What’s new and what’s next in glaucoma

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The plan for today is to:

Introduce you to all of us

Demonstrate our work across the spectrum of glaucoma research & innovation

Take questions

Tour our facilities
Our work covers the broad spectrum of important questions

What is glaucoma & why does it happen?

How can we find glaucoma before it is too late?

How can we treat glaucoma better?

How can we help glaucoma patients adjust to their disability?

Might we restore vision to those who have lost it?
What is glaucoma & why does it happen?

Dr. Harry Quigley
Director Emeritus, Glaucoma Center of Excellence

A. Edward Maumenee
Professor of Ophthalmology
## W.H.O. Estimates of Bilateral Blindness

<table>
<thead>
<tr>
<th>Condition</th>
<th>Estimated Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>50 million</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>12 million</td>
</tr>
<tr>
<td>Trachoma-Cornea</td>
<td>9 million</td>
</tr>
<tr>
<td>Macular Degen</td>
<td>7 million</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 million</td>
</tr>
</tbody>
</table>
Worldwide Glaucoma 2010

60 Million with Glaucoma
45 Million Open-Angle
16 million Angle-Closure

8.4 Million Bilaterally Blind

Quigley, Broman  *Br J Ophthalmol* 2006
Operational definition of OAG

Cup/disc ratio found in <2.5% of risk population

Humphrey Field with abnormal hemifield test

Risk Factors for OAG

- Age
- IOP
- Genetics (family history)
- Myopia
- Regional derivation
OAG Prevalence by Ethnicity

European 1.5%
Hispanic 2%
Indian 4%
African 8%
**Logarithmic scale**

Mean Normal IOP = 16
Mean OAG IOP = 19
3 of 4 glaucoma IOP < 21
“characteristic glaucoma cupping” defined by excavation
Disc Excavation

Normal

Glaucoma

Morrison JC, Dorman-Pease ME, Dunkelberger GR, Quigley HA
Total loss of rim

Vessels disappear

Base of cup out of focus relative to retina
Zeiss Humphrey Perimeter
Early damage: abnormal nasal, just below (or above) the horizontal
Moderate damage: spreads to include all of lower nasal field
Severe damage: includes all but center and temporal field (outside testing zone)
ACG blinds proportionately more than OAG and nearly as many

10% of all OAG are blind
25% of all ACG are blind,
Hence,
4.5 million blind from OAG
3.9 million blind from ACG
Risk factors for angle closure glaucoma

Older Age
Ethnicity: CHINESE
Gender: FEMALE
Small Ocular Dimensions
Lack of iris porosity
Choroidal expansion
Among 10 narrow angle persons, only 1 will develop AC. Do we do 50 million iridotomies in China or 5 million?

Gonioscopy and UBM aren’t predictive, they are a static view of a dynamic process.

Wilensky et al. Am J Ophth 1993
In 100 patients, half OAG, half AC
Iris volume estimated by cross-sectional area, comparing area in bright light to area in darkness
GLAUCOMA:
What Every Patient Should Know
A Guide from Dr. Harry Quigley
Glaucoma Center of Excellence
Wilmer Institute
Johns Hopkins School of Medicine
Available at:
www.createspace.com/3570763
How can we find those with glaucoma?

Dr. David Friedman
Director,
The Dana Center for Preventive Ophthalmology

Alfred Sommer Professor of Ophthalmology

Dr. Nazlee Zebardast
Fellow in Ophthalmology
Angle closure is the major cause of blindness worldwide

21 million worldwide; 5.3 million bilaterally blind  
– 1.6 million in Europe

Early detection and treatment with simple laser procedure may reduce progression and vision loss

Laser iridotomy

Angle closure is the ideal condition to screen for.

Need to screen on risk factors that do not require eye exam.

Based on experience with POAG, hypothesized family history one risk factor.

Partnered with colleagues at Aravind Eye Hospital in Tamil Nadu India.
Indian family angle closure evaluation

IFACE1: Is family history a risk factor for angle closure?

IFACE2: Is family history a risk factor for SEVERE angle closure?
Family history is a strong risk factor for angle closure

- Siblings of AC subjects had more than 1 in 3 risk of AC
- Odds of AC 14 x greater in AC siblings compared with OA siblings
Severe angle closure more prevalent among angle closure siblings

- Sibs with OA: 67.2%
- Sibs with AC suspect: 29.3%
- Sibs with AC glaucoma: 3.5%

AC suspect proband group
AC glaucoma proband group
Strong heritability of angle closure

Family history of angle closure major risk factor for angle closure
  – 14 times higher odds

Family history of SEVERE angle closure risk factor for SEVERE angle closure
  – 3 times higher odds
What does this mean for you?

If you have been diagnosed with angle closure, please ask your **FAMILY MEMBERS** to get **SCREENED**

Same is true for most other types of glaucomas: primary open angle, pseudoexfoliation, juvenile glaucoma
Screening for glaucoma in the community

David S. Friedman, MD, MPH, PhD
Glaucoma is mostly unrecognized

NO symptoms
Symptomatic!
# Glaucoma Worldwide

## Affected*

<table>
<thead>
<tr>
<th>Year</th>
<th>PACG</th>
<th>POAG</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>44 million</td>
<td>21 million</td>
</tr>
<tr>
<td>2020</td>
<td>63 million</td>
<td>30 million</td>
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</table>

## Blind from Glaucoma**

<table>
<thead>
<tr>
<th>Year</th>
<th>PACG</th>
<th>POAG</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>4.5 million</td>
<td>3.9 million</td>
</tr>
<tr>
<td>2020</td>
<td>5.9 million</td>
<td>5.3 million</td>
</tr>
</tbody>
</table>

*Tham, 2013*, **Quigley 2006**
Frequently not diagnosed

Baltimore Eye Survey

62% in Los Angeles

76% in Proyecto Ver
90% of glaucoma is undiagnosed in most of the world.
Hard to reach populations
Screening is difficult
Technology can improve performance and allow remote diagnosis.
Cataract
Macular degeneration
Refractive error
We have screened over 4,000 in East Baltimore, ongoing work as part of CDC-Funded Research = STOP Glaucoma

http://www.stopglaucomahopkins.org/

STOP Glaucoma Screening Summary Video
How can we treat glaucoma better?

Dr. David Friedman
Director, Dana Center for Preventive Ophthalmology
Alfred Sommer
Professor of Ophthalmology

Dr. Randy Craven
Director, Wilmer Bethesda Office
Associate Professor of Ophthalmology

Dr. Amanda Kiely Bicket
Assistant Professor of Ophthalmology

Dr. Henry Jampel
Director, Wilmer Green Spring Station Office Odd Fellows
Professor of Ophthalmology

Dr. Michael Boland
Residency Program Director
Associate Professor of Ophthalmology

Dr. Ian Pitha
Assistant Professor of Ophthalmology
Improving quality of care

Receiving frequent patient feedback

Bivarus will allow us to assess patient experience and to intervene
Rating of the providers’ performance by patients

A clinic at the Wilmer Eye Institute

<table>
<thead>
<tr>
<th>Name</th>
<th>Top-Box</th>
<th>Score</th>
<th>Overall Patient Experience</th>
<th>Provider Questions</th>
<th># of Responses</th>
<th>Download Report</th>
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<tbody>
<tr>
<td></td>
<td>65.5</td>
<td>4.53</td>
<td>4.55</td>
<td>4.50</td>
<td>403</td>
<td></td>
</tr>
<tr>
<td></td>
<td>77.7</td>
<td>4.59</td>
<td>4.61</td>
<td>4.58</td>
<td>169</td>
<td></td>
</tr>
<tr>
<td></td>
<td>68.1</td>
<td>4.44</td>
<td>4.28</td>
<td>4.59</td>
<td>341</td>
<td></td>
</tr>
<tr>
<td></td>
<td>61.0</td>
<td>4.61</td>
<td>4.60</td>
<td>4.61</td>
<td>122</td>
<td></td>
</tr>
<tr>
<td>Peer Group Average</td>
<td>75.85</td>
<td>4.64</td>
<td>4.61</td>
<td>4.67</td>
<td>235.17</td>
<td></td>
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<tr>
<td></td>
<td>81.6</td>
<td>4.68</td>
<td>4.60</td>
<td>4.76</td>
<td>369</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100.0</td>
<td>5.00</td>
<td>5.00</td>
<td>5.00</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>
Better communication with patients
Better communication with patients
Current Glaucoma Treatment

Reduce Eye Pressure
Prevents development of glaucoma
Prevents vision loss from glaucoma

Eye Drops
Poor adherence with daily medications
Ocular surface toxicity
Controlled Release

![Graph showing controlled release and pulsed delivery with annotations for increased side-effects and poor activity.](Image)
What do you want?

Would you accept controlled release to daily eye drops?

Varadaraj et al.  Unpublished Results

THE JOHNS HOPKINS CENTER FOR NANOmedicine AT THE WILMER EYE INSTITUTE
Glaucoma Surgery

- Disease progression
- Stable vision
- Vision loss due to low IOP

Pressure vs. Time

- Surgical Intervention
- Device Implantation
- Surgical Intervention

THE JOHNS HOPKINS CENTER FOR NANOMEDICINE AT THE WILMER EYE INSTITUTE
Nano-structured Glaucoma Shunts

Drug Release (µg) vs. Days

Shunt w/ template wire

Shunt w/o template wire

Inner lumen after flow
Using Information Systems to Improve Glaucoma Care

Michael V. Boland, MD, PhD

Associate Professor, Wilmer Eye Institute and Health Sciences Informatics
Director of Information Technology, Wilmer Eye Institute
Residency Program Director, Wilmer Eye Institute
Why all the computers?

• Ophthalmology (Medicine) is really about collecting data and then using them to make decisions
• Many clinical data are now (or soon will be) electronic
• Digital data can be used to:
  – Facilitate decision making
  – Assess quality
  – Communicate with others
Difference between IOP and Target IOP in 3 Months

- delta >=7
- delta 4-6
- delta 1-3
- delta <=0
- IOP <= 5
<table>
<thead>
<tr>
<th></th>
<th>Novice (score = 2)</th>
<th>Beginner (score = 3)</th>
<th>Advanced Beginner (score = 4)</th>
<th>Competent (score = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Universal precautions</td>
<td>Has not heard of universal precautions.</td>
<td>Able to perform team time-out but needs prompting to do so.</td>
<td>Independently initiates team timeout at beginning of case, identifies correct patient, procedure and side. Team members have been introduced. Alerts / allergies noted.</td>
</tr>
<tr>
<td>2</td>
<td>Draping:</td>
<td>Unable to start draping without help.</td>
<td>Lashes mostly covered, drape at most minimally obstructing view. Attains proper head position.</td>
<td>Lashes completely covered and clear of incision site, drape not obstructing view.</td>
</tr>
<tr>
<td>3</td>
<td>Corneal or superior rectus traction suture</td>
<td>Unable to describe purpose and method of inserting traction suture.</td>
<td>Able to load and handle needle appropriately. Some difficulty in finding correct depth of suture, needs instruction, needle track too deep or too shallow or bite not of ideal size.</td>
<td>Is able to consistently perform the step with the appropriate length of bite, depth of suture and achieve the desired rotation of the eye for exposure.</td>
</tr>
<tr>
<td>4</td>
<td>Conjunctival incision &amp; Tenon's dissection</td>
<td>Is able to describe but not able to perform limbal or fornix conjunctival incision but is inefficient and requires guidance. Has difficulty with judging appropriate length of incision, dissection down to sclera of both conjunctiva and Tenon's and the necessary force to apply to the tissue. Has difficulty avoiding damage to the superior rectus muscle with limbal-based conjunctival flap.</td>
<td>Is able to perform subconjunctival dissection, but needs occasional guidance. Able to describe the complications that can occur during conjunctival dissection and their management.</td>
<td>Is able to efficiently perform either limbal or fornix conjunctival incision. Judges appropriately the length of incision, adequately dissects down to sclera of both conjunctiva and Tenon's and handles the tissue with the appropriate tension. Takes condition of the patient's conjunctiva into account. Ensures that an adequate area of conjunctiva has been dissected, creating a pocket to facilitate application of antimetabolite.</td>
</tr>
</tbody>
</table>
There are 3 ways to lower the eye pressure

Medications (eye drops)
Office Laser

Operating room surgery

Equally good first steps
Eye drops

Difficult to instill
Difficult to remember to take
Bimatoprost insert
Latanoprostene bunod vs. latanoprost (VOYAGER)
Adverse events

<table>
<thead>
<tr>
<th></th>
<th>LBN 0.006%</th>
<th>LBN 0.012%</th>
<th>LBN 0.024%</th>
<th>LBN 0.040%</th>
<th>Latanoprost 0.005%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperemia</td>
<td>1%</td>
<td>6.0%</td>
<td>2%</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Pain</td>
<td>15%</td>
<td>17%</td>
<td>12%</td>
<td>17%</td>
<td>6%</td>
</tr>
</tbody>
</table>
Latanoprostene bunod vs. latanoprost (VOYAGER)
Don Zack, M.D., Ph.D.
Neuroprotection

Eye Pressure

Other factors

??

Optic nerve
Microscopic (MIGS) Stents

Figure adapted from reference 1
Red arrows denote aqueous outflow

Using patients’ preferences to inform new glaucoma therapies

MIGS (“minimally invasive glaucoma surgeries”) & other new treatments are being developed

www.glaucoma.org
Using patients’ preferences to inform new glaucoma therapies

MIGS (“minimally invasive glaucoma surgeries”) & other new treatments are being developed.

We want to balance:

Effectiveness (controlling disease)

&

Patient experience (side effects, recovery)
We are interviewing patients about their experiences living with glaucoma & its treatments. Assessing patient recovery after procedures.

Using patients’ preferences to inform new glaucoma therapies.

Using **patients’ preferences** to inform new glaucoma therapies

*We are...*

**Interviewing patients** about their experiences living with glaucoma & its treatments

Assessing patient **recovery** after procedures

...in order to...

Ensure **clinical trials** address patient priorities (not just physician priorities)

Help the **FDA accelerate approval** for therapies patients want most

How can we help glaucoma patients adjust to their disability?

Dr. Pradeep Ramulu
Director, Glaucoma Center of Excellence
Associate Professor of Ophthalmology
The easiest way to make you safer & to help you adjust to disability is to change the world around you
In FIGS, most falls occurred in or just outside the home

440 total falls reported by 152 participants

59% occurred in or near the home
Our FIGS patients also did most of their walking **AWAY** from home.

1,700 steps/day at home

2,100 steps/day away from home
Less walking at home

More falls at home

Walking at home is actually more dangerous than walking outside the home
Highest number of falls on stairs and in the bedroom

- **Bathroom**: 22 falls, 7 injurious
- **Hallway**: 7 falls, 3 injurious
- **Bedroom**: 30 falls, 9 injurious
- **Dining room**: 9 falls, 0 injurious
- **Stairs**: 34 falls, 13 injurious
- **Kitchen**: 25 falls, 10 injurious
- **Living room**: 25 falls, 8 injurious
- **Basement**: 8 falls, 4 injurious
- **Other**: 8 falls, 2 injurious
- **Bathroom**: 22 falls, 7 injurious
- **Hallway**: 7 falls, 3 injurious
- **Bedroom**: 30 falls, 9 injurious
- **Dining room**: 9 falls, 0 injurious
- **Stairs**: 34 falls, 13 injurious
- **Kitchen**: 25 falls, 10 injurious
- **Living room**: 25 falls, 8 injurious
- **Basement**: 8 falls, 4 injurious
- **Other**: 8 falls, 2 injurious
Lighting may be the easiest way to prevent falls.

Bedroom & stairs often poorly lit.

Poor light among the home hazards is the strongest predictor of the falls.

94% more likely to fall if lighting bad.
Home lighting the same for those of you with mild, moderate or severe glaucoma.
Might we restore vision to those who have lost it?

Dr. Pradeep Ramulu
Director, Glaucoma Center of Excellence
Associate Professor of Ophthalmology

Dr. Don Zack
Co-Director, JH Center for Stem Cells & Ocular Regeneration
Guerrieri Professor of Ophthalmology

Dr. Harry Quigley
Director Emeritus, Glaucoma Center of Excellence

A. Edward Maumenee
Professor of Ophthalmology

Dr. Thomas Johnson
Resident in Ophthalmology
The retina is an extension of the brain.
THE BRAIN BENEFITS OF EXERCISE

- Increases production of neurochemicals that promote brain cell repair
- Improves memory
- Lengthens attention span
-Boosts decision-making skills
-Prompts growth of new nerve cells and blood vessels
-Improves multi-tasking and planning
Worse glaucoma = less walking
For 100+ years, there has been one thing we can do to treat glaucoma...

More activity

Less worsening of glaucoma over time

Is physical activity the a 2\textsuperscript{nd} reversible risk factor for glaucoma?
Visual Improvement with Physical activity Study (VIPS)
Stem Cells as a Way to Protect and Restore Vision for Glaucoma Patients
Potential of Stem Cells for Glaucoma

1. Improve our understanding of Retinal Ganglion Cells (RGCs) and why they die in glaucoma

2. Develop new drugs and new therapeutic approaches for glaucoma

3. Replace RGCs and optic nerve
Stem Cells as a Way to Protect and Restore Vision for Glaucoma Patients
Healthy or diseased individual

Patient-derived somatic cells

Modified RNA encoding reprogramming factors (OCT4, SOX2, KLF4, cMYC, LIN28)

Patient-specific iPS cells

Modified RNA encoding specification factors for different cell types

Directed differentiation

Drug screening for disease-specific therapeutics

Transplantation (autologous)
GOAL: Protect and Replace

- Photoreceptor Cells
- Retinal Ganglion Cells
- ES-Derived RPE Cells
- ES-Derived RGCs
CRISPR GENE EDITING TECHNOLOGY
High-Throughput Screening System

Neuronal Profiling V3.5
Identified Drug that Potently Promotes RGC Survival and Function
Potential of Stem Cells for Glaucoma

1. Improve our understanding of Retinal Ganglion Cells (RGCs) and why they die in glaucoma

2. Develop new drugs and new therapeutic approaches for glaucoma

3. Replace RGCs and optic nerve
Stem cell transplantation to replace the optic nerve

A glaucoma treatment of the future?
Stem cell transplantation for other eye diseases is already in clinical trial

Schwartz et al., Lancet. 2014
Retinal ganglion cells are very complicated

Kay et al., Jneurosci 2011.
Step 1: Cells have to get into the retina

Without inhibition of barrier

With chemical inhibition of barrier cells
Step 2: Cells have to listen to other retinal neurons
Step 3: Cells have to talk to the brain

Leibinger et al., MolTher. 2016
We still have a lot to learn in order to re-grow a damaged optic nerve in human patients...

But I believe it will be feasible in the future!
A brief word of caution...

Clinical trials in human patients should:
1. Have oversight from an independent safety and ethics committee
2. Be based on convincing and reproducible data in non-human models
3. **Not** cost the patient any money to participate
Questions?