To Sleep Perchance to Dream

- To Sleep Perchance to Dream!
The Role of Sleep Dysfunction in Glaucoma

- To Sleep Perchance to Dream
  - Sleep Dysfunction: It’s Role in patient Health
  - Sleep Apnea: The Impact of sleep dysfunction in glaucoma

TO SLEEP PERCHANCE TO DREAM

- MOJON DS, et al
- OPTIC NEUROPATHY / SLEEP APNEA
- OPHTH 105:874-77 1998
  - SEVEN PATIENTS
    - 3 SEVERE / NASAL STEPS 2 / ARCUATE DEFECT 3
    - 2 MODERATE / ARCUATE DEFECT
    - 1 MILD
    - ETIOLOGY: DECREASED BLOOD FLOW

Obstructive Sleep Apnea

- Bendel, R et al. (Mayo Clinic, Jacksonville)
- OAS - Repeated apnea episodes
- Daytime symptoms
  - Daytime sleepiness
  - Chronic fatigue
  - Decreased cognitive function
- Etiology
  - Collapse of the pharyngeal airway
  - Last 10-60 seconds

OSA

- Diagnosis
  - Overnight polysomnography
  - EEG, EMG, EOG EKG, Nasal buccal airflow, and pulse oximetry (arterial oxygen)
  - Respiratory Disturbance Index 10 >= OASS
- 83 patients with apnea
- Outcomes
  - Median age 62
  - Median BDI 37
  - Median IOP 16mmHg
OSA

- Outcomes
- 2.4% patients with OHTN
- 33% COAG
- No relation to gender, age, or BMI
- Relation between IOP increase and BMI level

Sleep Apnea & NTG

- Mojon DS et al; Ophthalmologica 2002
- 16 patients with NTG had PSN
- RDI > defined as mild
- < 45 - 0%
- 46-64 - 50%
- 65 & > 63%

Sleep Apnea: The Silent Assassin

- Co-Morbidities of Sleep apnea
  - Increased risk of CVA
  - Irregular Menstrual Cycles (40%)
  - Children May exhibit “Failure to Thrive”: T & A removal
  - Psychologic Dysfunction (32%)

2. Will The Real IOP Please Stand Up!

A Comparative Study of Tonometry in Controlled Glaucoma Patients

J James Thimons, O.D., FAAO
Tonometry on LASIK-treated Eyes

Pre - LASIK vs. Post - LASIK

GAT vs. DC

Study Criteria:

- 50 consecutive glaucoma patients
- 45 full data base
- 11 AA's/ 5 L's
- Age, sex, race, general health
- Medications, Visual Fields (Sita 24-2 HVF), RNFL, C/D Ratio, Pachymetry & IOP's
- Alternating Pascal vs. Goldmann Tonometry

Pascal vs. Goldmann

- 15 (33%) Patients with Pascal IOP greater than 4 mmHg difference than Goldmann
- 13 (28%) Patients with Pascal IOP greater than Goldmann
- 2 (4%) Patients with Pascal IOP less than Goldmann

Average age: 60.33
Average Ta: OD 17.4/ OS 17.6
Pachymetry: 537/539
RNFL: 71.22/ 75.38
Medications: 1.22
Visual Fields: 10.66/10.82
C/D: 0.504 / 0.484
**Pascal vs. Goldmann**

- Pascal IOP lower than Goldmann
- Average IOP Ta: 30.6 / 34 mmHg
- Average IOP Tp: 23.25 / 25.15 mmHg
- Pachymetry: OD 623 / OS 625.5
- RNFL: OD 88.24 / OS 93.08
- C/D: 0.4 / 0.5
- VF loss: 3/2

**Pascal vs: Goldmann**

- Pascal IOP greater than Goldmann
- Goldmann IOP: 16.3 OD / 15.8 OS
- Pascal IOP: 21.9 OD / 20.6 OS
- RNFL: 66.56 / 69.32
- C/D: 0.7 / 0.72
- VF loss: 13.2 / 12.6
- Pachymetry: 516 / 518

**Pascal vs: Goldmann**

- 5 patients (11%) with increased therapy
- 2 patients (4%) with less therapy

---

**Ocular Response Analyzer**

**Corneal Hysteresis:**

A New Ocular Parameter

**CH distribution - Normals & Glaucoma**

Glaucoma subjects have lower CH than normals, especially those who are still progressing in the disease.

Data courtesy New England College of Optometry and Mitsugu Shimjo, MD

**Applanation Signal Plot**

- "a" Signal Peak
- "Out" Signal Peak
- Applanation Pressure 1
- Applanation Pressure 2

**CH distribution**

- Normals
- POAG
- NTO
3. Alternate Day Therapy in Glaucoma

Diurnal IOP Fluctuation & Visual Field Loss

- Greater diurnal IOP fluctuation resulted in greater visual field progression
  - Home applanation tonometry by 64 patients 5X daily for 5 days
  - Visual field progression of patients was tracked over 8 years

Asrani, et. al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma, J.Glaucoma, 9, 134-142, 2000

Alternate Day Therapy

- Twice daily dosing increases IOP relative to once daily dosing
- Xalatan and Lumigan combined can increase IOP, even to 50s
- anytime IOP is >30 with prostaglandin, it is overdosed
- Once daily can be overdose if there is inflammation/endogenous prostaglandin

Persistence of IOP Response

- Labovitz RA et al; Arch Ophth 2001
- Comparison of Lumigan vs: Timolol
- Maintenance of IOP at 48 hours post D/C 5.6mmHg
- 7.2 - 8.2 mmHg at peak effect
- 28 Day control showed less than
- Timolol was 3.4-3.9 mmHg at peak.
Alternate Day Therapy

- 30% reduction first day, 25% reduction second day
- IOP will be one point higher on second day
  - Doro. ARVO 2007

Alternate Day Therapy Post SLT

- SLT somewhat less effective in patients already on prostaglandin
  - Suggesting that part of SLT induces prostaglandin like effects
- QD prostaglandin could be an overdose after SLT
  - Especially first year after laser

Alternate Day Therapy: Compliance

- Not a problem for organized patients
- Some keep a calendar
- Some choose 3 or 4 days of the week
- Some choose odd or even days

Alternate Day Therapy: Practical Tips

- Starting every other day improves tolerability in prostaglandin novices
- Aching and high IOP suggest overdose
- Wash face after instillation

Alternate Day Therapy: Initial Review

- 22 patients with well controlled glaucoma over a two year period.
- Switched from daily therapy to alternate day treatment following complaints of cosmetic/anterior segment problems
- Average IOP pre-switch: 16.2 mmHg
- Post switch IOP at 1 week, 1 month and 3 months average: 16.67 mmHg
4. Size Really Does Matter!

**How to Evaluate Disc Size**
- Use a 60 D Lens at the Slit Lamp
- Make a Thin Vertical Beam
- Measure Vertical Disc Diameter by Adjusting Beam Height
- Read off Scale on Slit Lamp
- Vertical Disc Diameter Greater Than 2.2 Mm Is a Large Disc
- Vertical Disc Diameter Less Than 1.8 Mm Is a Small Disc

**Optic disc size does not indicate glaucoma**
Small hyperopic discs with glaucoma may have small cups
Watch out for small discs with large cups!

**Optic Disc Size**
Measurement of optic disc size with biomicroscopy
Volk lens
Measure length of slit beam
Correction factors
Volk 60D – x 1.0
Volk 78D – x 1.1
Volk 90D – x 1.3

<table>
<thead>
<tr>
<th>Disc Size</th>
<th>Avg Vertical Diameter</th>
<th>Avg Horizontal Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>1.8 mm</td>
<td>1.7 mm</td>
</tr>
<tr>
<td>Large</td>
<td>2.4 mm</td>
<td></td>
</tr>
</tbody>
</table>

**Optic Disc Size**
Size of cup varies with size of disc
Large discs have large cups in healthy eyes
Identify small and large optic discs
Small discs: avg vertical diameter <1.5 mm
Large discs: avg vertical diameter >2.2 mm

**Storing and Graphing Stereo Images and C/D Drawings**
A Retrospective Study of HRT Data on 244 Referred Patients

J. James Thimons, O.D., FAAO
Medical Director, OCC
Eric Conley, O.D.
Assistant Professor, ICO

Average Age of HRT Scanned Patients
- The Average Age of the 244 Scanned Patients = 53.25 years old
- The Representative Age Range = 8 years to 93 years

Overall Review Optic Disc Area OD vs OS (mm²)
- Mean Disc Area OD = 2.17 (0.86 - 4.69)
- Mean Disc Area OS = 2.13 (0.81 - 4.60)

Data Analysis of Representative 244 HRT III Patients
- 44 of 244 Patients Presented with Disc Areas > 2.82 mm²

Data Analysis of Representative 44 Large Disc Patients
- Only 9 of 44 Patients with Macrodiscs Demonstrated Apparent Visual Field Loss
- 80% of Patients Demonstrated No VF Loss
Data Analysis of Representative 44 Large Disc Patients

- The Overall Mean C/D Ratio of this Group = 0.55
- Average C/D OS = 0.65 (0.40 - 0.91)
- Average C/D OD = 0.61 (0.38 - 0.96)

5. Every Journey begins with The First Step

Staging Glaucoma & Target IOP

GON/Neuron Loss/HVF/OCT - RNFL/C/D

1. 0-35% 0 to -2 < 80 0.1-0.7/5
2. 35-65% -2 to -5 < 70 0.3-0.8/6
3. 65-90% -5 to -15 < 60 0.6-0.9/7-8
4. >90% > -15 < 50 0.8-1.0 >9

Target Pressures Are Determined by the Baseline IOP and the Amount of Optic Nerve Damage

- Mild Damage - 20-30% Reduction of Baseline IOP
- Moderate Damage - 30-40% Reduction of Baseline IOP
- Severe Damage - 40-50% Reduction of Baseline IOP

Visual Field Classification (Mild, Moderate, Severe)

- Mean Deviation (MD)
- Number of Abnormal Points on the Pattern Deviation Plots
- Decibel Value of the Four Points Just Off Fixation

Mild Visual Field Defect

- The Mean Deviation Index (MD) Is Better Than -6 dB
- On the Pattern Deviation Plot, Fewer Than 18 of the Points Are Depressed Below the 5% Level and Fewer Than 10 Points Are Depressed Below the 1% Level
- No Point in the Central 5 Degrees Has a Sensitivity < 20 dB
Moderate Visual Field Defect
- The Mean Deviation Is Better Than -12 dB
- On the Pattern Deviation Plot, Fewer Than 36 of the Points Are Depressed Below the 5% Level and Fewer Than 20 Points Are Depressed Below the 1% Level
- No Point in the Central 5 Degrees Has a Sensitivity < 10 dB

Severe Visual Field Defect
- The Mean Deviation Is Worse Than -12 dB
- On the Pattern Deviation Plot, More Than 36 of the Points Are Depressed Below the 5% Level or More Than 20 Points Are Depressed Below the 1% Level
- Any Point in the Central 5 Degrees Has a Sensitivity <10 dB
- There Are Points Within the Central 5 Degrees With Sensitivity <20 dB in Both Hemifields

6. The Role of Perfusion Pressure in Glaucoma

Hypoperfusion
- flow = pressure/resistance
- perfusion pressure = BP - IOP
- mean arterial BP = diastolic + 1/3 syst-diastolic
- nocturnal hypotension is greatest risk

Nocturnal Hypotension: Another Reason to Get a Good Nights Sleep
- TIBA Medical
- ABPM 2400
- 24 hour Serial BP Monitoring
- Role in Glaucoma Management

Nocturnal Hypotension
- TIBA Medical
- Reimbursement
  - Commercial
  - Medicare
- ICD-9 Codes
- www.tibamedical.com
How Low Can You Go!

- SM a 40 y/o white female was referred for evaluation of glaucoma. Current Tx was Betoptic-S and Alphagan.
- VA 20/20 OD/OS
- Ta 12/12 @ 10
- SLE: wnl
- DFE: 0.7 OD / 0.9 OS
- VF: Early near fixation loss OS
- Gonioscopy: CB 360 OU
- Medical Hx: LBP (100/65), pulse 54, Raynaud’s, Migraine HA
- Family Hx: Negative
How Low Can You Go!

- 4/21/07
- Meds: Alphagan P, Lumigan, Ginkgo
- Ta:14/11 @ 9:30
- Migraines increased x 4 weeks, episode of syncope x 1 week
- Serial BP 2 AM 58/30/ pulse 54

NTG- Differential Diagnosis

- Diurnal Variation
- Vasculitis
- Optic Atrophy
- Old AION
- Previous RBON
- Compressive ON
- Chronic marijuana use
- Prior Hypotensive episodes
- Systemic Beta-Blocker
- “Burned out” Glaucoma
- Sub-acute angle closure
- History steroid use
- Ocular Ischemic Syndrome

Nocturnal Hypotension: It’s role in Visual Field Progression

- Graham SL, Drance S: Surv Ophthalmol Jun 1999
- 84 patients 24 hour ambulatory BP
- Nocturnal BP variables were lower in patients with progressive VF loss
- Patients with > nocturnal dips were more likely to show VF loss even with good IOP control
- Increased risk of disc hem’s

NORMAL TENSION: ABNORMAL RESULTS

- ANDERSON et al AJO
- EXAMINED NTG’S FOR MULTIPLE VARIABLES (AGE, GENDER,BP AND MIGRAINES)
- MIGRAINES,DISC HEM’S MOST NOTABLE RISK FOR PROGRESSION
- AGE , RACE NEXT
- 230 PATIENTS/NTG/IOP< 20mm Hg

NTG

- 99 WOMEN/61 MEN
- 23 WOMEN WITH H/O MIGRAINES
- 2 MEN
- WOMEN WITH MIGRAINES HAD FASTEST RATE OF PROGRESSION

THE BIG DIPPER

- STIMADA K etal, CIRCULATION 1990
- COLLIGNON N etal INT OPH 1998
- NOCTURNAL HYPOTENSION OCURS IN 10% OF POPULATION
- "BIG DIPPERS" > 10%
- INCREASED RISK OF MI AND LOWER LIMB ISCHEMIA
- INCREASED RISK OF VF LOSS AND DISC DAMAGE
Habitual IOP (mm Hg)

<table>
<thead>
<tr>
<th>Sitting</th>
<th>Supine</th>
<th>Sitting</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>22</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>16</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Clock Time

- 3:30 PM
- 5:30 PM
- 7:30 PM
- 9:30 PM
- 11:30 PM
- 1:30 AM
- 3:30 AM
- 5:30 AM
- 7:30 AM
- 9:30 AM
- 11:30 AM
- 1:30 PM

Treatment of Low Blood Flow

- middle aged women with history of low BP
- increase salt
- licorice extract (glycerrhinic acid) is aldosterone agonist
- elderly patients taking BP meds with BP <130/75
- if no heart disease or stroke, discuss reduced anti-hypertensive therapy

Selective Laser Trabeculoplasty (SLT)

Selecta 7000
Glaucoma Laser System

Laser trabeculoplasty

- Stimulates trabecular cells to release mediators which improve outflow
- Improves both trabecular and uveoscleral outflow
- Useful in all open angle glaucoma except uveitic and neovascular
- Effectiveness and response rate similar to Xalatan (25% reduction in 80% of patients not receiving other treatment)

Trabecular Meshwork

- Cellular and Structural Components
- TM cells are phagocytic and contain variable amounts of melanin
- ALT induces focal scarring and coagulative damage with reduced flow through the laser-treated site
Selective Laser Trabeculoplasty
- Results comparable to ALT (argon laser trab.)
- 50 spots to nasal trabecular meshwork
- Less “traumatic” than ALT
- 70% of pts respond IOP reduced by > 3 mmHg, mean 23.5%

SLT Effectivity
- International studies show IOP reductions of 22%-28% with 36-49 weeks follow-up
- In a prospective, randomized clinical trial, SLT and ALT were shown to have a similar effect on IOP reduction

Laser Trabeculoplasty risks
- 20% of patients get minimal benefit
- IOP spike
  - Less likely if treatment is fractionated into 2-4 sessions per eye
  - Greater risk in pigment dispersion

Making Sense of Normal Pressure Glaucoma
- Asrani, S et al; ARVO 2006
- 24 eyes of 12 untreated patients
- Analyzed IOP fluctuation before and after SLT
- Outcomes:
  - Mean IOP decrease was 1.89 OS & 2.06 OD
  - Mean Diurnal pre SLT: 5.10 mmHg
  - Mean Decrease in Diurnal IOP 2.78 OS/ 5.73 OD
  - Greater decrease in Diurnal than Mean IOP

8. Trab’s vs Tubes: A New Paradigm
**TUBE SHUNT SURGERY**
- Tube in anterior chamber connects to a reservoir sutured to posterior globe
  - reservoir (plate) prevents scar from blocking tube opening
  - scar around reservoir will limit IOP

**Common tube types**
- **Ahmed** has a valve to limit early hypotony
- **Baerveldt** has larger surface area
  - 1-2 points lower than Ahmed
  - but greater risk of suprachoroidal hemorrhage

**TUBE PROBLEMS**
- Gradual failure due to scarring around reservoir
- Erosion of tube through conjunctiva
  - Consequent serious risk of infection
- **Decompensation of corneal endothelium**
  - can occur even without contact of tube and endothelium
  - corneal transplants usually fail over several years if tube is in anterior chamber
  - tube can be moved to posterior chamber after vitrectomy

**Physiologic outflow**
- Two subsections:
  - Trabecular meshwork
  - Schlemm's canal and episcleral veins
- Conventional fistulization surgery bypasses both
- Non-penetrating may bypass just TM or both sections

**Nerve Fiber Layer Analysis**
- OCT overestimates RNFL thickness in large discs
- Underestimates RNFL in Hypoplastic disc’s average thickness is best gauge of overall damage
- Sectoral damage must match ONH topography
- 70 microns is moderate loss, 60 advanced, 50 severe

Glaucoma: Not Just a Goal pressure
- Lee AJ et al; Ophthalmology 2006
- COAG & CAD Mortality: The Blue Mountain Study
- 3,654 patients 49-97 evaluated over 9 years
- All cause mortality 24.3% non COAG / 23.8% COAG
- Cardiovascular Mortality 8.4% non COAG/ 14.6% COAG
- Observed mainly in < 75 y/o with previously diagnosed disease
Glaucoma: Not Just a Goal Pressure

- Suh-Yuh Wu et al; Arch Ophth 2008
- Open angle Glaucoma & Mortality: The Barbados Eye Studies
- 4092 AC’s/ 40-84 / 9 year evaluation
- 764 deaths/ unrelated to overall mortality
- Cardiovascular mortality increased with previously diagnosed disease (1.38) and timolol maleate use (1.91)

Glaucoma: Not just a Goal Pressure

- Impact of Visual Impairment and Eye Disease on Visual-Related Quality of Life
- 4774 participants/ NEI-VFQ 25
- Glaucoma patients scored lower without decreased visual acuity than matched groups

IOP in glaucoma

- A risk factor
- Poor for diagnosing POAG
- Poor predictor of disc and field damage
- Used for management (AGIS - target IOP)
- Normal population distribution skewed (non-bell shaped)
- Overlap between normal and glaucoma groups

ANOTHER REASON NOT TO BE A COUCH POTATOE!

- PASSO, M etal; Arch Ophth-Vol 109 Aug 1991
- EXERCISE TRAINING REDUCES IOP AMONG GLAUCOMA SUSPECTS
- 13 SEDENTARY ADULTS/25-60 Y/O
- < 1 HOUR/WEEK OF EXERCISE PRIOR TO STUDY FOR 6 MONTHS
- IOP > 22mmHg MULTIPLE MEASUREMENTS

EXERCISE AND IOP

- BASELINE COMPREHENSIVE EXAM
- 12 WEEKS/ 40 MINUTES /DAY/4 DAYS
- OUTCOMES
  - BASELINE IOP 23.8 mmHg
  - POST TRAINING IOP 19.2 mmHg
  - SYSTEMIC RESPONSE SIMILAR( BP, HEART RATE )
  - IOP AFTER DECONDITIONING 24mmHg