The Eye & Systemic Disease

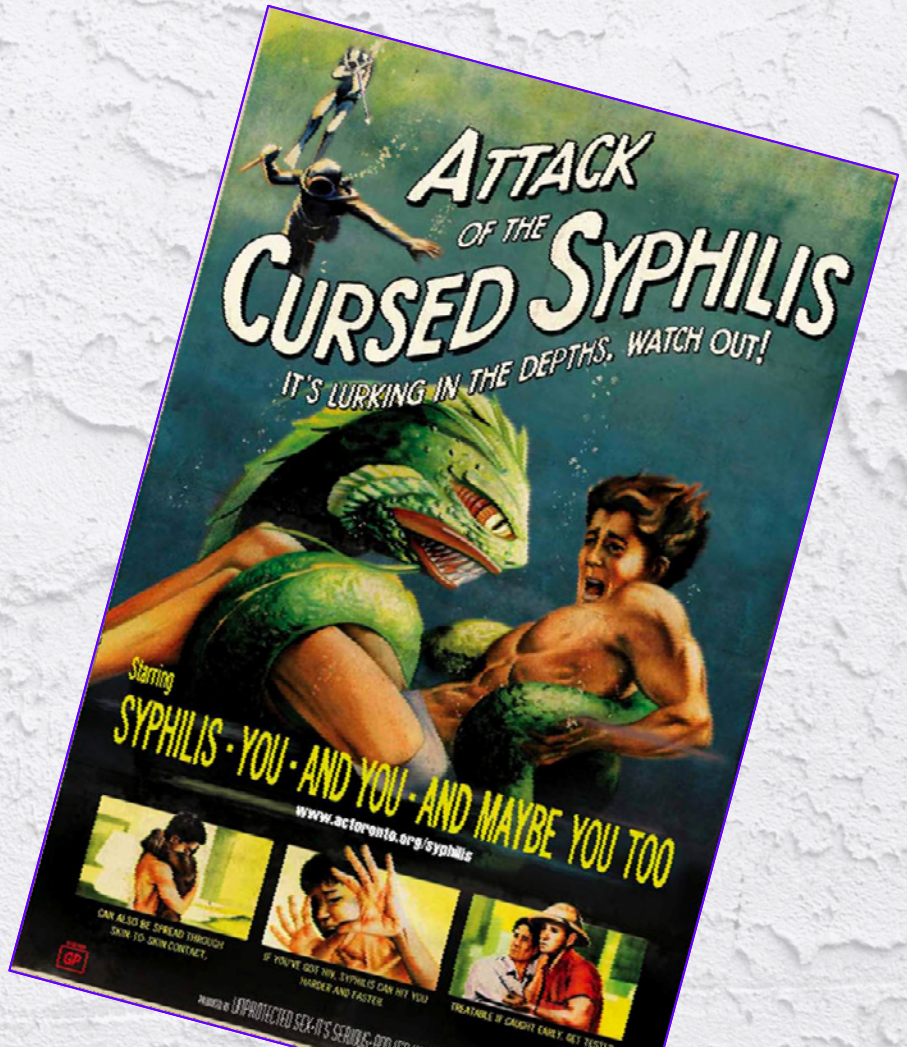
Rick Trevino, OD, FAAO

Rosenberg School of Optometry

University of the Incarnate Word

Eye & Systemic Disease

- Online notes
  - richardtrevino.net
- Email me
  - rctrevin@uiwtx.edu
- Disclosures
  - None



The Great Imitator

Case Report

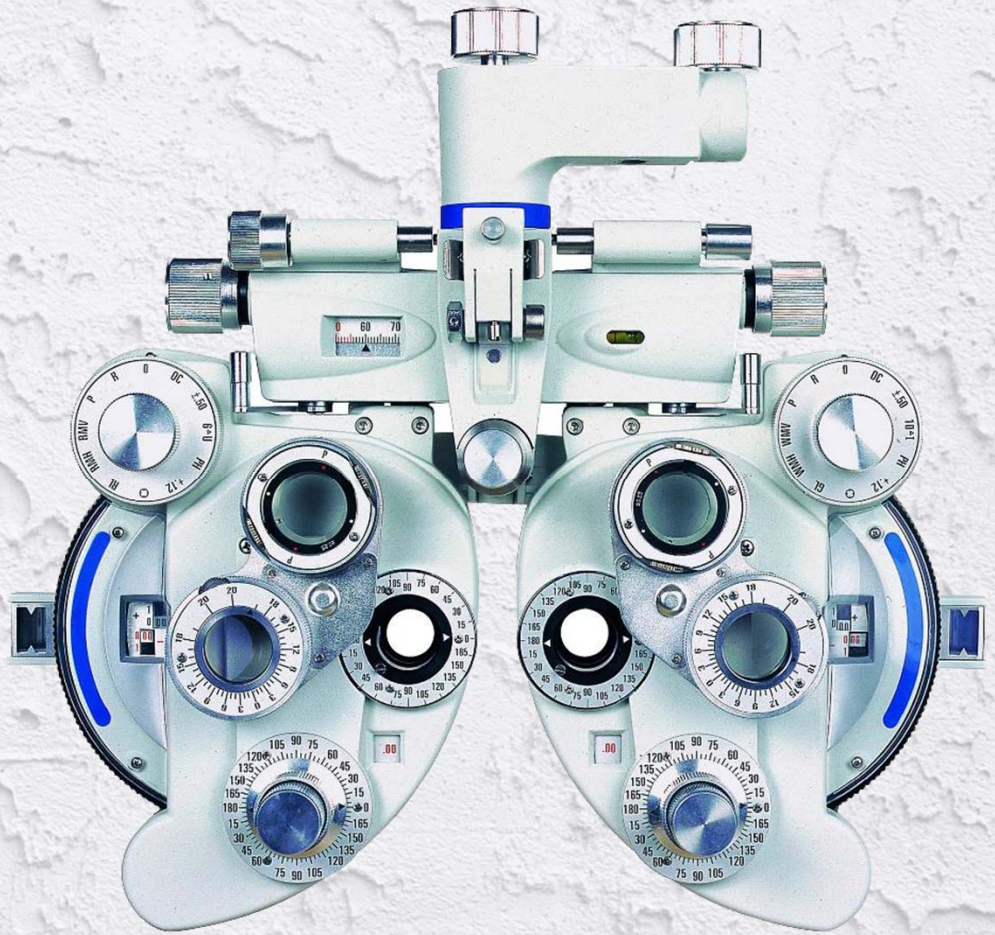
- 54yo WM presenting for a **routine annual eye exam**.
  - C/O blue/white flashes in peripheral vision OU.
  - Also c/o intermittent vertigo, tinnitus, muscle weakness, and nausea x several months
  - Specifically denies headache
- POH: OHT. LEE: 1yr.
- MH: HTN, HIV, depression

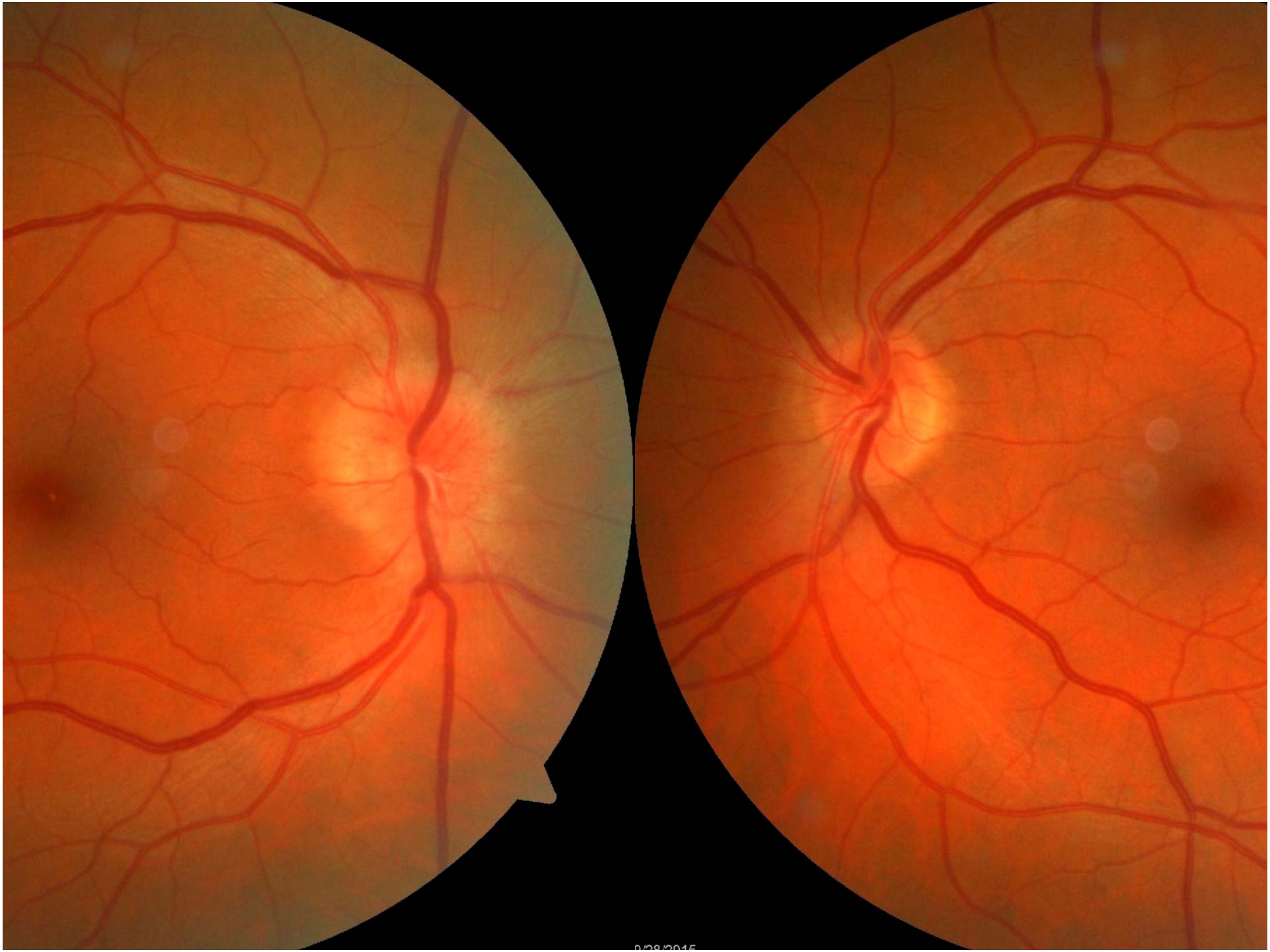
Case Report

Vcc

- OD: **20/25**
- OS: **20/20**

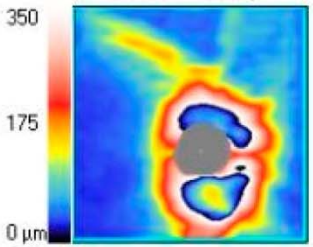
Ta 20/19 @ 9:40AM
PERRL, No APD
FROM, nontrabismic
Color: 8/8 (HRR)
SLE: Clear OU





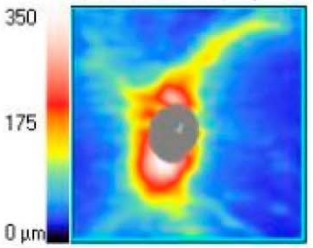
ONH and RNFL OU Analysis:Optic Disc Cube 200x200 OD ● | ● OS

RNFL Thickness Map

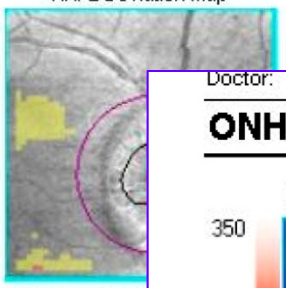


	OD	OS
Average RNFL Thickness	173 µm	79 µm
RNFL Symmetry	78%	
Rim Area	1.61 mm²	1.52 mm²
Disc Area	1.60 mm²	1.55 mm²
Average C/D Ratio	0.08	0.16
Vertical C/D Ratio	0.07	0.22
Cup Volume	0.002 mm³	0.008 mm³

RNFL Thickness Map

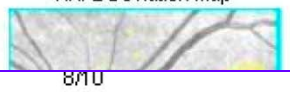


RNFL Deviation Map



Neuro-retinal Rim Thickness

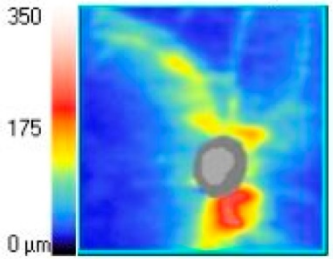
RNFL Deviation Map



Doctor: Signal Strength: 8/10 8/10

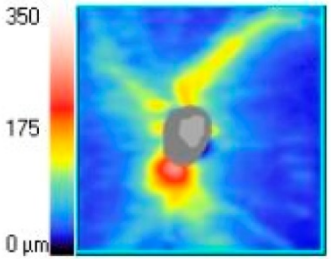
ONH and RNFL OU Analysis:Optic Disc Cube 200x200 OD ● | ● OS

RNFL Thickness Map



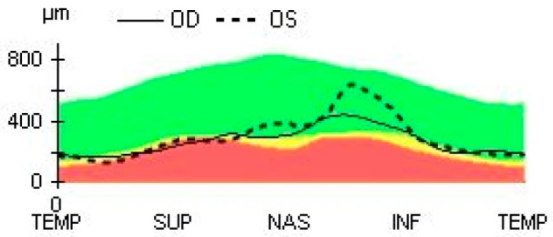
	OD	OS
Average RNFL Thickness	71 µm	72 µm
RNFL Symmetry	94%	
Rim Area	0.97 mm²	1.01 mm²
Disc Area	1.52 mm²	1.39 mm²
Average C/D Ratio	0.60	0.52
Vertical C/D Ratio	0.60	0.54
Cup Volume	0.240 mm³	0.085 mm³

RNFL Thickness Map

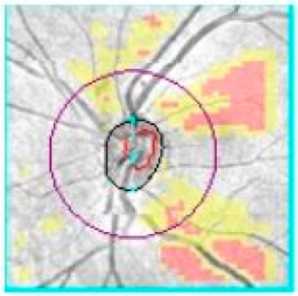


RNFL Deviation Map

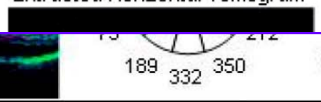
Neuro-retinal Rim Thickness



RNFL Deviation Map



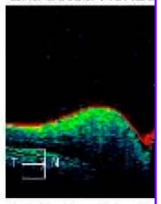
Disc Center(0.42,-0.87)mm
Extracted Horizontal Tomogram



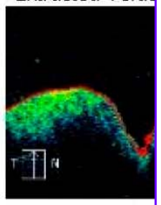
RNFL Thickness

Disc Center(-0.36,-0.12)mm
Extracted Horizontal Tomogram

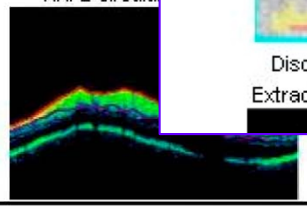
Disc Center(0.
Extracted Horizo



Extracted Vertic



RNFL Circula



Single Field Analysis | Eye: Right

Name: | DOB:

ID:

Central 30-2 Threshold Test

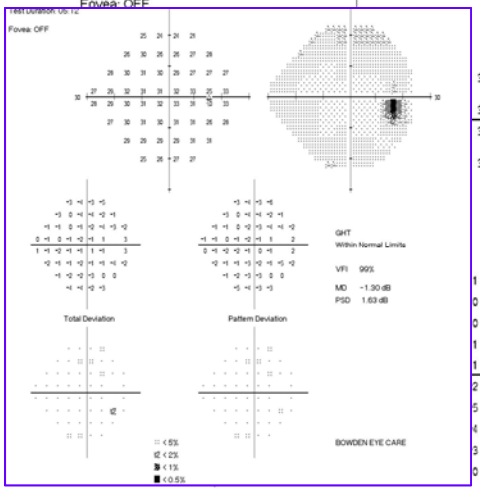
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 7/12 xx
False POS Errors: 60 % xx
False NEG Errors: 18 %
Test Duration: 04:58

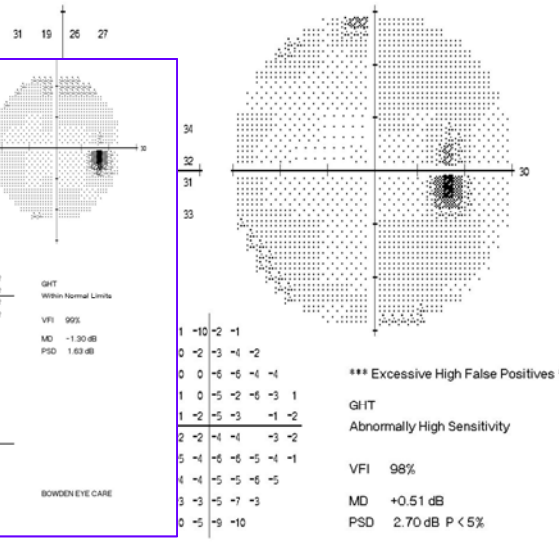
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast

Pupil Diameter:
Visual Acuity:
RX: +4.50 DS DC X

Date: 09-28-2015
Time: 9:07 AM
Age: 53

Fovea: OFF



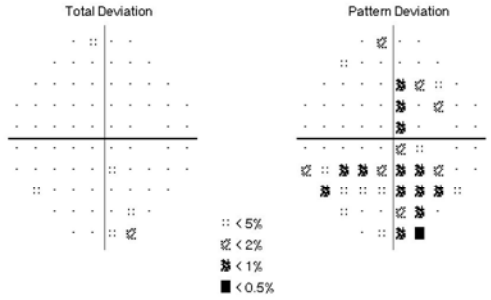


*** Excessive High False Positives ***

GHT
Abnormally High Sensitivity

VFI 98%

MD +0.51 dB
PSD 2.70 dB P < 5%



BOWDEN EYE CARE

HFA II 740-41128-5.1.2/5.1.2

Single Field Analysis | Eye: Left

Name: | DOB:

ID:

Central 30-2 Threshold Test

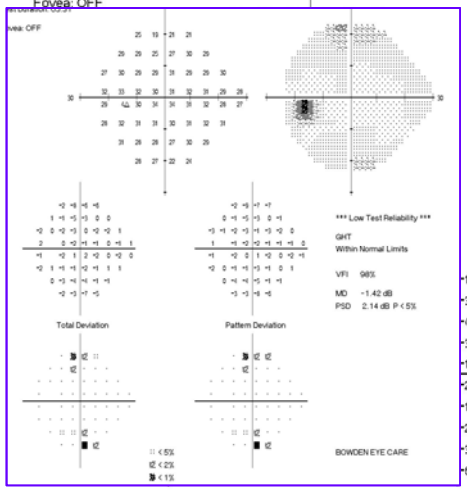
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 11/15 xx
False POS Errors: 28 % xx
False NEG Errors: 9 %
Test Duration: 04:37

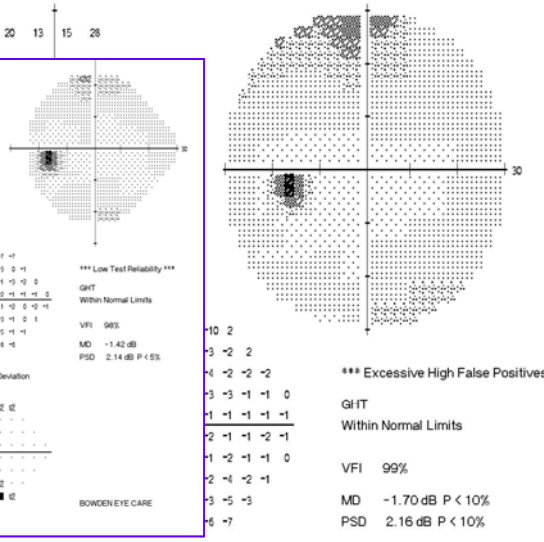
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Fast

Pupil Diameter:
Visual Acuity:
RX: +4.00 DS DC X

Date: 09-28-2015
Time: 9:14 AM
Age: 53

Fovea: OFF



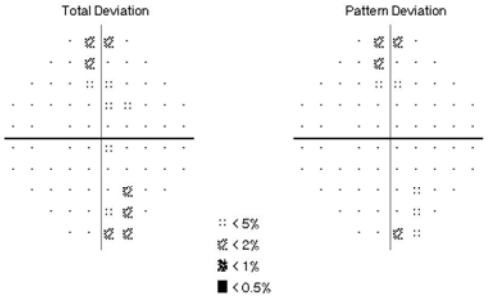


*** Excessive High False Positives ***

GHT
Within Normal Limits

VFI 99%

MD -1.70 dB P < 10%
PSD 2.16 dB P < 10%



BOWDEN EYE CARE

HFA II 740-41128-5.1.2/5.1.2

Case Report

Impression

- **Papilledema**
  - Normal visual function
  - Bilateral disc edema OD>>OS

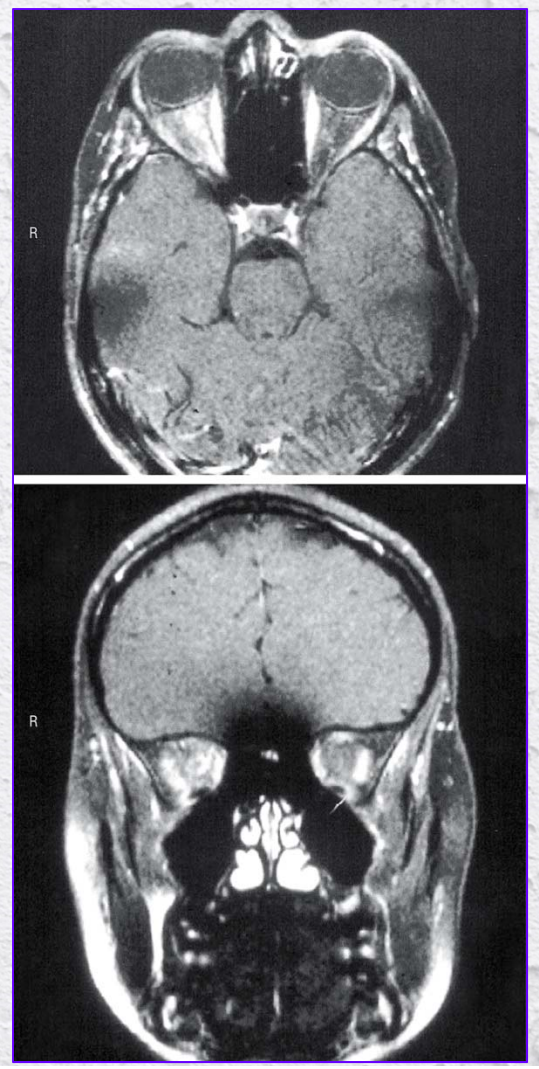
Plan

- **Telephone consult with PCP**
- Advise stat ER consult
- RCT 4 wks

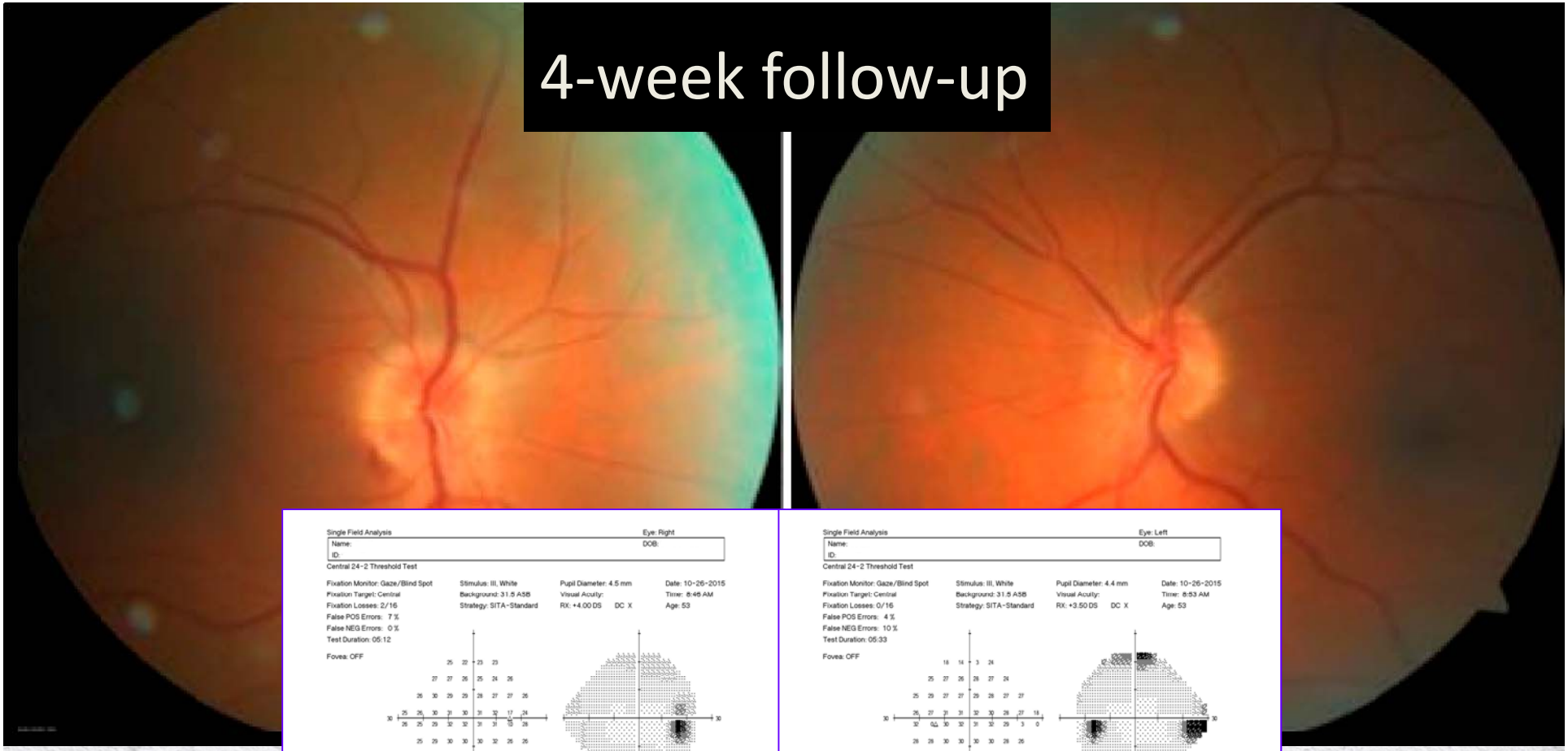
Case Report

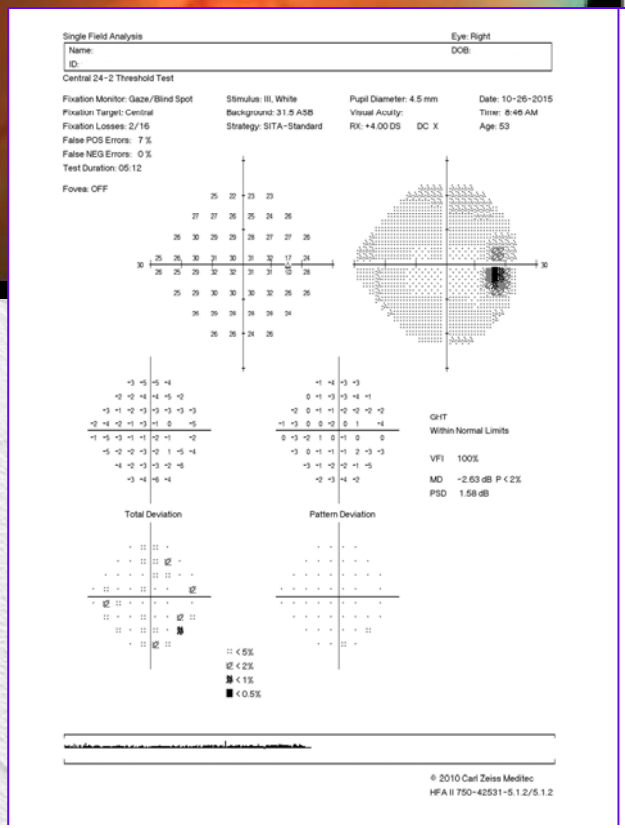
HOSPITAL VISIT

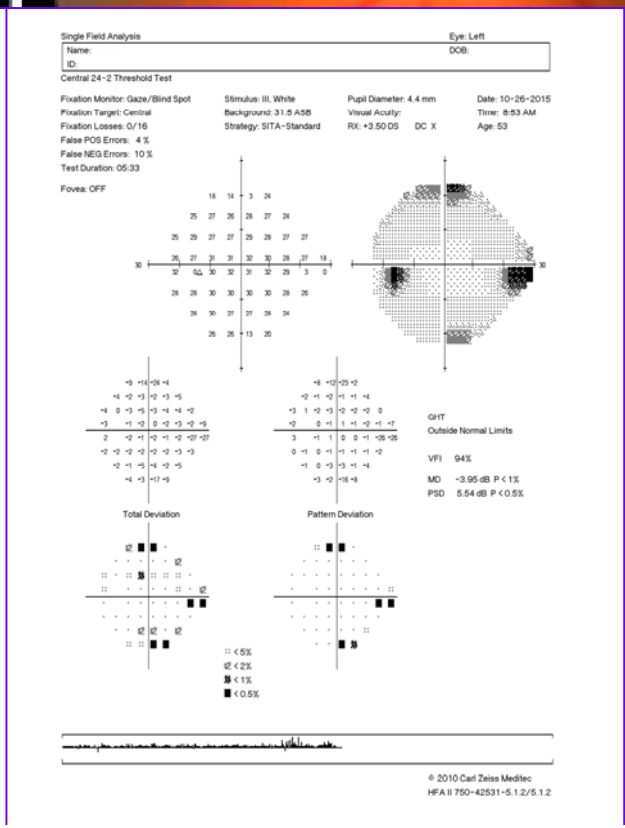
- MRI: Enhancement around right intraorbital optic nerve
- Lumbar puncture: Normal opening pressure, elevated WBC
- Neurology & ophthalmology
- Dx: **Optic perineuritis OD** secondary to syphilis
- Tx: IV Penicillin x 2 weeks



4-week follow-up

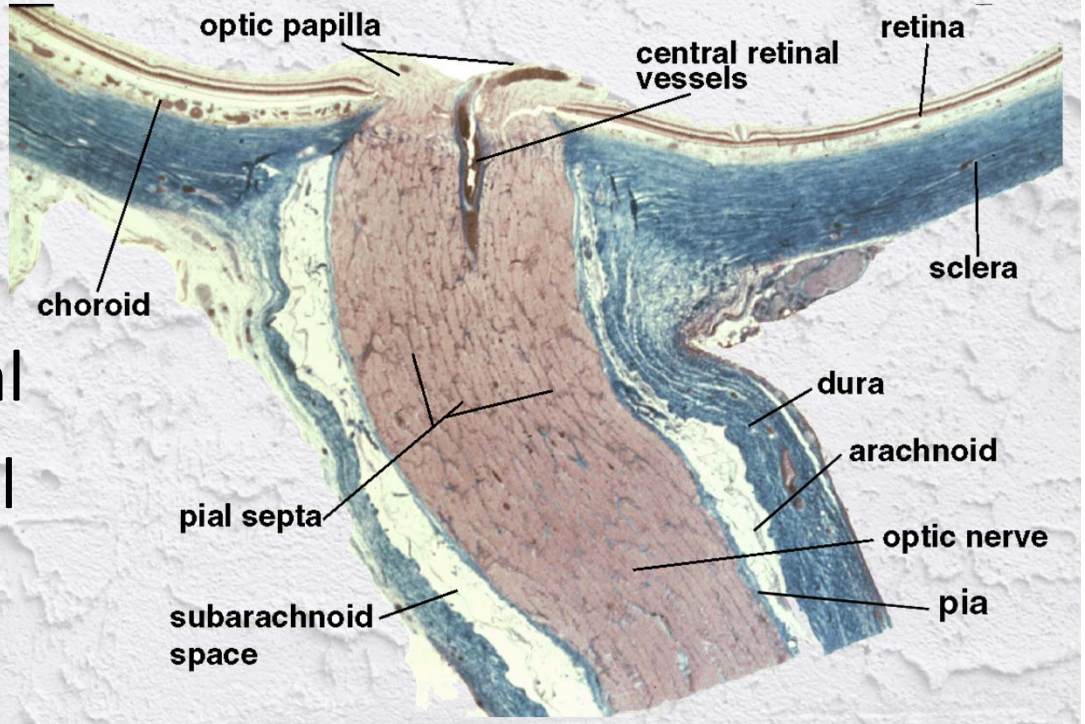






Optic Perineuritis

- A form of orbital inflammatory disease
- Optic nerve sheath is the target tissue
- **Key findings**
  - Optic disc swelling
  - Optic nerve may remain normal
  - Normal intracranial pressure



Optic Perineuritis

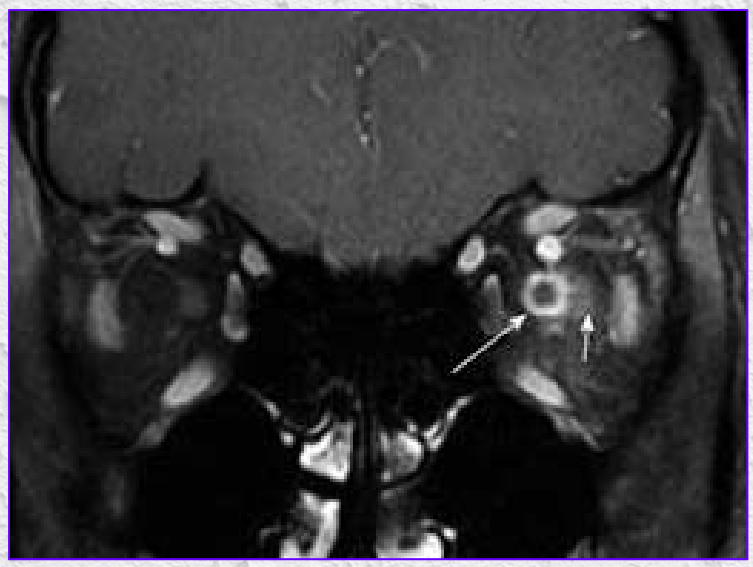
- Primary (Idiopathic, most common)
- Secondary
  - **Syphilis**
  - Sarcoid
  - Giant cell arteritis
  - Meningitis
  - Sinusitis
  - Behcet disease
  - Acute retinal necrosis
  - Wegener granulomatosis
  - Leukemia
  - Crohn disease

Idiopathic Optic Perineuritis

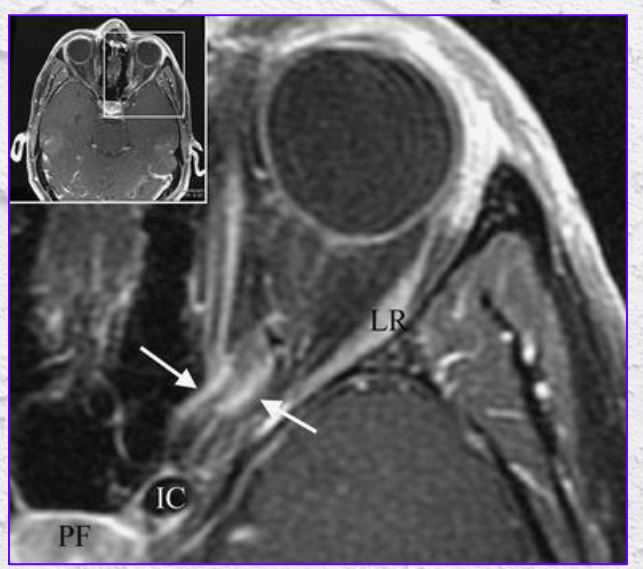
- Epidemiology
  - Mean age: 40 , Women 2x more common
- Clinical Features
  - Usually unilateral, but bilateral not uncommon
  - 50% report pain or painful eye movement
  - Visual sxs: Blur, dimness, spots
  - VA is typically normal, but may worsen
  - Paracentral or arcuate VF defects

Optic Perineuritis

- Diagnosis
  - Clinically resembles optic neuritis if painful
  - **MRI of orbits** (Tram Track and Doughnut signs)



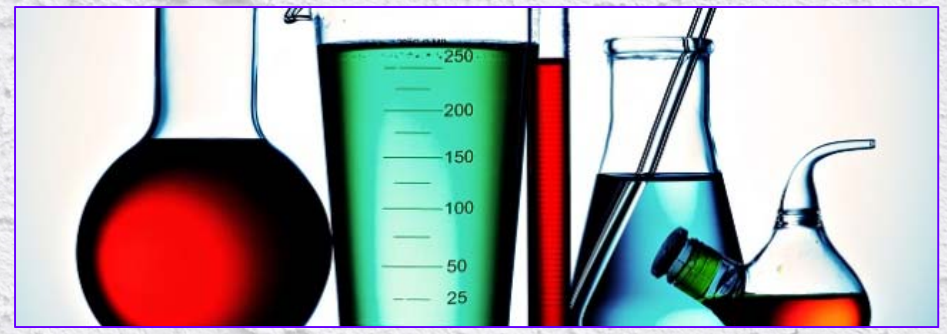
Doughnut sign



Tram Track sign

Optic Perineuritis

- Work-up
  - **MRI (orbits) & Lumbar puncture**
  - Labs (systemic infectious/inflammatory disease)
  - Team approach (rheumatology, neurology, etc)
- Treatment
  - Idiopathic: Steroids
  - Secondary: Address underlying cause



Syphilis + HIV

- **Co-infection is common**
- Most cases involve men
  - 64% of all syphilis cases involve MSM
- Co-infection worsens severity of syphilis
- **Increases risk of CNS involvement**

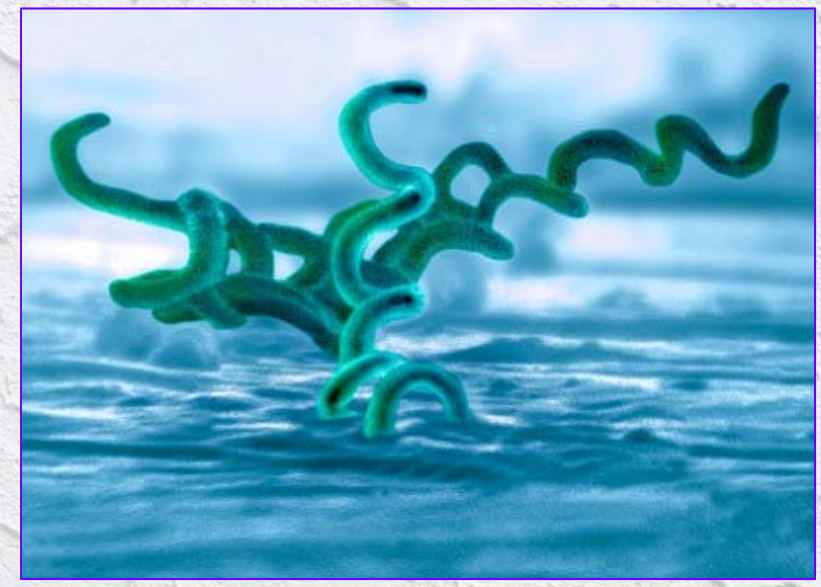
Neurosyphilis

1. Parenchymatous (**rare**)
   - Neurodegeneration
   - Tabes dorsalis and general paresis
2. Meningovascular (**common**)
   - Inflammatory
   - HA, confusion, symptoms of meningeal irritation
   - Acute hydrocephalus, cranial nerve abnormalities

Ocular Neurosyphilis

5% of syphilis cases develop ocular signs (may be higher with HIV co-infection)

- Uveitis (most common)
- Optic neuritis
- Optic perineuritis
- Neuroretinitis
- Papilledema
- Episcleritis



Key Points

- **High index of suspicion** of syphilis in HIV population
- **Urgent MRI and lumbar puncture** in any patient suspected of having papilledema
- **Optic perineuritis** may mimic optic neuritis or papilledema
- **MRI of orbits** is required to diagnose optic perineuritis

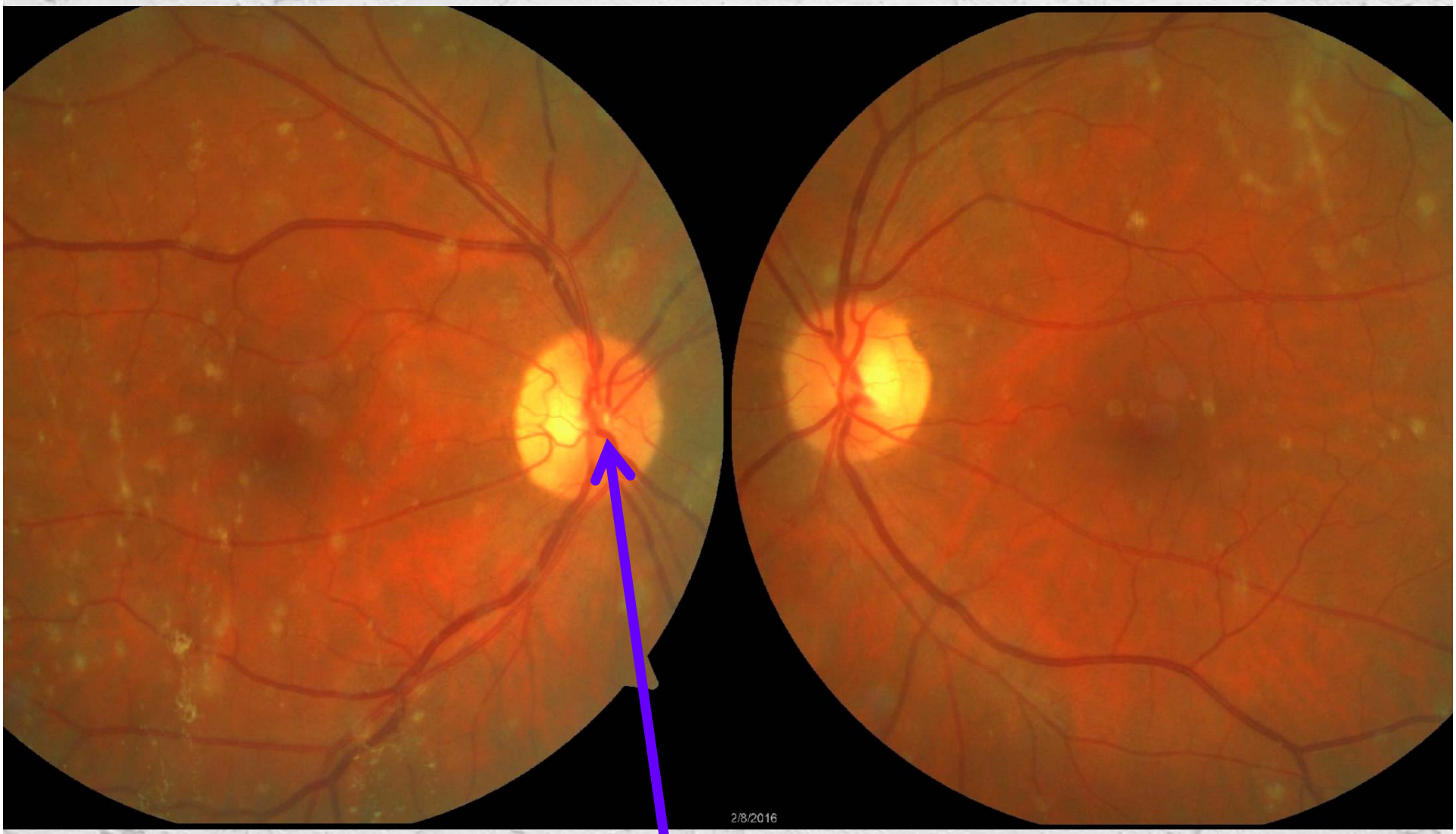
Now You See It, Now You Don't

Case Report

- 71yo WM presents c/o TVL OD
  - Occurred 30 min ago while driving car
  - Lasted several minutes
  - Only affected vision below fixation
  - No pain, headache, or any other associated sxs
- Pt pulled car over to side of road and called our office.
  - Was told to come in immediately

Case Report

- Medical Hx
  - H/O CABG, “stents”, Dyslipidemia, HTN
  - Meds: Plavix, ASA
- POH
  - Episode of transient diplopia 1yr ago
- VA: 20/20- OD, 20/25+ OS
- IOP, Pupils, Color: Normal OU
- External: Normal OU, No cells/flare



Hollenhorst Plaque!

Case Report

- Impression
  - **Amarousis fugax** with Hollenhorst plaque OD
- Plan
  - Urgent consult with patient's cardiologist
  - Recommend carotid duplex scan
  - RCT 4 weeks

4-week follow-up

- Pt was scheduled for **endarterectomy**

Is This TIA, or Something Else?

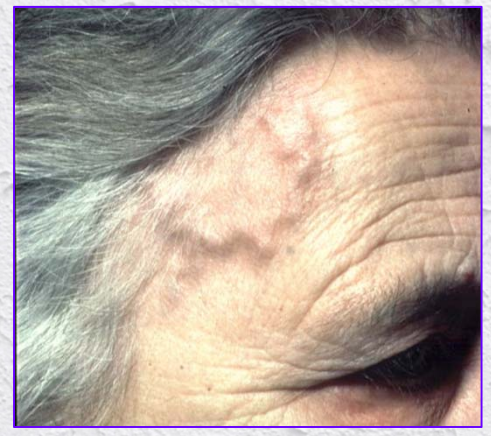
- Monocular vs Binocular
  - Monocular: Carotid artery disease most common
  - Binocular: Migraine most common
- Age
  - <50yo: Migraine most common, collagen-vascular disease possible
  - >50yo: Thromboembolism most common, giant cell arteritis possible

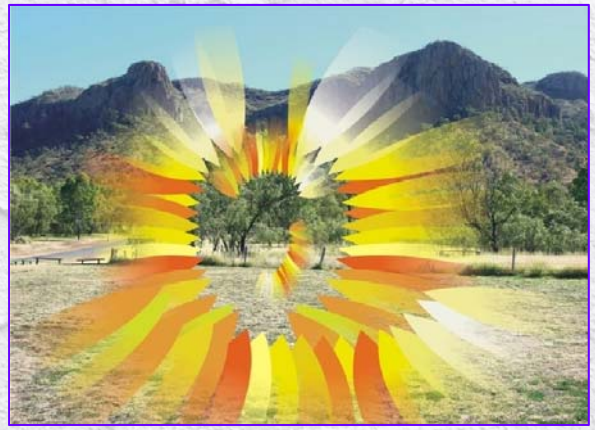
Is This TIA, or Something Else?

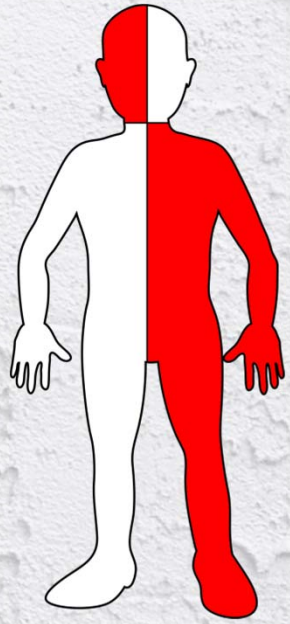
- Duration of loss
  - Seconds: Disc drusen, papilledema
  - <15 min: Embolism
  - >15 min: Migraine
- Pattern of loss & recovery
  - Altitudinal: Embolism, vasospasm
  - Geometric: Migraine (zigzag, migrates across visual field)

Is This TIA, or Something Else?

- Associated symptoms
  - Migraine: Lights, colors, headache
  - Giant cell: Headache, scalp tenderness
  - Hemispheric TIA: Muscle weakness, speech difficulties, loss of consciousness





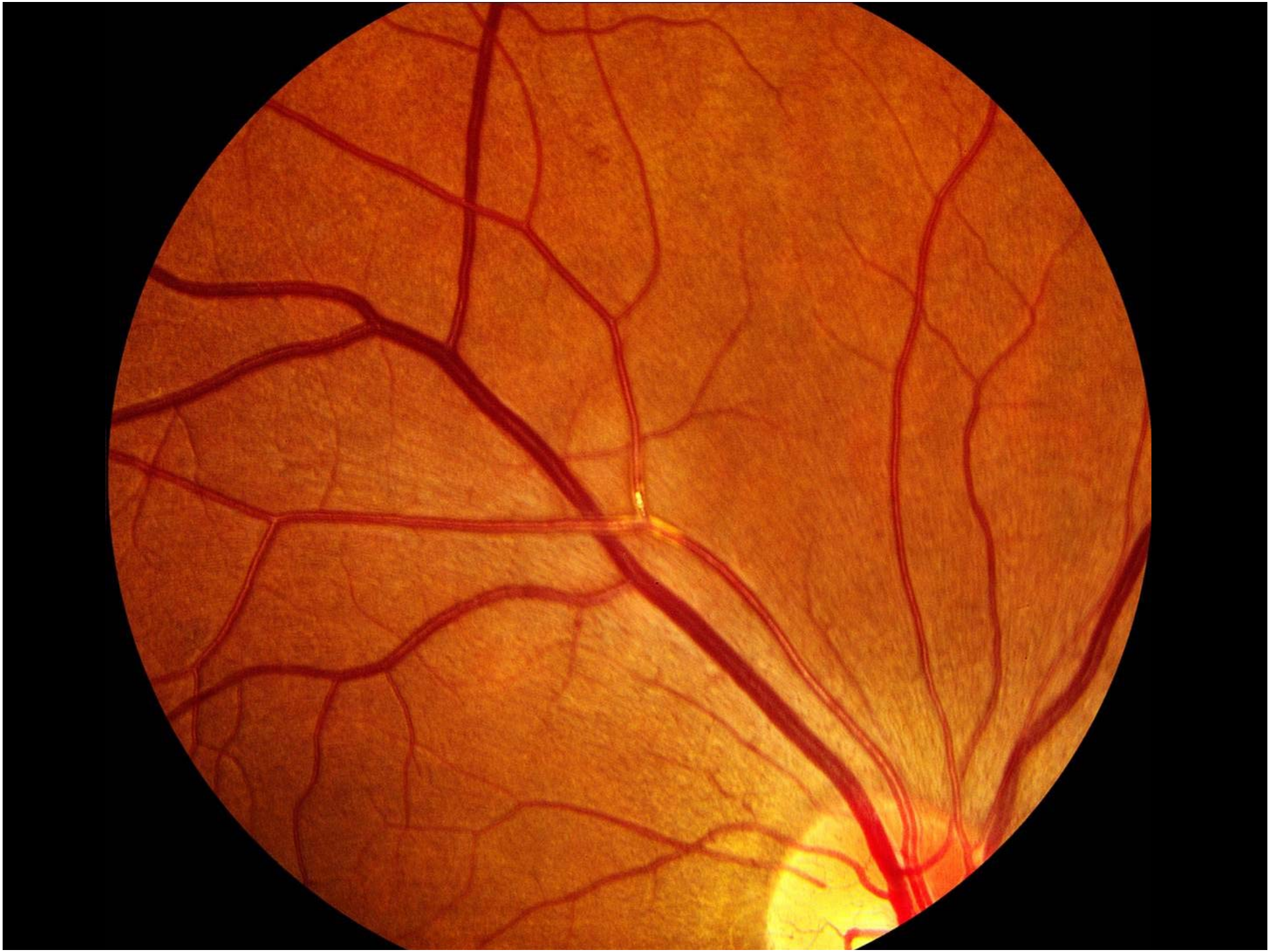


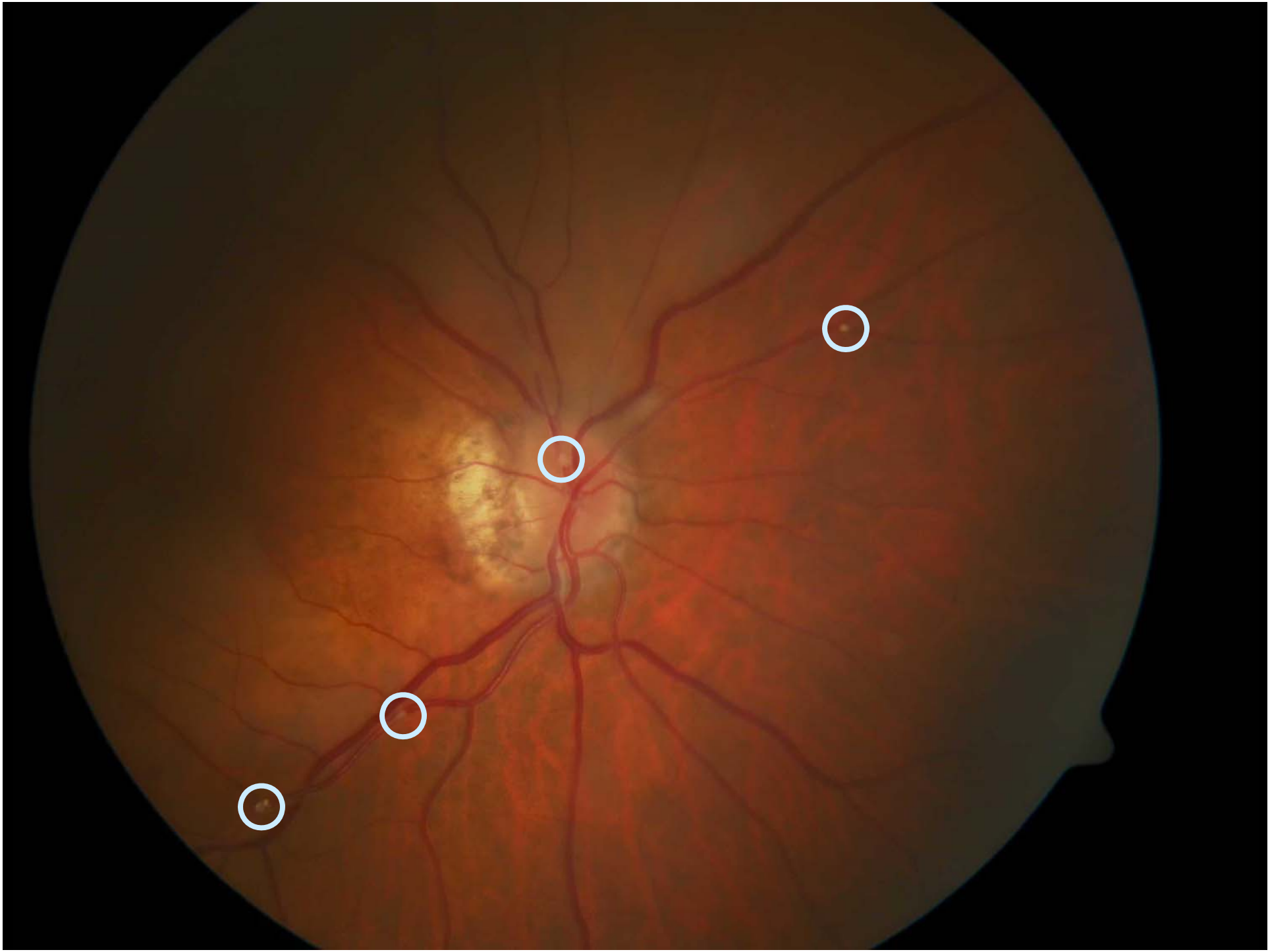
Differential Diagnosis

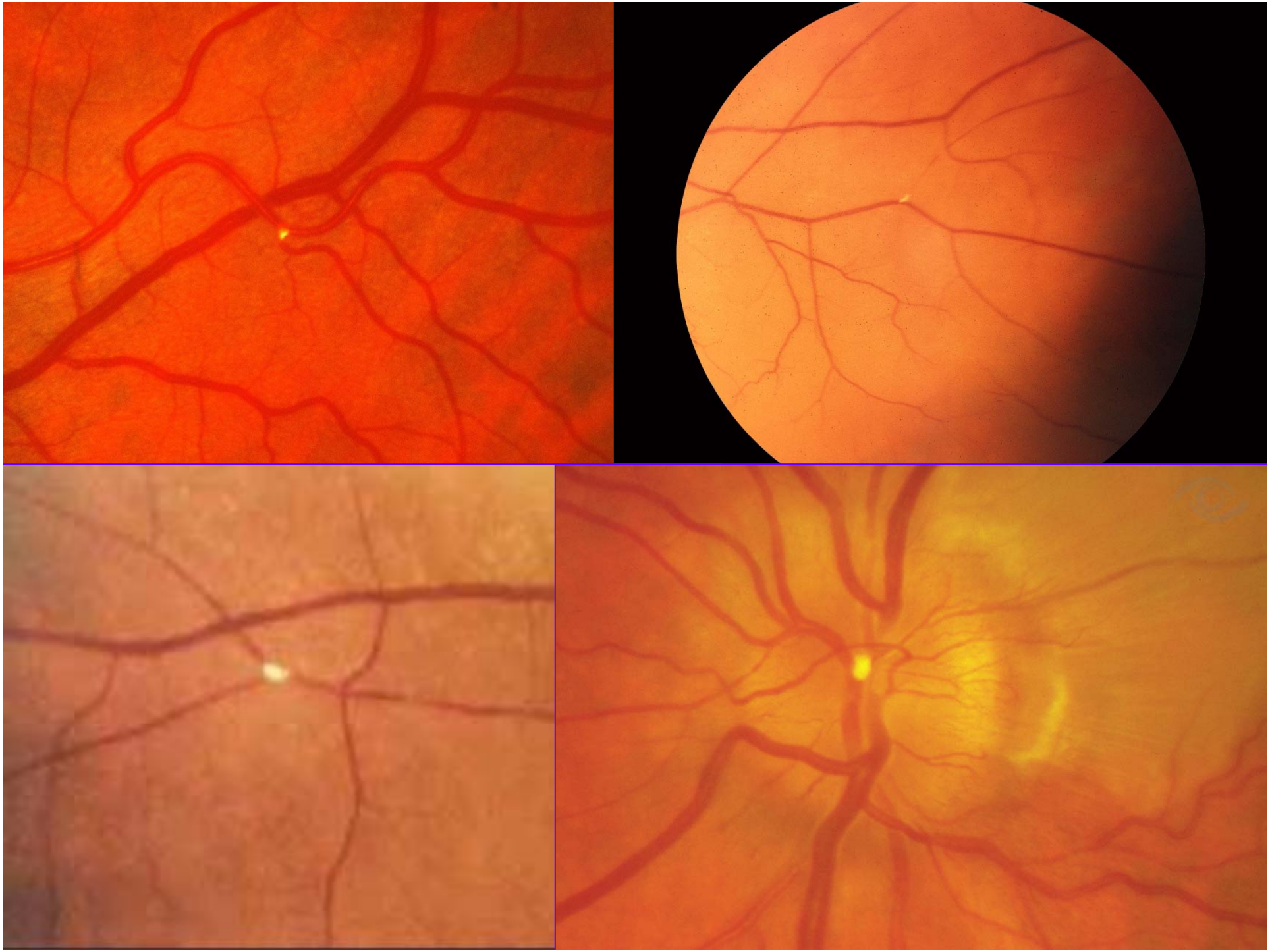
- Vascular
  - **Emboli**, carotid dissection, vasculitis (giant cell), vasospasm, systemic hypotension, hyperviscosity
- Migraine
- Optic nerve
  - Disc drusen, papilledema, demyelination
- Miscellaneous ocular nonvascular
  - Tear film, floaters, subacute ACG

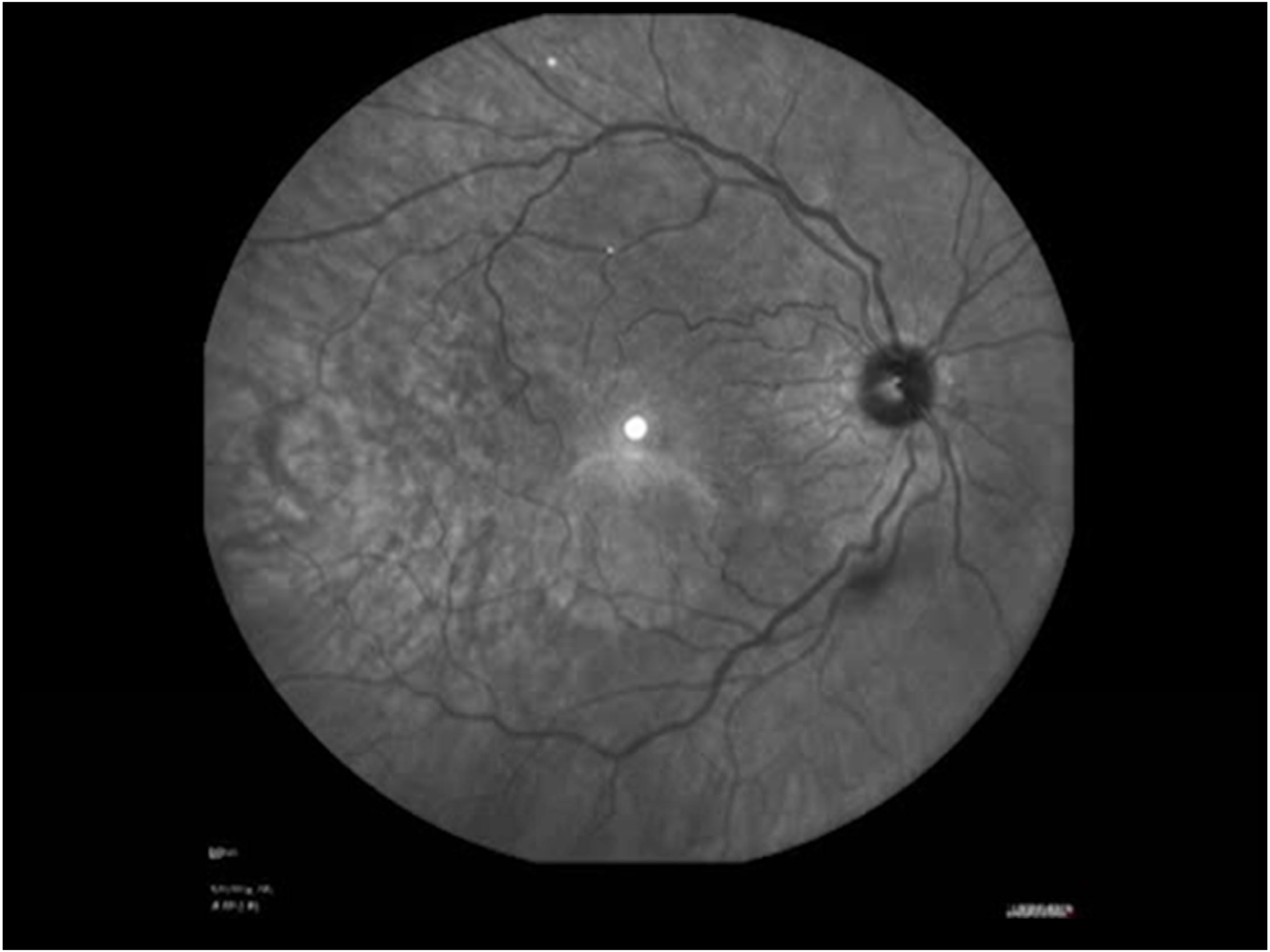
Amaurosis Fugax

- Transient monocular vision loss (TMVL) due to emboli
- **Sudden, painless loss**, typically lasting 10-15 min
- Vision loss may be partial or complete
- **No associated symptoms**
- Ocular exam often normal
- Emboli usually originate in the **carotid artery or heart**









Retinal Emboli

- Absence of visible emboli in setting of TMVL does not decrease risk of carotid disease
- Appearance of embolus (yellow [Hollenhorst], white, refractile) does not predict source
- **Asymptomatic emboli** may have been present for many years prior to discovery, and are poor predictors of significant carotid stenosis

What is the Risk?

- >50% of patients with TMVL have clinically significant carotid stenosis (≥70% stenosis)
- **Highest stroke risk**: men, >75yo, prior h/o hemispheric TIA or CVA, and stenosis >80%
- Treatment options
  - Carotid endarterectomy
  - Carotid stent
  - Medical therapy (anti-platelet, statin, etc)

What is the Risk?

Eur J Vasc Endovasc Surg (2015) 49, 137–144

Risk of Early Recurrent Stroke in Symptomatic Carotid Stenosis

S. Strömberg [a,b,*], A. Nordanstig [c], T. Bentzel [b], K. Österberg [a], G.M.L. Bergström [b]

[a] Department of Vascular Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden

The cumulative risk of stroke following TIA

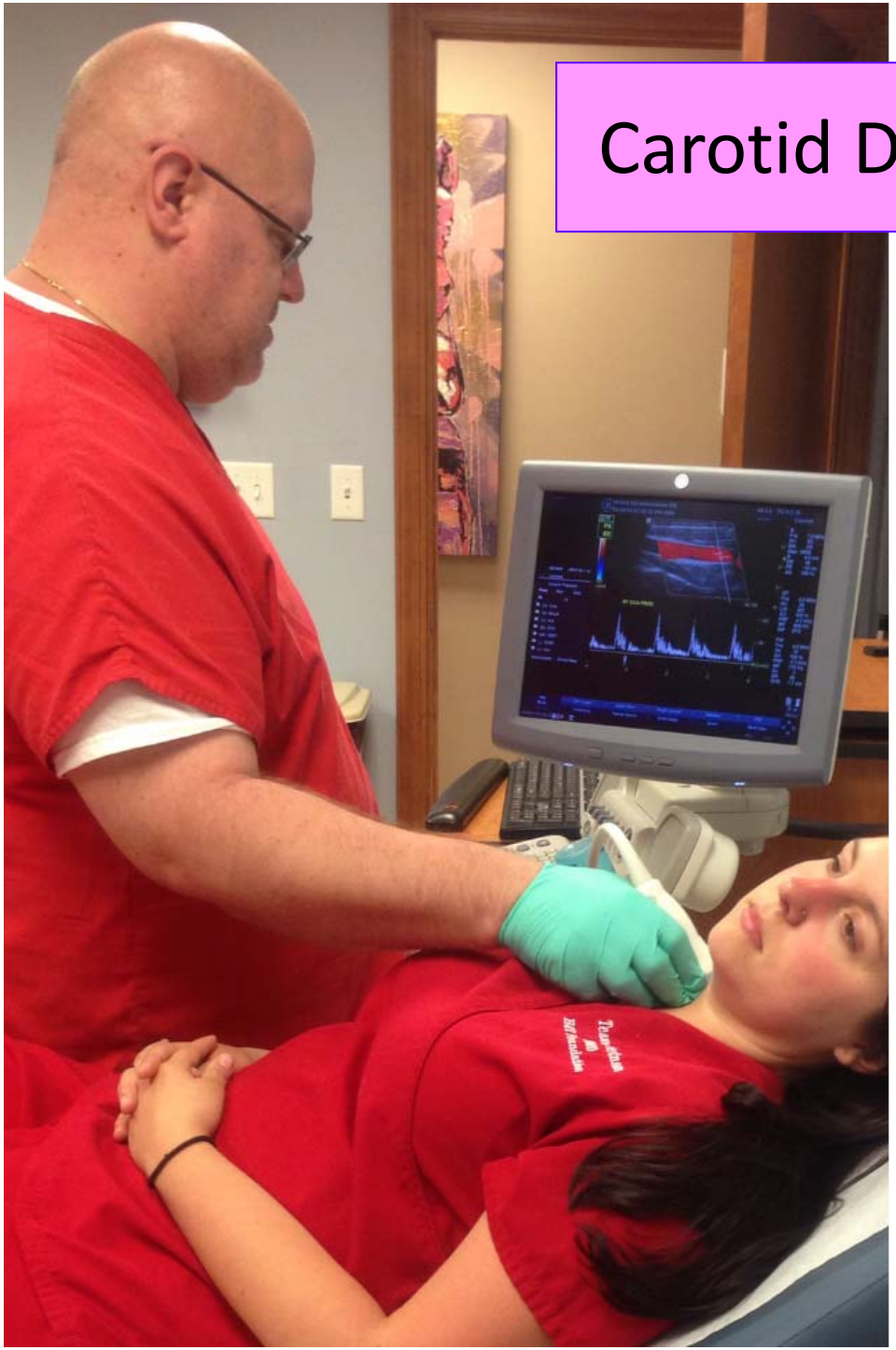
Day 2: 0.7%

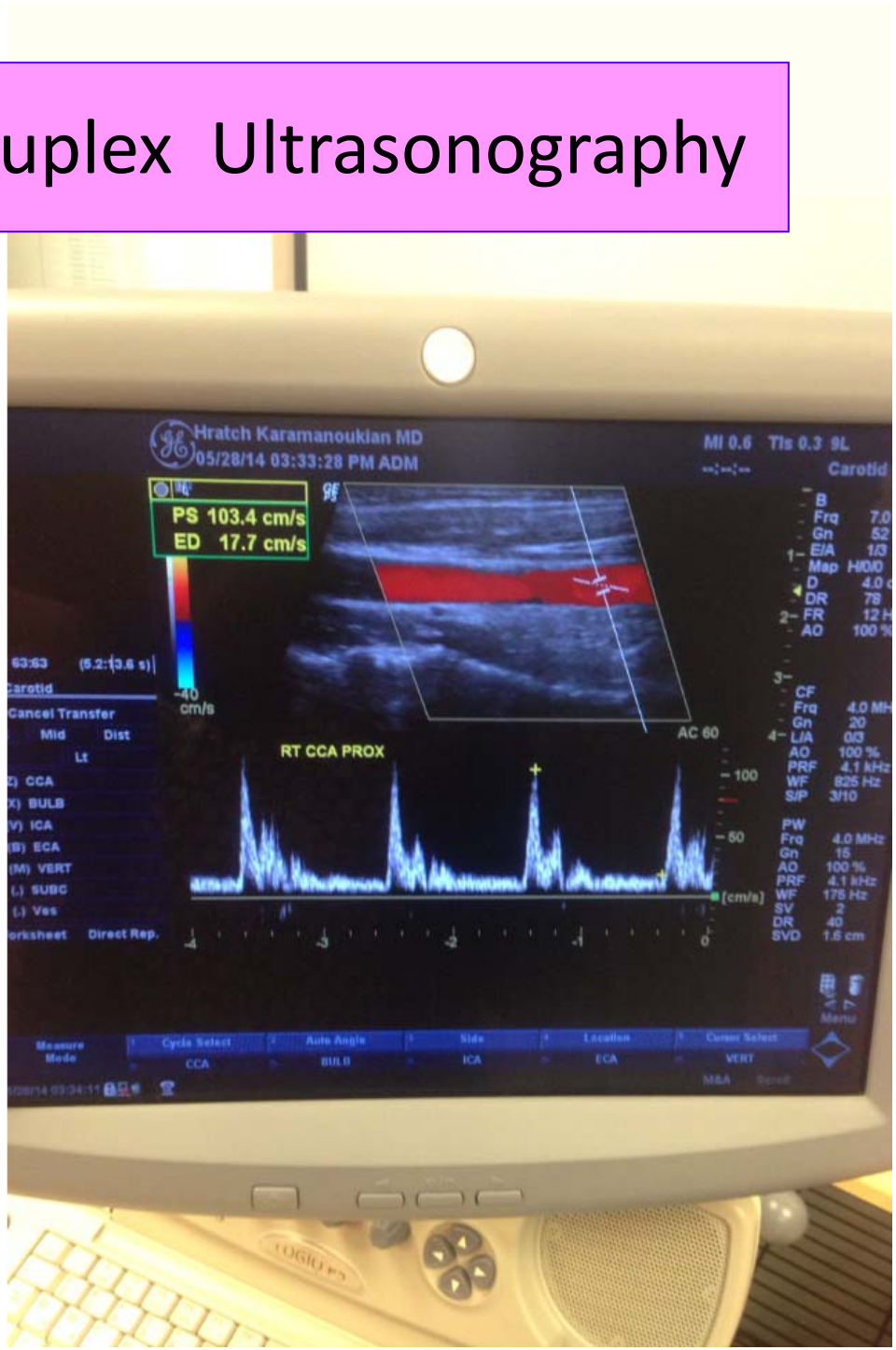
Day 7: 2.3%

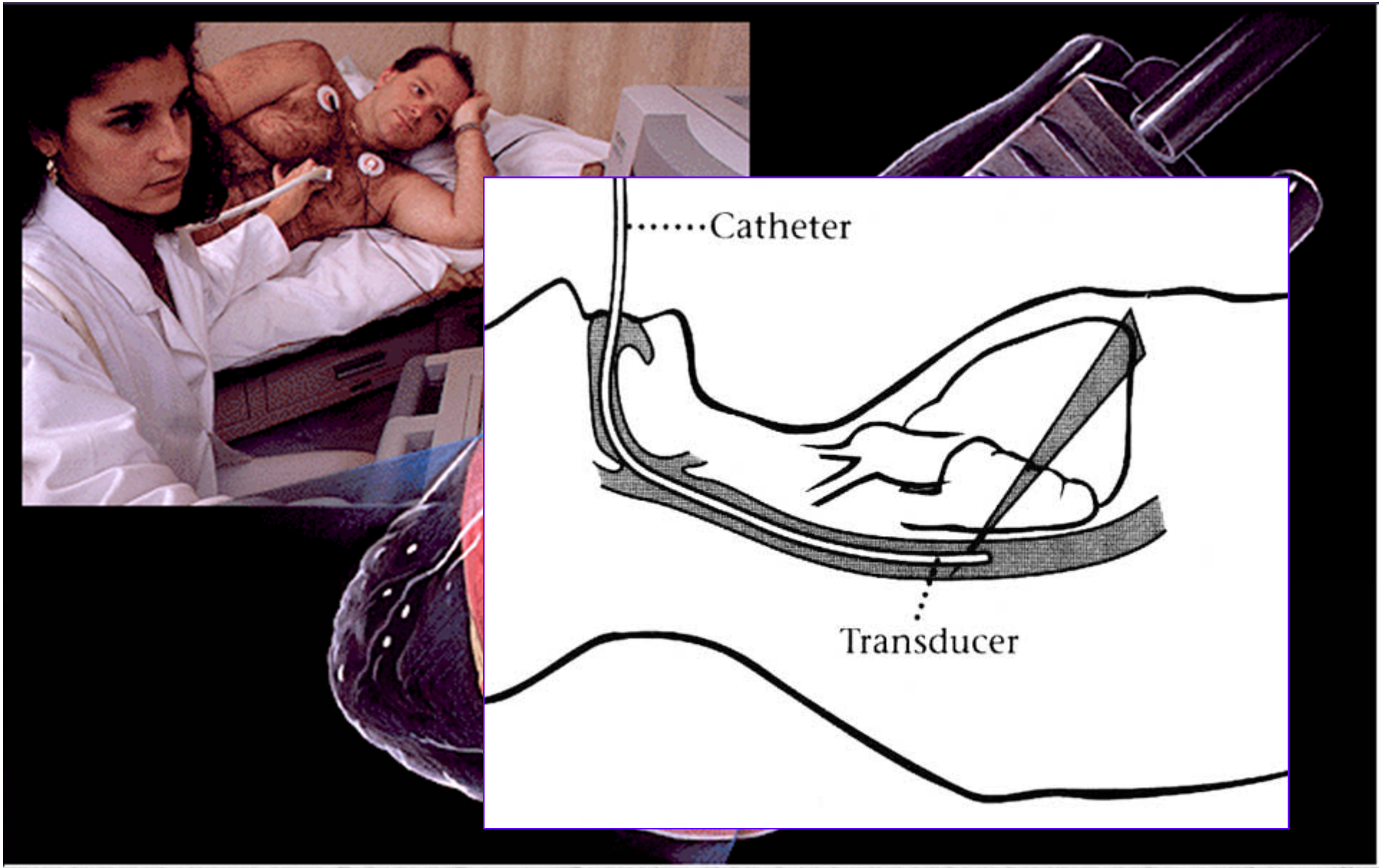
Day 30: 6.8%

weeks after a transient ischemic attack (TIA) or minor stroke and can be reduced with carotid endarterectomy

Carotid Duplex Ultrasonography







Echocardiogram

Management

- Asymptomatic emboli
  - Report to PCP
  - Patient instructed to seek medical follow-up
- **Transient monocular vision loss (>50yo)**
  - Urgent carotid duplex scan and medical evaluation
  - R/O giant cell if clinical picture warrants
- Transient monocular vision loss (<50yo)
  - Report to PCP
  - Patient instructed to seek medical follow-up

Key Points

- **Careful history** and exam needed to differentiate amaurosis fugax from other causes of TVL
- **Urgent carotid duplex scan** indicated for TMVL in patients >50yo
- Monitor **asymptomatic emboli**
- **Co-manage** all patients with TVL with their PCP

Plaquenil Screening Today

AMERICAN ACADEMY™
OF OPHTHALMOLOGY

American Academy of Ophthalmology Statement

Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)

Michael F. Marmor, MD,[1] Ulrich Kellner, MD,[2] Timothy Y.Y. Lai, MD, FRCOphth,[3] Ronald B. Melles, MD,[4] William F. Mieler, MD,[5] for the American Academy of Ophthalmology

Background: The American Academy of Ophthalmology recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy are revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools.

Pattern of Retinopathy: Although the locus of toxic damage is parafoveal in many eyes, Asian patients often show an extramacular pattern of damage.

Dose: We recommend a maximum daily HCQ use of $\leq$5.0 mg/kg real weight, which correlates better with risk than ideal weight. There are no similar demographic data for CQ, but dose comparisons in older literature suggest using $\leq$2.3 mg/kg real weight.

Risk of Toxicity: The risk of toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years. However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.

Major Risk Factors: High dose and long duration of use are the most significant risks. Other major factors are concomitant renal disease, or use of tamoxifen.

Ophthalmology. 2016 Mar 16. [Epub ahead of print]

Table 3. Clinical Examination Techniques

Recommended Screening Tests

1. Primary tests: ideally do both
   - Automated visual fields (appropriate to race)
   - SD OCT
2. Other objective tests (as needed or available):
   - mfERG
   - FAF
3. Newer tests of possible value in future
   - Microperimetry
   - Adaptive optics retinal imaging

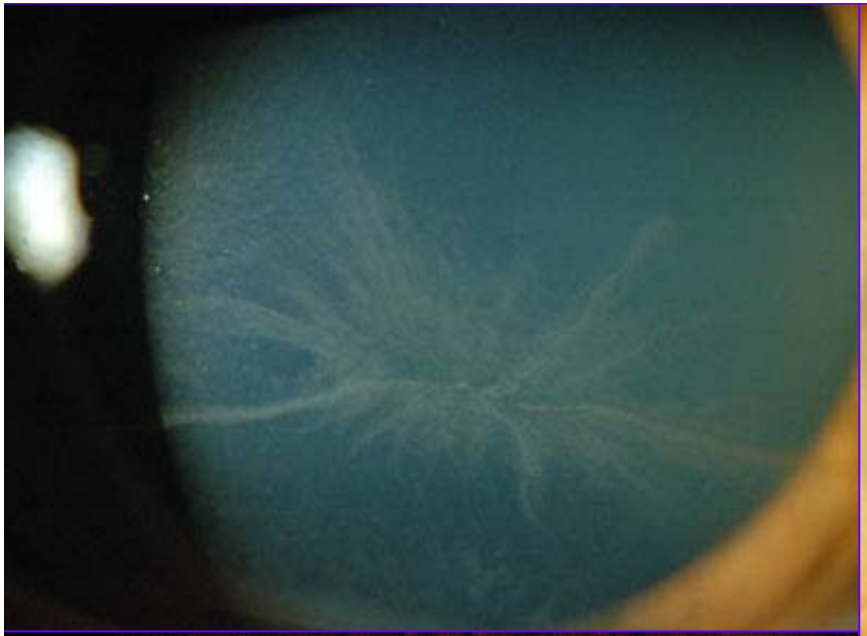
Not Recommended for Screening

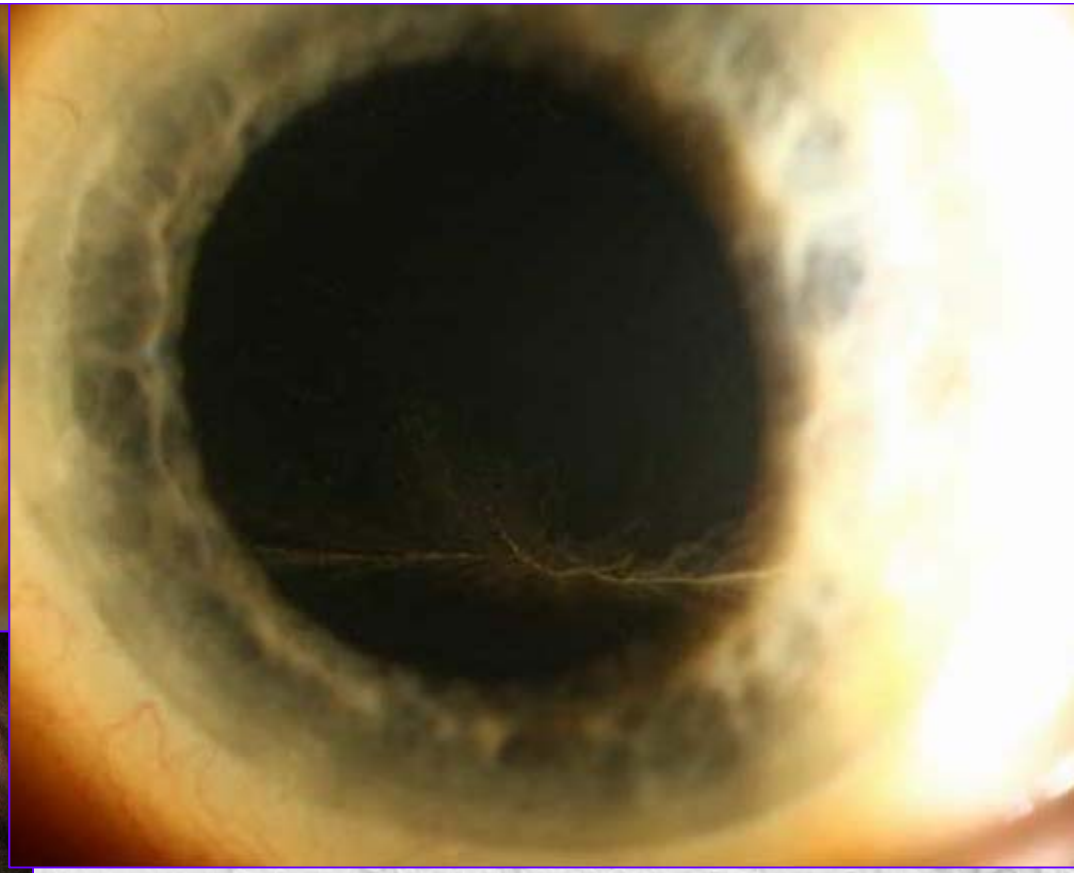
- Fundus examination
- Time-domain OCT
- Fluorescein angiography
- Full-field ERG
- Amsler grid
- Color testing
- EOG

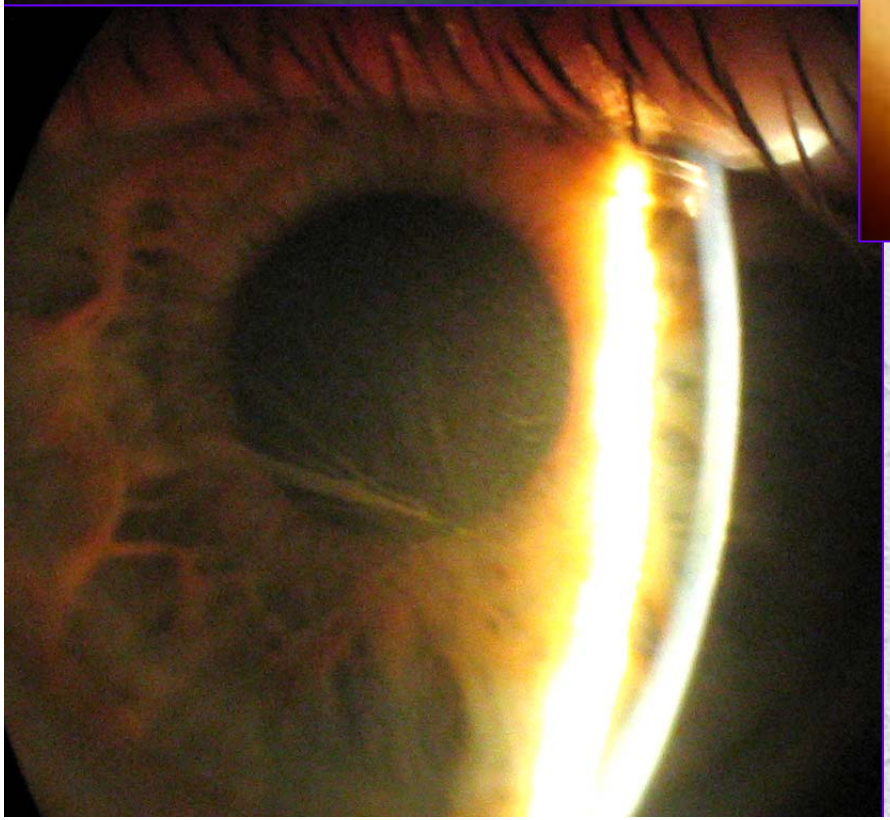
EOG = electro-oculogram; ERG = electroretinogram; FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; SD OCT = spectral-domain optical coherence tomography.

Chloroquine

- Antiparasitic and immunosuppressant
- Widely used to treat malaria, rheumatic disease, and lupus
- Mechanism of action unclear
- Very toxic to the CNS, eyes, ears, GI, and blood
- Chloroquine (CQ) use has been largely replaced by less toxic analog hydroxychloroquine (HCQ, **Plaquenil**)







Examples of corneal verticellata (“whorls”) which may be caused by CQ, HCQ, and amiodarone

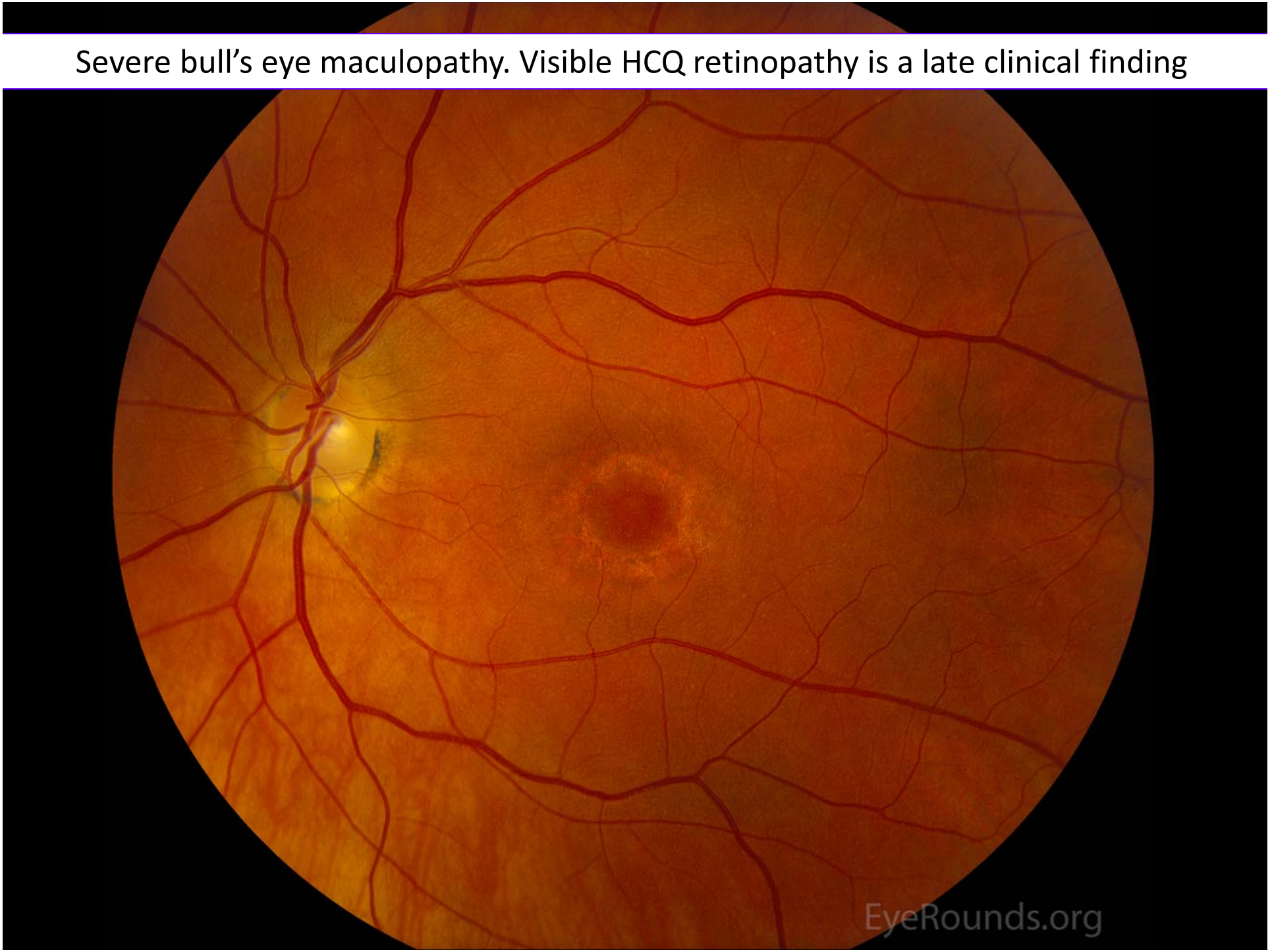
Chloroquine Retinopathy

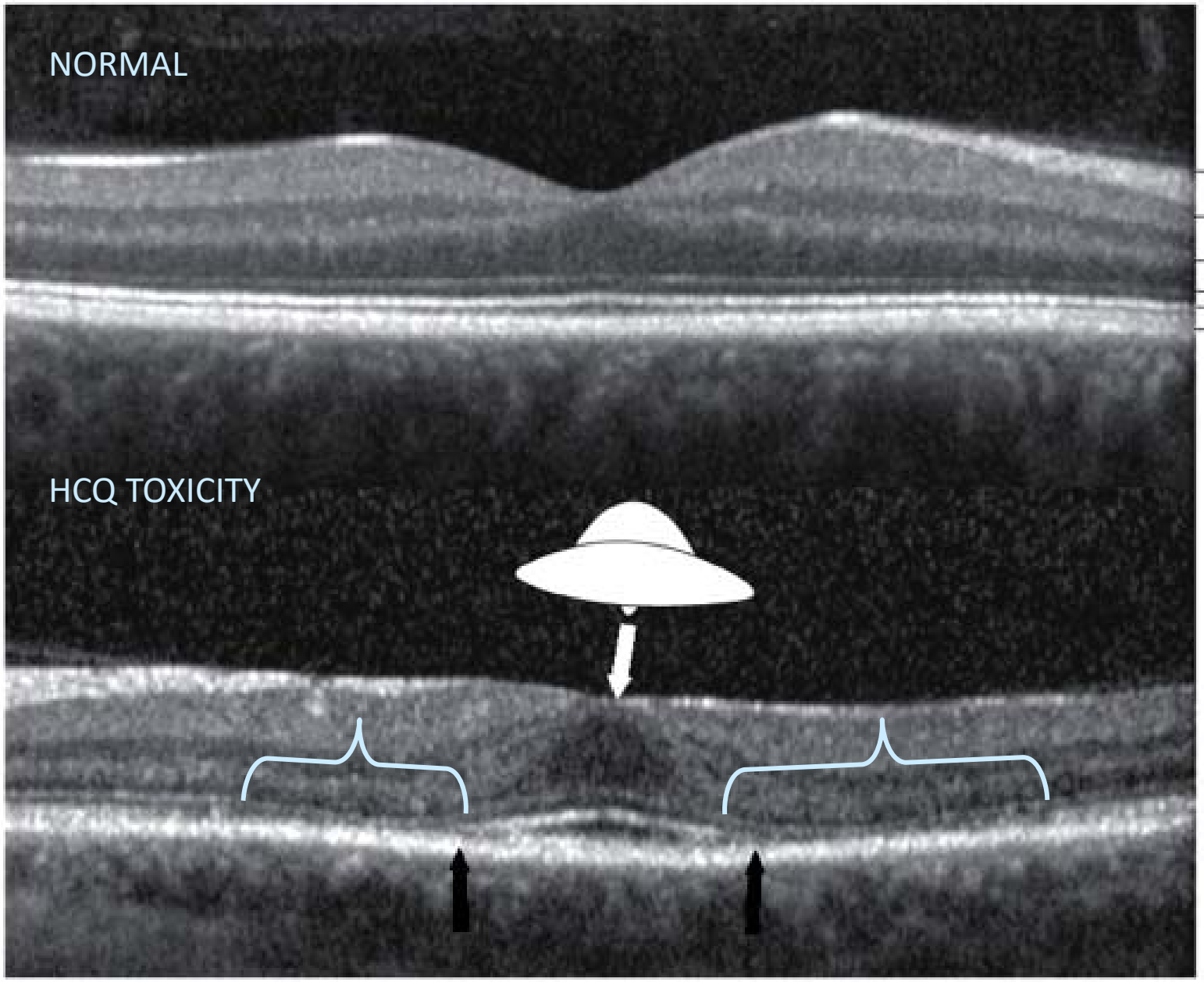
- Both CQ and HCQ bind to melanin and will concentrate within the RPE
- The drugs trigger **RPE atrophy and migration**
- There is also evidence of direct damage to ganglion cells and photoreceptors
- The reason for the **bull's eye pattern** is unknown

Chloroquine Retinopathy

- **Ophthalmoscopic**
  - Bilateral atrophic bull's eye pattern maculopathy
- **Morphologic**
  - OCT: Perifoveal IS/OS junction loss and thinning
  - FAF: Bull's eye pattern of hyper/hypofluorescence
- **Functional**
  - 10-2 Visual field: Paracentral scotomas
  - mfERG: Decreased amplitude in affected areas

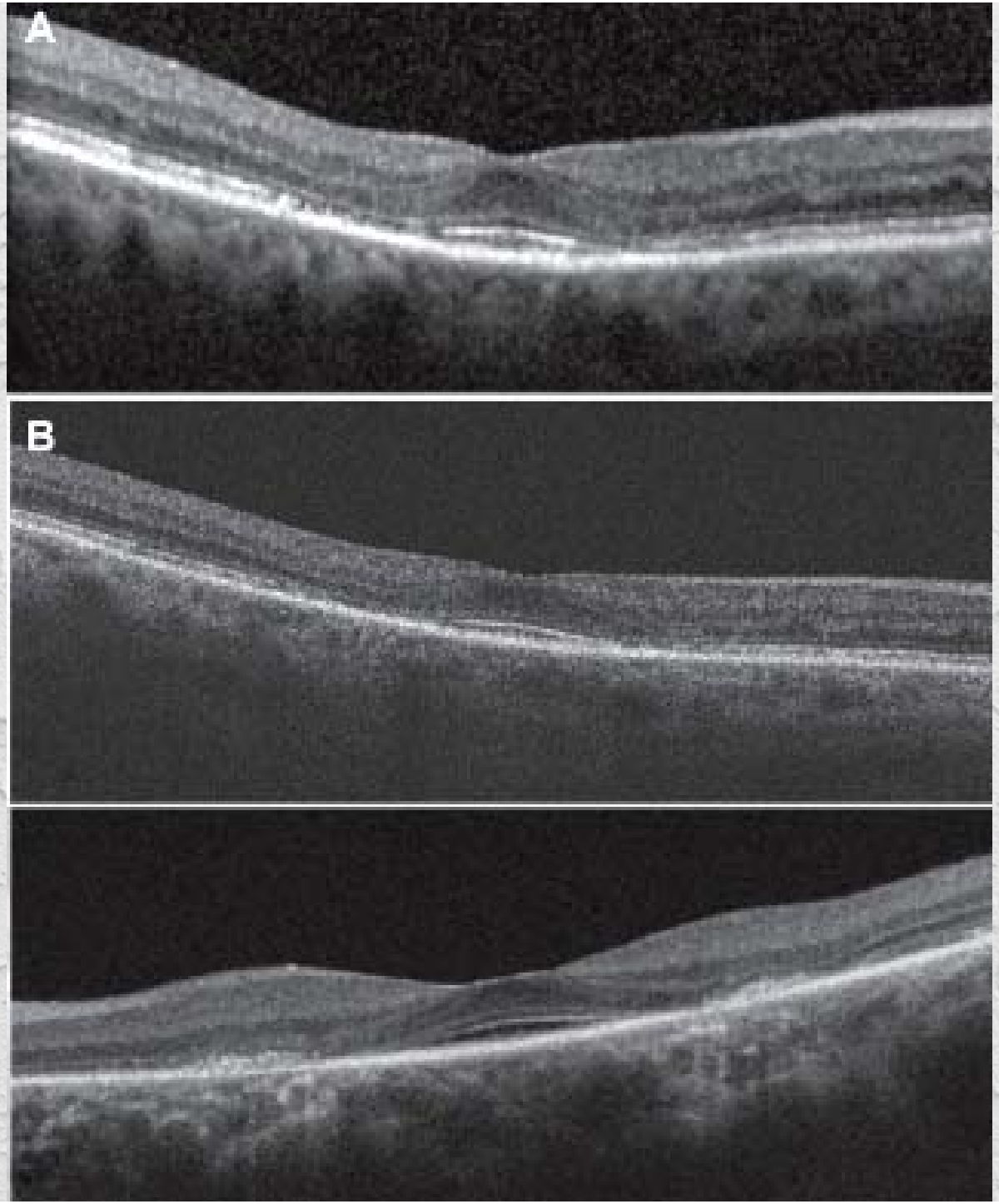
Severe bull’s eye maculopathy. Visible HCQ retinopathy is a late clinical finding





There is loss of the IS/OS junction (ellipsoid zone) in a concentric ring surrounding the fovea

Flying saucer sign of plaquenil toxicity on OCT



Examples of flying saucer sign in patients with plaquenil retinopathy

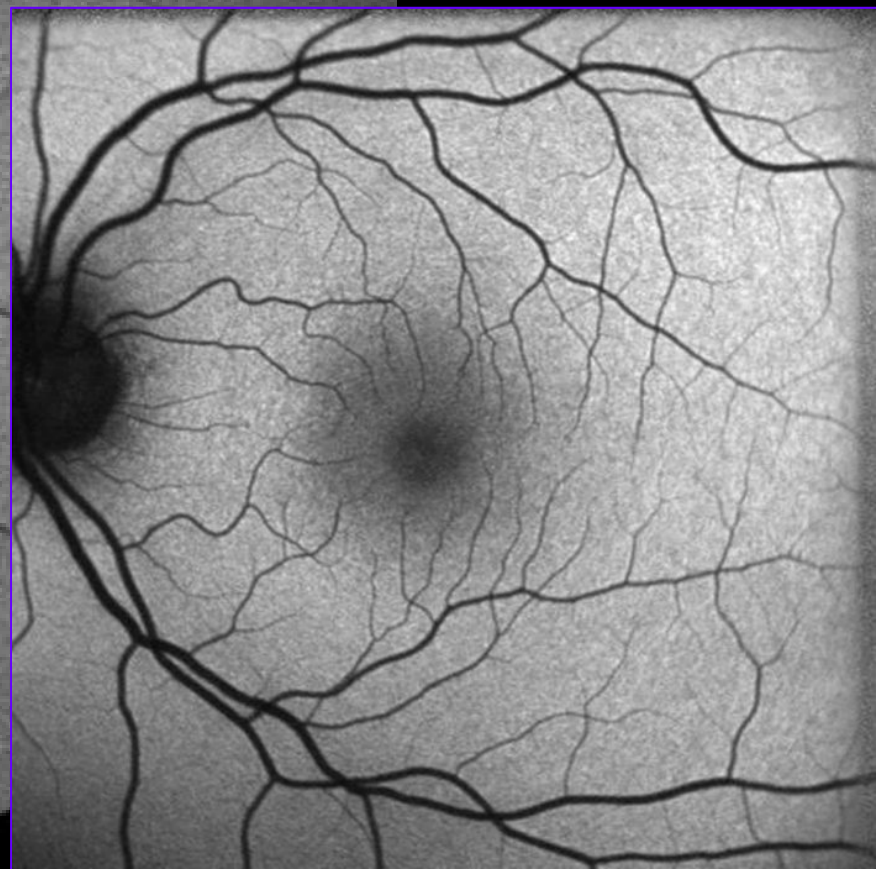
Note in each case the presence of a gap in the IS/OS junction line on either side of the fovea

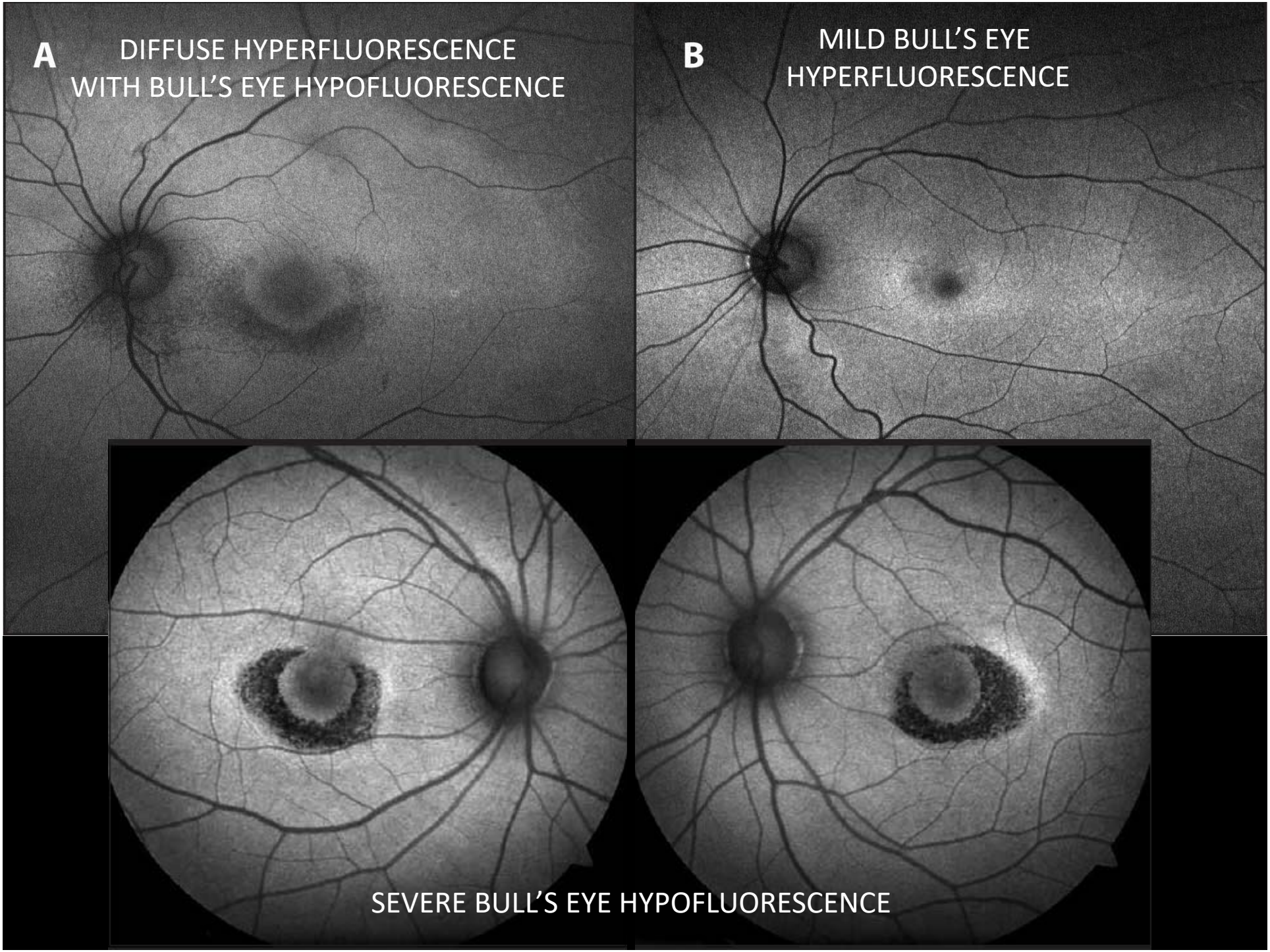
Normal

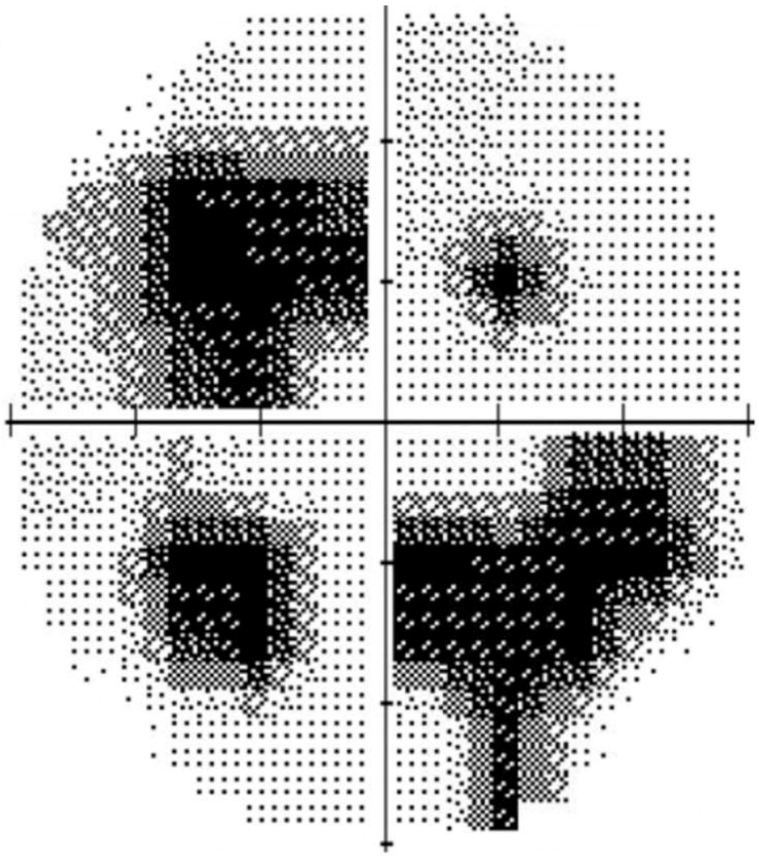
Fundus Autofluorescence (FAF)

Gradual darkening of macula as fovea is approached

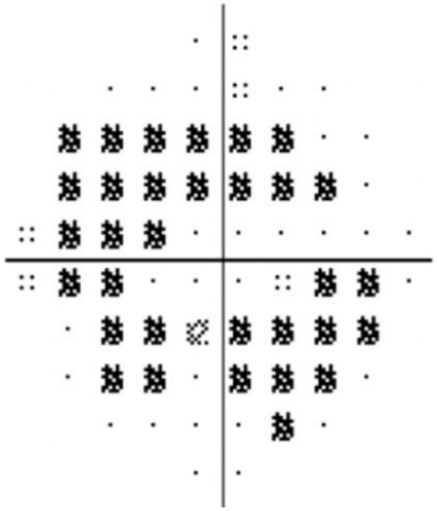
Uniform gray background

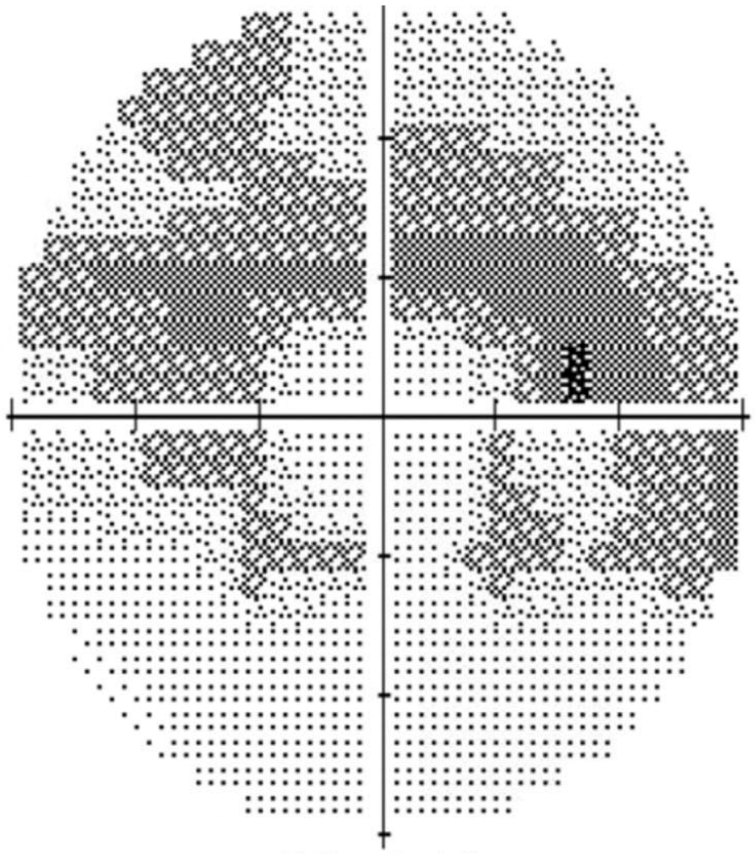



A
DIFFUSE HYPERFLUORESCENCE
WITH BULL'S EYE HYPOFLUORESCENCE
B
MILD BULL'S EYE
HYPERFLUORESCENCE
SEVERE BULL'S EYE HYPOFLUORESCENCE

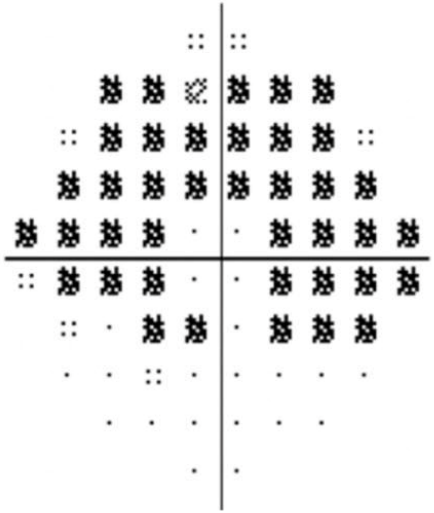


Pattern Deviation





Pattern Deviation



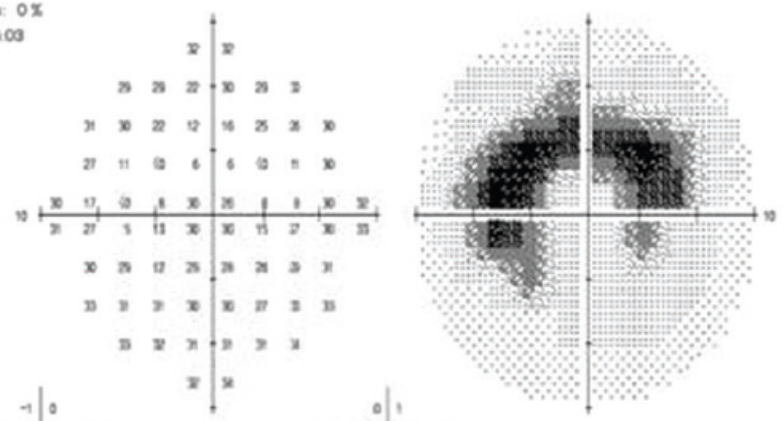
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 2/17
False POS Errors: 5 %
False NEG Errors: 0 %
Test Duration: 06:03

Fovea: 35 dB

Stimulus: III, White
Background: 315 ASB
Strategy: SITA-Fast

Pupil Diameter:
Visual Acuity:
RX: +0.00 DS +1.25 DC X 78

Date: 06-11-2014
Time: 3:06 PM
Age: 29



Total Deviation

Pattern Deviation

MD -11.03 dB P < 1%
PSD 11.19 dB P < 1%

:: < 5%
Ø < 2%
▒ < 1%

DEAN MCGEE

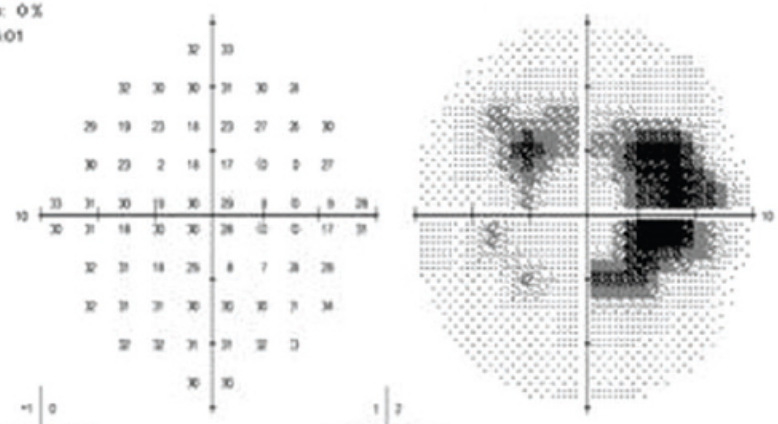
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 1/17
False POS Errors: 1 %
False NEG Errors: 0 %
Test Duration: 06:01

Fovea: 35 dB

Stimulus: III, White
Background: 315 ASB
Strategy: SITA-Fast

Pupil Diameter:
Visual Acuity:
RX: +0.00 DS DC X

Date: 06-11-2014
Time: 3:15 PM
Age: 29



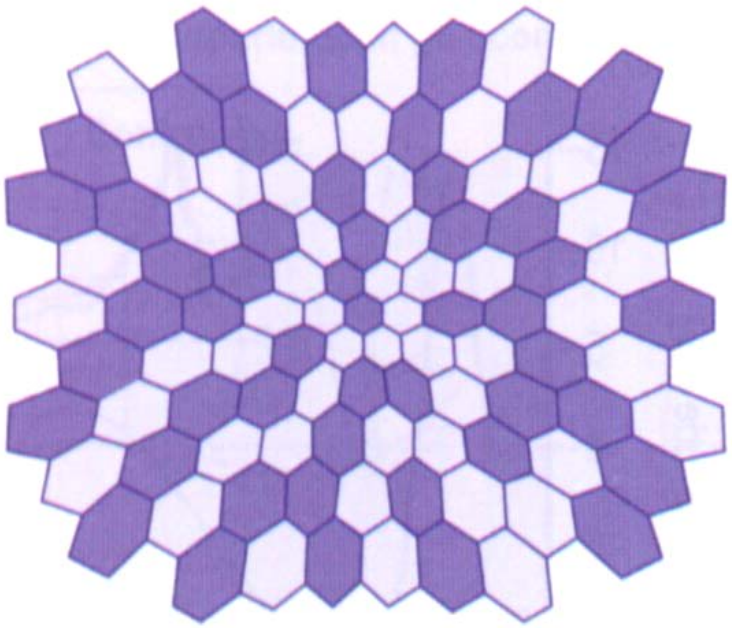
Total Deviation

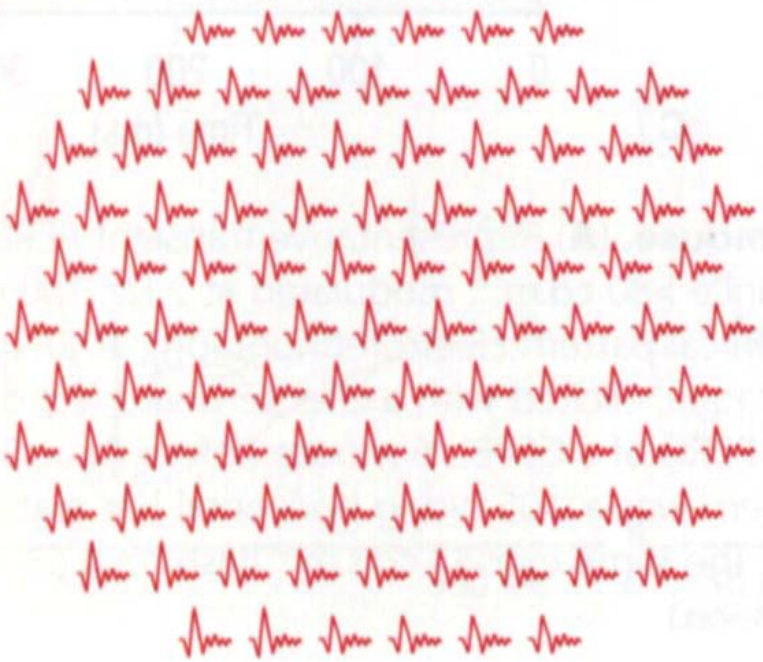
Pattern Deviation

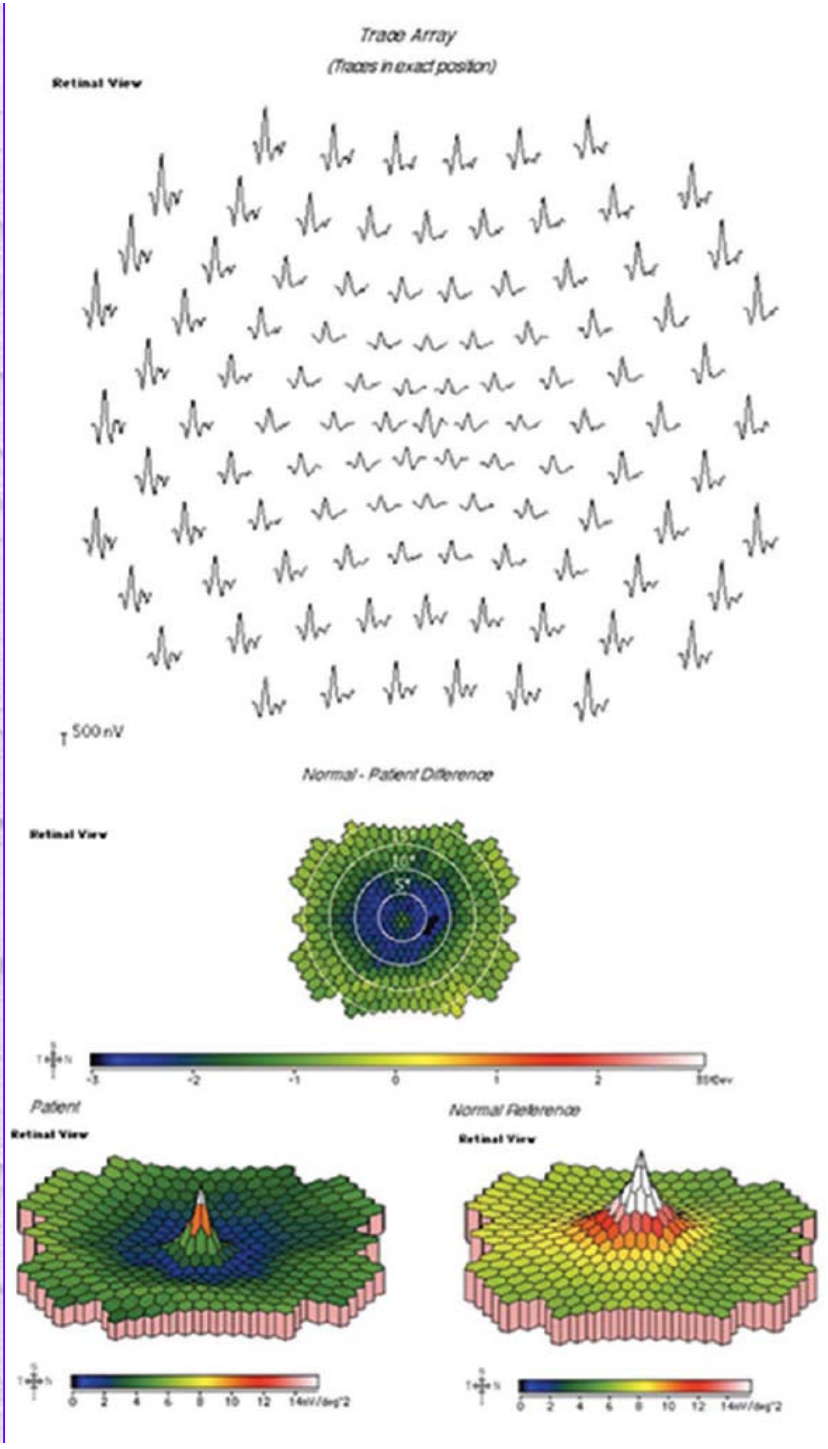
MD -10.99 dB P < 1%
PSD 11.53 dB P < 1%

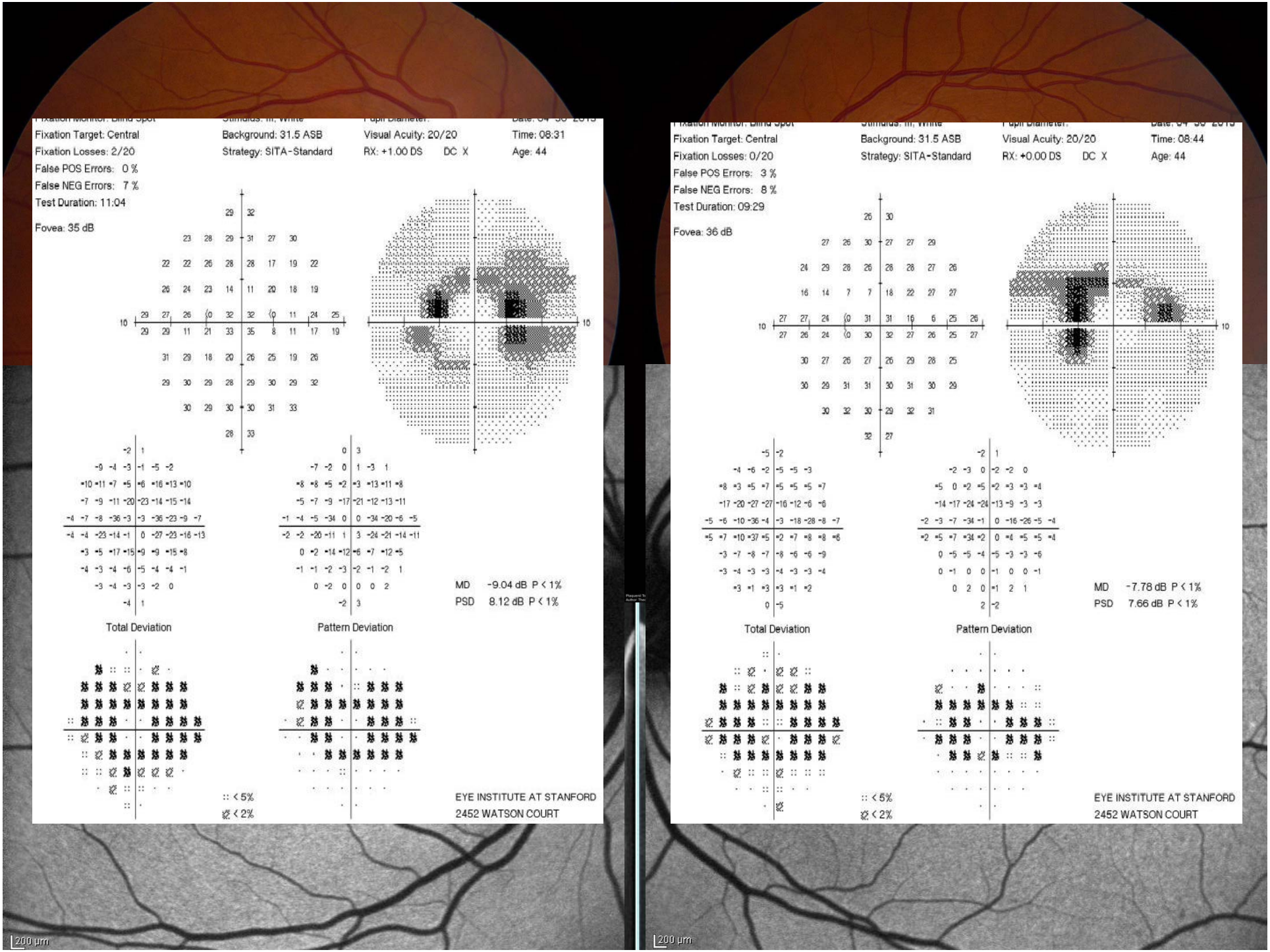
:: < 5%
Ø < 2%
▒ < 1%

DEAN MCGEE






Trace Array
(Traces in exact position)
Retinal View
500 nV
Normal - Patient Difference
Retinal View
10°
5°
Patient
Normal Reference
Retinal View
Retinal View
0 2 4 6 8 10 12 14dB/deg^2
0 2 4 6 8 10 12 14dB/deg^2

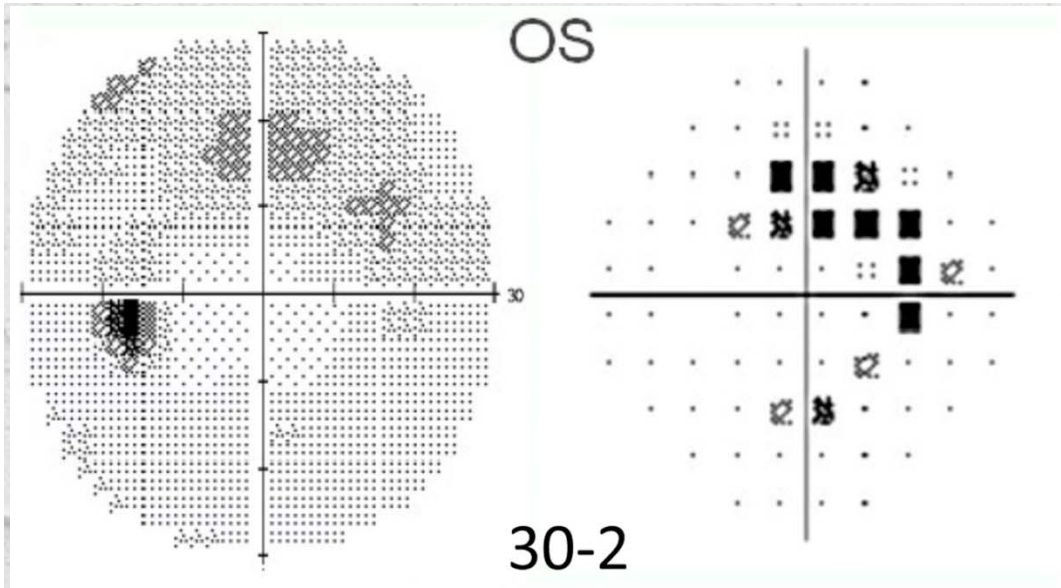

Fixation Target: Central
Fixation Losses: 2/20
False POS Errors: 0 %
False NEG Errors: 7 %
Test Duration: 11:04
Fovea: 35 dB
Background: 31.5 ASB
Strategy: SITA-Standard
Visual Acuity: 20/20
RX: +1.00 DS DC X
Time: 08:31
Age: 44
MD -9.04 dB P < 1%
PSD 8.12 dB P < 1%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
EYE INSTITUTE AT STANFORD
2452 WATSON COURT
200 µm
Fixation Target: Central
Fixation Losses: 0/20
False POS Errors: 3 %
False NEG Errors: 8 %
Test Duration: 09:29
Fovea: 36 dB
Background: 31.5 ASB
Strategy: SITA-Standard
Visual Acuity: 20/20
RX: +0.00 DS DC X
Time: 08:44
Age: 44
MD -7.78 dB P < 1%
PSD 7.66 dB P < 1%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
EYE INSTITUTE AT STANFORD
2452 WATSON COURT
200 µm

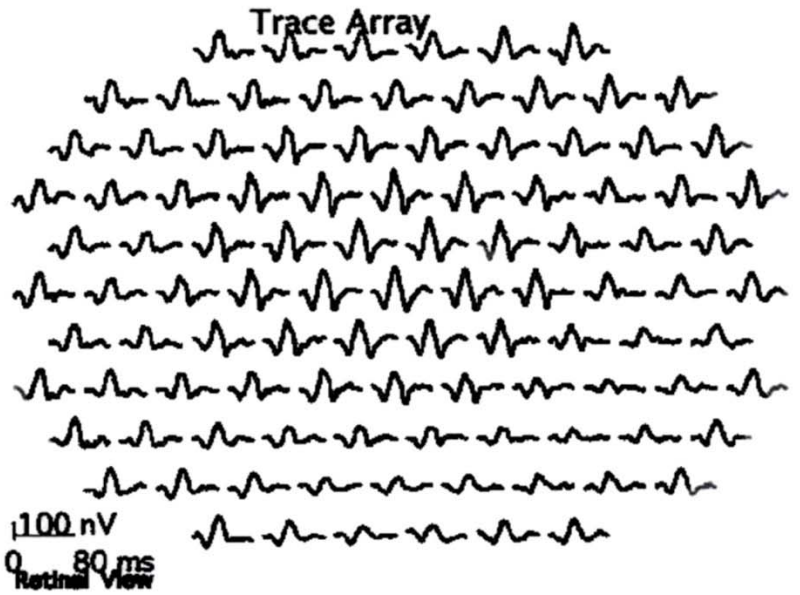
Risk Factors for Toxicity

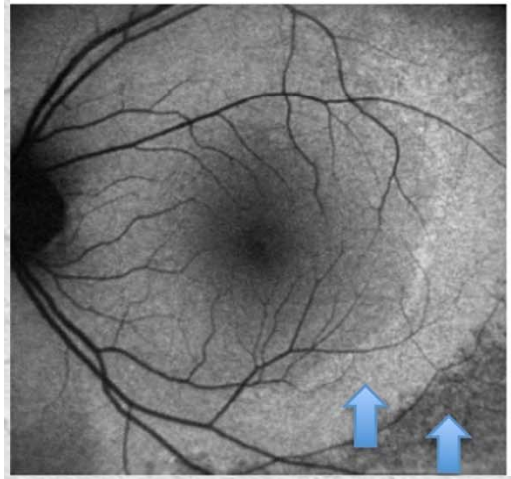
- Major Factors
  - **Dosage >5.0 mg/kg**
  - Renal disease
  - Tamoxifin use
- Lesser Factors
  - Older age, liver disease, genetic factors
- No diet or medical therapy can prevent, treat, or reduce risk of HCQ or CQ retinopathy other than cessation of the drug

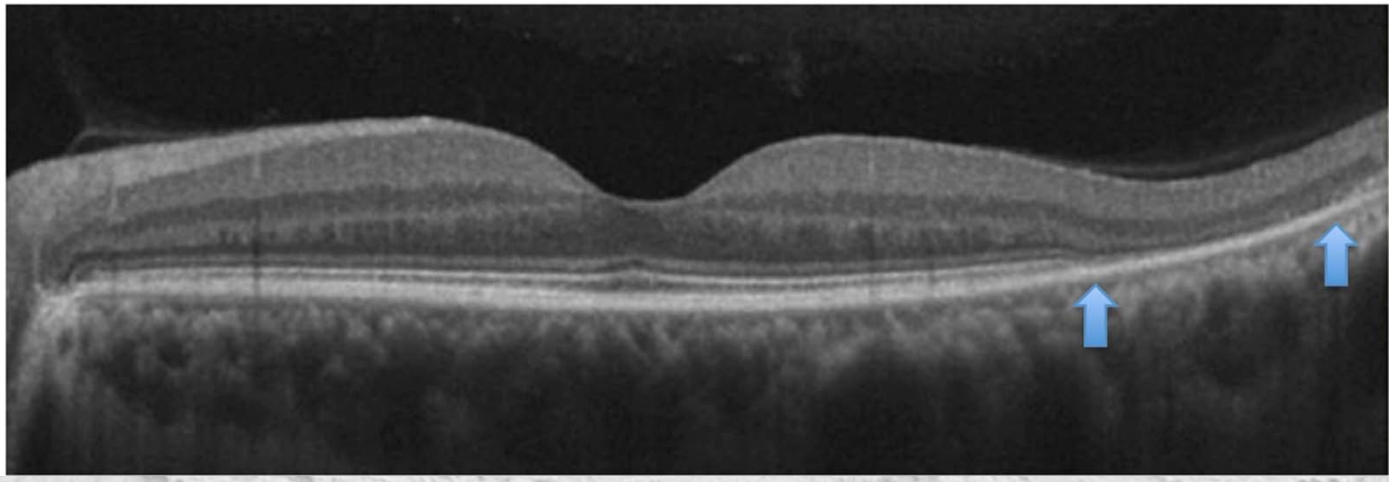
Racial Differences

- **Asians do not typically develop the classic bull's eye pattern of toxicity**
- Asian patients will normally develop early damage in the region of the vascular arcades
- Perform OCT scans at the vascular arcades
- Obtain a 30-2 rather than a 10-2 visual field









Typical pattern of CQ toxicity in Asians. Earliest signs of toxicity occur in the region of the vascular arcades.

Screening Exams

- Goal of screening exams is to detect retinal toxicity prior to onset of vision loss
- Vision loss is permanent and may continue to progress even after drug is discontinued
- Baseline exam within first year of starting drug
- Annual screening exams after 5yrs on drug
  - Sooner and more frequently if there are major risk factors (eg. kidney disease)
  - Check the dosage relative to weight at every visit

Key Points

- **Annual OCT and visual fields** are the primary means of detecting CQ toxicity
- **Asians do not develop the typical bull's eye** pattern of toxicity
- **Kidney disease and tamoxifen use** are major risk factors
- Speak directly to prescribing physician if toxicity is detected

Thank you!


UNIVERSITY OF THE
INCARNATE WORD
BOWDEN
EYE CARE &
HEALTH INSTITUTE
ROSENBERG
SCHOOL OF OPTOMETRY