

# Review of Normal Tension Glaucoma

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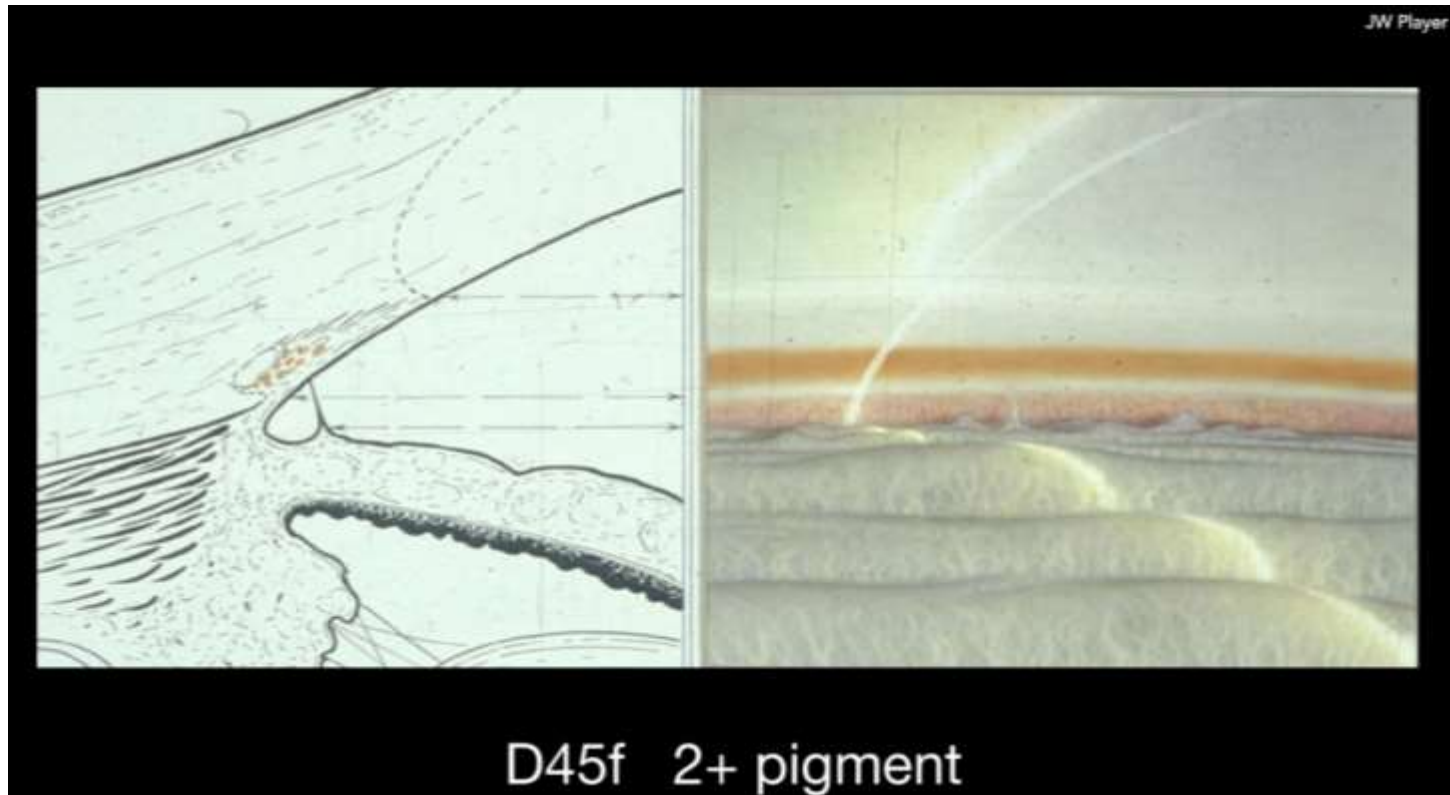
# Learning Objectives

- **Define** Normal Tension Glaucoma (NTG)
  - AKA low-tension glaucoma
- Identify **pertinent signs** of NTG
- **Distinguish** NTG from Primary Open Angle Glaucoma (POAG)
- Identify **risk factors** of NTG
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# Normal Tension Glaucoma (NTG): Definition

Glaucoma (optic neuropathy) WITH...

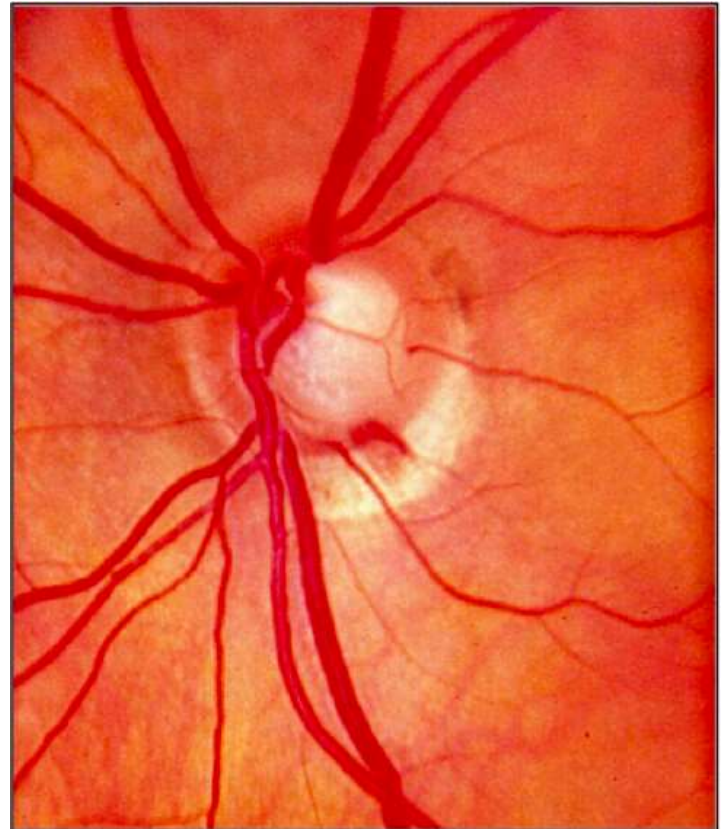
- Open, apparently **normal** anterior chamber angles



# Normal Tension Glaucoma (NTG): Definition

Glaucoma (optic neuropathy) WITH...

- Open, apparently normal anterior chamber angles
- Glaucomatous optic nerve damage
  - Thinning of neuroretinal rim
    - Focal thinning: **Notching\*\***
  - Progressive cupping of the optic disc
  - **Optic disc hemorrhages\*\***



# Normal Tension Glaucoma (NTG): Pertinent signs

Glaucoma (optic neuropathy) WITH...

- Open, apparently **normal anterior chamber angles**
- Glaucomatous **optic nerve damage**
  - Thinning of neuroretinal rim
    - Focal thinning: **Notching\*\***
  - Progressive cupping of the optic disc
  - **Optic disc hemorrhages\*\***
- **Visual loss** characteristic of that seen in patients with chronic glaucoma related to an elevated IOP
  - Common to POAG (nasal step, arcuate scotomas)
  - Defects more focal, closer to fixation (**paracentral\*\***)
- **WITHOUT** a clearly abnormal IOP (IOP within statistically normal limits, **around  $\leq 21$  mmHg**)
  - **Wide diurnal fluctuations\*\***
  - **Nocturnal IOP spikes\*\***

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# Etiology: Glaucomatous optic neuropathy

- Mechanical
- Vascular
- Neurodegenerative

Drance, S.M., R.W. Morgan, and V.P. Sweeney, Shock-induced optic neuropathy: a cause of nonprogressive glaucoma. *N Engl J Med*, 1973. 288(8): p. 392-5.

# Etiology: Glaucomatous optic neuropathy: NTG

- Mechanical
- **Vascular**
  - Non-progressive: Associated with **transient episode of vascular compromise**
  - Progressive: Resulted from **chronic vascular insufficiency** at the optic nerve
- Neurodegenerative



# POAG vs. NTG

## Similarities

- Open, apparently normal anterior chamber angles
- Characteristic glaucomatous optic neuropathy
- Characteristic visual field defects

## Differences

- Vascular dysregulation
- Hypotension
- Lamina cribosa abnormalities
  
- NTG: IOP at or below 21 mmHg
- POAG: IOP above 21 mmHg

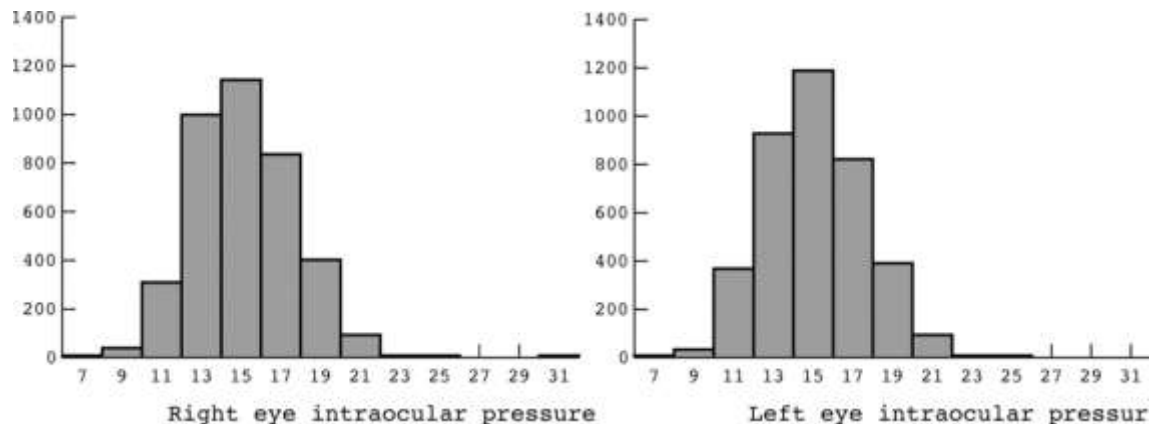
.... Is there really a “magic number”?

# POAG vs. NTG: “Magic number?”

- POAG and NTG are a continuum of OAG with a shift in mechanism?
  - POAG: Predominantly IOP-related
  - NTG: Enhanced sensitivity to what would otherwise be physiologic IOP
- Keep in mind
  - Influence of central corneal thickness of accuracy of applanation tonometry
  - Diurnal variations
  - Available treatment options

# POAG vs. NTG: “Magic number?”

- Mean IOP in a non-glaucomatous population is about 15 mmHg
  - ~21mmHg = Upper limit of normal (2 SD above the mean)



- At least 50% of patients with undiagnosed glaucoma may have IOP below 21 mmHg on an initial exam
  - IOP asymmetry unrelated to visual field asymmetry (LoGTS)
  - IOP alone cannot be relied upon for screening for glaucoma

# POAG vs. NTG: NTG Prevalence

- NTG occurs at an older age than POAG
  - NTG mean age: **66.5 years**
  - POAG mean age: 51.7 years
- NTG seen more frequently in **females** (59.5%)
- Patients of **Japanese decent** more likely to have NTG
  - 92% of Japanese with glaucoma >40 years had an IOP  $\leq$ 21 mmHg
- 20-39% of patients with open angle glaucoma (visual field loss and glaucomatous optic nerve alterations) have an IOP in the statistically normal range (less than 22 mmHg)

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# NTG Risk factors

- Vascular dysregulation
  - Systemic vascular risk factors
  - Local vascular risk factors
- Positive family history

# NTG: Vascular dysregulation: Systemic vascular risk factors

- Ischemic vascular diseases
  - **Diabetes**
  - History of **stroke**
- Hemodynamic crises: Prior history of...
  - **Gastro-intestinal and uterine hemorrhages**
  - **Cardiac arrest** and **severe hypotension** during general anesthesia
- Raynaud's
- Migraine headaches
- Sleep apnea
- Low blood pressure

# NTG: Vascular dysregulation: Systemic vascular risk factors: Raynaud's

- Vasospasm of blood vessels and **subsequent discoloration in the fingers, toes**
  - Exposed to cold temperatures: Skin turns **pale, cold, numb**
  - Oxygen supply depleted: Skin turns **blue**
  - Area warmed: Skin turns red, may also **swell, tingle, be painful**
- Found in 65% of NTG patients





# NTG: Vascular dysregulation: Systemic vascular risk factors: Migraine headaches

- **Chronic headaches** that can cause significant pain for hours or days
- Migraine headaches more common in NTG vs. POAG and normals
  - **Visual aura** more common
  - More frequent in **women**
- Migraine **an independent risk factor** for more rapid NTG progression



# NTG: Vascular dysregulation: Systemic vascular risk factors: Sleep apnea

- Characterized by **abnormal pauses in breathing** or instances of abnormally low breathing
  - **Excessive daytime sleepiness and fatigue**
  - May be recognized as a problem by others witnessing the individual during episodes



During normal breathing the throat is clear and open, allowing air to flow freely to and from the lungs.



While a person with OSA sleeps, tissue at the back of the throat collapse and block the flow of air.



Positive pressure therapy can keep the airway open so that air flows freely to and from the lungs.

# NTG: Vascular dysregulation: Systemic vascular risk factors: Sleep apnea

- Sleep apnea may create **transient hypoxemia** and increased vascular resistance
  - Consult with internist for **sleep study**
  - Seek treatment for sleep apnea if needed



During normal breathing the throat is clear and open, allowing air to flow freely to and from the lungs.



While a person with OSA sleeps, tissue at the back of the throat collapse and block the flow of air.



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# NTG: Vascular dysregulation: Systemic vascular risk factors: Sleep apnea: **STOP BANG** questionnaire

Height \_\_\_\_\_ inches/cm Weight \_\_\_\_\_ lb/kg

Age \_\_\_\_\_

Male/Female

BMI \_\_\_\_\_

Collar size of shirt: S, M, L, XL, or \_\_\_\_\_ inches/cm

Neck circumference\* \_\_\_\_\_ cm

## 1. Snoring

Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?

Yes                      No

## 2. Tired

Do you often feel tired, fatigued, or sleepy during daytime?

Yes                      No

## 3. Observed

Has anyone observed you stop breathing during your sleep?

Yes                      No

## 4. Blood pressure

Do you have or are you being treated for high blood pressure?

Yes                      No

# NTG: Vascular dysregulation: Systemic vascular risk factors: Sleep apnea: **STOP BANG** questionnaire

5. BMI

BMI more than 35 kg/m<sup>2</sup>?

Yes

No

6. Age

Age over 50 yr old?

Yes

No

7. Neck circumference

Neck circumference greater than 40 cm?

Yes

No

8. Gender

Gender male?

Yes

No

\* Neck circumference is measured by staff

*High risk of OSA: answering yes to three or more items*

*Low risk of OSA: answering yes to less than three items*

# NTG: Vascular dysregulation: Systemic vascular risk factors: Low blood pressure

- Patients with lower blood pressure (**90/60 mmHg**) may have periods of low perfusion pressure
  - Hypotension found in 31-59% of NTG patients
  - May also be **secondary to TREATMENT of HYPERtension**



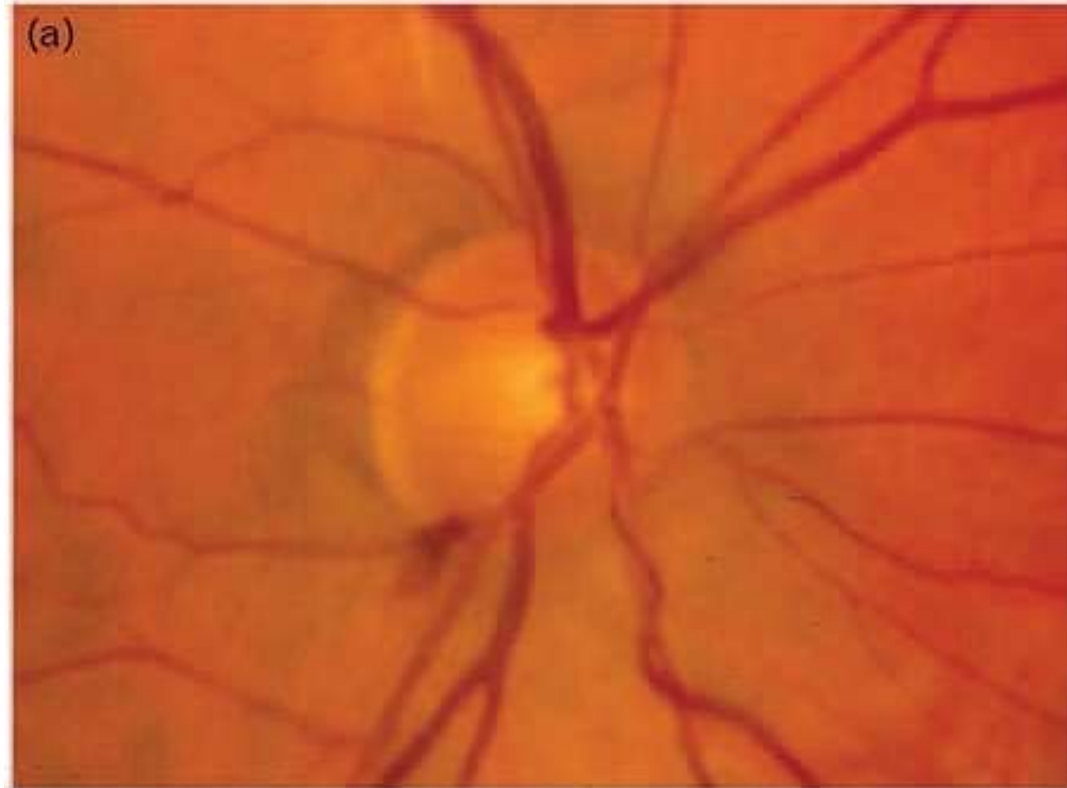
# NTG: Vascular dysregulation: Systemic vascular risk factors: Low blood pressure

- NTG patients with a dip of more than 20% in **nocturnal** blood pressure had a higher incidence of visual field progression
- IOP increases in supine position
- May consider **24-hour ambulatory BP monitoring**



# NTG Risk factors

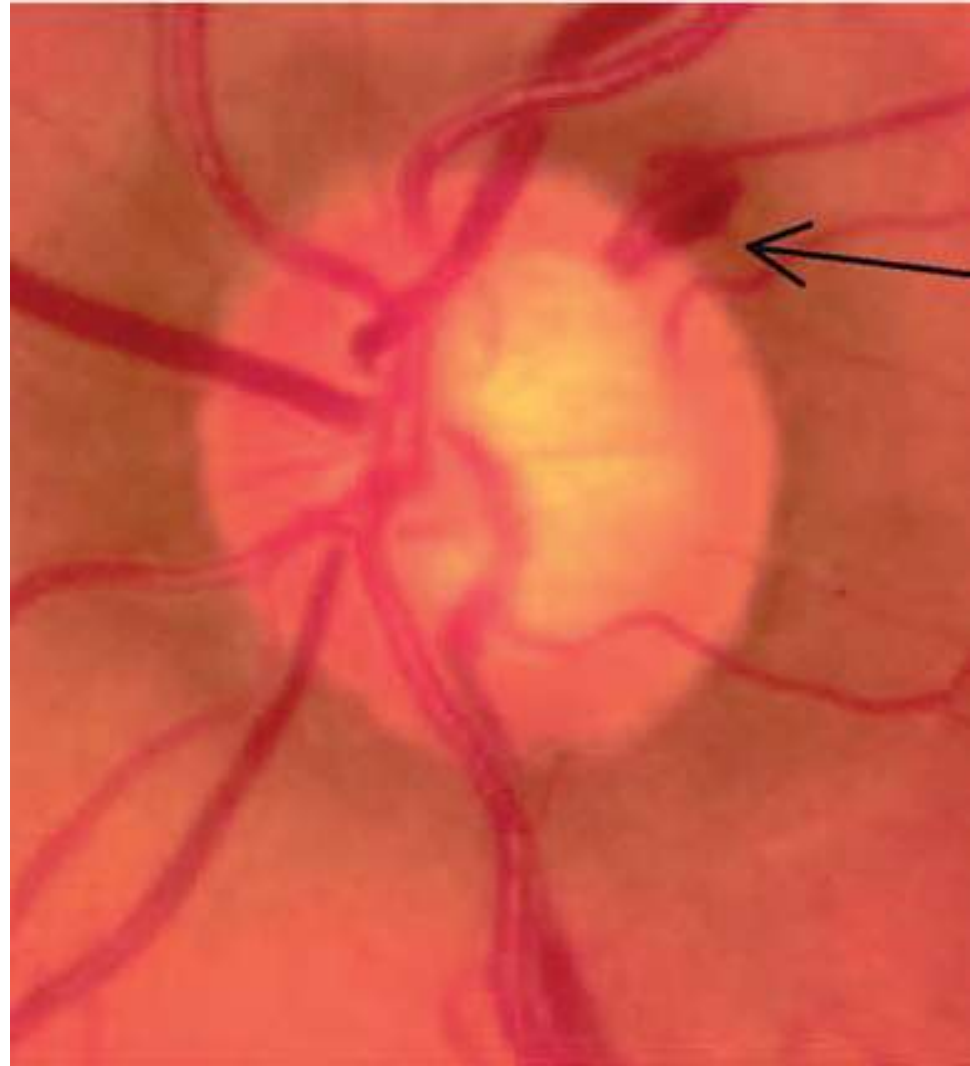
- **Vascular dysregulation**
  - Systemic vascular risk factors
    - Ischemic vascular diseases
    - Hemodynamic crises
    - Migraine headaches
    - Raynaud's phenomenon
    - Sleep apnea
    - Low blood pressure
  - **Local vascular risk factors**
    - **Disc hemorrhages**
- Positive family history





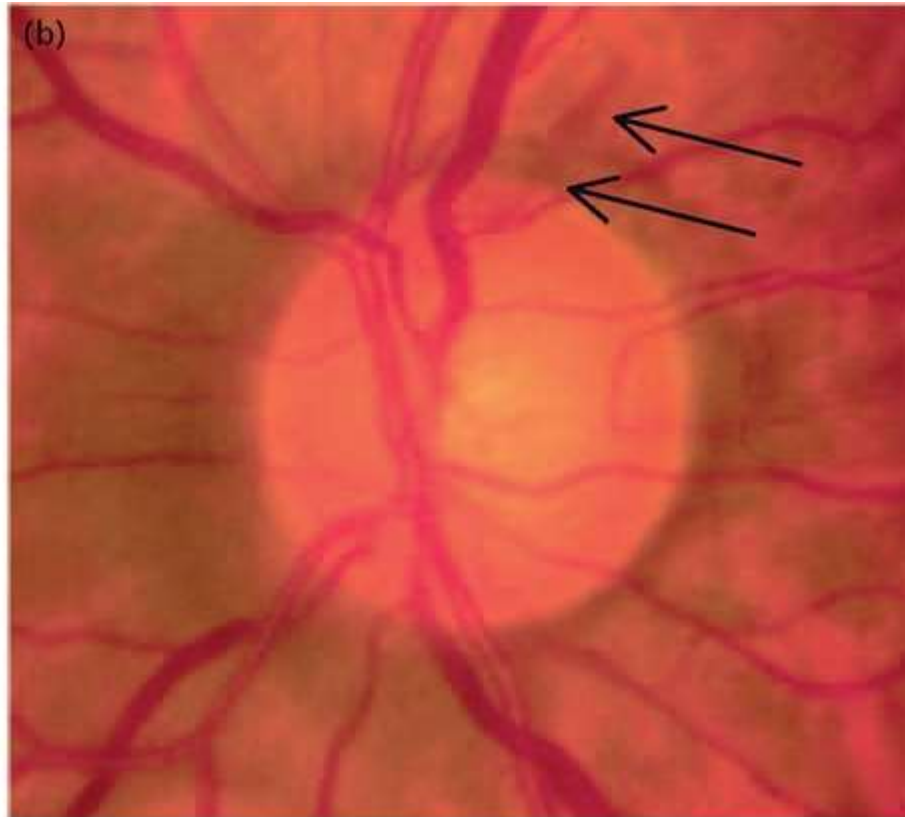
# NTG: Vascular dysregulation: Local vascular risk factors: Disc hemorrhages

- Splinter or **flame-shaped**
- Radially oriented
- **Perpendicular to the disc margin**
- Most commonly **inferotemporal** and **superotemporal**
- Associated with early glaucomatous change



# NTG: Vascular dysregulation: Local vascular risk factors: Disc hemorrhages

- Increased frequency of disc hemorrhages in patients with NTG:  
Predictive factor for **progression** of NTG
  - 11-42% in NTG patients (vs. 0-0.4% in normals)

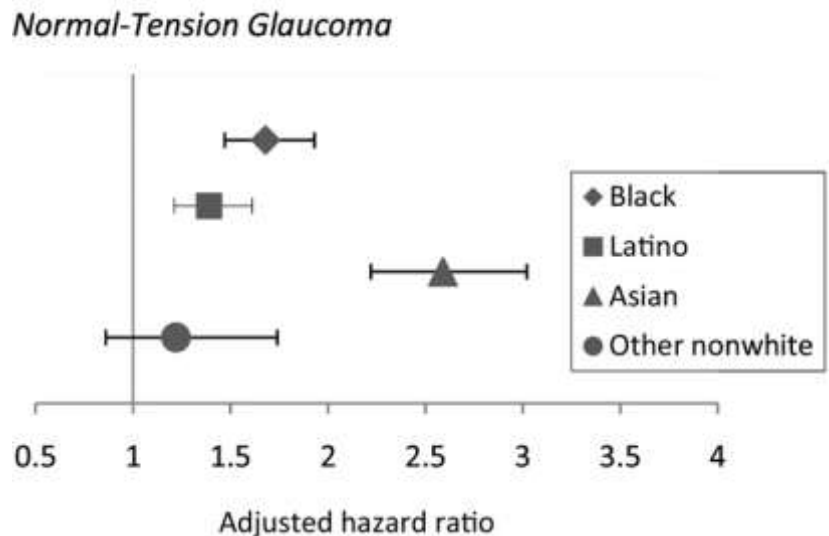


# NTG Risk factors

- Vascular dysregulation
  - Systemic vascular risk factors
  - Local vascular risk factors
- **Positive family history**
  - 34.7% of patients with NTG have a positive family history of glaucoma
  - POAG and NTG intermingle within the same families

# NTG: Positive family history: Asian American heritage

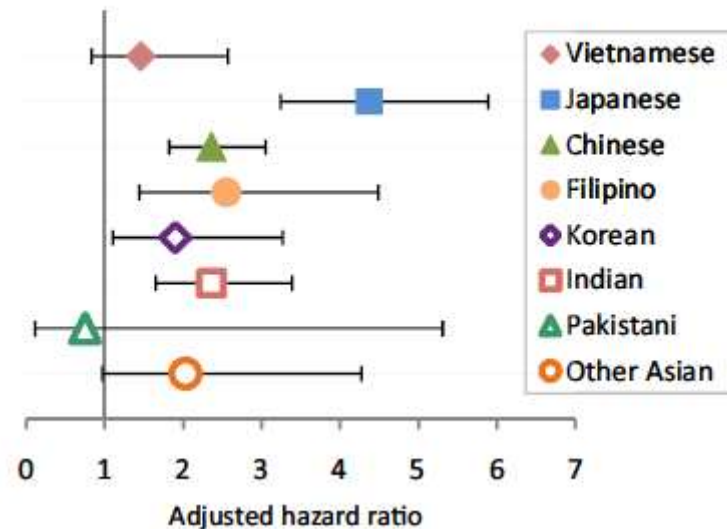
- NTG rates considerably higher among **Asian Americans** relative to other races
  - 159% increased hazard of NTG
  - Japanese Americans had a substantially higher hazard of NTG compared to non-Asian Americans



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*Normal-Tension Glaucoma*



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NTG: Treatment and management: CNTGS

30%

reduction in IOP can  
prevent progression of  
visual field loss

# NTG: Treatment and management

- Pharmacologic
  - Prostaglandin analogs
  - Alpha-2 agonists
  - Carbonic anhydrase inhibitors
  - Miotics: Poor local tolerability, frequent dosing required
  - Beta blockers: ?Decreases perfusion
- Surgical
  - Laser trabeculoplasty
  - Filtration surgery: Continued progression despite maximum tolerated medical therapy



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# Collaborative Normal-Tension Glaucoma Study (CNTGS)

- 30% reduction in IOP can prevent progression of visual field loss
  - 20% of treated patients with a 30% reduction in IOP showed continued progression
- 50% of untreated patients showed no further progression during 5 years of follow-up

# Low-Pressure Glaucoma Treatment Study (LoGTS)

- Patients treated with **brimonidine 0.2%** were less likely to have visual field progression compared to patients treated with timolol 0.5%
  - Neuroprotective effect of brimonidine?
  - Detrimental vascular effect of timolol?
- No relationship between IOP asymmetry and visual field asymmetry

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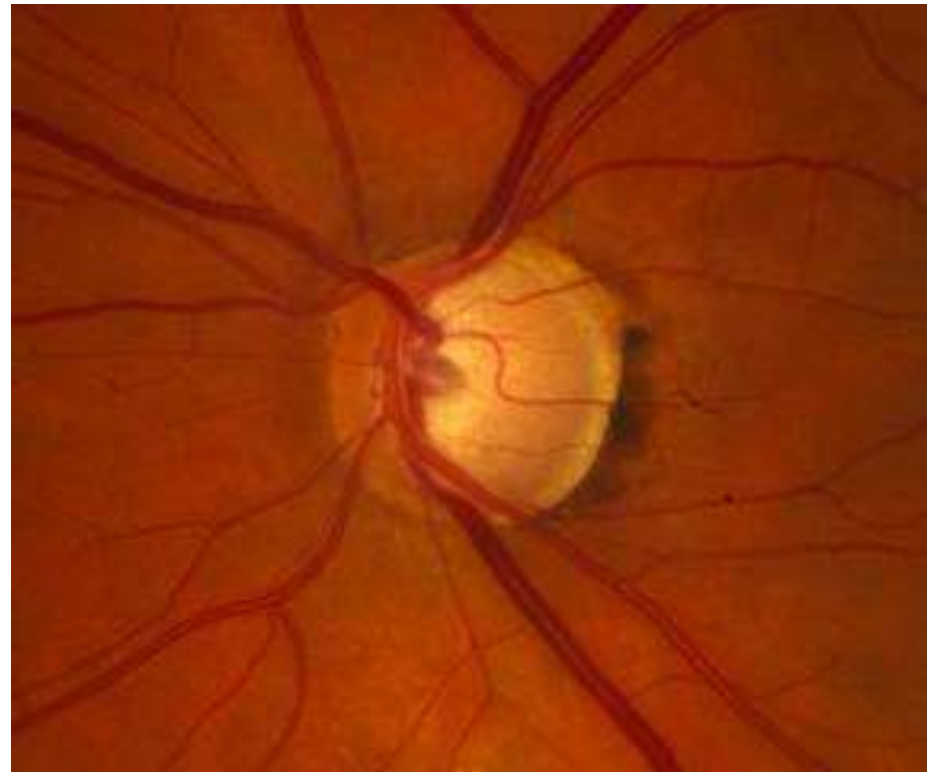
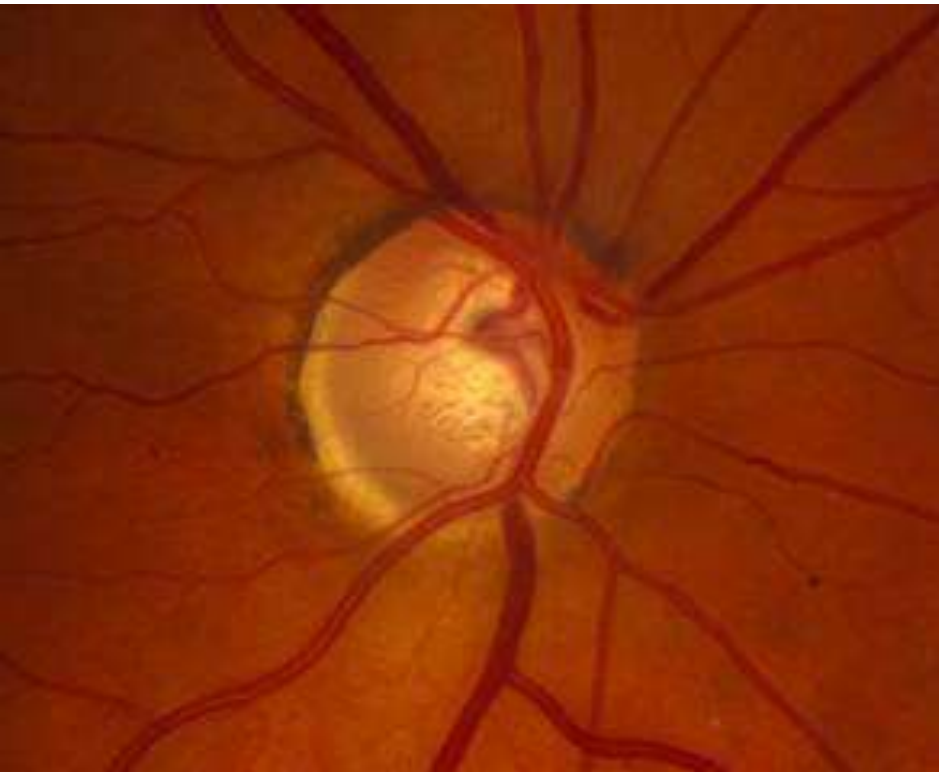
# NTG: Sample case

- Chief Complaint: **65 y.o. Japanese-American female** with progressive visual field loss, glaucomatous disc change and normal IOP
- History of Present Illness
  - Patient was diagnosed with glaucoma by her local optometrist one year ago
  - She has been using **latanoprost** in both eyes (OU) at nighttime since her diagnosis
  - Recent follow up detected **progressive visual field changes** in the left eye (OS) and the patient was referred for further evaluation
- Past Ocular History: No previous ocular procedures or trauma
- Past Medical History: **Diabetes** x 5 years; A1C 7%, BS range 130-150s
- Medications: **Atenolol qPM**, Metformin BID; NKDA
- Family History: No family history of glaucoma

# NTG: Sample case

- Manifest Refraction
  - OD: -3.75 +0.75 x 050 20/20
  - OS: -3.75 +0.25 x 020 20/20
- Motility: Full, OU
- Intraocular pressure: OD -- 18 mmHg; OS -- 16 mmHg
- Anterior segment examination: Unremarkable, OU
  - Pachymetry: 553/539
  - Gonioscopy: Flat approach, open angles to CB 360, grade 1 pigment OU
- Additional finding
  - BP 115/75 RAS
  - Changes in hand color consistent with possible Raynaud's was observed bilaterally during exam

# NTG: Sample case



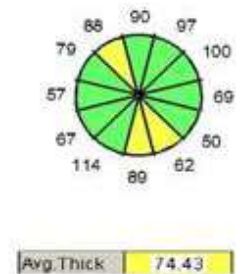
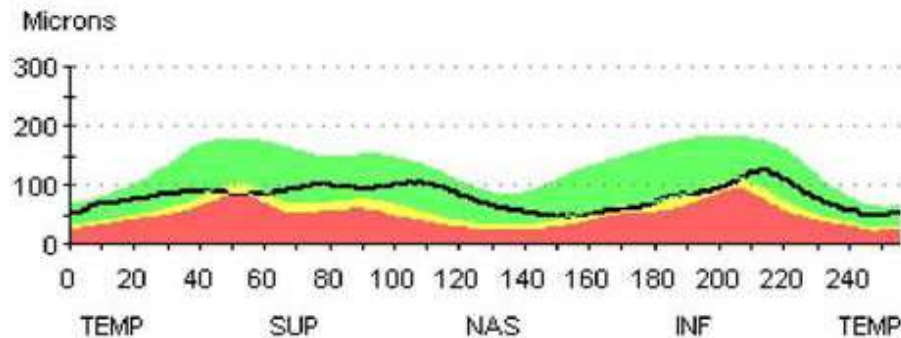
OD: 0.7 C:D with early superior and inferior notches

OS: 0.8 C:D with superior and inferior notches

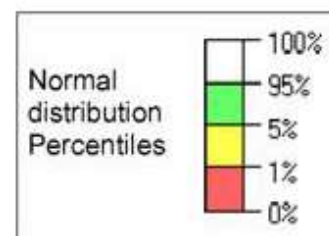
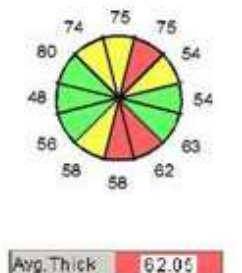
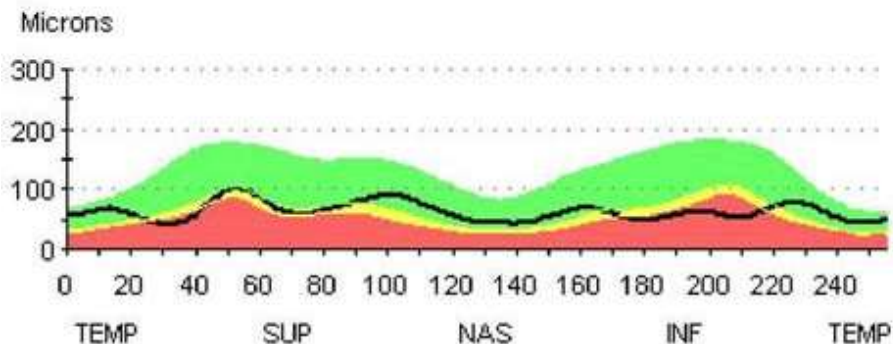
OU: Pink rims, distinct margins, no DH OU

# NTG: Sample case

A. OD



B. OS



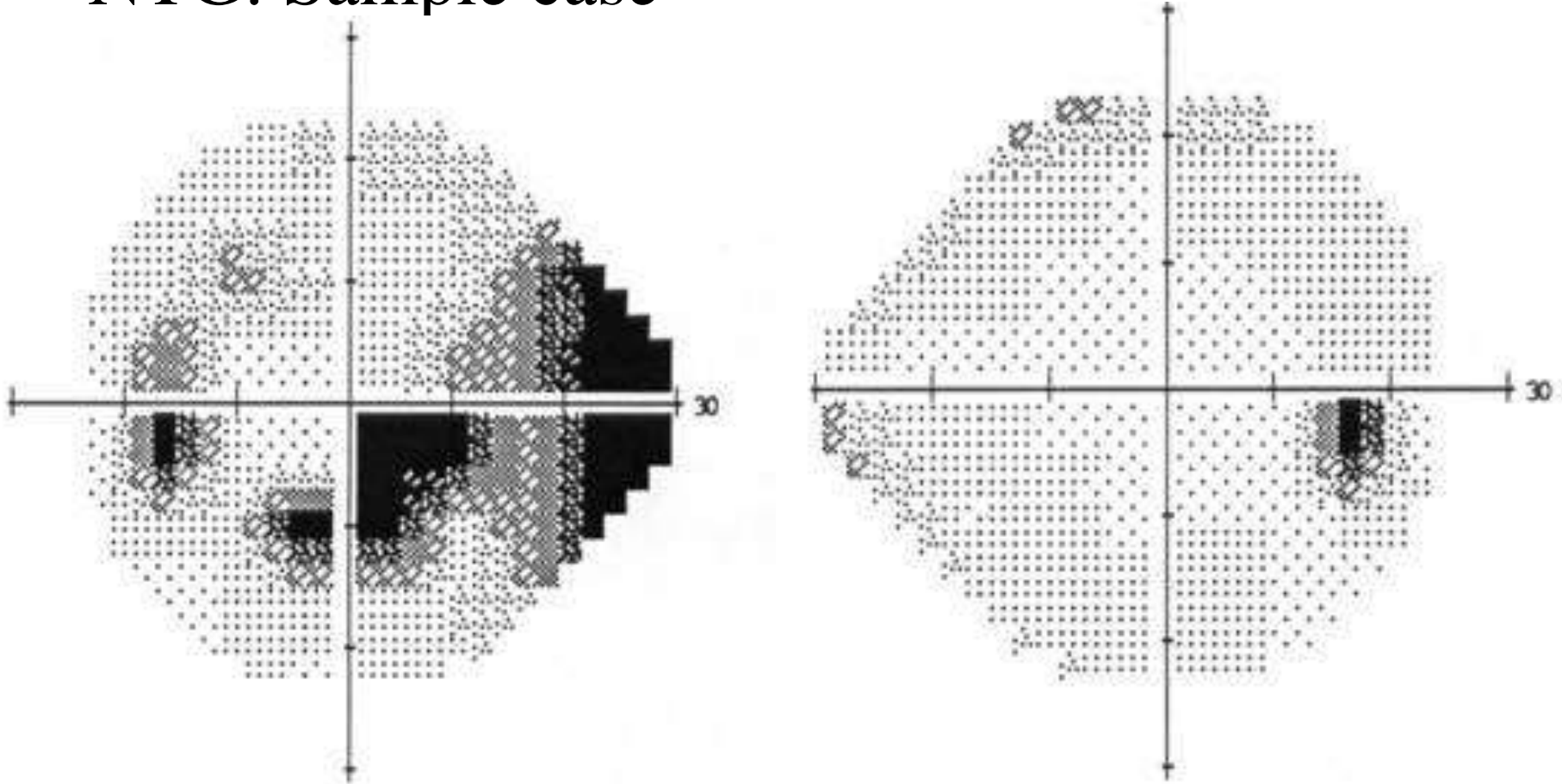
OD: Possible superior > inferior RNFL thinning

OS: **Inferior > sup/temp RNFL thinning**

OS >> OD; consistent with ONH appearance



# NTG: Sample case



OD: No pattern defects

OS: Inferior paracentral with superior and inferior nasal step defects

# NTG: Sample case

- 65 year old Japanese-American woman
- Diabetes
- Atenolol qPM
- Normal IOP
- Normal central corneal thickness
- Normal anterior chamber angles
- Possible Raynaud's disease
- Glaucomatous optic nerve cupping
- NFL thinning
- Corresponding visual field loss

What would you do?

# NTG: Sample case: What would you do?

- Rule out
  - Other forms of optic neuropathy
  - NTG-mimickers
- Request prior exam records: Prior visual fields, ONH OCT, IOP flow including **Tmax**
- **Update PCP**
  - Diabetes
  - NTG
  - Strongly consider switch from qPM to qAM Atenolol dosage
  - Signs and symptoms of possible Raynaud's
- Discuss adherence, drop instillation: Discuss SLT
- Recall prostaglandins generics: **Continue Latanoprost qhs OU**
  - Latanoprost qhs OU (Xalatan)
  - Bimatoprost qhs OU (Lumigan)

# NTG: Sample case: What would you do?

- Add additional medications: Expect a minimum of an **additional 15% reduction** in IOP when an adjunctive medication is added to a first-line agent
  - Alpha-2 agonists: **Brimonidine (Alphagan) BID-TID**
    - Mean IOP reduction: 4.2 mmHg (20.3% reduction)
    - Neuroprotection?: Interaction with retinal ganglion cells
  - Carbonic anhydrase inhibitors: **Brinzolamide (Azopt) BID**
- Consider combination pharmacologics thereafter
  - Brinzolamide / Brimonidine (Simbrinza) TID

# NTG: Sample case: What I did

- Continue Latanoprost QHS OU: 30% reduction from Tmax
- Add Brimonidine TID OU: Additional 15% reduction
- Switch Brimonidine to Brinzolamide / Brimonidine combo TID OU while continuing Latanoprost QHS OU
- Refer to glaucoma specialist: Filtration surgery
  
- Discuss SLT throughout

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