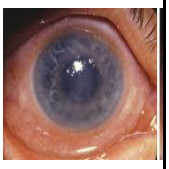
- Increased IOP is related to trabecular blockade or trabeculitis.
  - inflammatory cells, fibrin, and plasma proteins may produce a physical blockade of the trabecular meshwork
- Retrocorneal membrane obstruction of the angle may also contribute to rises in IOP



Slide 93

HSV Keratouveitic Glaucoma

- Thick and edematous trabecular bands, which may present clinically as limbitis, appears to obstruct trabecular outflow
- Posterior synechia formation could cause pupillary blockade and secondary angle-closure glaucoma.



Slide 94

HSV Keratouveitic Glaucoma

- glaucoma could be overlooked in a disease process that occurs in an acute, chronic, and intermittent fashion
- increased IOP as a consequence of prior damage to the trabecular meshwork by HSV keratouveitis can be overlooked.

Slide 95

HSV Keratouveitic Glaucoma

- The ocular signs of HSV keratouveitis that have presented with increased IOP include:
  - disciform keratouveitis (44%),
  - stromal keratouveitis (36%),
  - disciform keratitis (10%),
  - stromal keratitis (4%),
  - scleral keratitis/limbitis (2%), and
  - metaherpetic ulcer (4%).

Slide 96

HSV Keratouveitic Glaucoma

- The most striking feature noted by the authors was the preponderance of patients with uveitis in the group who developed increased IOP compared with the group who did not.
- Patients who developed herpetic ocular hypertension suffered an average of 2 attacks during the 4 years of observation.

Slide 97

HSV Keratouveitic Glaucoma

- The management of increased IOP and glaucoma occurring secondary to HSV keratouveitis is directed initially at halting or preventing activation of viral disease.
- After antiviral coverage has been provided, corticosteroids can have a profound and rapid effect on the inflammatory aspects of the disease, in particular the intraocular inflammation with a marked drop in IOP within a few days.

Slide 98

HSV Keratouveitic Glaucoma

- With long- term steroid use, the possibility of steroid-induced ocular hypertension should be kept in mind.
  - However, a drop in IOP from steroid suppression of the trabeculitis will precede any steroid-induced pressure rise.

Slide 99

HSV Keratouveitic Glaucoma

- Supplemental antiglaucoma medications may need to be added to adequately control the ocular hypertension.
- Suggested options include b-blockers, a-agonist, and carbonic anhydrase inhibitors (oral and topical).
- The IOP usually returns to normal as the intraocular inflammation resolves.
- Approximately 12% of patients with HSV keratouveitic glaucoma will develop persistent IOP elevation requiring chronic therapy.
  - Filtration surgery may be required occasionally.

Slide 100

Clinical Pearls

- **Patients who develop a uveitis with an HSV keratitis are more likely to develop an ocular hypertensive state.**
- **Patients who develop increased IOP are more likely to have had frequent flare ups over a shorter period of time.**
- **Treatment of the viral infection is foremost with trying to reduce the overall inflammatory state.**

Slide 101

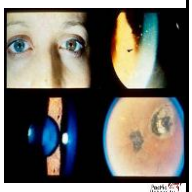
Fuch's Heterochromic Iridocyclitis

- mild form of anterior uveitis associated with cataract and glaucoma
- most cases are unilateral,
- affect men and women equally, and begin in the fourth decade.
- increased IOP is seen in 13% to 59% of affected patients.

Slide 102

Fuch's Heterochromic Iridocyclitis

- this condition is characterized by:
  - iris atrophy with or without heterochromia,
  - posterior subcapsular lens opacities
  - gray-white nodules on the anterior surface of the iris, and
  - opacities in the vitreous



Slide 103

Fuch's Heterochromic Iridocyclitis

- postulated that the chronic inflammation causes permanent scarring of the outflow channels
- this form of uveitis does not respond well to treatment
- the IOP often responds poorly to medical therapy, including corticosteroids

Slide 104

Glaucomatocyclitic Crisis

- also referred to as *Possner-Schlossman syndrome*,
- produces significant elevation in IOP in association with recurrent episodes of mild anterior uveitis
- The clinical features include:
  - ciliary flush,
  - IOPs up to 60 mm Hg,
  - faint flare, and
  - keratitic precipitates.

Slide 105

Glaucomatocyclitic Crisis

- It is thought that the elevated IOP is caused by a trabeculitis
  - possibly involving prostaglandins
- The disorder is recurrent in nature and the patient should be monitored for visual field defects and optic nerve cupping.
- Treatment typically includes the use of corticosteroids, beta blockers and CAI's.

Slide 106

Steroid Induced Glaucoma

- Corticosteroid-induced glaucoma must be considered in the long-term management of ocular inflammation.
- Intraocular pressure elevation has been detected as early as 1 week and as late as several months after initiating treatment.
- The amplitude of IOP increase is dose-related and is allied closely to:
  - the potency,
  - frequency, and
  - route of administration and
  - the susceptibility of steroid response on the part of the patient.

Slide 107

Steroid Induced Glaucoma

- It has been established that topical or systemic corticosteroid administration is associated with significant elevations in IOP in 18% to 36% of the general population.
- The response rate is increased to between 46% and 92% in patients with primary open angle glaucoma and to 87% in first-degree relatives of patients with open angle glaucoma.

Slide 108

Steroid Induced Glaucoma

- The proposed mechanism of steroid-induced elevated IOP relates to impaired outflow facility through the TM.
  - Corticosteroids may decrease availability of catabolic enzymes and thus decrease breakdown of mucopolysaccharides that accumulate in the anterior chamber angle, retain water, and obstruct the trabeculae.

Slide 109

Steroid Induced Glaucoma

- Corticosteroids may also have a direct impact on trabecular cells through their interaction with cytoplasmic receptors and DNA binding sites.
  - Corticosteroids inhibit phagocytosis by TM cells that may lead to accumulation of cellular debris and increased resistance to aqueous outflow.
- Corticosteroids also reduce outflow facility by increasing tight junctions between TM endothelial cells.

Slide 110

Steroid Induced Glaucoma

- corticosteroids administered topically, by intraocular injection, or systemically are associated with a rise in intraocular pressure (IOP) and the development of glaucoma
- The rise in IOP has been shown to be related to the:
  - dose,
  - duration of administration,
  - type and route of administration of steroid.

Slide 111

Steroid Induced Glaucoma

- Intravitreal injections of triamcinolone acetonide (TA) have recently become a frequently used treatment for various intraocular proliferative or edematous diseases, including diabetic macular edema and central retinal vein occlusion.
- There have been several recent studies demonstrating a rise in IOP and the development of secondary glaucoma after intravitreal TA injections.

Slide 112

Steroid Induced Glaucoma

- In some patients, postinjection IOP elevation has been unresponsive to maximum medical therapy, necessitating surgical intervention including:
  - removal of the corticosteroid,
  - trabeculectomy,
  - Ahmed valve placement,
  - pars plana vitrectomy, or
  - a combination of trabeculectomy and vitrectomy with removal of corticosteroid.

Slide 113

Clinical Pearls

- **Patients who have glaucoma or first degree relatives with glaucoma have a significantly increased prevalence of steroid induced IOP increases.**
- **IOP increase is directly related to:**
  - **Frequency of steroid use**
  - **Type of steroid**
  - **Route of administration**
  - **Duration of use**

Slide 114

ANGLE CLOSURE GLAUCOMA SECONDARY TO MEDICATIONS

Slide 115

Question

Drug induced glaucoma has been the MOST associated with which of the following groups of medications?

1. OTC flu medicine (containing ephedrine)
2. Anti-psychotic medications
3. Anti-asthma medications
4. Phenylephrine

Slide 116

Acute Angle Closure Secondary to Medications

- At least one-third of Acute Angle Closure (AAC) cases are related to an over-the-counter or prescription drug.
- Drugs with alpha-1 adrenergic or anticholinergic effects can precipitate attacks of AAC mainly by mydriasis.
- Some drugs with no pupillary effect induce AAC by ciliochoroidal effusion:
  - E.g. sulpha-based drugs and anticoagulants

Slide 117

Acute Angle Closure Secondary to Medications

- Mechanisms by which a substance can induce angle-closure glaucoma:
  - pupillary dilatation,
  - forward displacement of the iris-lens structures, and
  - swelling of the ciliary body

Slide 118

Acute Angle Closure Secondary to Medications

- Both:
  - local (ocular drops, nasal and nebulized agents) and
  - systemic drugs (e.g. atropine, adrenaline, ephedrine, some psychoactive and antiepileptic drugs) can induce AAC
- Alpha-adrenergic agents cause mydriasis that can precipitate an attack in predisposed individuals that have shallow anterior chambers.

Slide 119

Acute Angle Closure Secondary to Medications

- Phenylephrine drops may induce AAC in about 0.03% of nonselected patients
- Cases have been reported after systemic administration of ephedrine for the flu

Slide 120

Angle Closure Secondary to Medications

- Angle-closure glaucoma has been mainly associated with:
  - TCAs,
  - low-potency antipsychotics,
  - topiramate and,
  - to a lesser extent, SSRIs.
- When patients with narrow angles are given TCAs, they all appear to experience induction of glaucomatous attacks.

Slide 121

Angle Closure Secondary to Medications

- Antipsychotics and SSRIs may lead to an added risk of developing angle-closure glaucoma, but only in predisposed eyes.
- Topiramate (anti-convulsant/epilipesy) can lead to an allergic-type reaction whereby structures of the lens and ciliary body are displaced, which results in angle-closure glaucoma.

Slide 122

Angle Closure Secondary to Medications

- Nebulized b2-adrenergic agents:
  - salbutamol, albuterol, terbutaline
  - used for bronchodilation in patients with asthma or chronic obstructive pulmonary disease.
  - can increase the intraocular pressure and induce transient angle closure.
  - stimulating ciliary body b2-adrenergic receptors promotes aqueous humour secretion.
  - angle closure is exacerbated by pupil dilation caused by the parasympathetic inhibitory effect

Slide 123

Anticholinergic agents

- Tropicamide is a short-acting anticholinergic commonly used to induce pupil dilation for fundus examination.
- Atropine, homatropine and cyclopentolate used to relax the ciliary muscle and dilate the pupil have long-acting anticholinergic action, and more frequently induce AAC

Slide 124

Cholinergic agents

- Pilocarpine is used in some forms of glaucoma to constrict the pupil and increase aqueous outflow through the major outflow pathways.
- **However:**
  - it can induce AAC due to anterior movement of the iris-lens diaphragm, thus resulting in complete angle closure
  - eyes with zonular weakness or exfoliation syndrome seem to be particularly prone to developing miotic-induced angle closure

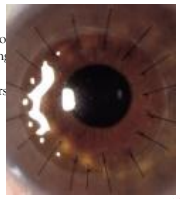
Slide 125

PKP AND GLAUCOMA

Slide 126

PKP and Glaucoma

- Irvine and Kaufman first reported a higher incidence o elevated IOP after PKP notin intraocular pressures higher than 25mmHg during the firs post-operative week after corneal transplant surgery:
  - 37% of phakic eyes and
  - 88% in aphakic eyes



Slide 127

PKP and Glaucoma

- The incidence of glaucoma after PKP varies with the indication for PKP
  - increased IOP develops most frequently after PKP for aphakic bullous keratopathy and less frequently for eyes with Fuchs' corneal dystrophy and keratoconus
- risk factors for the development of glaucoma after PKP include:
  - pre-existing glaucoma,
  - presence of peripheral anterior synechiae,
  - corneal re-grafting,
  - history of ocular trauma, and
  - combined PKP and cataract extraction surgery

Slide 128

Mechanisms of Post-Keratoplasty Glaucoma

- Postsurgical glaucoma can be caused by:
  - pupillary block,
  - iritis,
  - hemorrhage,
  - steroid response,
  - malignant glaucoma, or
  - retained viscoelastic.

Slide 129

Mechanisms of Post-Keratoplasty Glaucoma

- Although increased IOP after PKP can develop in eyes with open or closed angles
  - **peripheral anterior synchiae is present in 87% of patients post-PKP.**
- Distortion of the angle, anterior and posterior to the trabecular meshwork, has also been implicated as a cause for increased IOP after PKP.

Slide 130

Mechanisms of Post-Keratoplasty Glaucoma

- Peripheral anterior synechiae secondary to corneal transplantation leads to progressive angle closure glaucoma that is often difficult to treat with medications or laser and frequently requires surgical intervention for adequate IOP control
- Corneal transplant donor size may also affect postkeratoplasty IOP.
  - using oversized donor tissue may decrease the incidence of increased IOP after PKP in the early post-operative course

Slide 131

Medical Management of PK-Glaucoma

- The most commonly used and successful glaucoma medications are:
  - **topical beta-blockers and alpha-adrenergic agonists.**
- Prostaglandins are effective in lowering the IOP,
  - but case reports of increased incidence of inflammation associated with their use may compromise graft outcome and visual outcome if cystoid macular edema develops

Slide 132

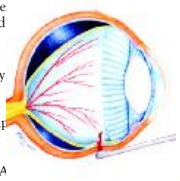
Medical Management of PK-Glaucoma

- The use of miotics is usually ineffective and not recommended in the early post-operative period
  - pilocarpine causes break-down of the blood–aqueous barrier and shallows the anterior chamber with subsequent intraocular inflammation and potential development of peripheral anterior synchiae.
- Carbonic anhydrase inhibitors (CAIs) can be used topically or systemically.

Slide 133

Cyclodestructive Procedures

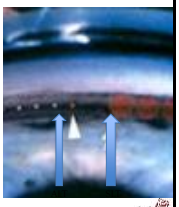
- By ablating a portion of the ciliary body, IOP is lowered by decreasing aqueous humour production
  - destruction of the ciliary body can be achieved through transscleral application of cryotherap or transscleral or endoscopic delivery of diode, krypton or Nd:YA laser.



Slide 134

Laser Trabeculoplasty

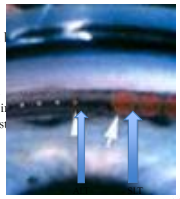
- Argon laser trabeculoplasty (ALT) has been reported to successfully treat PK glaucoma
  - use of this modality is often limited by the formation of PAS after keratoplasty.
  - Poor visibility of the TM through the corneal transplant may also limit its use as the laser may be applied ineffectively, possibly resulting in further angle closure.



Slide 135

Laser Trabeculoplasty

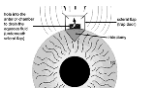
- Use of selective laser trabeculoplasty is also limited visibility of the trabecular meshwork.
- Both procedures have limited data to support their efficacy i glaucoma following keratoplas



Slide 136

Trabeculectomy

- Trabeculectomy with and without mitomycin-C has been shown to be successful in controlling intraocular pressure after keratoplasty
- The use of anti-metabolites improves IOP control and the success of trabeculectomy



Slide 137

Summary

- **Glaucoma following penetrating keratoplasty (PKP) is one of the most common causes for irreversible visual loss and the second leading cause for graft failure after rejection.**
- **The management of penetrating keratoplasty and glaucoma (PKPG) remains controversial mainly because of the high risk of graft failure associated with the treatment.**