

# NORMAL TENSION GLAUCOMA UPDATE



Scott J. Sands M.D.  
Associate Professor of Ophthalmology  
TTUHSC

## DEFINITION

GLAUCOMAS: A group of optic neuropathies characterized by progressive retinal ganglion cell and axonal degeneration

Two Broad Categories:

+Open Angle 80%

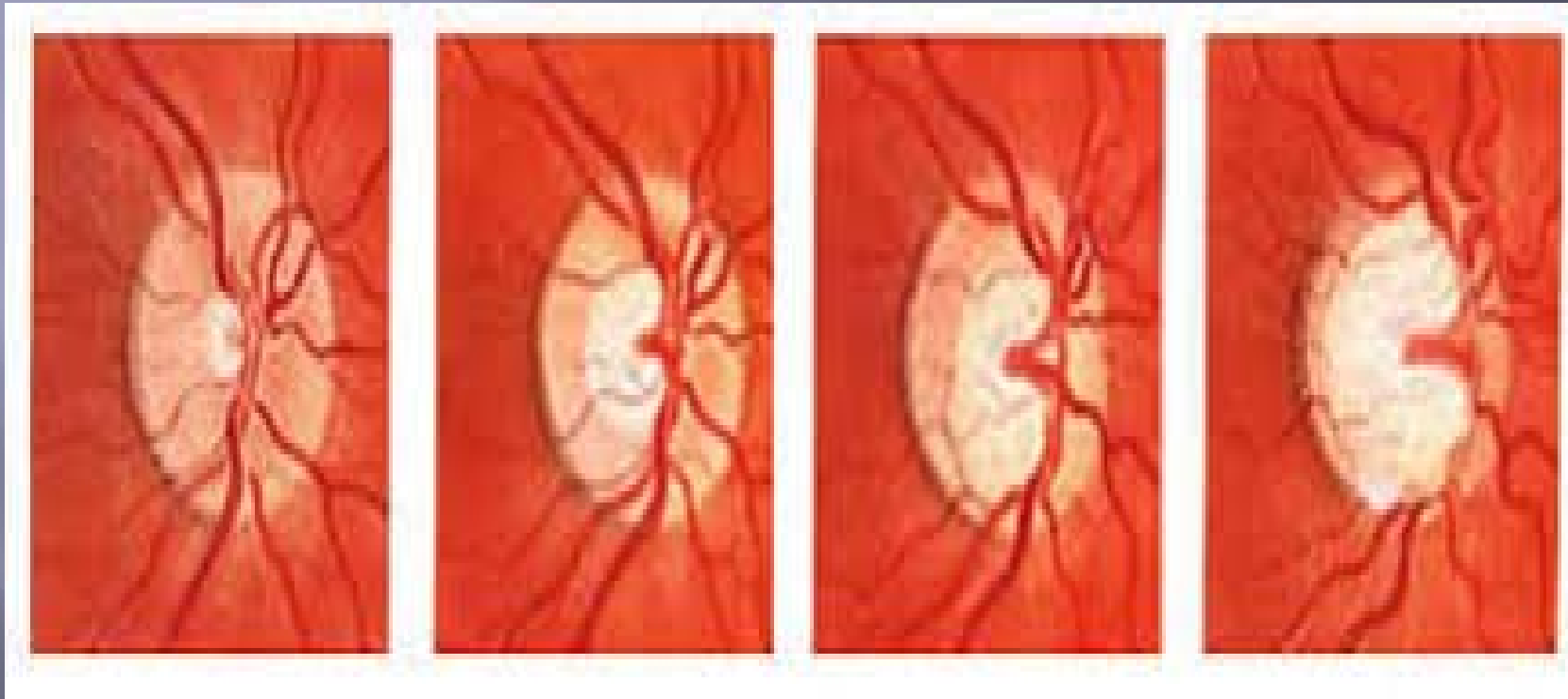
+ Angle Closure 20%

## Open Angle Category

Normal-tension Glaucoma accounts for 25-50% of open angle glaucoma individuals with IOP's < 22mmHg in several population based studies\*

\*JAMA. 2014; 311(18):1901-1911.doi;10.1001/jama.2014.3192(See references 1,14)

## NTG Update




## A Typical Presentation

- Often 60 years and older
- Blurred vision
- No visual symptoms
- IOP < 22 mmHg
- Increased optic nerve cupping, especially vertically
- Often significant asymmetrical cupping
- Higher incidence of splinter hemorrhages
- VF loss tends to be more paracentral and deeper ?
- OCT RNFL thinning consistent with VF and optic nerve changes

## Work Up Strategies

### Good Baselines:

- Best corrected visions
  - Multiple IOP's
  - Comprehensive dilated eye exam
  - Reliable VF's
  - OCT glaucoma
  - Disc photos
  - Gonioscopy
  - Detailed present and past medical history
- 

## Present and Past Medical History

- Obstructive sleep apnea(OSA)- snoring and daytime sleepiness
- Systemic vascular or immune related illnesses
- Past history of major hypotensive event
- Head injury
- Current or prior use of systemic or topical steroids
- Migraine
- Past episodes of angle closure glaucoma

## Current Systemic and Topical Meds

- Blood pressure meds- morning or evening dosage?
- Steroid: systemic, nasal, and topical routes

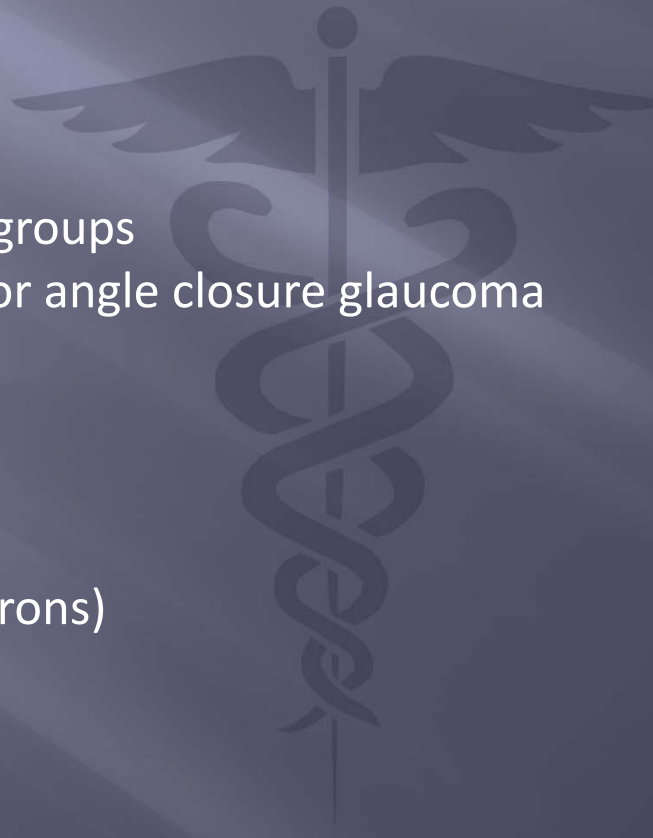




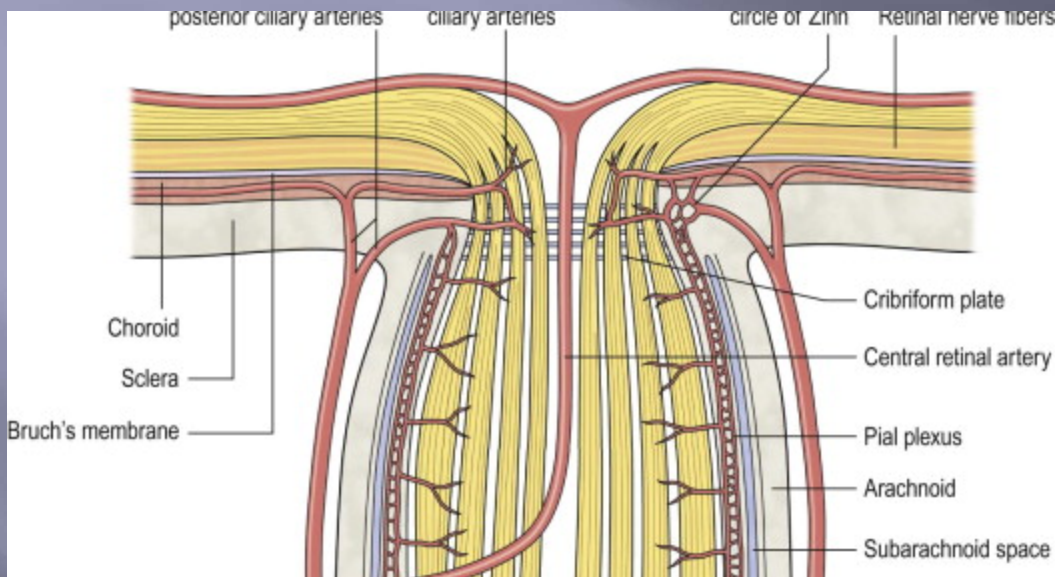
# Glaucoma Risk Factors

## High Risk groups:

- African Americans
- Over 60 years
- Family history
- Hispanics in older age groups
- Asians-increased risk for angle closure glaucoma
- Steroid users
- Eye Injuries
- High Myopia
- Hypertension
- Thin corneas(<500 microns)
- OSA

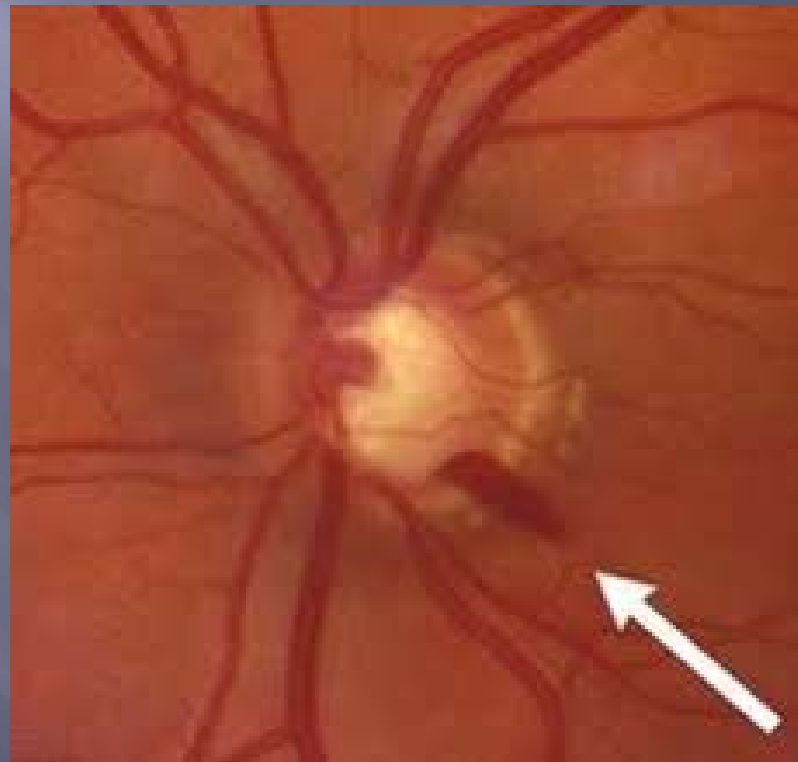


## Pathophysiology of NTG



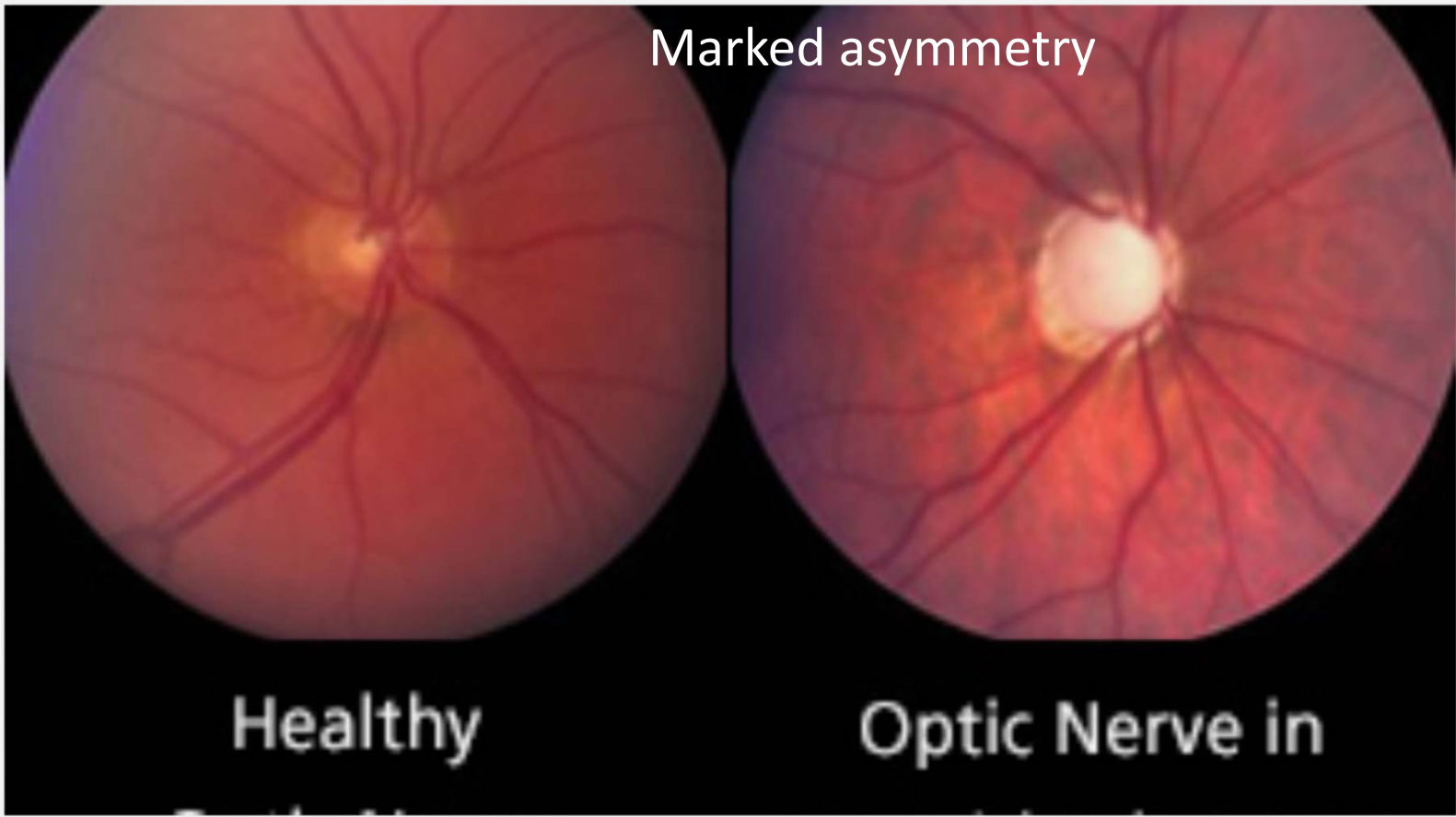
- Lower tolerance of normal IOP causing mechanical damage
- Perfusion deficit and vascular dysregulation
- Translaminar pressure gradient
- Impaired CSF circulation(compartment syndrome)

## Optic Nerve Anatomy



ADVANCED CUPPING

Marked asymmetry



CENTRAL 24-2 THRESHOLD TEST

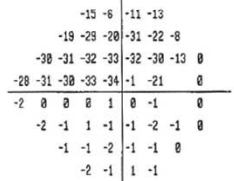
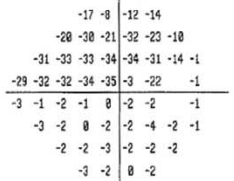
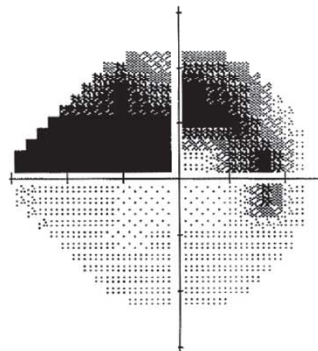
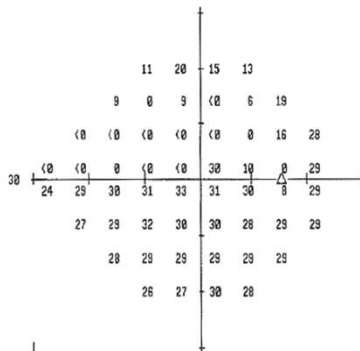
FIXATION MONITOR: GAZE/BLINDSPOT  
 FIXATION TARGET: CENTRAL  
 FIXATION LOSSES: 1/15  
 FALSE POS ERRORS: 0 %  
 FALSE NEG ERRORS: 13 %  
 TEST DURATION: 08:24

STIMULUS: III, WHITE  
 BACKGROUND: 31.5 ASB  
 STRATEGY: SITRA-STANDARD

PUPIL DIAMETER: 3.2 MM  
 VISUAL ACUITY:  
 RX: +0.00 DS DC X

DATE:  
 TIME:  
 AGE:

FOVEA: 36 DB

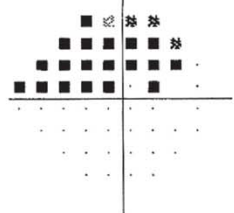
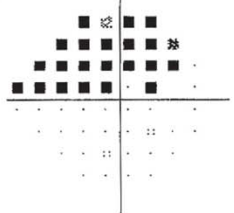


GHT  
 OUTSIDE NORMAL LIMITS

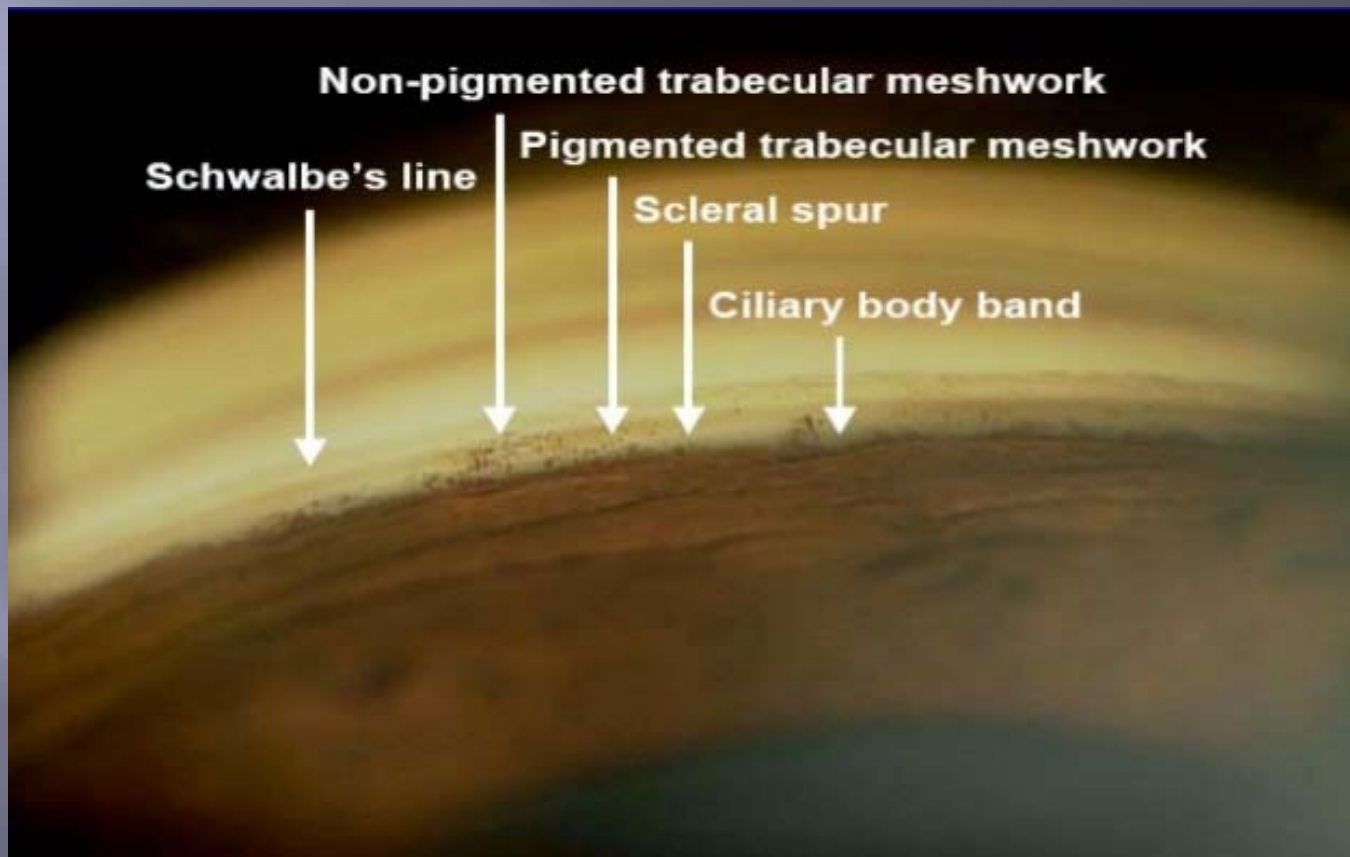
MD -12.11 DB P < 0.5%  
 PSD 14.59 DB P < 0.5%

TOTAL  
 DEVIATION

PATTERN  
 DEVIATION



● < 5%  
 ■ < 2%  
 ■ < 1%  
 ■ < 0.5%



## Neuro Imaging

- Indications:
- Progressive optic nerve cupping and VF loss despite meeting target pressures and no other obvious cause for the progression
- Unexplainable Headaches
- Unexpected VF loss especially if loss respects the vertical midline
- Rapid unexplained vision and/or VF loss

## Clinical Case

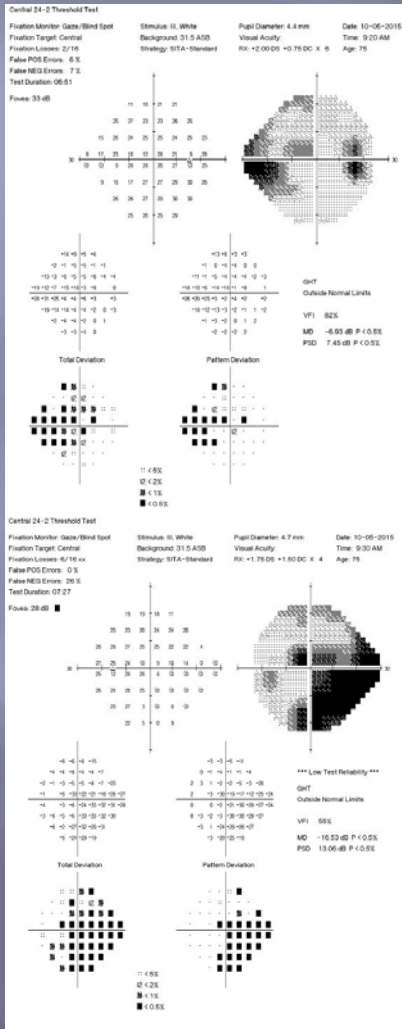
80 yo female who first presented to TTUHSC at 70 yrs of age with:

- + 20/20 Va OU (with correction)
- + IOP 16/17
- + C/D 0.55/0.7
- + F/U one month later: IOP 12/12 and pach 585/585 and now C/D is described as 0.7/0.85

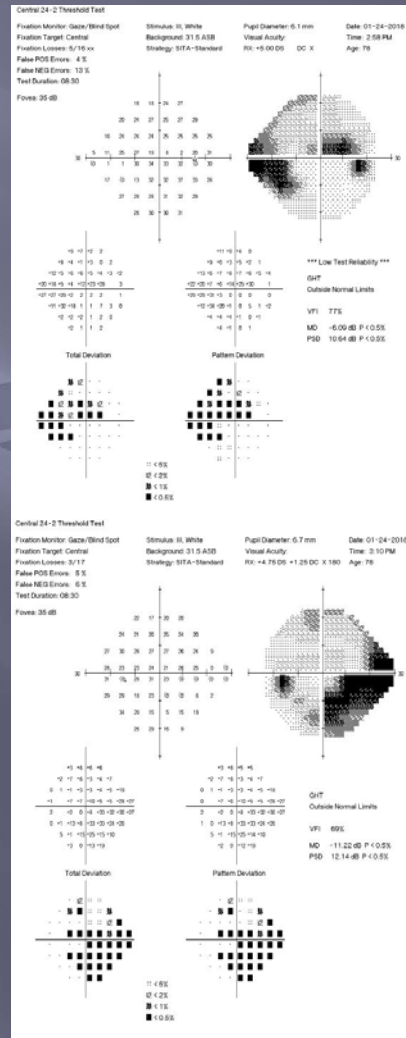
Here's what happened to her over a 10 year period:

- + slow progressive VF and optic nerve progression despite "normal" IOP's
- + What questions should have been asked and what further work up would you recommend

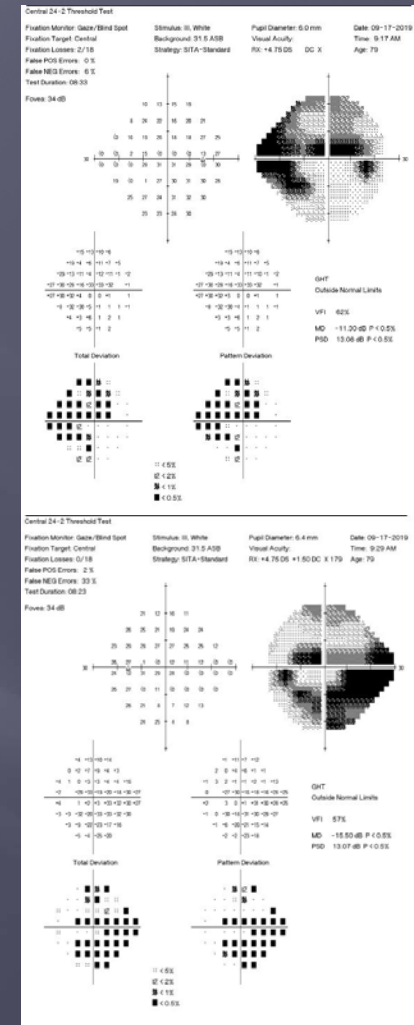




2015



2018



2019

## Clinical Case

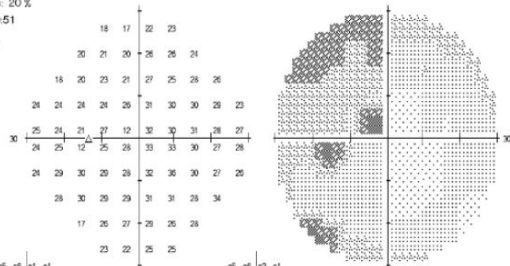
- 63 year old female who presented with blurred vision and headaches:
- Exam findings: Va(uncorrected) 20/100 ph 20/80-2 OU  
IOP's 16/17 mmHg  
C/D 0.5 OD and 0.55 OS with mild temporal pallor OU  
Posterior segment : normal except for a 2 DD choroidal nevus inferotemporally OD
- VF findings: somewhat diffuse overall decrease in sensitivity

Central 30-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot      Stimulus: III, White      Pupil Diameter: 6.4 mm      Date: 12-16-2019  
 Fixation Target: Central      Background: 31.5 ASB      Visual Acuity:      Time: 12:06 PM  
 Fixation Losses: 4/20 xx      Strategy: SITA-Standard      RX: +3.25 DS      DC X      Age: 63

False POS Errors: 17 % xx  
 False NEG Errors: 20 %  
 Test Duration: 10:51

Fovea: 31 dB



|                            |                            |
|----------------------------|----------------------------|
| -5 -6 -1 -1                | -5 -6 -2 -1                |
| -5 -5 -7 -1 -1 -2          | -5 -5 -7 -1 -1 -2          |
| -6 -7 -6 -8 -2 -4 -1 -1    | -6 -8 -6 -8 -3 -4 -1 -1    |
| -3 -4 -6 -6 -5 0 0 0 1 -3  | -3 -4 -6 -7 -5 0 0 1 0 -3  |
| -3 -5 -4 -20 0 -2 0 -2 0 0 | -3 -5 -5 -20 0 -2 0 -2 0 0 |
| -5 -4 -6 -4 0 1 -1 -2 1    | -5 -5 -6 -4 0 0 -1 -2 1    |
| -5 -1 0 -2 -4 0 5 -1 -1 0  | -6 -1 0 -2 -4 0 4 -1 -2 -1 |
| 1 0 -1 -2 0 0 -1 7         | 1 -1 -1 -2 0 0 -1 7        |
| -12 -3 -2 0 -3 0           | -12 -4 -2 0 -3 0           |
| -5 -6 -3 -2                | -5 -6 -3 -2                |

\*\*\* Excessive High False Positives \*\*\*

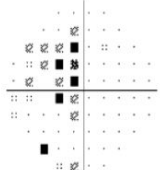
GHT  
 Outside Normal Limits

VFI 91%

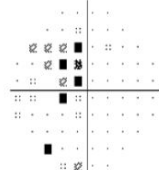
MD -2.43 dB P < 5%

PSD 4.49 dB P < 0.5%

Total Deviation



Pattern Deviation



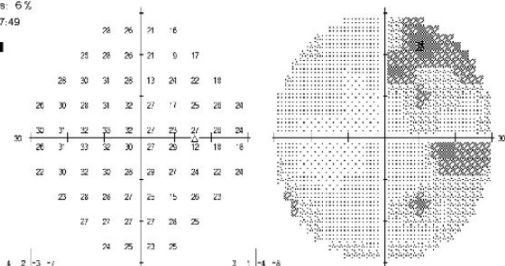
:: < 5%  
 ☺ < 2%  
 ☹ < 1%  
 ■ < 0.5%

Central 30-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot      Stimulus: III, White      Pupil Diameter: 7.2 mm      Date: 12-16-2019  
 Fixation Target: Central      Background: 31.5 ASB      Visual Acuity:      Time: 11:56 AM  
 Fixation Losses: 0/18      Strategy: SITA-Standard      RX: +3.00 DS      DC X      Age: 63

False POS Errors: 14 %  
 False NEG Errors: 6 %  
 Test Duration: 07:49

Fovea: 21 dB



|                             |                              |
|-----------------------------|------------------------------|
| 4 2 -3 -7                   | 3 1 -4 -8                    |
| 0 1 - -5 -16 -6             | -1 0 -2 -7 -18 -10           |
| 1 1 2 - -16 -5 -6 -5        | 0 0 0 -3 -7 -6 -7 -10        |
| 0 1 -2 0 - -4 -13 -5 -3 -3  | -2 0 -4 -1 0 -5 -15 -6 -4 -5 |
| 2 2 1 1 0 -5 -6 -3 -5       | 2 0 0 -1 -1 -6 -9 -5 -6      |
| -1 2 2 0 -2 -6 -2 -11 -11   | -2 0 0 -2 -4 -7 -4 -12 -12   |
| -7 2 1 -1 -4 -5 -4 -6 -7 -5 | -6 0 0 -3 -5 -4 -6 -5 -9 -7  |
| -1 -1 -2 -4 -6 -15 -4 -6    | -6 -3 -4 -5 -6 -17 -6 -7     |
| 0 -2 -2 -2 -1 -4            | -2 -3 -4 -4 -3 -6            |
| -2 -2 -5 -5                 | -1 -1 -7 -4                  |

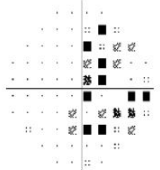
GHT  
 Outside Normal Limits

VFI 89%

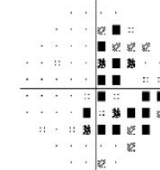
MD -2.97 dB P < 2%

PSD 4.92 dB P < 0.5%

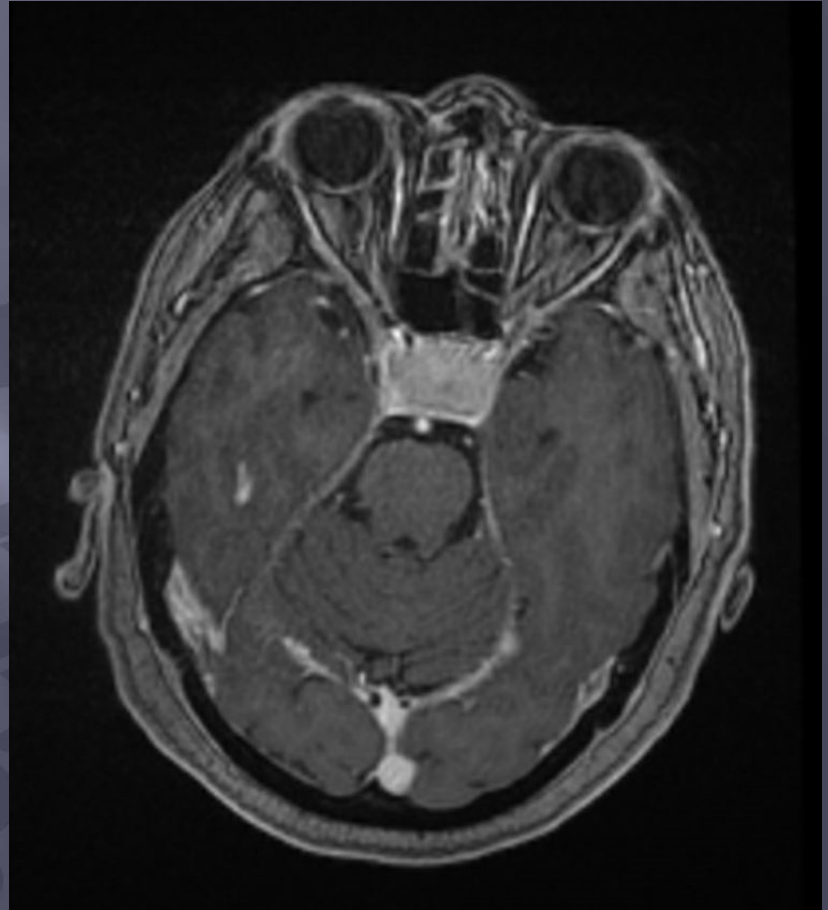
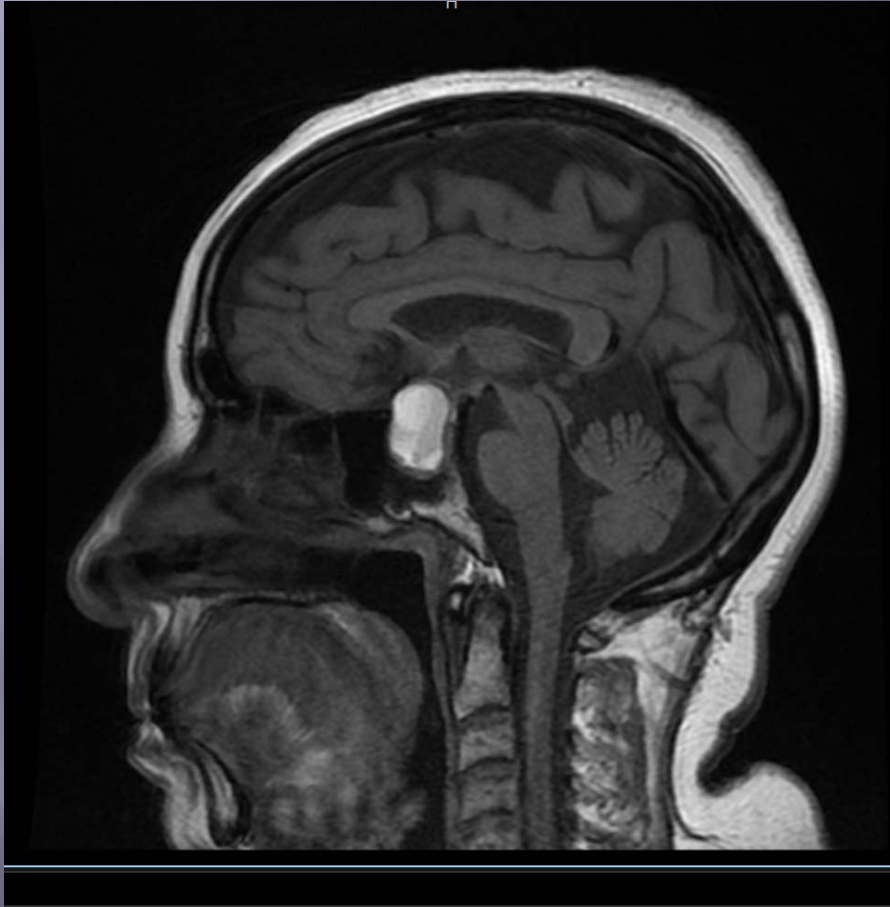
Total Deviation



Pattern Deviation



:: < 5%  
 ☺ < 2%  
 ☹ < 1%  
 ■ < 0.5%



|               |                      |                      |                         |
|---------------|----------------------|----------------------|-------------------------|
| Case:         | Collected:           | Received:            | Requested by:           |
| SR-20-0000766 | 01/21/2020 10:51 CST | 01/21/2020 10:56 CST | Benedicto Baronia, M.D. |

1 Surgical Pathology Report

|               |                      |                   |     |
|---------------|----------------------|-------------------|-----|
| Status:       | Date:                | By:               | At: |
| Authenticated | 01/23/2020 10:32 CST | Safaa Labib, M.D. | UMC |

**B. Sellar tumor:**

**Hemorrhagic Pituitary adenoma.**

**C. Sellar tumor liquid in trap #1:**

**Hemorrhagic Pituitary adenoma.**

**D. Sellar tumor liquid in trap #2:**

**Mostly hemorrhage with scant Pituitary tissue.**

# Sleep Study

## When to Recommend

- OSA characterized by:
  - repeated episodes of partial(hypopnea) or complete(apnea) upper airway obstruction during sleep
  - Snoring
  - Daytime sleepiness

\*5/18/2013 presentation by Jess Whitson M.D. UTSW

## OSA Risk Factors\*

- Upper Body Obesity
- Male gender
- Upper airway abnormalities
- Smoking
- ETOH use
- Snoring
- Neck girth of >17 inches for male and >16 inches for female
- Diabetes and Hypertension
- Family History

\*Jess Whitson M.D. , UTSW presentation 5/18/2013

## Definitive Dx of OSA\*

- ▣ Requires: Sleep Study
- ▣ Interpretation:
- ▣ Apnea/Hypopnea Index(AHI)- number of apneas and hypopneas per hour of recorded sleep
- ▣ AHI >5 is abnormal
- ▣ AHI>15 requires intervention due to increased risk of cardiovascular morbidity and mortality

\*Phillips B, et al, eds, Principle and Practice of Sleep Medicine, 2005



# OSA Syndrome Associated Systemic Conditions\*

- Systemic Hypertension
- Cardiac arrhythmias
- Pulmonary arterial Hypertension
- CHF
- Stroke
- Health-related quality of life issues:
  - -motor vehicle crashes and occupation accidents
  - -pregnancy issues

\*Young T, et al. Epidemiology of osa. Am J Respir Crit Care Med 2002;165:1217-1239

## OSA syndrome-Associated Ocular conditions\*

- Floppy Eyelid Syndrome
- NAION
- Papilledema
- Papillary conjunctivitis
- Retinal vascular tortuosity
- Central Serous Chorioretinopathy

\*Faridi O, et al. Glaucoma and OSA syndrome. Clin Exp Ophthalmol 2012;40:408-419

## OSA Syndrome Association with Glaucoma

- Surgi\* and Coworkers found:
  - NTG in 3 of 51 patients with OSA(5.9%)
  - No OSA in 40 controls
- As AHI increased the following were found:
  - greater IOP
  - more extensive VF loss
  - RNFL thickness decreased

\* Sergi M, et al. Prevalence of Normal tension glaucoma in obstructive sleep apnea syndrome patients. J Glaucoma 2007;16:42-46

## OSA Syndrome Association with Glaucoma

- Marcus and coworkers\* found OSA in 55% of NTG patients(5/9) and 50%(2/4) of NTG suspects
- Blumen and coworkers\* found OSA in 50% of NTG patients(3/6)and 48% of POAG patients(12/25)

\* Marcus DM,et al. Sleep disorders: a risk factor for normal tension glaucoma? J Glaucoma 2001;10:177-83

\* Blumen , et al. Primary open-angle glaucoma and snoring; prevalence of OSAS. Eur Ann Otorhinolaryngol Head Neck Dis 2010;127:159-64

## Glaucoma and OSA (UTSW)\*

- Comparison of 14 POAG and 34 GS patients with OSA to a control group of POAG and GS patients with out OSA:
  - +POAG patients with OSA:
    - 5 times more likely to have diabetes(20 vs. 4,  $p= 0.0001$ )
    - > 4 times more likely to be pseudophakic (9 vs. 2,  $p = 0.04$ )

\*Mahasneh S, et. Al. Glaucoma and obstructive sleep apnea (poster). American Academy of Ophthalmology, Chicago, IL, Nov. 10-13, 2012

## OSA Syndrome Association with Glaucoma

- ▣ Geyer and coworkers found POAG in 5 out of 228 patients with OSA, similar to the expected 2% prevalence in the general population\*

\*Geyer O , et al, The prevalence of patients with sleep apnea syndrome: same as in the general population. Am J Ophthalmol 2003; 136:1093-6

## Glaucoma and OSA Treatment Effects

- Kremmer et al\* reported two cases of NTG which continue to progress despite low IOP's following trabeculectomy
- Following initiation of CPAP, visual field and RNFL indices stabilized for over 3 years

\*Kremmer S, et.al. Obstructive sleep apnea syndrome, normal tension glaucoma, and nCPAP therapy-a short note. Sleep 2003;26:161-2

## Glaucoma and OSA Treatment Effects

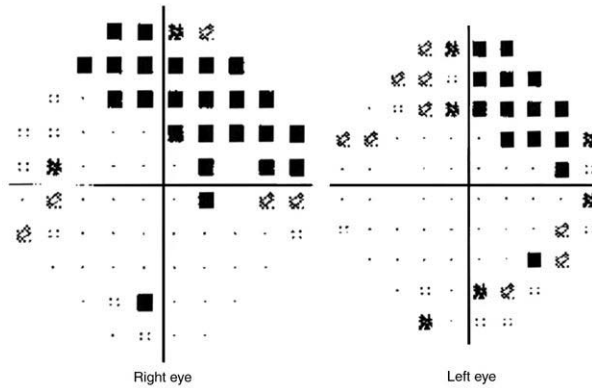
- ▣ Sebastian and Associates\* described a 49 yo male with moderately advanced POAG and severe OSA.
- ▣ Two years after CPAP therapy, visual field indices improved significantly

\* Sebastian RT, et al. Treating obstructive sleep apnoea syndrome: does it improve visual field changes? Eye 2006;20:118-20

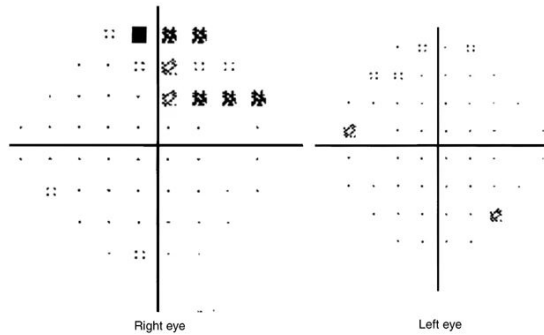


# Glaucoma and OSA

## Effect of Treatment



Humphrey's Visual field-pattern deviation: right eye before treatment (test duration: 10 min 16 s); left eye before treatment (test duration: 9 min 37 s).



Humphrey's Visual field-pattern deviation: right eye after treatment (test duration: 3 min 49 s); left eye after treatment (test duration: 3 min 54 s).

# OSAS

## Treatment Options

- Weight loss
- Avoid supine sleep posture
- Positive Airway Pressure (CPAP)
- Oral Appliance
- Surgery



## Glaucoma and OSA Causal Factors\*

- Ischemia(hypoxia)
- Ocular perfusion pressures
- IOP
- Autonomic dysfunction
- Inflammation and oxidative stress
- Hypercapnia

\* Faridi O, et al. glaucoma and obstructive sleep apnea syndrome. Clin Exp Ophthalmol 2012;40:408-419.

## Conclusions for glaucoma and OSA\*

- Evidence is increasing that strongly suggests an association between OSA and glaucoma.
- Episodic hypoxia may be the link between IOP-independent mechanisms and these two disorders
- Primary eye care professionals should be aware that OSA is a not infrequent modifiable mechanism in addition to IOP's associated with the development and progression of glaucoma

\* Jeff Whitson MD, presentation at UTSW 5/8/2013

# Treatment Modalities

- Observation:  
Maybe appropriate in borderline and low risk patients  
Follow-up IOP checks at differing times of day  
Annual VF's and OCT's
- Medical Therapy:  
Determine target IOP's  
Take into consideration contraindicated topical meds
- Surgical Therapy:  
SLT  
MIGS  
Filtering procedure

## Summary

- ✓ NTG is a diagnosis of exclusion
- ✓ Systemic Hypotension and/or Hypoxic events are more common associated factors than expected
- ✓ Don't exclude the Dx of Glaucoma based on normal IOP's
- ✓ Early detection of modifiable medical co-morbidities can be transformative in the life of your patients