Glaucoma CAQ Assessment Outline

Definition of Primary Open Angle Glaucoma

1. No universal definition established. Generally regarded as an insidious, asymmetric, bilateral progressive optic neuropathy with characteristic optic nerve, retinal ganglion cell and nerve fiber changes which can lead to characteristic visual field loss and, ultimately, blindness.
2. Leading cause of irreversible blindness world wide
3. An estimated 50% of those with glaucoma have not been diagnosed
4. OAG is the most common glaucoma – representing ~ 90% of cases
    a. HTG – IOP > 21mmHg
    b. NTG – IOP $\leq$ 21 mmHg (30-50% of POAG)
5. Proposed pathophysiology
    a. Biomechanical – elevated pressure causes bowing of lamina resulting in damage to axons and impedes perfusion
    b. Vascular – vascular dysregulation and poor oxygenation due to reduced perfusion creates ischemia (believed to be non-pressure dependent (NTG))
    c. Genetic – genetically predisposed individuals have accelerated apoptosis (a form of programmed cell death) of ganglion cell axons

Assessing the Patient at Risk of Open Angle Glaucoma

1. Non-ocular risk factors
    a. Age
    b. Race
        i. Asian – NTG (Japanese, Korean)
        ii. AAs and Hispanics ancestry
    c. Family history
        i. Most significant RF
        ii. First degree
    d. Hypertension, hypotension
        i. Overmedication
    e. Diabetes
    f. Vascular dysregulation/vasospasm
        i. Migraine (NTG)
        ii. Raynaud's Syndrome
    g. Obstructive Sleep Apnea
    h. Steroid use

2. Ocular risk factors
    a. IOP
        i. Acquire measurements on 3 separate days and times for baseline
        ii. Angle abnormalities affecting IOP
            a. Pigmentation
            b. Pseudoexfoliation
            c. Recession
            d. Neovascularization
            e. Narrow angle
        iii. Steroid use
    b. Corneal Hysteresis (CH)
    c. Central Corneal Thickness (CCT)
    d. Myopia
    e. Ocular Perfusion Pressure (OPP)
    f. Disc Hemorrhages
3. Genetic markers in glaucoma

Evaluating the Optic Nerve in OAG

1. Ophthalmoscopy (BIO/Photography)
    a. Cup
        i. Size/CDR
            a. Relevance of disc diameter
            b. Inter-eye asymmetry
        ii. Depth
            a. Laminar exposure
    b. Rim
        i. ISNT rule
            a. Relative thickness of Inferior, Superior, Nasal and Temporal rim
            b. Inter and intra-eye asymmetry
        ii. Focal notching
    c. Vasculature
        i. Baring
        ii. Bayonetting
        iii. Nasalization
        iv. Drance hemorrhage
    d. Peripapillary Region
        i. Beta zone atrophy
        ii. NFL
            a. Focal wedge defects
            b. Diffuse loss
                i. Choroidal exposure

c. Differentiation from pseudo-wedge defects

2. OCT Evaluation
    a. Peripapillary Nerve Fiber Layer (PPNFL)
        i. Wide range of normal thickness leading to ambiguity in early diagnosis
    b. Ganglion Cell Complex (GCC)
        i. More anatomically uniform thickness
        ii. Often the first detectable structural sign of glaucomatous damage
    c. Morphologic characteristics
        i. Disc area
        ii. Rim area
3. Peripapillary NFL Thickness Considerations
    a. Wide range of normal
        i. Statistically normal average does not preclude disease.
    b. Asymmetric nature of glaucoma in OCT
        i. Ipsilateral asymmetry
            a. Primary focus is on superotemporal and inferotemporal rim sectors
        ii. Contralateral asymmetry
            a. Primary focus is on corresponding superotemporal and inferotemporal sectors
    c. Non-glaucomatous NFL changes
        i. Prior retinal vascular events, ischemia
        ii. Congenital Disc anomalies
            a. Drusen
            b. Optic pit
            c. Hypoplasia
            d. Situs inversus
        iii. Optic atrophy
    d. Monitoring Progressive Structural Loss
        i. Normal rate of thinning
            a. 0.4% per year (~5000 axons)
        ii. GCC Progression report
        iii. RNFL progression report

Assessing Function in Glaucoma: Visual Fields

1. Testing Strategies
    a. 30-2: Largely obsolete
    b. 24-2: Most commonly used field for glaucoma; faster, more reliable
    c. 24-2C: Adds 10 central points to better reveal central loss
    d. 10-2: 6 times more sensitive centrally vs 24-2

        i. Often better for diagnosing and monitoring advanced and severe stages of disease
2. Reliability Indices
    a. Fixation losses
        i. Limited metric that does not always predict field reliability
        ii. Improperly plotted BS common source of error
    b. False positive errors
        i. Limited metric that does not always predict field reliability
        ii. Associated with understated field loss
    c. False negative errors
        i. Limited metric that does not always predict field reliability
        ii. Specifically limited in that an abnormal visual field typically has increased FNEs
        iii. Not included in SITA Faster due to above limitations.
        iv. Associated with overstated field loss
    d. Gaze tracking
        i. Best overall assessment of fixation consistency (vs FLs)
3. Global Indices
    a. Mean Deviation (MD)
        i. Older metric with limitations due to center weighted avg and potential influence of cataract.
    b. Pattern Standard Deviation (PSD)
        i. Identifies patterned loss
        ii. Best in early to moderate defects – less useful in advanced, generalized loss
    c. Visual Field Index (VFI)
        i. Enhancement of MD less influenced by media
            1. More sensitive to central loss
        ii. Correlates better with GC loss
        iii. Useful for measuring progression
4. Typical Glaucomatous Defects
    a. Nasal step: most common defect
    b. Arcuate loss: hemispheric vs bi-hemispheric
    c. Central loss
5. Staging Glaucoma
    a. Hoddap-Parish-Anderson Criteria
    b. AAO Glaucoma Stage Definitions
    c. Modified Glaucoma Staging System (Harikawa)
6. Monitoring Progressive Visual Field loss
    a. Establish reliable baseline of fields
    b. Match frequency of follow up to severity/stability
    c. Confirm suspected progression with repeat field
    d. Match field testing strategy to severity

i. 24-2 vs 10-2

e. Guided progression analysis (GPA)

i. MD

ii. VFI

iii. Assessment of progression slope, projected VFI and life expectancy

Assessing Function in Glaucoma: Electroretinography

1. Sensitive to early glaucomatous loss
2. May identify reversible glaucoma

Ocular Hypertension and Glaucoma Suspect

1. Characteristics of glaucoma suspect
   a. Individuals are usually regarded as a glaucoma suspect due to the presence of any of these following characteristics:
      i. Elevated intraocular pressure (IOP)
      ii. Optic nerve head (ONH) or retinal nerve fiber layer (RNFL) appearance suggestive of glaucomatous damage
      iii. Unexplained visual field (VF) defect consistent with glaucoma
      iv. Abnormal angles
      v. strong family history of severe glaucoma and other risk factors.
2. Definition of ocular hypertension (OHT)
   a. Defined as IOP >22 mmHg (2 standard deviations above the mean), but without any other abnormal features in the optic discs, VFs, or RNFL.
   b. In the absence of other features of glaucoma, if IOP is found to be consistently high on 3 consecutive examinations then, a diagnosis of OHT can be made.
   c. Therefore, the diagnosis of OHT is one of exclusion after ruling out any features suggestive of primary open-angle glaucoma (POAG).
3. Establishing a baseline for glaucoma suspect
   a. **I**ndividuals with elevated IOP should be evaluated as any other glaucoma patient.
   b. Initial investigations should include:
      i. serial IOP measurements
      ii. gonioscopy
      iii. optic disc photos (if possible, stereoscopic)
      iv. central corneal thickness (CCT)
      v. VF assessments
      vi. RNFL thickness (RNFLT) assessments
   c. Additional investigations - individually customized depending on their availability or indication:
      i. ultrasound biomicroscopy
      ii. scanning laser polarimetry
      iii. confocal scanning laser ophthalmoscopy

4. Importance of serial tonometry
    a. IOP should be checked on three different days at different times of the day so that any IOP spikes are not missed.
    b. Time should be recorded duly in the medical records to determine any diurnal fluctuation of IOP.
5. Number of VF during the first year
    a. Attempts should be made to obtain at least 3 VFs during the 1st year of assessment.
6. Importance of OCT and VF testing
    a. Whenever possible, both structural (OCT) and functional (VF) changes should be analyzed since one could precede the other.
7. Factors associated with an increased risk of conversion to POAG
    a. High initial IOP
    b. Positive family history of glaucoma
    c. History of retinal vein occlusion (RVO)
    d. High myopia (>6 D)
    e. Increasing age (>70 years)
8. Importance of IOP measurements based on The Ocular Hypertension Treatment Study (OHTS)
    a. IOP is an important parameter in the management of glaucoma since it is the only modifiable risk factor at present.
    b. OHTS found that high IOP alone can be a risk factor for the development of glaucoma
    c. 1 mmHg increase in IOP was associated with a 10% increase in relative risk of conversion to POAG
    d. 22.5% decrease in IOP in treatment arm (vs 4% in control arm) was associated with a reduction in the development of POAG from 9.5% in controls to 4.4% in the treatment group at 60 months of follow-up.
9. Causes of overdiagnosis of glaucoma
    a. Due to the perceived risks of high IOP and fear of lawsuits, individuals are often started on antiglaucoma medications, despite the absence of other features of glaucoma.
10. Importance of family history in glaucoma suspects
    a. Epidemiologic and genetic studies have found a positive linkage of glaucoma with family history
    b. The Baltimore Eye Survey reported that after considering age-adjusted associations of POAG with a family history of glaucoma, there is a 3.69 times higher risk of development of POAG in siblings than in parents (odds ratio=2.17) or children (odds ratio=1.12)
11. Importance of disc hemorrhages in patient with ocular hypertension
    a. The presence of disc hemorrhages in a patient with OHT, increases the risk of conversion to POAG by 6 times (by univariate analysis) and 4 times (by multivariate analysis).
    b. The Asia Pacific Glaucoma Guidelines mention that compared to a single episode of disc hemorrhage, recurrent hemorrhages increase the risk of optic nerve damage by 3–4 times.

12. Importance of screening all patients over 40 for glaucoma
    a. Increasing age as a risk factor for the development of glaucoma has been identified in a number of studies.
    b. The Barbados Eye Study and Blue Mountains Eye Study found age to be a major risk factor for the development of POAG.
    c. Since age is positively associated with a higher prevalence of glaucoma, it is recommended to screen all possible persons above 40 years of age for this disease.

13. Importance of central corneal thickness in glaucoma suspects
    a. Both OHTS and the European Glaucoma Prevention Study found that the risk of developing POAG was greater in eyes with CCT <555 µ compared with eyes having CCT of 588 µ or greater.
14. Factors influencing CCT and IOP measurements
    a. The actual IOP can be overestimated on Goldman applanation tonometry in eyes with thicker corneas, whereas an underestimation may happen in eyes with less than average CCT.
    b. Refractive surgery can alter the corneal biomechanics and corneal thickness, thus resulting in falsely low IOP readings.
    c. In the presence of corneal edema IOP tends to be underestimated
    d. IOP is overestimated in presence of corneal scars due to the increased rigidity of fibrous tissue.
    e. Mandatory that all glaucoma suspects undergo pachymetry so that their IOP can be assessed in the proper perspective.

Progression in Glaucoma Overview

1. Increased degradation of optic nerve
    a. Increased CDR (generalized rim thinning)
        i. Best by comparison of stereo disc photos
    b. Development of focal notching
        i. Best by comparison of stereo disc photos
    c. New disc hemorrhage
2. Increased thinning of peripapillary RNFL and/or macula (GCC)
    a. Progression/change reports
    b. Negative slope greater than age related thinning
3. Worsening of Visual Field
    a. PSD
        i. Best for staging and monitoring early to intermediate loss vs generalized loss or advanced disease
    b. MD
        i. Cataract may simulate glaucomatous loss
        ii. Best for end stage, central loss
    c. VFI
        i. Improvement vs MD – cataract less significant vs MD

ii. Better for moderate loss
iii. Not present on 10-2

d. GPA
    i. Establish reliable baseline of fields
    ii. Determine slope of progression: slope likely not linear
    iii. Estimate life expectancy
    iv. Extend current slope to end of life
        1. Determine if EOL VFI/MD is acceptable
            a. If VFI/MD is acceptable: may maintain current tx
            b. If VFI/MD unacceptable
                i. Determine necessary slope percentage
                ii. Determine corresponding IOP reduction to achieve necessary percentage
                    1. Assume 10-12% reduction for each mmHg of IOP reduction
                iii. Decide how to address necessary IOP reduction
                    1. Medical
                    2. Surgical

Treatment and Management of Open Angle Glaucoma

1. Goal of treatment: lower the IOP in a target range to slow disease progression
    a. Initial target pressure should be set at least 25% lower than pretreatment IOP
        i. Target pressure is an estimate that must be individualized and adjusted
            1. Level of disease, past rate of progression, age, and family history are additional risk factors which impact target pressure
    b. IOP may be lowered through utilization of medical therapy, laser therapy, and/or incisional surgery - all may be appropriate first line therapy
    c. If a single medication fails to lower IOP to within the target range:
        i. switch to an alternative medication within the same drug category
        ii. add medication from an alternative class of medication is appropriate
        iii. perform laser trabeculoplasty
        iv. adherence to medical therapy is reduced with increased complexity of the medication regimen
    d. If disease progression is identified at the target pressure:
        i. evaluate patient's adherence to therapy and potential IOP fluctuation
        ii. the target pressure should be lowered
2. Medical therapy
    a. Prostaglandin analogs
        i. First line medical therapy due to efficacy, tolerability, and lack of systemic adverse effects
            1. Medication: Latanoprost, bimatoprost, latanoprostene bunod, tafluprost, travoprost
            2. Mechanism of action: Increased uveoscleral outflow
                a. Latanoprostene bunod also increases trabecular outflow through release of nitric oxide into the anterior chamber

3. IOP reduction: 25-33%
4. Most frequently encountered adverse effects: conjunctival hyperemia, increased eyelash growth, increased iris pigmentation, perioribitopathy, periocular hyperpigmentation
    a. Possible adverse effects: keratitis, allergic conjunctivitis, uveitis, cystoid macular edema, migraine-like headache
5. Potential contraindications: Macular edema, active intraocular inflammation, history of herpetic keratitis

b. Beta antagonists (blockers)
1. Medication: timolol, levobunolol, carteolol, metipranolol, Betaxolol (selective)
2. Mechanism of action: decreased aqueous production
3. IOP reduction: 20-25%
4. Most frequently encountered adverse effects:
    a. Possible adverse effects: bronchospasm, bradycardia, hypotension, congestive heart failure, reduced exercise tolerance, depression, impotence
5. Potential contraindications: chronic obstructive pulmonary disease, asthma, congestive heart failure, bradycardia, hypotension, greater than first-degree heart block

c. Alpha adrenergic agonists
1. Medication: apraclonidine, brimonidine
2. Primary mechanism of action: decreased aqueous production
    a. Secondary mechanism of action: increased uveoscleral outflow, decrease episcleral venous pressure
3. IOP reduction: 20-25%
4. Most frequently encountered adverse effects:
    a. Possible adverse effects: Follicular conjunctivitis, dry mouth and nose, hypotension, headache, fatigue, somnolence
    b. Potential contraindications: Monoamine oxidase inhibitor therapy, infancy and childhood (brimonidine)

d. Carbonic anhydrase inhibitors
1. Medication: brinzolamide, dorzolamide
2. Mechanism of action: decreased aqueous production
3. IOP reduction: 15-20%
4. Most frequently encountered adverse effects: allergic dermatitis, allergic conjunctivitis
    a. Possible adverse effects: corneal edema, keratitis, metallic taste
5. Potential contraindications: sulfonamide antibiotic allergy, sickle cell disease with hyphema, low endothelial cell count

e. Oral carbonic anhydrase inhibitors
1. Medication: acetazolamide, methazolamide
2. Mechanism of action: decreased aqueous production
3. IOP reduction: 20-30%
4. Most frequently encountered adverse effects: Metallic taste, abdominal cramps, diarrhea, paresthesia
    a. Possible adverse effects: Stevens-Johnson syndrome, malaise, anorexia, depression, electrolyte imbalance, blood dyscrasia

b. Potential contraindications: sulfonamide antibiotic allergy, kidney stones, aplastic anemia, thrombocytopenia, sickle cell disease

f. Rho-kinase inhibitors
    1. Medication: netarsudil
    2. Mechanism of action: increased trabecular outflow, decreased episcleral venous pressure, decreased aqueous production
    3. IOP reduction: 10-20%
    4. Most frequently encountered adverse effects: Conjunctival hyperemia, corneal verticillata
        a. Possible adverse effects: conjunctival hemorrhage
        b. Potential contraindications: possibly low endothelial cell count

g. Parasympathomimetic agents
    1. Medication: pilocarpine
    2. Mechanism of action: increased trabecular outflow
    3. IOP reduction: 20-25%
    4. Most frequently encountered adverse effects: increased myopia, decreased vision, headache, eye pain
        a. Possible adverse effects: increased salivation, abdominal cramps, retinal tears, retinal detachment, conjunctival shrinkage, periocular contact dermatitis, decreased vision
    5. Potential contraindications: Peripheral retinal thinning, neovascular, uveitic, malignant glaucoma, posterior synechiae

h. Osmotics
    1. Medication: glycerol, mannitol
    2. Mechanism of action: dehydration of vitreous
    3. IOP reduction: no data
    4. Most frequently encountered adverse effects: headache, nausea, vomiting, diarrhea
        a. Possible adverse effects: congestive heart failure, renal failure, diabetic complications, mental confusion
        b. Potential contraindications: renal failure, congestive heart failure

i. Prostanoid EP2 receptor agonist
    1. Medication: omidenepag isopropyl
    2. Mechanism of action: increased uveoscleral outflow, increased trabecular outflow
    3. IOP reduction: 20-25%
    4. Most frequently encountered adverse effects: conjunctival hyperemia
        a. Possible adverse effects:
        b. Potential contraindications: keratitis, allergic conjunctivitis, uveitis, cystoid macular edema, migraine-like headache

j. Fixed combination medications
    i. Dorzolamide 2% + timolol 0.5% solution
    ii. Brimonidine 0.2% + timolol 0.05% solution
    iii. Brinzolamide 1% +brimonidine 0.2% suspension
    iv. Netarsudil 0.02%-latanoprost 0.005%

3. Medical therapy in pregnancy and breastfeeding
    a. IOP naturally decreases during pregnancy
    b. First trimester-consider: brimonidine, beta-blockers, timolol, prostaglandin analogs
        i. Caution with topical carbonic anhydrase inhibitors; avoid oral carbonic anhydrase inhibitors
        ii. Brimonidine is considered pregnancy category "B"
    c. Second trimester-consider: brimonidine, beta-blockers, prostaglandin analogs, carbonic anhydrase inhibitors
    d. Third semester-consider: carbonic anhydrase inhibitors, beta-blockers
        i. Avoid brimonidine and prostaglandin analogs
            1. Prostaglandin analogs carry the theoretical risk of premature labor
    e. Breastfeeding-consider: timolol, carbonic anhydrase inhibitors
        i. Avoid brimonidine
            1. Crosses the blood-brain barrier and can result in somnolence and decreased alertness
        ii. American Academy of Pediatrics has approved oral and topical carbonic anhydrase inhibitors during lactation
4. Sustained drug delivery systems
    a. Bimatoprost intracameral implant 10mcg
5. Selective laser trabeculoplasty
    a. 532nm, Q-switched, frequency doubled Nd:YAG laser
        i. Laser energy selectively absorbed by pigmented trabecular meshwork cells
    b. The Selective Laser Trabeculoplasty Versus Eye Drops for First-Line Treatment of Ocular Hypertension and Glaucoma (LiGHT Study) 2019
        i. 360-degree SLT had a similar quality of life and IOP lowering over three years with better cost effectiveness compared to medical therapy
6. Incisional glaucoma therapy
    a. Trabeculectomy
        i. Indicated when medications and laser therapy fail to control disease
        ii. Allows aqueous to leave the eye via a subconjunctival pathway
        iii. Failure rates have reduced with adjunctive intraoperative and postoperative antimetabolites (mitomycin C, 5-fluorouracil)
        iv. Complications include hypotony, bleb leak, endophthalmitis, cataract
    b. Ex-PRESS shunt
        i. Device inserted as part of a modified trabeculectomy procedure
            1. Greater surgical cost, similar IOP reduction, similar surgical success rate, potential for greater endothelial cell loss vs. trabeculectomy alone
    c. Aqueous shunts, glaucoma drainage devices, tube shunts
        i. Divert aqueous through a rube to an endplate located within the subconjunctival space near the equator
        ii. Valved vs. nonvalved devices differ in the presence of a valve mechanism to limit flow through the tube
            1. Nonvalved: Baerveldt, ClearPath, Molteno
            2. Valved: Ahmed
        iii. Similar complication profile to trabeculectomy with the additional risk of extrusion, corneal decompensation,
        iv. Primary tube versus trabeculectomy (PTVT) study

1. Compared safety and efficacy of tube shunt (350-mm^2 Baerveldt) implantation and trabeculectomy with mitomycin C in eyes without prior ocular surgery
2. Trabeculectomy had a lower rate of failure and higher likelihood of defined success at 1 and 3 years

7. Minimally invasive glaucoma surgery (MIGS)
   a. Utilize an ab interno approach and involve minimal trauma to ocular tissues
   b. Generally indicated for mild-moderate open angle glaucoma and are commonly performed with phacoemulsification
   c. Trabecular meshwork/Schlemm's canal-based procedures:
      i. Excise, cleave, dilate, or stent the trabecular meshwork or inner wall of Schlemm's canal
         1. Ab interno trabeculectomy: Trabectome, Kahook Dual Blade (KDB)
         2. Gonioscopy-assisted transluminal trabeculotomy (GATT): ab interno cannulation of Schlemm's canal and goniotomy
         3. Ab interno canaloplasty: ab interno dilation of Schlemm's canal with viscoelastic
         4. iStent inject, iStent inject W: 2 stents inserted through the pigmented trabecular meshwork into Schlemm's canal
            a. iStent infinite: 3 stents, on-label for the treatment of primary open angle glaucoma in whom previous medical and surgical treatment has failed as a stand alone treatment
         5. Hydrus microstent: Intracanalicular scaffold inserted into Schlemm's canal
      ii. Subconjunctival MIGS
         1. Xen gel stent: on label for the treatment of refractory glaucoma
            a. Utilization of antimetabolites increases surgical success
8. Cyclodestructive surgery
   a. Reduce aqueous production through damage to the ciliary processes
   b. Post-operative complications include pain and inflammation, decreased visual acuity, pain, hypotony, macular edema, sympathetic ophthalmia

Angle Closure Glaucoma

1. Classification
   a. PACS v PAC v PACG
      i. PACS = $\geq$ 180 degrees ITC* (no elevated IOP/PAS or glc nerve damage)
      ii. PAC = $\geq$ 180 degrees ITC* + elevated IOP and/or PAS (no glc nerve damage)
      iii. PACG = $\geq$ 180 degrees ITC* + elevated IOP and/or PAS + glc nerve damage
      *dark room dynamic gonioscopy without compression
   b. Acute angle closure crisis
      i. Sudden, symptomatic, marked IOP elevation w/ 360 degrees of complete ITC, iris bombe
   c. Plateau
      i. Plateau iris configuration – narrow angle w/ ITC 2' anteriorly rotated CB w/ deep central AC; double hump sign
      ii. Plateau iris syndrome – PIC with persistent ITC after LPI
2. Characteristics
   a. Prevalence

i. 0.7% of people over 40 are estimated to have PACG, world-wide
ii. PACG is a leading cause of blindness world-wide
iii. Main idea: much less common than POAG but responsible for a lot more blindness –> more devastating form of glaucoma.
iv. Considerable differences in the prevalence of angle closure among ethnoracial groups:
    1. Highest in Inuit, Chinese, and other Asian
    2. Lower in African, African-derived, European and European-derived

b. Progression of PACS to PAC
    i. Risk for progression from PACS to PAC ranges from 4-22% over 5-6 years and may be influenced by population.
    ii. 22% PACS (southern India population) to 4% (Chinese population) progressed to PAC (developed IOP elevation or PAS) over 5 and 6 years respectively.

c. Demographics
    i. Family history of angle closure
    ii. Older age
    iii. Asian (Chinese, Vietnamese, Pakistani) or Inuit descent

d. Ocular risk factors
    i. Hyperopia
    ii. Short axial length
    iii. Shallow anterior chamber depth (peripherally and centrally)
    iv. Steep corneal curvature
    v. Anterior position of CB (plateau iris)
    vi. Thick crystalline lens
    vii. Anteriorly positioned crystalline lens

e. Plateau iris configuration/syndrome
    i. Age 30-50
    ii. NOT associate w/ small, hyperopic eyes or lens effects

3. Assessment
    a. Clinical signs/symptoms
        i. Acute angle closure crisis
            1. c/o blurred vision, halos around lights, red eye, eye pain, headache, nausea/vomiting
            2. Unilateral reduced acuity, mid-dilated pupil, conjunctival injection, corneal edema, markedly elevated IOP, fully closed angle 360 (viewed w/ gonioscopy), possible AC cell, shallow AC,
        ii. PACS and PAC
            1. Probably asymptomatic
            2. Possible h/o painful blurred vision and red eye, halos, headache
        iii. PACG
            1. As above + evidence of glaucomatous damage to ON
    b. Gonioscopy
        i. Should be performed on both eyes on all patients in which PACS/PAC/PACG is suspected
        ii. Attention to ITC and PAS and plateau configuration
        iii. Compression (indentation) w/ 4 mirror gonio lens helps determine appositional closure from synechia

iv. Performed in dark room w/ a bright, short (1mm) beam that does not pass through pupil

c. Optic nerve assessment
    i. Ophthalmoscopy and or OCT to gauge status of optic disc health
d. Anterior segment OCT
    i. What it can add to exam
    ii. Quantitative measures include: angle opening depth, trabecular-iris space area, angle recess area, iridotrabecular contact index, lens vault, iris volume
    iii. Does not image posterior iris or CB so not useful in plateau iris configuration
    iv. Misses subtle iris neo and pigmentation changes
e. Biometry/axial length/anterior chamber depth
    i. Can measure axial length, AC depth
    ii. Nanophthalmos <20.0mm AL
f. Ultrasound biomicroscopy
    i. Indications for use – i.e. plateau iris
    ii. Better characterizes posterior iris and CB compared to AC-OCT
    iii. More operator dependent
g. Provocative testing
    i. Dark-room prone positions and pre- and post-dilation IOP measurement replaced by careful gonioscopy exam
    ii. ZAP trial – no participants experienced IOP elevation with prone-dark testing.

4. Differential diagnoses
    a. PACS and PAC tend to be bilateral, thus a presence of wide-open angle in the fellow eye should prompt consideration of a diagnosis other than PAC
    b. Secondary pupillary block
        i. PS complication of uveitis
        ii. Lens malposition
        iii. Pupillary block from vitreous prolapse
    c. Secondary PAS (pulling mechanism)
        i. Neovascularization of iris/angle (NVG)
        ii. ICE syndrome
        iii. Contracture from inflammation
        iv. Axenfeld-Rieger syndrome
        v. PAS following anterior segment surgery
    d. Posterior pushing mechanism
        i. Choroid/uveal effusion 2' retina conditions (CRVO, PRP, SB, meds (topiramate, sulfonamides)
        ii. Aqueous misdirection syndrome/malignant glaucoma
        iii. Gas or SO pushing lens-iris forward
        iv. Chronic serous choroidal detachment
        v. Hemorrhagic choroidal detachment
        vi. Intraocular tumors
        vii. ROP/persistent fetal vasculature
5. Management
    a. Acute angle closure crisis
        i. Initial treatment is aimed at lowering IOP to minimize potentially harmful effects of high IOP and relieve acute symptoms:

ii. Immediate medical treatment to lower IOP: aqueous suppressants (BB, CAI (including oral), AA), pilocarpine (ineffective at very high IOP), hyperosmotic agents (if needed).
iii. LPI in both eyes (assuming fellow eye is anatomically similar)
    1. Relieves pupillary block
    2. Half of untreated fellow eyes develop AACC w/in 5 years
iv. Possible lens extraction to follow
v. Chronic management of residual stage glaucoma

b. PACS
    i. LPIs are effective in reducing risk of development of PAC
        1. 50% reduction in risk of PAC development over 6 years (ZAP)
    ii. Progression rate from PACS to PAC is very low in some populations (Chinese, 4% (ZAP)); thus treating all PACS may not be justified
    iii. Careful discussion and education with patient about risks/benefits of LPI vs monitoring without LPI and the signs/symptoms of angle closure
    iv. Careful monitoring for further angle narrowing, IOP elevation or PAS development which may warrant a change in management
    v. Other considerations: patients requiring frequent dilations, chronic use of medications known to provoke pupillary block (anticholinergic meds), symptoms that suggest prior intermittent AACC, patient situation making access to urgent care difficult (works at sea, very remote)

c. PAC and PACG
    i. LPI for all vs lens extraction – no clear consensus
    ii. Older publications advocate for LPI in all PAC and PACG
    iii. LPI has been shown to increase angle width at all stages of angle closure and has a favorable safety profile (see complications from LPI).
    iv. Studies have shown less benefit with LPI with greater amounts of PAS (>180) and with extensive ON damage
    v. EAGLE trial showed benefit of clear lens extraction over LPI in patients with PAC (IOP$\underline{\geq}$30) and PACG. Thus, cataract or clear lens extraction can also be considered for management of PAC or PACG.
    vi. Patients with primary angle closure glaucoma/PAC are 10 times more likely to maintain drop-free good IOP control with initial CLE surgery than LPI.
    vii. Non-Chinese ethnicity, higher baseline IOP and using glaucoma drops prior to randomization are predictors of worse long-term IOP response.

d. Plateau Iris Configuration and Syndrome
    i. LPI
    ii. Persistent ITC after LPI = Plateau Iris Syndrome
    iii. No strong evidence or consensus for treatment of PIS w/ elevated IOP
        1. No randomized controlled trials have been conducted to evaluate argon laser peripheral iridoplasty
        2. Other options: chronic parasympathomimetic therapy, cataract/clear lens extraction, endoscopic cystoplasty

e. Laser peripheral iridotomy
    i. LPIs have been shown to significantly increase angle width and lower IOP in PAC
    ii. Post-LPI
        1. Should be routinely evaluated for patency (visualizing zonules, anterior lens capsule, ciliary processes)

2. Goniosocopy to monitor angle structures
3. Monitor IOP
4. Dilate as indicated

iii. Complications from LPI
1. Increased IOP
2. Laser burns to other tissues (cornea, lens, retina)
3. Late-onset corneal edema
4. PS
5. Hyphema
6. Iritis
7. Light-induced visual disturbance
a. Some studies show improvement with 3 and 9 o'clock placement; others show no difference

f. Lens extraction for angle closure
i. Lens extraction significantly opens AC angle
ii. May lower medication burden
iii. Decreased complications compared to LPI, iridectomy and trab for PACG
iv. Phaco soon after AACC is effective in maintaining IOP control and reducing med burden but also carries higher risk in these smaller eyes
v. EAGLE study –clear lens extraction w/ PCIOL for PAC (IOP $\geq$ 30) and PACG more effective than LPI at lowering IOP and improving QOL.
vi. Patients with primary angle closure glaucoma/PAC are 10 times more likely to maintain drop-free good IOP control with initial CLE surgery than LPI.
vii. Non-Chinese ethnicity, higher baseline IOP and using glaucoma drops prior to randomization are predictors of worse long-term IOP response.
viii.

Secondary Glaucomas (adult)

1. Primary disorders of the corneal endothelium
a. Iridocorneal endothelial (ICE) syndrome
i. Early-middle adulthood
ii. Female>male
iii. Unilateral (viral origin?)
iv. The spectrum (not distinct clinical entities)
1. Progressive iris atrophy
2. Chandler syndrome
3. Cogan-Reese syndrome
v. Mechanism for glaucoma
1. Synechia or membrane formation
2. Peripheral anterior synechia
a. Extending to or beyond Schwalbe's line
b. Progressively close
3. Descemet-like membrane
a. Single layer of endothelial cells
b. Extends from peripheral cornea across the anterior chamber angle
vi. Management

1. In early stages, like POAG
2. High percentage eventually require incisional surgery
    a. ~45% of trabs ultimately need to be repeated

b. Posterior polymorphous corneal dystrophy
    i. A common finding in Alport syndrome
        1. Renal abnormalities
        2. Neurosensory hearing loss
        3. Hernias
        4. Glaucoma in 15%
    ii. Mechanism for glaucoma
        1. Similar to ICE syndrome
        2. Synechia or membrane formation
    iii. Management
        1. May respond to medical treatment
        2. SLT often ineffective
        3. Incisional surgery when medical management fails

c. Fuchs endothelial dystrophy
    i. Higher incidence of angle-closure glaucoma
        1. Axial hypermetropia
        2. Shallow anterior chambers
    ii. Management
        1. Angle open: like POAG but avoid CAIs
        2. Angle-closure: iridotomy/incisional surgery

2. Disorders of the Iris and Ciliary Body Associated with Glaucoma
    a. Iris atrophy with corneal disease (see Disorders of the Cornea Associated with Glaucoma)
    b. Pigmentary
        i. Etiology
            1. Iridozonular and iridociliary contact liberates pigment
            2. Glaucoma related to accumulation of pigment in the trabecular meshwork
            3. Subsequent alteration in trabecular beams
        ii. Epidemiology
            1. Young, myopic, male (2:1), onset third decade of life
        iii. Ocular Manifestations
            1. Iris transillumination defects
            2. Dispersed pigment on the iris
            3. Dispersed pigment on the corneal endothelium (Krukenbuerg spindle)
            4. Dispersed pigment in the anterior chamber angle
            5. Dense homogeneous trabecular meshwork pigmentation
                a. May accumulate on Schwalbe line (Sampaolesi line)
        iv. Treatment
            1. Miosis
                a. Theoretically addresses iris/lens contact
                b. Often rejected by young patients
                    i. Brow ache

ii. Decreased Retinal Illumination
c. Risk of retinal detachment
2. Medications like POAG
3. SLT
a. First line
b. Supplemental to meds
4. LPI - Insufficient evidence
5. Incisional

c. Iridoschisis
i. Uncommon
ii. Usually 6-7th decade of life
iii. Bilateral separation of the layers of the iris stroma
iv. Occasionally associated with glaucoma
v. Management
1. Angle open: treat like POAG
2. Closed angle mechanism: LPI/surgical iridotomy
3. Incisional as needed

d. Disorders of the Lens Associated with Glaucoma
i. Ectopia Lentis
1. Traumatic dislocation
a. Most common form of ectopic lentis (~50% of all cases)
2. Associated with Exfoliation Syndrome
a. Spontaneous
b. Traumatic
3. Marfans
a. Autosomal dominant
b. 5% have glaucoma
i. Lens dislocation into anterior chamber
ii. Anomaly of the anterior chamber angle
4. Homocystinuria
a. Autosomal recessive
b. Glaucoma more common vs Marfans
i. Lens dislocation into anterior chamber accounts for 50% of glaucoma surgical intervention
c. Retinal detachment is common
5. Weill-Marchesani Syndrome
a. Glaucoma more common vs Marfans and Homocystinuria
i. Forward shift in position of lens
ii. Pupillary block glaucoma
6. Spontaneous dislocation
ii. Lens Particle Glaucoma
1. Mechanical obstruction of trabecular meshwork by free lens particles
iii. Phacoanaphylaxis
1. Unknown

2. Immune response (wbc's lymphoid/epitheliod/giant cells) may accumulate in trab

iv. Intumescent Lens Phacomorphic Glaucoma
1. Phacomorphic glaucoma
2. Lens vault from advanced cataract causes pupillary block

v. (Pseudo) Exfoliation syndrome/glaucoma
1. Systemic
a. Pseudoexfoliation syndrome (PEX) is a systemic disorder
b. (Pseudo)exfoliative material isolated from various body tissues: blood vessels, lungs, heart, liver, kidneys, and skin
2. Etiology
a. Incompletely understood
b. Inherited microfibrillopathy
c. Associated with polymorphisms in LOXL1
3. Epidemiology
a. Most common identifiable cause of secondary open-angle glaucoma
b. Incidence increases as a function of advanced age (60s-70s)
4. Ocular Manifestations
a. May be unilateral or bilateral: >50% unilateral will be bilateral over 20 years old
b. Most apparent on lens capsule, pupillary margin
c. Uneven pigment in angle vs pigment dispersion
d. Pigment may accumulate on Schwalbe line (Sampaolesi line)
e. Also present on ciliary processes, zonules, trabecular meshwork
f. Even in eye without clinical findings (77%)
g. Strongly associated with raised IOP in up to 44% of patients
h. Greater diurnal variation in IOP
i. IOP can spike out of control in a short period of time
j. Development of pseudoexfoliation glaucoma (PEG)
5. Treatment
a. Same as COAG
b. Prophylactic LPI should be considered in setting of shallow peripheral and center anterior chamber depth
6. Cataract surgery complicated by zonule/capsule weakness

e. Disorders of the Retina Associated with Glaucoma
i. Neovascular glaucoma
1. Retinal ischemia/chronic hypoxia (majority of cases)
a. Diabetic retinopathy
b. Central retinal vein occlusion
c. Ocular ischemic syndrome
d. Others
2. Irradiation (e.g. photoradiation, external beam)
3. Neoplasm (e.g. chroidal/ciliary body/iris melanoma, retinoblastoma)

4. Inflammatory (e.g. chronic uveitis, sympathetic ophthalmia)
5. Surgical causes (e.g. carotid endarterectomy, cataract extraction, pars plana vitrectomy)
6. Extraocular Vascular Disorders (e.g. carotid artery obstructive disease, carotid-cavernous fistula, internal carotid artery occlusion)
7. Treatment
    a. Address ischemia/hypoxia
        i. Anti-VEGF
        ii. PRP
    b. Lower IOP (medical)
    c. Lower IOP (surgical)
        i. Incisional
        ii. Cyclodestructive procedures

f. Glaucoma associated with increased episcleral venous pressure
    i. Venous obstruction
        1. Thyroid-associated ophthalmopathy
        2. Superior Vena Cava Syndrome
    ii. Orbital Amyloidosis
    iii. Arteriovenous Fistulas
        1. Carotid-Cavernous Fistula
        2. Orbital Varices
        3. Sturge-Weber Syndrome
    iv. Idiopathic Episcleral Venous Pressure Elevation
    v. Treatment
        1. Eliminate the cause
        2. Medical/surgical glaucoma management

g. Glaucomas associated with intraocular tumors
    i. Primary uveal melanomas
    ii. Choroidal Melanomas
    iii. Systemic Malignancies
        1. Metastatic carcinomas
        2. Metastatic melanomas
        3. Leukemias
        4. Lymphomas
        5. Histiocytosis X
        6. Multiple Myeloma
        7. Myelodysplastic Syndrome
    iv. Treatment
        1. Enucleation
        2. Excision of tumor
        3. Photocoagulation
        4. Medical glaucoma management
            a. Surgery may seed the neoplasm
                i. Ab externo cyclodestruction

h. Glaucoma Associated with Ocular Inflammation
    i. Iridocyclitis
        1. Sarcoidosis
        2. Juvenile Idiopathic Arthritis
        3. Ankylosing Spondylitis
        4. Pars Planitis
        5. Glaucomatocyclitic Crisis
        6. Fuchs Heterochromic Cyclitis
        7. Behcets Disease
        8. Reactive Arthritis
    ii. Infectious Disease
        1. Congenital Rubella
        2. Hansen Disease
        3. Hemorrhagic Fever with Renal Syndrome
        4. AIDS
    iii. Associated with Keratitis
        1. Interstitial Keratitis
        2. Herpes Simplex Keratouveitis
        3. Herpes Zoster Keratouveitis
    iv. Associated with Scleritis
    v. Treatment
        1. Control underlying inflammatory component
        2. Medical/surgical glaucoma management

i. Steroid-Induced Glaucoma
    i. Treatment
        1. Discontinue steroid
        2. Medical/surgical glaucoma management

j. Glaucoma Associated with Trauma
    i. Acute
        1. Angle concussion
        2. Hyphema
            a. Most common s/p blunt globe trauma
        3. Early post-injury
            a. IOP elevation usually transient
        4. Treatment
            a. Medical/surgical glaucoma management
            b. Hyphema may require irrigation/aspiration
    ii. Late post-injury
        1. Angle recession glaucoma
        2. Ghost cell glaucoma
        3. Treatment
            a. Medical/surgical glaucoma management

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