Glaucoma: The Silent Blinding Disease

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Main Causes of Blindness

- Cataract
- Glaucoma
- Retinal Disease
  - Macular Degeneration
  - Diabetic Retinopathy

Ocular Anatomy

Cataract
White Cataract

Cataract

Cataracts

Cataract Surgery
Cataract Surgery

Ocular Anatomy

Glaucoma

- Leading cause of irreversible blindness worldwide
- Second leading cause of blindness in the US
- Divided into
  - Open Angle Glaucoma
  - Closed Angle Glaucoma

Glaucoma-Racial Differences

- African Americans have 4X more glaucoma than whites (8-10% vs 2-3%)
- Hispanics in between (5-6%)
- Asians have a wide variation (2-5%)
  - Chinese have a large amount of Closed Angle
  - Japanese and Korean have mostly Normal Tension type
Glaucoma

Drainage angle and fluid flow

Normal Angle

Open Vs Closed Angle
**Occludable Angle**

**Pre-Laser PI**

- Used in the treatment or prevention of angle closure glaucoma
- Creates a “bypass” for fluid and helps “open the angle”

**Laser Iridotomy**

**Post-Laser PI**
**Diagnosis**

- Intraocular pressure
- Optic nerve exam
- Visual field test
- Gonioscopy (angle exam)

**Eye Pressure Test**

**Optic Nerves—Normal vs. Glaucoma**

- Normal optic nerve
- Early glaucoma
- Advanced glaucoma

**Visual fields—Normal vs. Glaucoma**

Visual Field Examination

- Normal result
- Abnormal result
Gonioscopy – Angle Structures

Diagnosing Glaucoma

Gonioscopy

- Open or normal angle
- Narrow or closed angle

Normal Tension Glaucoma

- Glaucoma in patients with normal eye pressures
- More common in Japanese

Treatment

- Aim: Lower the intraocular pressure
- Types
  - Medical – usually eyedrops
  - Surgical – laser, incisional surgery
- Future: medications to protect the optic nerve (Neuroprotection)

Pathways to Lower Intraocular Pressure

<table>
<thead>
<tr>
<th>Outflow</th>
<th>Inflow</th>
</tr>
</thead>
<tbody>
<tr>
<td>prostamides</td>
<td>α₂-agonists</td>
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<td>α₂-agonists</td>
<td>CA inhibitors</td>
</tr>
<tr>
<td>cholinergics</td>
<td>β₁-blockers</td>
</tr>
<tr>
<td>prostaglandins</td>
<td></td>
</tr>
</tbody>
</table>

Inflow

- α₂-agonists
- β₁-blockers
- CA inhibitors

Outflow

- prostamides
- α₂-agonists
- cholinergics
- prostaglandins
**Xalatan**
- Prostaglandin class
- Best-selling glaucoma medication
- Once-a-day dosing
- Minimal systemic side effects
- Eye side effects: iris color change, eyelash growth, skin pigmentation

**Timolol**
- Beta blocker class
- Prior best-selling drug
- Twice-a-day dosing
- Many systemic side effects
- Contraindicated in asthma, severe heart disease/block, depression, etc.
- Eye side effects mild

**Alphagan**
- Alpha-2 agonist class
- Third level drug
- Twice-a-day dosing
- Systemic side effects: drowsiness
- Eye side effects: 15% local allergy

**Trusopt**
- Carbonic anhydrase inhibitor class
- Fourth tier agent
- Twice-a-day dosing
- Systemic side effects minimal
- Ocular side effects include significant burning
Pilocarpine

- Cholinergic (miotic) class
- Fifth level drug
- Four-times a day dosing
- Systemic side effects uncommon
- Ocular side effects include induced myopia and temporal headache

Neuroprotection

- Memantine – glutamate receptor inhibitor
  - Shown to protect neuronal cells from dying
  - Clinically used in Europe for the treatment of Parkinson’s disease and dementia
  - Proposed to protect the nerve cells of the optic nerve in glaucoma

Memantine

- Currently in Phase III clinical trials in U.S.
- UCSF is a major University site
- Over 3000 glaucoma patients have been enrolled
- Duration: 48-month study
- Primary endpoint: Visual field loss

Laser Trabeculoplasty

- Used in the treatment of open-angle glaucoma
- Modifies the trabecular meshwork to encourage fluid outflow
- Newer laser has less side effects and can be repeated
**Trabeculectomy**

- Penetrating surgery to create a controlled outflow pathway
- “Gold standard” surgical procedure for glaucoma

**Ahmed Tube Surgery**

- Uses a valved device to shunt fluid from the eye
- Usually used in more difficult glaucomas or after trabeculectomy has failed

**Asians and Glaucoma**

**Financial Interest Disclosure**

- Research Affiliation
  - Allergan, Inc.
  - Memantine Study
  - National Eye Institute
  - OHTS study
  - Carl Zeiss Meditec
  - Visante OCT study
  - Genentech
  - Lucentis/Ahmed valve study

- Speakers Bureau
  - Alcon
  - Allergan

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Personal Disclosure

I’m Asian

Overview

• Asian Americans and Glaucoma
• Mechanisms for Angle Closure Glaucoma

Asian-Americans and Glaucoma

• Chinese-Americans
• Japanese-Americans
• Filipino-Americans
• Vietnamese-Americans

Narrow Angles-Chinese Americans

• Retrospective, clinic-based study within San Francisco Chinatown district (Shiu Kwok, MD)
• 163 Chinese-Americans with glaucoma or suspicion
• Mean age: 68 for women, 65 for men
• Gender: 61% women, 39% men

Narrow Angles-Chinese Americans

- Results:
  - Overall: 57% narrow by gonio (Shaffer Gr. ≤2)
  - 73% narrow among those 60 and older
  - Narrow angles correlated with:
    - Older age
    - Greater hyperopia
    - Female gender


Prospective Chinese-American study

- Prospective study comparing mainland Chinese, Chinese-Americans, and Caucasians
- Relative risk factors and ocular biometric parameters among Chinese and Caucasians for Narrow Angles
- Measures:
  - A-Scan (Ax. Length, Lens Thickness)
  - UBM, AS-OCT (Angle, iris, and ciliary body parameters)
  - Refraction, Pachymetry


Pilot Study in Chinatown

Wang D…Lin S.
Japanese-Americans

• Retrospective, Clinic-based study in San Francisco
  • 1732 Japanese-American patients
    • 1321 were ≥ 40 years
    • 64% female, 36% male


Japanese-Americans

• Glaucoma prevalence (clinic pop.)
  • 112 patients (6.4%)
• Glaucoma suspects
  • 181 patients (10.5%)

### Japanese-Americans

<table>
<thead>
<tr>
<th></th>
<th>Glaucoma</th>
<th>Non-glaucoma</th>
<th>p</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA (LogMAR)</td>
<td>0.30±0.60</td>
<td>0.11±0.24</td>
<td>&lt;0.0001</td>
<td>0.035</td>
</tr>
<tr>
<td>SE (D)</td>
<td>-0.82±3.05</td>
<td>-2.21±3.28</td>
<td>&lt;0.0001</td>
<td>0.905</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td>19.23±9.59</td>
<td>15.92±3.03</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CCT (µ)</td>
<td>524.08±38.97</td>
<td>554.79±38.79</td>
<td>&lt;0.0001</td>
<td>0.068</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>53.8</td>
<td>26.5</td>
<td>&lt;0.0001</td>
<td>0.123</td>
</tr>
<tr>
<td>Coronary Artery Disease (%)</td>
<td>16.5</td>
<td>7.1</td>
<td>0.001</td>
<td>0.089</td>
</tr>
<tr>
<td>Family History of Glaucoma (%)</td>
<td>16.5</td>
<td>7.1</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>


### CCT and NTG

- Many studies support association of low CCT with NTG

### Japanese-Americans

- Risk factors for Glaucoma
  - Poor visual acuity
  - Higher IOP
  - Presence of family history of glaucoma
  - Lower CCT
  - Systemic hypertension
  - Coronary artery disease
  - Low Blood Pressure


### Filipino-Americans

- Prospective observational study
  - 98 patients, 194 eyes—consecutive patients of randomly selected clinics within a single practice (Anthony Agadzi, MD)
  - Main results:
    - 31% narrow angles in at least one eye
    - 36% narrow angles aged 55 and older
    - Correlating factors: more hyperopia

Seider M…Agadzi A, Lin S. J Glaucoma 2010 Apr 30
Filipino-Americans

- Clinic study of Filipinos Vs. Whites
  - 1112 patients within 2 clinics
  - Higher rate of Glaucoma in Filipinos (15% vs. 9%)
  - Proportion of Glaucoma that was Angle Closure higher (8% vs. 0%)
  - Proportion of Glaucoma that was NTG higher (47% vs. 27%)

Vietnamese-Americans

- Retrospective, cross-sectional study
- 2,247 Vietnamese patients
- Glaucoma in 311 (14%)
  - 53% POAG
  - 31% PACG
  - 10% Combined Mech Glaucoma
  - 5% Secondary Glaucoma

Thailand

- Population-based study (Rom Klao Dist.)
  - N=701
  - 50 years and older
  - Total Glaucoma = 3.8%
    - PACG = 0.9% (21% of all Glau)
    - NTG was 69% of POAG cases
    - NTG was 41% of all Glau
Singapore Malay Eye Study

- N=3280
- Age 40-80 years
- Overall Glaucoma rate 3.4% (adjusted)
  - PACG 0.12%
  - POAG 2.5%
  - 85% was NTG (IOP<22)

Optic Disc

- Optic Disc Size among glaucoma and suspect patients
- Heidelberg Retinal Tomogram (HRT)
  - African, Asian, Hispanic, and Filipino statistically identical
  - Whites were significantly smaller than all other groups

<table>
<thead>
<tr>
<th>Race</th>
<th>Mean Disc Size (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>2.15</td>
</tr>
<tr>
<td>African American</td>
<td>2.55</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.57</td>
</tr>
<tr>
<td>Asian</td>
<td>2.38</td>
</tr>
<tr>
<td>Filipino</td>
<td>2.48</td>
</tr>
</tbody>
</table>


CCT in Populations

- Large racial differences
  - Whites 1-2% of glaucoma
  - Chinese 30-35% of glaucoma
  - Accounts for 90% of bilateral blindness in China

Anatomic Risk Factors for Closed Angle Glaucoma

- Anterior chamber depth (ACD)
- Anterior chamber width (ACW)
- Lens vault (LV)
- Iris thickness (IT)
- Angle/Iris change from light to dark
- Anterior chamber area (ACA)

Prospective Chinese Vs Whites

- Collaborative Study – Zhongshan Ophthalmic Center (Guangzhou, China) and Beijing University
- Total enrollment: 486 subjects (non-glaucoma)
- Chinese Americans
- White Americans
- Northern mainland Chinese
- Southern mainland Chinese

Anatomic Risk Factors

- Anterior chamber depth
- Corneal arc depth
- Anterior chamber area

Lower in Chinese than in Whites


Anatomic Risk Factors

- Anterior chamber area
- Anterior chamber volume

Lower in Chinese than in Whites

Anatomic Risk Factors

- Iris thickness (750 μ)
- Iris Area

Thicker in Chinese than in Whites


Anatomic Risk Factors

- Δ Iris thickness (750 μ)
- Greater in Chinese than in Whites


Anatomic Risk Factors

- Angle recess area
- Trab-Iris space area

Smaller in Chinese

Wang D., Lin S. IOVS. 2011;52:9404-10

Anatomic Risk Factors

- Iris thickness (750 μ)
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Anatomic Risk Factors

- Angle recess area
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Smaller in Chinese

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Summary

• Asians have a wide spectrum of glaucoma among the different races
  • Japanese, Koreans—Southeast Asia influences
  • Vietnamese—closer to Chinese glaucoma
  • Filipino—mixture of many races
• Mechanism of Angle Closure
  • May be related to Iris Thickness, particularly at the iris root
  • Dynamic change in iris behavior
  • Related to ACD, ACW, CAH

Summary

• Glaucoma is the main cause of irreversible blindness in the world
• Asians have a wide spectrum of glaucoma among the different races
  • Vietnamese—closer to Chinese glaucoma
  • Japanese, Koreans—Normal Pressure Glaucoma
  • Filipino—mixture of many races, types of Glaucoma
• You should get a check up!