What We Know

Glaucoma: What We Know, How We Should Practice, and What the Future May Hold

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What We Know

NFL Thinning
RGC Death

Vascular Dysfunction
Metabolic Dysfunction
Pigmentation
CSF Pressure
Intraocular Pressure
Aging
Excitotoxicity
Oxidative Damage
Genetics

What is Glaucoma?

Glaucoma is:

• A neurodegenerative disease
• The most common neurodegenerative disease
• More common than all other neurodegenerative diseases put together!!
• Alzheimer’s, Parkinson’s, Huntington’s, ALS…
  • 30 million (Exp Gerontology, 2009)
• Glaucoma
  • 60 million (BJO, 2006)

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Glaucoma is a chronic, degenerative optic neuropathy that can be distinguished from most other forms of acquired optic neuropathy by the characteristic appearance of the optic nerve. In glaucoma, the neuroretinal rim of the optic nerve becomes progressively thinner, thereby enlarging the optic nerve cup. This phenomenon is termed as optic nerve cupping. It occurs in the loss of retinal ganglion cell axons, along with supporting cells and vascular connections.

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What the Future May Hold

12 Topics for Discussion
- Biomarkers
- Ocular Blood Flow
- Progression
- IOP
- Combining Structure and Function
- Advances in Imaging
- Examining the Angle
- Cerebral Spinal Fluid Pressure
- Neuroprotection
- Drug Administration
- Surgical Alternatives
- Modifiable Lifestyle Factors

1. Biomarkers
What do we know?
- Genes and Genetics
  - Myocilin
  - Exfoliative disease
  - The studies
- Epigenetics
- Proteins

1. Biomarkers
How should we practice?
- Early days
  - Commercial interests
    - e.g. Illumina
- Ethical considerations
- Family History

What the future may hold
- Proteomics
  - ARVO workshop 2013
- Lipidomics
- Genetic Markers
  - CDKN2B-AS1
2. Ocular Blood Flow

What do we know?
• Highly variable across the population
• Difficult to measure (even more variability)
• Frustrating as should be “no brainer” for ocular disease

How should we practice?
• With great care
• Evaluation of dysfunction is the key; how the vasculature “reacts” rather than “is”

What the future may hold
• Vascular dysregulation key to early diagnosis
• OCT Doppler Flowmetry
• OCT Angiography

3. Progression

How do we know?
• Rate of progression important
• Early progression easier to detect in structural measures?
• Function increasingly important as disease progresses

What the future may hold
• Highly sensitive, individually based progression analysis
• Earlier diagnosis
• More confidence in calling clinically significant progression

How should we practice?
• Evaluate rate of progression
  – Trend Analysis
• Evaluate change from known baseline
  – Event Analysis
• Progression the key to diagnosis
• Progression the key to management
4. IOP

What do we know?
• Highly variable
• Many assumptions
• Difficult to measure accurately
• Diurnally sensitive

How should we practice?
• Understand the limitations
• Repeat before making clinical decisions
• Only modifiable treatment
• Neuroprotective?

What the future may hold
• Understanding corneal biomechanics – Corneal hysteresis
• 24-hour IOP – Smart technologies

5. Combining Structure and Function

What do we know?
• Linear relationship between S & F
• Different ranges of normality and variability
• Temporal factors

How should we practice?
• Combined printouts
• Look for concordance

What the future may hold
• Combined S-F indices
• New visual field patterns to optimize S-F relationship
• S-F progression analysis
6. Advances in Imaging

What do we know?
- OCT currently c.55,000 scans per second
- SLO currently unavailable
- Doppler blood flow

How should we practice?
- Understand the limitations
- Acquire carefully
  - Rubbish in equals rubbish out
- Analyze carefully
  - Red disease
  - Problems of normal databases
- Progression is the key

What the future may hold
- Doppler blood flow
- OCT angiography
- Faster, better, deeper
- SLO
- Adaptive Optics
- Real-time biomechanics

7. Examining the Angle

What do we know?
- Essential to the diagnosis
- Essential to management

How should we practice?
- Frequent gonioscopy on every glaucoma patient and suspect
- Understand the clinical definitions and implications of the abnormal angle (WGS Consensus)
- www.gonioscopy.org

What the future may hold
- Better understanding of angle structure and function
- Risk factors
  - Ethnicity
- New imaging techniques
8. Cerebral Spinal Fluid Pressure

What do we know?
• Trans-scleral pressure difference
• Low CSF pressure associated with NTG
• Finally provides a reasonable explanation of aspects of NTG

How should we practice?
• With knowledge but no clinical measure
• Implications for perfusion pressure
  – BP medications

9. Neuroprotection

What do we know?
• Glaucoma is the world’s most common neurodegenerative disease
• Mechanisms and potential interventions
• Failed clinical trials
  – Memantine
• The marketing myths

How should we practice?
• Do no harm
• Careful of marketing without evidence
• How to define Neuroprotection?

What the future may hold
• Neuroprotective strategies
• Targeted drug delivery
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<td>• Tear film</td>
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<td>How should we practice?</td>
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<td>• Know the alternatives</td>
<td>• Minimally invasive, non-bleb surgery</td>
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## 12. Modifiable Lifestyle Factors

### What do we know?
- Very little evidence
- Healthy lifestyle, healthy patient, better outcomes

### How should we practice?
- Be able to offer advice
- Promote healthy lifestyle
- Be careful of fads and marketing; help protect your patient
- Placebo

### What the future may hold
- Coenzyme Q10
- Cyclosporin A
  - Cyclophilin D inhibition
- Resveratrol
  - Sertuins
- Caloric restriction
  - CR mimetics