Covering Glaucoma from A to Z:
Glaucoma Grand Rounds

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Financial Disclosure

Glaukos
Bausch + Lomb
Alcon
Allegan
Reichert
Aerie

Johnson & Johnson
Shire
Sun Pharma
Equinox
Patient LM, 65 year old female
CC: “I was told I am at risk for glaucoma”

- BCVA: 20/20 OD, 20/20 OS
- No Meds
- IOP: 27 OD, 27 OS
- Pachymetry: 583 OD, 583 OS
- ONH Eval: 0.50/0.50 OD, 0.55/0.55 OS

Tmax: Unknown
Corneal Hysteresis:
OD: 10.5 OS: 10.5

RNFL Analysis
Age
Family History
Corneal Thickness
Visual Field
Corneal Hysteresis
ONH Appearance
OCT

Pay attention to TSNIT curve.
Pay attention to the actual numbers in the segmentation plot.
Pay attention to the numbers between eyes in the segmentation plot.
Look at the B Scan for accuracy.

OCT-Angiography

Images retinal and peripapillary microvasculature without dye injection.
Displays structure and function from a single imaging system.
Moderate Glaucoma

Advanced Glaucoma

Corneal Hysteresis (CH)

Corneal Hysteresis reflects the ability of the corneal tissue to dissipate energy. It is a function of viscoelastic damping.

It provides insight into ocular properties that were not previously understood or conceived of.

1. Katz J, Zangwill L. [Ref]
2. Drance S. [Ref]
3. Drance S, et al. [Ref]
Average CH in Normal Subjects

<table>
<thead>
<tr>
<th>Country</th>
<th>N</th>
<th>CH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>105</td>
<td>10.1 ± 1.8</td>
</tr>
<tr>
<td>UK</td>
<td>277</td>
<td>10.2 ± 1.2</td>
</tr>
<tr>
<td>China</td>
<td>125</td>
<td>10.9 ± 1.5</td>
</tr>
<tr>
<td>Japan</td>
<td>204</td>
<td>10.2 ± 1.3</td>
</tr>
<tr>
<td>Spain</td>
<td>188</td>
<td>10.8 ± 1.5</td>
</tr>
<tr>
<td>USA</td>
<td>44</td>
<td>10.5 ± 1.2</td>
</tr>
</tbody>
</table>

Clinical Evidence
Why is CH relevant in Glaucoma?

(Low) CH has been consistently shown to be independently and strongly associated with or predictive of glaucoma progression.
What We Do Know - OHTS

TABLE 1. Hazard Ratios for Baseline Factors Predictive of Primary Open-angle Glaucoma

<table>
<thead>
<tr>
<th>Baseline Factor</th>
<th>Model Including PDR, VCD</th>
<th>Model Excluding PDR, VCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (decade)</td>
<td>1.29 (1.04, 1.59)</td>
<td>1.29 (1.09, 1.53)</td>
</tr>
<tr>
<td>IOP (mm Hg)</td>
<td>1.11 (1.05, 1.18)</td>
<td>1.10 (1.03, 1.17)</td>
</tr>
<tr>
<td>CCT (per 50 μm decrease)</td>
<td>0.82 (0.91, 2.19)</td>
<td>0.92 (1.00, 2.09)</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>0.39 (0.15, 0.78)</td>
<td>0.38 (0.17, 0.86)</td>
</tr>
<tr>
<td>PSSD (per 10 cells)</td>
<td>1.28 (1.06, 1.46)</td>
<td>Excluded</td>
</tr>
<tr>
<td>VCD/D (per 0.1)</td>
<td>1.32 (1.00, 1.45)</td>
<td>Excluded</td>
</tr>
</tbody>
</table>

VCD/D = central corneal thickness; IOP = intracocular pressure; PSSD = pattern standard deviation; VCD/D = vertical cup-to-disc ratio.

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Patient LM returns for scheduled F/U approximately 15 months after initial presentation. She reports no changes in vision.

BCVA: 20/20 OD
20/20 OS

IOP: 23 OD
23 OS

VF = normal OU

ONH Eval: 0.50/0.50 OD
0.60/0.60 OS

No Meds

Tmax: 27

OCT = see next slide
Serial OCT shows progressive RNFL loss OD but still “in the green”. OS findings were similar.

1 Year Later

BOVA: 20/20 OD 20/20 OS
Med: PGA OD 20/20 OS
IOP: 18 OD: 18 OS
Pachymetry: 583 OD 583 OS
ONH Eval: 0.65/0.65 OD 0.70/0.70 OS
Tmax: 27 OU

Selective Laser Trabeculoplasty

Selectively targets and laser burns pigmented TM cells
**Efficacy**

- **SLT as 1st Line Treatment**
  - 100%
  - 0%

**IOP Decrease (Pre-Tx 25 mmHg)**

- 1-2 mmHg
- 3-5 mmHg
- >5 mmHg

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**Primary Outcome** - Quality of life at 3 years

**Secondary Outcome** - Cost, cost-effectiveness, clinical effectiveness, and safety

**Conclusions:**
- No significant difference in QOL
- 97% probability of SLT as 1st treatment being more cost-effective
- SLT at target IOP 93% of visits vs 91.3% at target for meds

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**Controlling Post-op Inflammation**

- ~ 50% present with AC reaction at 1 week

- **Topical corticosteroids** QID x 5-7 days
IOP Spikes and Control

~4.5% to 27% - Transient postoperative IOP Spike
Alpha-blockers (brimonidine or apraclonidine)
Instituted before and after

Steady-state of SLT 6-8 weeks

Prostaglandins

latanoprost 0.003% (Kalta)
travoprost 0.004% (Travatan Z)
bimatoprost 0.03% (Lumigan)
tafluprost 0.015% (Zioptan PF)

latanoprostene bunod 0.024% (Vyzulta)
Nitric Oxide

Endogenous in the human body
Causes alterations in the cytoskeletal network
Reduced NO in TM, Schlemm's canal, and ciliary muscle

VOYAGER Study
Interactions enhanced after 6-12 h (Yasuda)

JUPITER Study
Interactions weakened by 6-12 h (Yasuda)

Nocturnal IOP Lowering

Interactions enhanced after 6-12 h (Yasuda)
latanoprost ophthalmic emulsion 0.005% (Xelpros)

- BAK-free latanoprost ophthalmic emulsion
- Swollen Micelle Microemulsion (SMM) Technology
- Reduces IOP up to a mean of 6 mmHg to 8 mmHg in randomized clinical trials

Single Agent Adjunctive Agents

**Beta Blockers**
- Timoptic (timolol 0.25%, 0.5%, Merck)
- Timolol Alternative Formulations
  - Timoptic XT, timolol maleate 0.25%, 0.5%
  - Timoptic in OcuDrop 0.25%, 0.5%
- Traditional - Ointment
- Betaxolol 0.5%

**Alpha-adrenergic Agonists**
- Brimonidine tartrate 0.2%, 0.5%
- Carbachol (pilocarpine HCl, solution 2%)
- Pilocarpine (pilocarpine 4% suspension)

**Mechanisms of Action**
- Miotics stimulate the ciliary muscle to contract, which increases aqueous humor production
- Miotics induce cyclical constriction of the pupil which reduces aqueous humor outflow

Netarsudil 0.02% (Rhopressa)
Rhopressa (netarsudil 0.02%)

- 15% 20% hyperemia at baseline
- 6% dropout rate for hyperemia


Combination Therapy
Combigan Ophthalmic Suspension
Timolol 0.25%
Dorzolamide 0.2%

Simbrinza
Brimonidine 1%
Timolol 0.2%

Combigan Ophthalmic Solution
Brimonidine 0.2%
Timolol 0.5%
netarsudil 0.02% + latanoprost 0.005% (Rocklatan)

- RHO protein kinase (destabilizes actin in TM)
- Rock inhibitor (lowers EVP)
- Latanoprost (uveoscleral outflow)

Ocular AEs

- Conjunctival hyperemia
- Cornea epithelias
- Epiphora

Patient KR 68 year old male
CC: "VA is blurry. My doctor told me I need a VAG. I was put on a drop 1 month ago"

BCVA: 20/25 OD
20/15 OS

Latanoprost qd
IOP: 12 OD; 12 OS
Tmax: 14 OD, 14 OS

Pachymetry: 532 OD
533 OS

ONH Eval: 0.70/0.70 OD
0.65/0.65 OS

CH: OD 9.0 OS 9.0
SLE: Trace PCO
Long-Term IOP Fluctuation Is Associated With VF Progression – Advanced Glaucoma Intervention Study
Common Belief:

Glaucoma is a 1 Pressure Disease

Likely Truth

Glaucoma is a 2 Pressure Disease

The pressure imbalance between IOP and ICP here is critical.
ICP changes with age

Our solution

We are Pressurized
Patient JT: 55 year old female presents with recent blurred vision in both eyes. Started 2-3 months ago, but worsening.

BCVA: 20/40 OD, 20/20 OS

No medications and no significant medical history.

Special thanks to Elizabeth Muckley OD, FAAO for her contribution to this case.

Gonioscopy

OD = no structures

OS = PAS in multiple quadrants

Undilated Exam

All other structures normal on examination.
Diagnosis

Primary Angle Closure OD
ONH Suspicious
Need VFT/OCT

Primary Angle Closure Glaucoma OS
PAS
Advanced Cupping
Technically need a VFT, but
our eyes tell us advanced

IOP due to closure of drainage canal of eye

Pupillary block
- Hyperopia
- Shallow AC
- Steep X curvature
- Thick lens
- Short axial length

Plateau Iris

Anatomical Narrow Angle/Primary Angle-closure Suspect

Peripheral iris is located close to,
but not touching the posterior TM
What Angle’s are at Risk?

If TM 360 – monitor
If SL in 2 quadrants refer for LPI

Primary Angle Closure

PAS, elevated IOP
Iris whorling or sectoral atrophy, and excessive pigment deposited on TM

Primary Angle Closure Glaucoma

Iridotrabecular contact in 3 or more quadrants
Secondary Angle Closure
Caused by underlying pathologic etiology
Neovascularization of iris or angle
Uveitis

Our Goal for JT
Attempt to get IOP in the low 30s or less
Oral Diamox 2 x 250 mg in office
Rotate meds every 5 minutes
Send patient home with topical meds and oral Diamox
until LPI performed
1% Pilo qid – an option
Prednisolone qid

LPI Post op
1. Plateau Iris
Elevated IOP
Angle still Closed

LPI Post op

Elevated IOP
Angle still closed

2. PAS Present

Goniosynechialysis

Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial

- Prof Augusto Aurora, MD, PhD
- Dr. Craig Carrier, MD
- Dr. Craig D. Cooper, MD
- Prof. Philip L. Frishberg, MD
- Prof. David F. Friedman, MD - all authors

30% reduction in IOP and 5.1% decrease in number of medications

ACUTE AG – 71% IOP reduction and almost no need for post-phaco medications

64 year old male
CC: “Blurry vision x 6 months. Driving at night is terrible”

BCVA: 20/40 OD bimatoprost qd 20/40 OS
IOP: 16 OD; 16 OS
Max IOP’s: 25 OD; 25 OS
Pachymetry: 500 OD
500 OS
ONH Eval: 0.65/0.65 OD
0.85/0.85 OS

Goniral Hysteresis: OD: 8.5 OS: 8.5
A Case for Tubes and Trabs?

Powerful and effective at lowering

Covered by the vast majority of insurance companies

TVT

<table>
<thead>
<tr>
<th>5-year data</th>
<th>Tubes</th>
<th>Trab</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP</td>
<td>14±4</td>
<td>12±4</td>
</tr>
<tr>
<td># of Metals</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Failure Rate</td>
<td>30%</td>
<td>47%</td>
</tr>
<tr>
<td>Conversion</td>
<td>58%</td>
<td>66%</td>
</tr>
<tr>
<td>Complication</td>
<td>22%</td>
<td>12%</td>
</tr>
<tr>
<td>Reoperation</td>
<td>9%</td>
<td>29%</td>
</tr>
</tbody>
</table>
Treatment Outcomes in the PTVT Study (3 Years)

<table>
<thead>
<tr>
<th>Tube Group</th>
<th>Trab Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP: 13.9 mmHg</td>
<td>IOP: 12.1 mmHg</td>
</tr>
<tr>
<td>2.1 medications</td>
<td>1.6 medications</td>
</tr>
<tr>
<td>32.1% failure rate</td>
<td>28.1% failure rate</td>
</tr>
</tbody>
</table>

No significant difference in the rate of surgical success was observed between the two surgical procedures at 3 years.
Xen

Xen 45 Gel Stent: US Pivotal Clinical Trial

<table>
<thead>
<tr>
<th>Vital - IOP and Medications</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>Median IOP</td>
<td>25.1 (8)</td>
</tr>
<tr>
<td>Median Max IOP</td>
<td>5.3 (1.2)</td>
</tr>
<tr>
<td>12 Month</td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td>15.9 (5.2)</td>
</tr>
<tr>
<td>Max IOP</td>
<td>7.7 (5.5)</td>
</tr>
</tbody>
</table>

76.3% of patients reported a mean diurnal IOP reduction of > 20% from medicated baseline at 12 months.

Postoperative Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotony (IOP &lt; 5 mmHg at any time)</td>
<td>16 (24.6%)</td>
</tr>
<tr>
<td>Anterior chamber shallow</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Anterior chamber + flaps</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Bleb Needling</td>
<td>21 (32.3%)</td>
</tr>
</tbody>
</table>