

Glaucoma 2023: Evaluation, Treatment, and the Future

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Financial Disclosures

Nothing to disclose

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Speaker Bio –



Arizona Glaucoma Specialists Scottsdale

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Glaucoma 2023

- Evaluation of glaucoma
- Treatment of glaucoma
- Future of glaucoma

Glaucoma Worldwide

- The leading cause of irreversible blindness
- In adults over 50
 - 4 million with moderate/severe vision impairment - 11% of all global blindness
- Variable by nationality/region African descent
 - 6.5% to 7.3%
 - East Asian descent 2.59% to 3.54%
- By 2040 → 112 million affected

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Glaucoma in the U.S.

- Approximately 3 million affected – 2.7 million OAG
- Costs the U.S. economy \$2.86 billion yearly
- Prevalence \rightarrow 4x higher in African Americans and Hispanics



Strong Risk Factors

- Elevated IOP
- Family history
- Optic nerve cupping
- Thin central cornea
- Older age
 - Age 40+ in African Americans
 - Age 60+ in general population (especially Hispanics)

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Patient History

Three subjects ALWAYS

- 1. Family history?
 - Level of severity?
 - Surgery?Blindness?
 - Dimuness:
- 2. Steroid exposure?
 - Current AND historicalNose sprays especially!
- 3. Blunt trauma?

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Patient History

- Angle closure suspicion...
 - Headaches? Migraines?
 - Episodes of blurry vision, halos, pain, redness?
 - Ethnicity?
 - Medications?
 - Antidepressants, antihistamines, sulfonamides (e.g. topiramate)

Patient History

- Normal tension glaucoma suspicion...
 - Any blood pressure medications?
 - History of low blood pressure?
 - Dizziness with standing or change in position?

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Vision

- 20/20 is possible in advanced disease
- High refractive error
 - Pay extra close attention!
 - Don't forget about patients s/p LASIK/PRK

Intraocular pressure (IOP)

- Goldmann applanation remains gold standard
- Pachymetry important to put IOP into context
- Hx of LASIK/PRK or high astigmatism will also affect measurement



Pupil Exam

• Subjective RAPD can be first moment of realization for patient with new diagnosis

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Anterior Segment Exam

- Extra focus on:
 - Conjunctiva (prior surgery, surgical planning)
 - Endothelium (pigment dispersion)
 - Retroillumination (pigment dispersion, UGH)
 - Pupil margin (pseudoexfoliation)
 - Anterior lens capsule (pseudoexfoliation)



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Gonioscopy

Considerations

- Is there risk for acute angle closure glaucoma?
- Is there risk for chronic angle closure glaucoma?
- Angle recession?
- Neovascularization
- Heavy pigmentat
- Asymmetry?
- Prior angle closure (pseudophakic patients)?
- Personally I don't favor any particular grading systems
- Don't be afraid to refer for a second opinion!

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Central corneal thickness

- In OHTS and European Glaucoma Prevention Study
 - Average CCT was 570 um
 - Risk of developing POAG was greater if <555 um
- Still no accepted correction formula for IOP based on CCT
- Future evaluation standards may include corneal hysteresis

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OCT RNFL

- Low-coherence interferometry
- Often precedes visual field loss (preperimetric disease)







| Glauco | oma | | | | | | | |
|--|---|---|---|---|--|--|--|---|
| | | | | | | | | |
| Repr | oducib | ility of I | Peripa | pillar | y Retina | I Nerve | e Fibe | r |
| Layer | · Thick | mess an | d Opti | c Ner | ve Head | Param | eters | |
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- Macula contains 50% of RGCs of the entire retina
- Benefits of macular OCT
 - Early detection
 - Evaluation for progression
 - Myopic/abnormal discs
 - Peripapillary atrophy





Anterior Segment OCT

- Helpful with...
 - Reinforcing gonioscopic findings
 - Corneal disease
 - Poor patient compliance with gonioscopy
 - Patient education
- Cons
 - In clinical practice, typically a cross section (3:00 and 9:00)
 - Not dynamic
 - Misses patchy pigment from iridotrabecular contact
 - Artificial pupil constriction from room lights
- NOT A SUBSTITUTION FOR GONIOSCOPY



OD O OS

Anterior Chamber Analysis : Anterior Chamber

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Visual Field Testing

- Typically performed using *perimetry* Measures differential light sensitivity
- Most common is automated static perimetry – E.g. Humphrey Field Analyzer
- Limitations
 - Subjective test
 - Many sources of artifact
 - Data overload
 - No gold standard algorithm for diagnosis/monitoring

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Glaucoma Hemifield Test

- Within normal limits
- Borderline
- Outside normal limits
- Abnormally high sensitivity
- General reduction in sensitivity

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4.5 mm 20/20

3.5 mm 20/15

Visual Field Testing

- Visual field index (VFI)
 - Represents the entire visual field

 - Good for trending and creating plots
- Mean deviation (MD)
 - Compares results to age-matched controls
 - Starts at 0 and ends around -30
- Good for trending • Pattern standard deviation
 - Represents focal deficits
 - Higher values with dense arcuate or focal defects
 - Can "re-normalize" if an arcuate defect becomes global
- 43

3.5 mm 20/15

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Visual Field Testing

- Glaucomatous patterns
 - Nasal step
 - Arcuate
 - Altitudinal
 - Paracentral
 - Temporal wedge
 - Generalized depression
 - Central island

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Glaucoma 2023

- Evaluation of glaucoma
- Treatment of glaucoma
- Future of glaucoma

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Setting an IOP Goal

- I'm more in favor of a ~2 point general ballpark
- Always flexible
- Many factors to consider
 - Starting IOP (Tmax)
 - Severity of disease
 - Life expectancy/health of patient
 - Rate of progression
 - Risk factors
 - Type of glaucoma
 - Patient's tolerance for risk (or risk aversion)
 - Toleration of treatment side effects

Table 45-2 Delphi Panel Recommendations for Initial Target Pressu High IOP at d Target IOP e IOP Range ients with sentation Recommended M % IOP Reduction Preferred (mmHg) Accepta (mmHg) 16-21 mr 14-18 18-24 18-24 Ha 20% 20% 30% Not determined Not determined Not dete Not dete as First-Line T

Setting an IOP Goal

Lifestyle

- Healthy diet and exercise Caution heavy weightlifting
 Caution yoga (head down positioning)
- Avoid excess salt
- Unless NTG
- Avoid excess caffeine
- Avoid excess alcohol (does briefly reduce IOP)
- Avoid smoking
- Marijuana not helpful (does briefly reduce IOP)
- Some evidence CBD raises IOP
- Caution collagen joint supplements

Medical Treatment

- Prostaglandin analogues
 - Caution
 - Uveitis/macular edema
 - HSV
 - Trichiasis
 - Other considerations
 - Young patients/aesthetic concerns



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ADE THER-DR-IT Tomolol Malente Ophthalmic Solution, USP

Conversed Frances

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Medical Treatment

Beta blockers

Caution

- Heart disease (bradycardia, heart block, CHF, hypotension)
- Pulmonary disease (asthma, COPD)
- Other considerations
 - Caution if concern for systemic hypotension
 - Patients on a systemic beta blocker (less potential efficacy)
 - Exercise intolerance
 - Depression

Medical Treatment • Topical CAI inhibitors - Caution • Fuchs/corneal endothelial disease/transplants Other considerations

- Burning (dorzolamide)
- White deposits (brinzolamide)
- Bitter taste, blurred vision



Medical Treatment

- Miotics (pilocarpine, echothiophate iodide) - Caution
 - Risk for retinal detachment
 - History of ocular inflammation
 - Need for regular fundus exams
 - Other considerations
 - Brow ache, dimmed vision
 - QID dosing





Medical Treatment

• ROCK inhibitors (netarsudil)

- Caution
 - Corneal disease?
- Other considerations
 - Conjunctival hyperemia
 - Corneal verticillata
 - Conjunctival hemorrhage
 - Keratitis (reticular epithelial edema)

Medical Treatment

- Nitric oxide donating PG analogs
 - (Latanoprostene Bunod)
 - Caution
 - Same as other prostaglandin analogs

- Other considerations

- Same as other prostaglandin analogs
 - Extra NO-donating moiety (butanediol mononitrate) relaxes TM and increases aqueous outflow

 Latanoprost → primarily uveoscleral pathway

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Medical Treatment

- Technique
 - Eyes closed 2 minutes
 - Punctal occlusion
 - Okay if some "misses"
 - Wait 5-10 minutes before next drop (or lubrication)

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Laser Surgery

- Laser trabeculoplasty (SLT, ALT)
- Laser iridotomy
- Iridoplasty
- Cyclophotocoagulation

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Argon Laser Trabeculoplasty (ALT)

- Increased outflow facility through release of chemical mediators from TM cells
- Induction of matrix metalloproteinases (MMPs)
- ALT → thermal damage
 - Not repeatable
 - Local shrinkage of collagen fibers with adjacent stretching/widening
- Glaucoma Laser Trial
 - ALT reduces IOP in 75% of eyes
 - More effective than timolol in IOP lowering
 - Over 5.5 years, equally effective at preserving visual field and disc status

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Selective Laser Trabeculoplasty (SLT)

- Delivers less energy

 Selectively absorbed by pigmented TM cells
- Similar in efficacy to ALT and prostaglandins
- Excellent safety profile
- Repeatable, cost effective

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Laser Iridotomy

- Primary indications/uses
 - Narrow or occludable angle
 - Primary angle closure (+/- glaucoma)
 - Acute angle closure (affected or fellow eye)
 - Diagnosis of plateau iris
 - Pigment dispersion syndrome (select cases)

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Laser Iridotomy

Goals

- Reduce risk of acute angle closure glaucoma
- Reduce risk of chronic angle closure glaucoma
- Reduce IOP
- Reduce symptoms
- Most affective BEFORE elevated IOP/PAS/glaucoma develop!



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Laser Iridoplasty

- Large, peripheral burns at low power 360 degrees
- Induces shrinkage/contraction of peripheral iris and mechanical widening of angle
- Can widen angle in plateau iris syndrome or iris root crowding unresponsive to LPI

Cyclophotocoagulation (CPC)

- Reduces rate of aqueous production by reducing ciliary body function
- "Traditional" CPC
 - Reserved for end-stage eyes with limited visual potential and/or poor surgical candidates
- "Micropulse" CPC
 - Less "aggressive" alternative
 - Repetitive short bursts of diode laser energy → less collateral destruction

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Cyclophotocoagulation (CPC)

- Risks
 - Reduced vision
 - Inflammation
 - Pain
 - Hypotony
 - -CME
 - Poor efficacy
 - Phthisis

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Cataract Surgery

Sloppy surgery can also cause glaucoma...
 – E.g. UGH, residual cortex



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Cataract Surgery

- Generally 1-2 mmHg IOP reduction
- Probably proportional to starting IOP
- Higher yield in narrow angles

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Minimally Invasive Glaucoma Surgery (MIGS)

| Α | В | С | D 58 |
|---|--|------------------------------------|--|
| Schlemm's canal Trabecular bypass | Suprachoroidal space | Subconjunctival space Ab interno | Ciliary body |
| iStent iStent inject High frequency deep sclerotomy | CyPass (withdrawn) iStent Supra (not commercially available) | XEN Gel Stent Ab externo Preserflo | Endocyclo -photocoagulation Ab externo Transscieral photocoagulation |
| Schlemm's dilatation Ab interno canaloplasty Hydrus | | | / Micropulse |
| Trabeculotomy GATT Trabeculome Kahook Dual Blade Excimer laser trabeculotomy | c. b. | a 0 | |

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MIGS – Trabecular Bypass

iStent inject

- 2 microstents spaced 2-3 clock hours apart

~30%

- Efficacy
 - Reduction in IOP
 - Reduction in meds ~34%
- Traditionally combined with phaco

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MIGS – Schlemm's dilatation

OMNI

- Hollow dilating catheter for viscoelastic injection into Schlemm's +/- goniotomy
- Efficacy
 - Reduction in IOP ~35%
 - Reduction in meds ~39-55%
- Hydrus
 - Single microstent for trabecular bypass/stenting
 - Efficacy
 - ~34% Reduction in IOP
 - Reduction in meds ~62%

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MIGS – Goniotomy

- 90 to 120 degrees of TM excision
- Stand alone or at time of phaco
- E.g. SION/KDB/TrabEx
- Efficacy

- Reduction in IOP ~25% - Reduction in meds

~64%

MIGS – Suprachoroidal Space

- Utilizes the uveoscleral pathway via stenting
- Examples
 - CyPass (withdrawn due to endothelial cell loss)
 - MINIject (not currently available)

Incisional Surgery - XEN

- Gelatin stent designed for subconjunctival injection from ab-interno approach
- Intended for bleb creation similar to a trab

Incisional Surgery - XEN

Pros

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- Less invasive than trab/tube
- Requires less available conjunctiva
- Probably lower risk than trab/tube
- Cons
 - Probably higher rates of failure vs. trab
 - Probably less IOP lowering vs. trab, ?tube

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Incisional Surgery - Tubes

- Permanent sclerostomy (tube) in anterior chamber to drain aqueous to equatorial sub-Tenon's space
- <u>Tube vs. Trabeculectomy Study</u>
 - Compared Baerveldt 350-mm² tube shunts to trabeculectomy/MMC (0.4 mg/ml for 4 minutes)
 - Trabeculectomy had higher failure rate at 5 years
 - Trabeculectomy had higher reoperation rate
 - Trabeculectomy had more early complications
 - However, all patients had undergone prior cataract and/or glaucoma surgery
 - Nonetheless, lead to increased popularity of tube shunts

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Incisional Surgery - Trabs

- Creates a new pathway (fistula) allowing aqueous to flow out of anterior chamber into subconjunctival space
- Cost-effective, no hardware required
- Primary Tube vs. Trabeculectomy Study
- Patients <u>WITHOUT</u> prior incisional surgery
 Compared Baerveldt 350-mm² tube shunts to
- trabeculectomy/MMC (0.4 mg/ml for <u>2 minutes</u>)
- Similar failure rates at 5 years
- Similar IOPs at 5 years
- Trabeculectomy patients were on fewer meds (higher rate of *complete* success)

Incisional Surgery - Trabs

- Recent trends
 - Popularity has returned
 - Training in residency/fellowship more difficult
 - Fornix-based > limbus-based
 - Still the gold-standard for IOP-lowering surgery
 - Especially if very low IOP is required

Glaucoma 2023

Laser in Glaucoma and Ocular Hypertension

- Evaluation of glaucoma
- Treatment of glaucoma
- Future of glaucoma



Will SLT become first-line therapy over drops?

Ultimately, any surgical decision depends on many variables related to both the patient and surgeon

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Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial

Six-Year Results of Primary Selective Laser Trabeculoplasty versus Eye Drops for the Treatment of Glaucoma and Ocular Hypertension

- After 6 years, SLT group had...
 - Equivalent QOL scores
 - Less disease progression
 - Fewer trabeculectomies
 - Fewer cataract surgeries
 - More cost effective
 - 70% at goal without need for drops or surgery
 - Higher IOP at 6 years vs. drop group (16.3 vs. 15.4)

Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial

Six-Year Results of Primary Selective Laser Trabeculoplasty versus Eye Drops for the Treatment of Glaucoma and Ocular Hypertension_____

- Take home points
 - SLT does not require patient's adherence
 - SLT probably reduces IOP fluctuation
 - I offer drops or laser as first line, but do favor SLT in most circumstances
 - If drops chosen, I do recommend laser as second line prior to adding a second agent
 - Don't underestimate the effect on the conjunctiva of having years of drop exposure (also QOL)





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Home IOP Monitoring

• Pros

– Better diurnal monitoring potential

- Cons
 - Patient anxiety
 - More patient calls/triaging

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Home VF Monitoring

- Humphrey remains gold standard
- No strong data to support virtual reality testing yet
- Stay tuned...



Genetic Testing

- Polygenic risk scores have shown ability to identify higher risk disease
- Not yet widely available
- AAO Preferred Practice Patterns has not yet endorsed widespread use



Polygenic Risk Score Is Associated With Intraocular Pressure and Improves Glaucoma Prediction in the UK Biobank

Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA Departments of Ophthalmology and Visual Science and Biomedical Informatics, Division of Human Genetics, The Ohio State University, Journbus, OH, USA

Association of High Polygenic Risk With Visual Field Worsening Despite Treatment in Early Primary

X. Raymond Gao^{1,2}, Hua Huang¹, and Heejin Kim¹

JAMA Ophthalmol. 2023;141(1):73-77. doi:10.1001/jamaophthalmol.2022.4688

Open-Angle Glaucoma Owen M. Siggs, MD, DPhil^{1,2}; Ayub Qassim, MBBS, PhD¹; Xikun Han, PhD³; <u>et al</u>

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Research Article

Cohort

> Author Affiliation

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Will neuroprotective agents be available to supplement our IOP-lowering therapies?

Neuroprotection

• Treatment other than eye pressure control that prevents retinal ganglion cell death

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A Randomized Trial of Brimonidine Versus Timolol in Preserving Visual Function: Results From the Low-pressure Glaucoma Treatment Study

THEODORE KRUPIN, JEFFREY M. LIEBMANN, DAVID S. GREENFIELD, ROBERT RITCH, AND STUART GARDINER, ON BEHALF OF THE LOW-PRESSURE GLAUCOMA STUDY GROUP

- Brimonidine has shown neuroprotective effects in animal studies
- LOGTS study
 - Brimonidine superior to timolol in rate of visual field progression (despite similar IOPs)

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JAMA Ophthalmology | Original Investigation Nicotinamide and Pyruvate for Neuroenhancement in Open-Angle Glaucoma A Phase 2 Randomized Clinical Trial

Carlos Gustavo De Moraes, MD, MPH, PhD; Simon W. M. John, PhD; Pete A. Williams, PhD; Dana M. Blumberg, MD, MPH; George A. Cioffi, MD; Jeffrey M. Liebmann, MD

- High dose nicotinamide (1000 to 3000 mg) and pyruvate (1500 to 3000 mg) vs. placebo in POAG patients
- Treatment group showed more improvement in visual field testing
- Small (N = 42) and short-term (~2 months)

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Oral Memantine for the Treatment of Glaucoma

Design and Results of 2 Randomized, Placebo-Controlled, Phase 3 Studies

Robert N. Weinreh, MD,¹ Jeffrey M. Liebmann, MD,² George A. Cioffi, MD,² Ivan Goldberg, MBBS, FRANZCO,³ James D. Brandt, MD,² Chris A. Johnson, PhD, DSc,⁵ Linda M. Zangwill, PhD,¹ Susan Schneider, MD,⁶ Hanh Badger, PharmD,⁶ Marina Bejanian, PhD⁶

 "Based on 24-2 SAP, FDT, and optic disc photograph assessments, long-term daily treatment with memantine did not slow or prevent progression"

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Conclusion

Evaluation

- Many glaucoma patients remain undiagnosed
- Identification requires thorough history, ocular examination, and acquisition/interpretation of data
- Treatment
 - Options continue to expand, but the goal remains primarily IOP control
- Future
 - Expansion of current diagnostic and treatment technologies
 - Will likely bring shifts in the paradigm of glaucoma management

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