Disclosures

- Principal investigator for iVue OCT trial
- Principal investigator Topcon FDA trials for Maestro and OCT 2000
- Consultant for Topcon
- Speakers bureau Sanofi-Genzyme and Allergan

What is glaucoma?

- Definition:
  - "Ocular tissue damage at least partially related to intraocular pressure"

Where glaucoma is concerned agreement is limited among clinicians and scientists.

Prevalence studies

- Prevalence in different studies varies
  - Different populations
  - Different methods used to obtain a sample
  - Definition of glaucoma
Prevalence of POAG in Caucasians

<table>
<thead>
<tr>
<th>Study</th>
<th>Age range</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roscommon</td>
<td>Over 50</td>
<td>1.9</td>
</tr>
<tr>
<td>Beaver Dam</td>
<td>43-84</td>
<td>2.1</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>Over 55</td>
<td>1.1</td>
</tr>
<tr>
<td>Dalby</td>
<td>55-69</td>
<td>0.9</td>
</tr>
<tr>
<td>Blue Mountain</td>
<td>Over 49</td>
<td>2.4</td>
</tr>
<tr>
<td>Barbados Caucasians</td>
<td>40-84</td>
<td>0.8</td>
</tr>
<tr>
<td>Baltimore Caucasians</td>
<td>Over 40</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Prevalence of POAG in African American & African Caribbean

<table>
<thead>
<tr>
<th>Study</th>
<th>Age range</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbados</td>
<td>40-84</td>
<td>7.1</td>
</tr>
<tr>
<td>Baltimore</td>
<td>Over 40</td>
<td>4.2</td>
</tr>
<tr>
<td>St Lucia</td>
<td>Over 30</td>
<td>8.8</td>
</tr>
<tr>
<td>London</td>
<td>Over 35</td>
<td>3.9</td>
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</tbody>
</table>

Prevalence of OAG in LALES

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number who received on examination</th>
<th>Prevalence rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>2393</td>
<td>1.9</td>
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<tr>
<td>50-59</td>
<td>1883</td>
<td>2.0</td>
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<tr>
<td>60-69</td>
<td>1195</td>
<td>2.2</td>
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<tr>
<td>70-79</td>
<td>584</td>
<td>2.6</td>
</tr>
<tr>
<td>80+</td>
<td>147</td>
<td>2.9</td>
</tr>
<tr>
<td>Total</td>
<td>6142</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Risk factors for glaucoma examined in population based studies

- Demographic
  - Age
  - Gender
  - Race
- Ocular
  - IOP
  - Optic nerve head
  - Myopia
  - Hypermetropia
- Systemic
  - Diabetes
  - Systemic hypertension
- Genetic
  - Family history
- Other
  - Cigarette smoking
  - Alcohol intake
  - Socio economic factors

Intraocular pressure

- Major risk factor
  - Not as fundamental as once thought.
  - Prevalence increases with increase in IOP
  - Visual field loss slows down with decrease in IOP
  - Even if both eyes have IOP lower than 21. The eye with greater IOP will lose field quicker.
Systemic hypertension and glaucoma

- Blood pressure and pathogenesis of glaucoma
  - Hospital based study
  - Baltimore Eye Survey examined perfusion pressure
  - Ocular Perfusion pressure= Blood pressure-IOP (Systolic or Diastolic or mean pressure)

Genetic factors

- Positive family history
- Bias:
  - +ve Family history makes a person have frequent check ups
  - Recall bias
    - Sibling with glaucoma odds ratio 3.69
    - Parents with glaucoma odds ratio 2.67
    - Children with glaucoma odds ratio 1.12

Summary

- Prevalence of POAG is Caucasians over 40 years of age 2% and in African American and African Caribbean is “four times” that.
- Hispanics greater risk than African American as they grow older
- Overall quite underdiagnosed- 50% unknown
- Glaucoma suspects- increases need for care dramatically

Intraocular pressure

- Diagnosis- not helpful
- Treatment- only proven method
- Progression- very closely associated with IOP
- Risk factor- without a doubt most important risk factor
- In fact only alterable risk factor!
1. Observe the scleral ring to identify the limits of the optic disc and evaluate its size.

**Measure Disc Size**

- Observe the scleral ring to identify the limits of the optic disc and evaluate its size.
  - 66D 1 X magnification
- Cup size is associated with disc size
- Effects any casual observer for cup to disc ratio measurement
- Rim thickness varies with disc size

**Disc size**

- Small < 1.5 mm
- Medium > 1.5 but < 2.5 mm
- Large > 2.5 mm

**Neuroretinal rim characteristics**

- Color of rim- pale rims not good
- Width of rim in all sectors
- ISNT rule
- ISNT rule is accurate about 70% of times

**RNFL**

- Healthy eye has striations
- A certain amount of NFL is required for visibility
- RNFL loss can be diffuse, localized or mixed
RNFL cont...
- Diffuse – reduction in RNFL brightness
- Localized – wedge shaped defect
- Localized RNFL defects should traced back the disc

Peripapillary atrophy
- Where
- How large
- 1/8, ¼, ½, ¾, 1, > 1 DD

Optic disc hemorrhages
- Transient
- Inferior temporal or superior temporal regions mainly
- Record present or absent
- If present where

Retinal vessels
Look for this in patients that you suspect NTG

CD ratio
- Vertical
- Horizontal
- Largest
- CD ratio of imaging devices will not match your findings!
Focal atrophy of neural rim

Optic disc hemorrhages

Optic disc hemorrhages-3

Barring of circumlinear vessels

- Vessels that runs along margin between cup and neural rim.
- Found supero and infero temporally
Barring of circumlinear vessels
- As rim becomes thinner it leaves an area of pallor between the rim and the circumlinear blood vessel.

Nasal cupping
- Usually seen in advanced glaucoma.
- Space between Nasal rim and blood vessels.

Bayonetting
- Double angulation of blood vessel.

Barring of circumlinear vessels

Laminar dot sign

Nerve fiber bundle defect
- Rim changes also produces RNFL defects.
- Dark stripes or wedge shapes defect paralleling the normal striations.
- Common after disc hemorrhages
Visual field analysis: A systematic approach

- Watch out for Pupil size
- Reliability index
- Type of test 24-2 SITA STD
- Age
- Refractive error

- Look for patterns
- Grey Scale
- Global view
- Not for diagnosis
- Types of visual field defects

- Raw data
- Normals centrally low 30's
- Peripherally high 20's

- Total deviation
  - Deviation from average

- Total deviation probability plot

- Pattern deviation
  - Removes any generalized defects
  - Cataract
  - Pupil miosis

- Pattern deviation probability plot

- Glaucoma hemifield test
  - Outside normal limits
  - Borderline
  - Generalized reduction in sensitivity

- Global indices
  - MD mean deviation
  - PSD pattern Standard Deviation

- Gaze tracking
Criteria for glaucomatous damage

- GHT outside normal limits in at least two occasions
- PSD < 5% of normal individuals
- A cluster of three or more non-edge points (pattern deviation plot) all of which are depressed at a p<5% and one of which is depressed at a p<1% on two occasions (respecting horizontal meridian)
- This criterion was written for 30-2, if 24-2 field is analyzed edge points are included.

Staging based on MD

- Better than -6 dB - Mild
- Worse than -6.0 dB but better than -12 dB - Moderate
- Worse than -12.0 dB - Severe

Optical coherence tomography

Gonioscopy

A = Above Schwalbe line, totally occluded angle.
B = Behind the Schwalbe line, peripheral iris is in contact with TM.
C = Scleral spur Iris root at the level of scleral spur.
D = Deep anterior ciliary body seen.
E = extremely deep
Van Herrick angle estimation

- 1:1 – Open angle, VH grade 4
- 1:1/2 – Open angle, VH grade 3
- 1:1/4 – Narrow angle, VH grade 2 (Angle Closure Possible)
- 1: <1/4 – Angle closure likely, VH grade 1

Ultrasound pachymetry is standard

- As central data as possible
- Greater number of measurements increase your reproducibility of data
- Always use lowest data

Why lowest data?

- Perpendicular measurements are lowest or smallest in value

Why not average the data?

- Average 484 microns
- Lowest 473 microns
- Averaging helps decrease error but does not eliminate it.

Anterior segment OCT

Difference between optical and ultrasound pachymetry measurements

<table>
<thead>
<tr>
<th>Author</th>
<th>Difference in OCT and ultrasound values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al AJO 2008</td>
<td>26 microns</td>
</tr>
<tr>
<td>Wang et al J Refract Surg 2008</td>
<td>38 microns</td>
</tr>
<tr>
<td>Gunvant &amp; Darner Medical Imaging 2011</td>
<td>13 microns</td>
</tr>
</tbody>
</table>

How to use CCT data in glaucoma management?

- Error in IOP measurements
- Ocular hypertensive patients
- Thinner cornea at greater risk of developing glaucoma

The Scoring Tool for Assessing Risk (S.T.A.R. II) calculator

- OHTs and EGPS data
- Intended for use only in untreated OHT patients
- Age (30-80)
- IOP 20-32 mmHg
- CCT 475 to 650 microns
- PSD 0.50 to 3.00 dB
- C/D ratio vertical 0.00 to 0.8

Probability of conversion in 5 years
- <5% observe and monitor
- 5 to 15% consider treatment
- >15% treat

Medications first advantages

- Drugs are safer than surgery-
  - Less complications
  - Less discomfort
  - Drug effects can reversed or is short acting
  - Less expensive in the short run
  - Multiple drugs can be combined to achieve successful reduction in IOP
  - Better quality of life when compared to surgery first (Lichter et al., Ophthalmology 2001)
Medications first disadvantages

- May be more expensive in the long run
- Multiple drugs
  - Compliance, adherence and persistence issues
- Chronic drug uses and its effect on future surgical outcomes?
  - Preservatives effect?
  - Inflammation leading to failure of future procedures*
- Increased chances of cataract formation

Surgery first - advantages

- If successful and large drop in IOP may be obtained
- No issues related to patient compliance, adherence and persistence
- Good in situations where obtaining continuous supply of medications is a problem
- May be cheaper long term

Surgery first - disadvantages

- Outcomes may be variable
- Long term may loose efficacy
- May still require additional topical medications
- Complications may be dire
- Comfort and quality of life may be lower
- Chances of cataract formation is greater than topical medications
- Age- young vs. older individuals

Race and management options

- Race – white versus individuals with greater pigment
- Individuals with greater pigment - greater risk of post-operative scarring*
  - Medications – first choice

Age and management options

- Younger individuals
  - Accelerated wound healing systems
  - Thick fleshy periocular tissues heals rapidly
- Thus older individuals better suited for surgical options

Current practice patterns

- Unacceptable high pressures will inevitably destroy optic nerve tissue
- Safe levels of IOP by any means warranted
  - If these don't work or not sufficient
  - drugs like – prostaglandins
  - reduction in inflow – beta blockers
- Maximal medical therapy
- Consider surgery

*Broadway DC et al., Adverse effects of topical antiglaucoma medications II Arch Ophthalmol 1994
*Broadway DC et al., Racial differences in the results of glaucoma filtration surgery: are racial differences in conjunctival cell profile important? BJO 1994
Maximal tolerated medical therapy

-β-Blockers
  - Timolol
  - Betaxolol
  - Levobunolol
  - Carteolol
  - Metipranolol

Carbonic anhydrase inhibitors (CAIs)
  - Systemic:
    - Acetazolamide
    - Methazolamide
  - Topical:
    - Dorzolamide
    - Brinzolamide

Adrenergic Agonists
  - Nonspecific:
    - Dipivefrin (epinephrine)
  - α2-Agonists:
    - Brimonidine
    - Apraclonidine

Conventional/Trabecular
  - Cholinergic agonists (parasympathomimetics):
    - Pilocarpine
    - Echothiophate iodide
    - Carbachol
  - Prostaglandin derivatives:
    - Bisonephrine
  - Nonsteroidal adrenergic agents:
    - Epinephrine (epinephrine)

Nonconventional/Uveoscleral
  - Prostaglandin derivatives:
    - Latanoprost
    - Travoprost
    - Bimatoprost
  - α2-Agonists:
    - Brimonidine

...and how exactly do I use them?

Stage of disease
  - Visual field status
Stage of nerve damage
  - Rim tissue remaining
Type of glaucoma
  - POAG – medical first makes sense
  - Secondary glaucoma
  - Congenital glaucoma
  - Complete angle closure
Adherence, compliance, persistence issues
Effect of medications and future outcomes of surgery

Target pressure

- A theoretical value below which visual field and ONH appear stable (not deteriorating).
- Calculated from highest recorded IOP.
- Conventionally 20-30% decrease in IOP.
- 40% or more if severe glaucoma
- Consider having a range rather than one number.

Medications

- First line drugs- prostaglandin analogs
- Second line: Beta blockers, Alpha 2 agonist, Carbonic anhydrase inhibitor
- Third: Combination with prostaglandin
  - Eg: PGA (Travatan z) and CAI+ Beta blocker (COSOPT)

  - PGA + brinzolamide/brimonidine (Simbrinza)
Where should the IOP be?

- No real number
- Start with 30% drop
- Monitor for progression

- Advanced glaucoma you want IOP to be less than 12
- Pressure should not fluctuate much

ALT versus SLT

- SLT preferred
- Unlike ALT, SLT does not scar
- Autopsy specimens – confirm no coagulative damage after SLT
- SLT can be repeated

Mechanisms of action SLT

- 5-8 fold increase in monocytes and macrophages in TM after treatment with SLT
- Hypothesis
  - Injury via laser causes releasing of chemoattractant
  - This in turn recruits monocytes that are transformed into macrophages
  - Macrophages clear pigment granules and exit via Schlemm's canal


Selective Laser trabeculoplasty

- Selectively targets melanin pigment of TM
- More safe compared to ALT (because lower power)
- Equally effective as ALT
- Can be repeated if first attempt is not effective
Main adverse events:
- Blurred vision 82%
- Hyperemia 80%
- SPK 15%

Correlation for repeatability:
Overall $r=0.59$
That is $r^2 = 35\%$

Overall sensimed is "sensitive" to IOP fluctuations

Summary of contact lens IOP devices:
- Long way to go
- The ability of device to capture peak accurately is not excellent.
- Cautiously optimistic.
- FDA cleared on March 2016 not yet available for sale
- Prediction ...
Latanoprostene Bunod - Bausch and Lomb

- Latanoprostene bunod (LBN, BOL-303259-X) is a nitric oxide (NO)-donating prostanoid FP receptor agonist

**Mechanism of action**

Latanoprostene Bunod

- Cellular esterase
- Latanoprost acid
- 4-hydroxybutyl nitrate (Butanediol mononitrate)
- Acts on changing ECM
- 1,4 butanediol
- Nitric oxide
- Changes trabecular meshwork cells that are highly contractile in nature

**The APOLLO Study**

Timolol Maleate 0.5% or Latanoprostene Bunod 0.024%

IOP measured at 8 AM, 12 noon and 4 PM at week 2, 6, and 3 months
Treatment protocol - Acute angle closure - ABC procedure

- Alpha-2 agonist - Brimonidine
- Beta blocker - Timolol (caution in asthmatics) or Betaxolol
- Carbonic anhydrase inhibitor - Dorzolamide (Caution sulpha allergy contraindication)

- Each medication given every 15 minutes
- Perform 3 times

Oral medications

- Oral Carbonic anhydrase inhibitor
- Two tablets of 250 mg acetozolamide (Caution sulpha allergies contraindication)

- Works good when patient can retain medication - Vomiting common with angle closure glaucoma

- Check intraocular pressure after 1 hour if lower than 40°
- Add Pilocarpine every 15 minutes for 45 minutes and repeat procedure ABC procedure
- Seek ophthalmologist opinion - refer patient
Take home medication

- Prednisolone acetate 1% q1-6 hours (approx every 3 hours)
- Acetazolamide 500 mg sequel BID
- Alpha agonist or beta blocker BID
- Pilocarpine 2% QID

Laser therapy

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Laser used.</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irisotomy</td>
<td>Neodymium</td>
<td>Cataractal eye of an acute ASC</td>
</tr>
<tr>
<td></td>
<td>YAG</td>
<td>Narrow or closed angle in more than 180 degree</td>
</tr>
<tr>
<td></td>
<td>Argon</td>
<td>with optic nerve damage and high IOP</td>
</tr>
<tr>
<td></td>
<td>Sequential</td>
<td>Acute ASC</td>
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<tr>
<td></td>
<td>Argon-YAG</td>
<td>Cataractal eye of an acute ASC</td>
</tr>
<tr>
<td>Peripheral</td>
<td>Argon</td>
<td>Plateau iris</td>
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<td>Endolaserplasty</td>
<td>Argon</td>
<td>In preparation for laser trabeculectomy</td>
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<tr>
<td></td>
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<td>After incision of iris, posterior is still present</td>
</tr>
<tr>
<td></td>
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<td>Before an iridotomy: In case of thick, inflamed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or neovascular cases.</td>
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