Check for Diabetes?
Check for Hypothyroidism?
Do Diurnal IOP Variations?
Do Postural IOP Variations?
Screen VF or Digitized Imaging—WELL MAYBE?
Do Routine Anti-cardiolipin Antibodies?
Do Routine MRIs?
Check for Raynaud’s?

Hemi-Structure and Hemi-Function Sym-Metrix

LOOK FOR BALANCE IN LIFE

THE OPTIC NERVE AND ASYMMETRY

IS OD A MIRROR IMAGE OF OS?

THE OPTIC NERVE AND ASYMMETRY

IS OD A MIRROR IMAGE OF OS?
DISC SIZE DIFFERENCE IS A GREAT INDICATOR OF A CONGENITAL VARIATION BUT CAN ALSO INDICATE DISEASE..LOOK AT THE CONTEXT...OS IS PROPTOTIC

RETINAL SYMMETRY IS A GREAT INDICATOR OF A CONGENITAL VARIATION OR DYSTROPHY

RETINAL SYMMETRY IS A GREAT INDICATOR OF A CONGENITAL VARIATION..BUT IT MUST BE EVALUATED IN CONTEXT...

RETINAL ASYMMETRY IS A GREAT INDICATOR OF ACQUIRED DISEASE

RETINAL ASYMMETRY IS A GREAT INDICATOR OF ACQUIRED DISEASE

GROWTH HORMONE USE

OCULAR ISCHEMIC SYNDROME
RETINAL ASYMMETRY IS A GREAT INDICATOR OF ACQUIRED DISEASE

IS OD A MIRROR IMAGE OF OS?

OCULAR ISCHEMIC SYNDROME

“We tend to see what we expect to see or what we decide we have seen.” Edwards

OPTIC NERVE HEAD SYMMETRIX® IN ACTION®

53 YO

- ROUTINE P/O FOLLOW-UP
- RECENT PHACO OU, OS LAST
- NO COMPLAINTS EXCEPT THE P/O GTTS
- IOP UNATTAINABLE BECAUSE OF BLINK BUT REPORTED AS 15 MM HG AT LAST POST OP
DO YOU SEE ANYTHING WRONG?

NOW DO YOU SEE ANYTHING WRONG?

ASYMMETRY WITH MORE RIM OD THAN OS

RNFL THINNING OS > OD

SIGNIFICANT ASYMMETRY
4/11/12

CONCLUSION
NORMAL TENSION GLAUCOMA
NA-AION

Prevalence of Glaucoma as Related to Axial Length

<table>
<thead>
<tr>
<th>Axial Length in mm</th>
<th>Total Subjects</th>
<th>Total Subjects with Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.0 to 26.4 mm</td>
<td>192</td>
<td>3.125%</td>
</tr>
<tr>
<td>26.5 to 33.6 mm</td>
<td>196</td>
<td>11.224%</td>
</tr>
</tbody>
</table>

GLAUCOMA IS MORE PREVALENT IN LONGER EYES

IS THERE A RELATIONSHIP BETWEEN
MYOPIA AND GLAUCOMA?
**Responses to Topical Corticosteroids**

<table>
<thead>
<tr>
<th>N</th>
<th>&lt;20 mm Hg</th>
<th>20-31 mm Hg</th>
<th>&gt; 31 mm Hg</th>
</tr>
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<tbody>
<tr>
<td>Volunteers</td>
<td>100</td>
<td>70%</td>
<td>26%</td>
</tr>
<tr>
<td>POAG</td>
<td>50</td>
<td>0%</td>
<td>8%</td>
</tr>
<tr>
<td>POAG Offspring</td>
<td>100</td>
<td>10%</td>
<td>68%</td>
</tr>
<tr>
<td>POAG Siblings</td>
<td>50</td>
<td>22%</td>
<td>52%</td>
</tr>
<tr>
<td>&gt; -5 D</td>
<td>17</td>
<td>12%</td>
<td>59%</td>
</tr>
</tbody>
</table>

**Pigmentary Glaucoma and Refractive Error**

<table>
<thead>
<tr>
<th>Refractive Error</th>
<th>% of Eyes with Pigmentary Glaucoma - 78.22 % Myopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>+3 D</td>
<td>0.49%</td>
</tr>
<tr>
<td>+.5 to +2 D</td>
<td>6.44%</td>
</tr>
<tr>
<td>-2.5 to +2.5 D</td>
<td>14.85%</td>
</tr>
<tr>
<td>-5.0 to -2.0 D</td>
<td>31.19%</td>
</tr>
<tr>
<td>-2.25 to -4.00 D</td>
<td>23.27%</td>
</tr>
<tr>
<td>-4.25 to -6.75 D</td>
<td>19.80%</td>
</tr>
<tr>
<td>-7.00 to -9.00 D</td>
<td>1.98%</td>
</tr>
<tr>
<td>-10.00 to -13.50 D</td>
<td>1.98%</td>
</tr>
</tbody>
</table>

**POAG LTG and Refractive Error**

<table>
<thead>
<tr>
<th></th>
<th>POAG</th>
<th>LTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>71</td>
<td>63</td>
</tr>
<tr>
<td>Mean Refract</td>
<td>0.0D</td>
<td>-5.1 D</td>
</tr>
<tr>
<td>Mean AL</td>
<td>22.9 mm</td>
<td>25.2 mm</td>
</tr>
<tr>
<td>Mean Max IOP</td>
<td>34.3 mm Hg</td>
<td>19.8 mm Hg</td>
</tr>
</tbody>
</table>

**In longer eyes the sampling location of the RNFL layer is further away from the center of the ONH yielding artificially thinner measurements.**


**Signal strength and scan circle placement affects RNFL measurements.**


**Steroid response higher in higher myopes**

**Pigmentary glaucoma higher in myopes**

**LTG higher in myopes and long eyes**
Images further out from the ONH giving thinner RNFL.

**Conclusion??**

**Is there a relationship between**

**Systemic disorders and glaucoma**

**Neurology and glaucoma**

*When the RNFL dies, the brain dies*

*When the brain dies, the RNFL dies*

*The optic nerve is part of the brain*

*Stuff that is good for the brain is also good for the RNFL*
Degeneration of RGC and axons represent a substantial loss of neural activity in the brain as 50% to 60% of the cerebral cortex spread over 40-45 visual areas represent visual function. This RGC degeneration entails downstream caspase and mitochondrial dependent apoptotic cascades resulting in actual loss of cortex.


Grey density reduction occurs in the primary visual cortex in patients with advanced glaucoma.


Measuring the optic nerve diameter at the orbital apex (15 mm behind the eye) shows significant correlation with RNFL loss.

Lagnoux WR, Giacca M, Weigel M et al. Retrobulbar optic nerve diameter measured by high-speed magnetic resonance imaging as a biomarker for axonal loss in glaucomatous optic atrophy. Invest Ophthalmol Vis Sci 2006;47:422-4238

Progressive visual field loss in NTG is associated with silent cerebral infarcts as defined by CT.

CEREBROSPINAL FLUID PRESSURE AND GLAUCOMA

Lamina separates two distinctive pressurized zones, IOP 10-21 mm Hg and ICP 5-15 mm Hg. Average IOP is 16 and Average ICP is 12 and the IOP-ICP is called the Trans-laminar pressure.


Both IOP and ICP affected by BP.

?? Systemic Hypotension

?? CAI use for glaucoma

?? Positional Effects
Alteration of Trans-laminar pressure may bow the lamina creating a pinching of axons. Both intraocular fluid and intracranial fluid are created by carbonic anhydrase reactions and ultrafiltration.


MIGRAINE OCCURS IN 43% OF WOMEN AND 18% OF MEN. AURA IN 25%. CNTGS STATES MIGRAINE WAS RISK FACTOR FOR PROGRESSION OF GLAUCOMA. OTHER STUDIES REPORT NO STATISTICAL RELATIONSHIP.


What About Internal Carotid Stenosis and NTG?

Conclusion???
IS THERE A RELATIONSHIP BETWEEN

HORMONES AND GLAUCOMA

Suggestions that estrogens are neuroprotective in degenerative disorders and possibly within the retina and in glaucoma.

ESTROGEN LEVELS MAY HAVE SOME EFFECT ON GLAUCOMA

ESTRADIOL LEVELS 1/2 IN GLAUCOMA VERSUS NORMALS

ESTRADIOL POTENTIATES FLOW, TESTOSTERONE INHIBITS FLOW

RIM STRUCTURE ALTERED DURING MENSTRUAL CYCLE

SUGGESTION THAT FEMALE SEX HORMONES MAY BE PROTECTIVE OF THE OPTIC NERVE.
There are suggestions that “Topical estrogen drops may be a new alternative treatment of glaucoma.” Ozcura F, Aydin S. Med Hypotheses 2007;68:458.

Conclusion???

IS THERE A RELATIONSHIP BETWEEN

SLEEP APNEA AND GLAUCOMA
...the odds of an individual diagnosed with sleep apnea having glaucoma is **1.736 times the odds of individuals without sleep apnea (73.6 % MORE LIKELY)** having glaucoma in this patient population. We recommend that questions concerning sleep-disturbed breathing be included for patients suspected of having glaucoma. Similarly, we recommend that patients diagnosed with glaucoma be questioned about the risk factor of sleep-disturbed breathing.

Boyle M, Semes L, Fuhr P, Clay D. AAO Poster Session

Obstructive sleep apnea leads to reduced sensitivity in the visual field.


Oxygen desaturation was not found to be statistically related to glaucoma or sleep disorder.


The use of CPAP actually causes an additional IOP increase in OSA.


Report a high prevalence of glaucoma in OSAS. Visual field defects in glaucoma patients with OSAS may be due to ON perfusion defects.

Karakucuk S, Goktas S.

Sleep apnea patients should be referred for assessment of associated eye disorders.

The prevalence of glaucoma in patients with obstructive sleep apnoea is an estimated 27%. Sex, age, body mass index or apnoea plus hypopnoea index are not factors influencing the presence of glaucoma in this population of patients. Bendel RE, Kaplan J, Heckman M, et al. Prevalence of glaucoma in patients with obstructive sleep apnoea: a cross-sectional case-series. Eye (Lond) 2008;22:1105-1109


There is not a strong support of the impact of sleep apnea on the eventual development of glaucoma relative to other putative factors. Gallo CA, McGavin D, Ashraf SP, Dewey C. Is there an association between pre-existing sleep apnea and the development of glaucoma? Br J Ophthalmol 2006;90:679-681


Prevalence of sleep apnea in NTG 0% under 45, (AGE RELATED) 50% ages 45-64, 63% over 64. NTG patients should be checked for sleep apnea. Mojon DS, Hess CW, Goldbulu D, et al. Normal-tension glaucoma is associated with sleep apnea syndrome. Ophthalmologica 2002;216:180-184


There is also an association to ION and ODE. Br J Ophthalmol 2007;91:1524, Am J Ophthalmol 2007;144:853

Moderate to severe OSA is associated with a higher incidence of VF defect and glaucomatous optic nerve changes. Tsang CS, Chong SL, He DK, Li MF. Moderate to severe obstructive sleep apnoea patients is associated with a higher incidence of visual field defect. Eye (Lond) 2003;17:89-92.

The sleep apnoea syndrome is correlated with a proportional decrease in the RNFL. Decreased ocular perfusion related to hypoxia and vasospasm associated with OSAS may cause RNFL thinning, which may precede clinically detectable glaucoma. Kargi SH, Altin R, Koksal M, et al. Retinal nerve fibre layer measurements are reduced in patients with obstructive sleep apnea syndrome. Eye (Lond) 2003;17:875-879
SO SHOULD PATIENTS WITH SLEEP APNEA BE WORKED UP FOR GLAUCOMA AND SHOULD GLAUCOMA PATIENTS BE UNDER SUSPICION FOR SLEEP APNEA???

IS THERE A RELATIONSHIP BETWEEN BEHAVIORAL ISSUES AND GLAUCOMA

SMOKING AND GLAUCOMA

Smoking increases the risk for virtually every human affliction including glaucoma (often defined by increased IOP in studies) because of the interference with the oxygenation of the blood and the increase in oxidative stress.

References:
- Arch Ophthalmol. 1987;105(8):1066-1071
- Surv Ophthalmol. 1996;40(5-6):505-517
The direct relationship to glaucoma, however, appears to be controversial as studies and reviews fail to establish a firm link between either smoking or environmental smoke and glaucoma development. Yet the same studies recommend that cessation of smoking is important in the management of glaucoma patients.

The issue of smoking is proven to be a risk factor for the presence of glaucoma. 

The most critical risk factors associated with blindness in high tension glaucoma, however, were elevated initial IOP, fluctuation, poor control, noncompliance and late detection while the for angle-closure the risks include hypertension, family history, shallow anterior chamber and large CD.

In one large collaborative study it was shown that surgically treated patients with glaucoma had lower IOPs if they were non-smokers. From a functional standpoint, cigarette smoking is associated with reductions in retinal sensitivity. In an interesting study on the effects of smoking on normotensive patients it was found that both IOP and BP increased secondary to the nicotine in cigarettes.

**OBESITY AND GLAUCOMA**

**IS THERE A RELATIONSHIP BETWEEN**
Presence of metabolic syndrome increases risk of OHTN in males 2X and females 5X. Metabolic syndrome defined as having three or more of the following:
1. high blood pressure
2. elevated serum triglycerides
3. low HDL
4. elevated fasting glucose levels
5. large waist circumference

Imai K, Hamaguchi M, Mori K et al. Metabolic syndrome as a risk factor for high-ocular tension. Int J Obes. 2010;34:1209-1217

There is certainly a suggestion that there is an association of insulin resistance and the metabolic syndrome to increased intraocular pressure.


Body Mass Index appears to have an association with elevated intraocular pressure.


Certainly initial reaction to this fact among clinicians would be to point to neck size and positive pressure as a related factor with sleep apnea falling into the picture.


The relationship of cerebrospinal fluid pressure elevation, Idiopathic Intracranial Hypertension, serum cortisol, and sleep apnea also create an interesting scenario for elevated intraocular pressure.

Am J Ophthalmol. 2007;143:635

IS THERE A RELATIONSHIP BETWEEN

EXERCISE AND GLAUCOMA

Caution: Pigmentary Dispersion
Exercise reduces IOP and the reduction is sustainable. Int J Neurosci 2006;116:1207

In another study it was shown that in persons with increased IOP, regular, moderately intense aerobic exercise rather than short-lived intense exercise is more useful. Int J Neurosci 2006;116:351

Another study showed that exercise changes Ocular Perfusion Pressure and produces increased tissue blood flow in the retina in the immediate post-exercise period, while blood flow increases more persistently in the choroid-retina. Eye 2006;20:796

It is further confirmed the ocular hypotensive effect of strenuous exercise on the IOP and demonstrates that Pulsatile Ocular Blood Flow increases significantly after exercise. Optom Vis Sci 2002;79:A46

Suggestion that running distances (25 miles/week) may be of benefit in minimizing the risk for the development of glaucoma. Williams PT. Relationship of incident glaucoma versus physical activity and fitness in male runners. Medicine and Science in Sports and Exercise 2009;41:1566-1572

Exercise has an additive effect of lowering intraocular pressure regardless of the class of IOP medication or the number of medications. There is a 2-3 mm Hg reduction after just 5 minutes of aerobic activity. CAUTION WITH PIGMENTARY DISPERSION. Natsis K, Asouhidou I, Nousios G et al. Aerobic exercise and intraocular pressure in normotensive and glaucoma patients. BMC Ophthalmology 2010;5

IS THERE A RELATIONSHIP BETWEEN

VASCULAR SYSTEM AND GLAUCOMA
OHTS study photo review 84% detection of disc heme, observation gave 16%. Disc heme related to age, CCT, family history and smoking. Presence of heme increased risk of progression by 6X and 13.6% in eyes with previous heme 5.2% without previous heme.

BUT!!!
87% of eyes with disc hem did not progress in the 31 month follow-up.

Kass MA, Heuer DK, Higgenbotham EJ et al. The ocular hypertension treatment study: a randomized trial determines that topical ocular hypertensive medication delays the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120:701-713.


Simvastatin significantly protected against the development of progression of visual fields in a cohort of 121 patients with normal tension glaucoma.


WHY?

VASCULAR PERFUSION IS AN ISSUE.
DIFFERENCE OF SYSTOLIC AND DIASTOLIC IOP IS OCULAR PULSE AMPLITUDE (OPA) AND IS LOWER IN PATIENTS WITH POAG AND NTG. AVE OPA IS 2.09 TO 2.8 MM HG

This Vascular Perfusion Stuff is All over the Place. Logic Dictates it is an Issue, But the Issue is Yet to Be Defined.
ASSOCIATIONS WITH POAG AND NTG

• TREATED SYSTEMIC HTN ESPECIALLY WITH Ca BLOCKERS (Current Eye Research 2007;32:152, Ophthalmology 2007;114:221)


BLOOD FLOW

• SVP GONE 46% GLAUCOMA AND PRESENT 98% CONTROLS. (Br J Ophthalmol 2007:91:450, ARVO 2007 Abstract 1879)

• CCT AND INCR IN RVO (ARVO 2007 Abstract 3080/ B57)

• GLAUCOMA HAS LOWER OCULAR SURFACE TEMP (Br J Ophthalmol. 2007;91:878)

DORZOLAMIDE AS A VASOREGULATOR

• MAY INCREASE BLOOD VELOCITY AND FLOW (Microcirc Res 2006;72:191)

• DOES THIS ALSO LOWER ICP AND ALTER THE TRANS-LAMINAR PRESSURE GRADIENT?

• SHOULD NOT USE IN PATIENTS WITH A DEFECTIVE CORNEAL PUMP (Arch Ophthalmol 2007;125:1345)

Conclusion???
IS THERE A RELATIONSHIP BETWEEN

ANATOMICAL ISSUES AND GLAUCOMA

CENTRAL CORNEAL THICKNESS

IS THERE A RELATIONSHIP BETWEEN

NUTRITIONAL ISSUES AND GLAUCOMA

Patients with Normal Tension Glaucoma have Thinner Corneas.


WHY?
Natural and synthetic compounds have been reported to have neuro-protective capabilities including all antioxidants, inhibitors of glutamate release, calcium channel blockers, polyamine antagonists, nitric oxide synthase inhibitors, cannabinoids, aspirin, melatonin and vitamin B-12. (Curr Opin Ophthalmol 2000;11:78)

It has also been suggested that metabolic inhibition-EATING LESS- is also neuroprotective. (Ann NY Acad Sci 1998;890:240)

Mitogenol-bilberries + pycnogenol significantly increased velocity of blood flow through ophthalmic arteries, central retinal arteries, and posterior ciliary arteries while lowering IOP in ocular hypertension.


Ascorbate and glutathione concentrations decreased in exfoliation syndrome while reactive oxygen species are increased. Antioxidant potential (ROS) plays some role in the pathogenesis of glaucoma.


IS THERE A RELATIONSHIP BETWEEN

HYPERHOMOCYSTEINEMIA AND GLAUCOMA
The plasma level of Hcy was found to be increased only in PXG patients and the plasma levels of vit-B6 were found to increase in the NTG and POAG sample groups. Using homocysteine and vit-B6 levels as the determinants of hyperhomocysteinemia still needs further research. Turgut B, Kaya M, Arslan S, et al. Levels of circulating homocysteine, vitamin B6, vitamin B12, and folate in different types of open-angle glaucoma. Curr Interv Aging 2010;5:133-139.

Hyperhomocysteinemia was found in 27.1% of PXFG patients, 30.6% of POAG patients, and 29.4% of NTG patients. Clement CL, Goldberg I, Healey PR, Graber SL. Plasma homocysteine, MTHFR gene mutation, and open-angle glaucoma. J Glaucoma 2008;17:73-79.

PEXG and Alzheimer’s disease share common associations such as the higher prevalence of hyperhomocysteinemia in both disorders. Folate, vitamin B12 and B6 levels were significantly decreased and associated with elevated Hcy levels in PEXG. Roedl JB, Bleich S, Reulbach U, et al. Vitamin deficiency and hyperhomocysteinemia in pseudoexfoliation glaucoma. J Neural Transm 2007;114:571-575.

Hyperhomocysteinemia is a risk factor for thromboembolic vasculopathy in patients with PEXS and PEXG. Therefore, vitamin B supplementation should be considered in these patients when hyperhomocysteinemia is detected. Saricaoglu MS, Karakurt A, Sengun A, Hasiripi H. Plasma homocystine levels and vitamin B status in patients with pseudoexfoliation glaucoma. Turk J Med J 2006;27:473-477.


Elevated homocysteine levels have also been associated with WMLs. (JGMS 2007;9:15)

Nutrition. 2006 Apr;22(4):441-3. continued

- Serum vitamin E, serum alpha-carotene, and dietary intake of antioxidants and vitamin B6 were associated with lower levels of plasma HCY, whereas hypertension was associated with increased HCY.
- C-reactive protein and HCY levels are related to traditional dietary and behavioral factors associated with age-related macular degeneration.

TREATMENT

400 to 1000 mcg of folic acid per day, 10 to 50 mg of vitamin B6, and 50-300 mcg of vitamin B12 per day + N-ACETYLCYSTEINE (Acta Cardiol 2007;62:579)

SO THEN

HOW DO YOU MANAGE GLAUCOMA?
GET THE PRESSURE DOWN WITH
MINIMAL FLUCTUATION

HOPE THAT THE PATIENT COMPLIES

HOPE THAT THE PATIENT DOES NOT
RUN OUT OF MONEY

HOPE THE PATIENT GOES TO A
BETTER PLACE BEFORE THEY GO
BLIND

What is the overall recommendation for
patients with glaucoma?

Do Not Smoke
Get Quality Sleep
Maintain the Ideal Weight
Exercise Daily
Control Hypertension and Cholesterol
Control Diabetes
Eliminate Stress
Control Inflammation
Maintain an Anti-Inflammatory Diet

Use Nutritional Supplementation if
Needed (Conservative)

<table>
<thead>
<tr>
<th>Nutritional Supplement</th>
<th>Recommended Action</th>
<th>Dosage</th>
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</thead>
<tbody>
<tr>
<td>1000 mg Nigricorne</td>
<td>Nigrocin</td>
<td>500 mg</td>
</tr>
<tr>
<td>1000 mg Vitamin D3</td>
<td>Vitamin D3</td>
<td>500 IU</td>
</tr>
<tr>
<td>High quality Multivitamin with 400 mg Folic Acid, 2 mg B6 &amp; 500 IU Vitamin D3</td>
<td>Immune System</td>
<td>As recommended by AHA guidelines</td>
</tr>
<tr>
<td>100 mg Cystamine</td>
<td>Anti-Glaucoma</td>
<td>q.d.</td>
</tr>
</tbody>
</table>
| Other Optional
Supplements for Anti-Oxidant Protection |

<table>
<thead>
<tr>
<th>Nutritional Supplement</th>
<th>Recommended Action</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg Alpha Lipoic Acid</td>
<td>Anti-oxidant</td>
<td>q.d. to b.i.d. but there is no established RDA</td>
</tr>
<tr>
<td>500 mg Acetyl L-Carnitine</td>
<td>Anti-oxidant</td>
<td>q.d. to b.i.d. but there is no established RDA</td>
</tr>
<tr>
<td>500 mg Curcumin</td>
<td>Anti-oxidant</td>
<td>q.d. to b.i.d. but there is no established RDA</td>
</tr>
<tr>
<td>60 mg Ginkgo biloba</td>
<td>Anti-Oxidant</td>
<td>q.d. to b.i.d. with caution as it can thin blood</td>
</tr>
</tbody>
</table>

Roll Tide