Ocular Disease: Part I

Presented by MBKU | SCCO

Live Interactive CE Webinar | Day One | PM Session

Sunday | July 11, 2021 | 12:10 p.m. - 4:00 p.m.

Marshall B.
KETCHUM UNIVERSITY
Southern California College of Optometry

Department of Continuing Education

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Ocular Disease: Part II

Marshall B. KETCHUM UNIVERSITY
Southern California College of Optometry
Department of Continuing Education

Saturday, July 10

Pacific Time Zone | Live Webinar | COPE-Approved

8:00AM - 9:50AM
Comanaging Corneal Transplants: MD & OD Perspective
Presented by Lisa Wahl, OD & Asha Balakrishman, MD

10:00AM - 10:55AM
Thyroid Eye Disease: An Update on Clinical Management and Assessment
Presented by Jessica Yuen, OD

10:55AM - 11:50AM
Marine Omega-3s in Dry Eye Disease: Uncovering the Facts, Dispelling the Myths
Presented by Mark Roark, OD

11:50AM- 12:10PM
Lunch Break

12:10PM - 1:05PM
Evidence-Based Management of Retinal Artery Occlusions
Presented by Edward Chu, OD

1:05PM - 2:00PM
Neurotropic Keratitis: Rare, or Hiding in Plain Sight?
Presented by Douglas Devries, OD

2:10PM - 3:05PM
Anterior Segment Cases: OMD vs OD
Presented by David Sendrowski, OD & John Maher, MD

3:05PM - 4:00PM
Update on Cataract Work Up and Use of Multifocal IOLs
Presented by John Maher, MD & David Sendrowski, OD

Sunday, July 11

Pacific Time Zone | Live Webinar | COPE-Approved

8:00AM - 9:50AM
Oral Pharmaceuticals in Anterior Segment Disease
Presented by Blair Lonsberry, OD, MS, ME

10:00AM - 11:50AM
Legends of the Posterior Segment
Presented by Blair Lonsberry, OD, MS, ME

11:50AM- 12:10PM
Lunch Break

12:10PM - 1:05PM
Un-Nerved Conundrums of the Optic Disc
Presented by Mark Sawamura, OD

1:05PM - 2:00PM
PAMM, Plagues, and RAM: Uncommon Retinal Manifestations from Common Systemic Diseases
Presented by Xiao Xi Yu, OD

2:10PM - 3:05PM
Stargardt's Macular Dystrophy: A Family Affair
Presented by Ashley Deemer, OD

3:05PM - 4:00PM
Minimally Invasive Glaucoma Surgery (MIGS) Updates and Options
Presented by Igor Bussel, MD

This activity is supported by an unrestricted educational grant from the following education partners. We sincerely thank them for their support!

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Ocular Disease: Part II

Day Two | Sunday | July 11, 2021

Marshall B. KETCHUM UNIVERSITY
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Department of Continuing Education

Instructor Biographies

Blair Lonsberry, OD, MS, MEd

Professor, Pacific University Oregon

Dr. Blair Lonsberry was named the Pacific Eye Clinic Portland Director in 2005. Prior to joining Pacific University he was an assistant professor at Southern College of Optometry, where he was the instructor for Anterior Segment Disease courses and named Teacher of the Year for 6 years in a row. During his time at SCO, he completed a Masters in Education degree with an emphasis in Post-Secondary Education. Dr. Lonsberry also practiced at a vitreoretinal surgery and low vision rehabilitation practice. Dr. Lonsberry's current responsibilities include supervising students during their clinical rotations and overseeing the Clinical Grand Rounds course. Dr. Lonsberry is a Fellow in the American Academy of Optometry, the Optometric Glaucoma Society and the Optometric Retina Society. He is also a Diplomate of the American Board of Optometry.

Mark Sawamura, OD

Associate Professor, MBKU | SCCO

Dr. Mark Sawamura is currently an Associate Professor with Tenure at the Southern California College of Optometry. He is a 1991 graduate of the Southern California College of Optometry and returned to teach at his alma mater following a post-graduate residency at the Pennsylvania College of Optometry / Hahnemann University. He joined the faculty of the Southern California College of Optometry in 1993. Dr. Sawamura serves as the Chief of the Jarnagin Center for Primary Eye Care and Chief of Ocular Disease at the University Eye Center at Ketchum Health as well as attending faculty in the Special Testing Service. He teaches the neuro-ophthalmic disease track at the College as well as advanced ophthalmic procedures, application of lasers in ophthalmic practice and ocular disease courses. He has presented multiple lectures up to the national level in the area of ocular disease management and has been involved in many therapeutics courses for California, Hawaii, and Washington. Dr. Sawamura currently is a Fellow of the American Academy of Optometry, Oral Examination Chair for the Diplomate in Neuro-ophthalmic Disease, Webmaster for the Disease Section of the AAO, Committee member of the National Board of Examiners in Optometry, Past Chairman of the ASCO SIG on Optometric Informatics, and has authored TPA guides for California Optometrists. He authors medical abstracts for the Optometry Journal and was recently President of the Faculty Council at SCCO.

Xiao Xi Yu, OD

Chief, Low Vision, Greater Los Angeles VA Healthcare System

Dr. Xiao (Shawn) X. Yu is a graduate of Pennsylvania College of Optometry at Salus University. He completed his residency training in 2011 at State University of New York College of Optometry and the Lighthouse International in the field of Low Vision Rehabilitation. He has served as an assistant professor at Nova Southeastern University College of optometry for nearly 3 years and since joined the optometric staff at the West LA and Sepulveda VA. He is currently serving as the Chief of Low Vision at the greater Los Angeles VA system and continuing to pursue his academic interest in low vision rehabilitation, ophthalmic disease, and traumatic brain injury.

Ocular Disease: Part II

Day Two | Sunday | July 11, 2021

Instructor Biographies

Ashley Deemer, OD

Assistant Professor, MBKU | SCCO

Ashley Deemer, OD received her undergraduate degree at the University of California San Diego and her Doctor of Optometry degree from the New England College of Optometry. She completed her residency training at the Jamaica Plain Veterans Affairs Medical Center in Boston, MA with a focus in primary care optometry, low vision rehabilitation, and vision therapy. She then completed the Lions Vision Rehabilitation Fellowship at the Johns Hopkins Wilmer Eye Institute in 2016. During her training, Dr. Deemer was a recipient of the Charles Robert Soltes Scholarship, Beider Scholarship, and Bill Mattingly Memorial Scholarship. She also received grant awards for her work in functional outcome measures and depression prevention in patients with age-related macular degeneration. She now focuses her research on the development and implementation of low vision enhancement systems using head-mounted video displays and virtual reality. Dr. Deemer previously practiced at the Johns Hopkins Wilmer Eye Institute providing low vision rehabilitation care to optimize the remaining sight of patients with chronic visual impairment. She is a Fellow of the American Academy of Optometry.

Igor Bussel, MD

Ophthalmologist, UCI Health

Dr. Igor I. Bussel is a UCI Health ophthalmologist who specializes in cataract, glaucoma and advanced anterior segment surgery. Bussel earned his medical degree from Rosalind Franklin University of Medicine and Science in Chicago, where he also earned master's degrees in biomedical science and healthcare administration. He completed his residency in ophthalmology at the University of Pittsburgh School of Medicine and a fellowship in glaucoma and advanced anterior segment surgery at Washington University School of Medicine in St. Louis, as well as a hybrid fellowship in glaucoma at UCI School of Medicine. Bussel's clinical research interests include the development of micro-invasive glaucoma surgical devices, novel ophthalmic imaging modalities and glaucoma clinical trials. He has presented research and given talks at national and international meetings, and has written numerous peer-reviewed publications and book chapters. He speaks English and Russian.

Un-Nerved Conundrums of the Optic Disc

Presented by Mark Sawamura, OD

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Un-Nerved Conundrums of the Optic Disc

Mark Sawamura, OD, FAAO
Chief, Jarnagin Center for Primary Eye Care
Southern California College of Optometry @MBKU
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*I have no financial disclosures

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Objectives

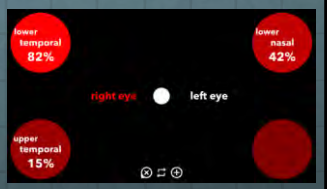
- Briefly discuss the general evaluation of optic disc
  - Dysfunction
  - Diagnostic testing
- Differential Diagnoses
- Optic Neuropathies
  - 3 to focus on
    - Optic Neuritis
    - Papilledema
    - AION
      - New thoughts and how OCT may be helpful

2

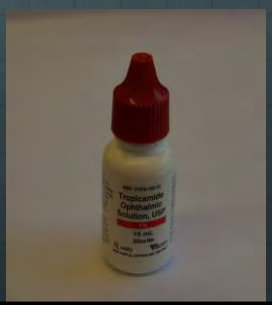
2

How to assess the Optic Nerves

- Visual acuity: Variable dysfunction
  - Quantitative vs. Qualitative
- Pupil function: Look for an APD
- Color vision: Red green color vision loss/desaturation
  - Red cap testing/Brightness sense



Smart Optometry App



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Visual Fields

- Kinetic vs. Static
- Threshold perimetry is the preferred method
  - Unless severely contracted or poor VA
- Test both eyes!
- What type of pattern?
  - Individual eye vs. Homonymous/Bitemporal

4

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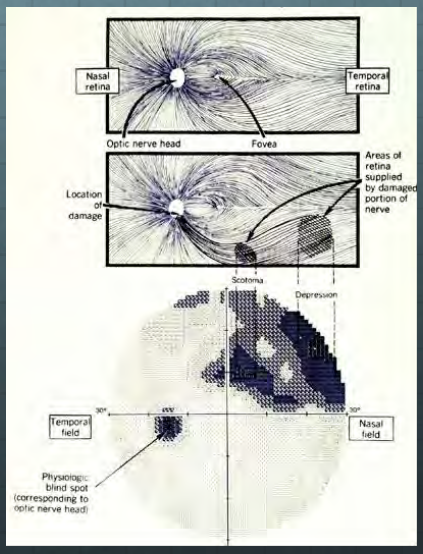
Visual Field characteristics

- Patterns
  - Paracentral scotoma
  - Nasal Step
  - Enlarged blindspot
  - Central-cecal scotoma
  - Bitemporal
  - Altitudinal defects
- Midlines
  - Vertical:
    - Chiasm and beyond
  - Horizontal:
    - Glaucoma, Disc Drusen, Papilledema



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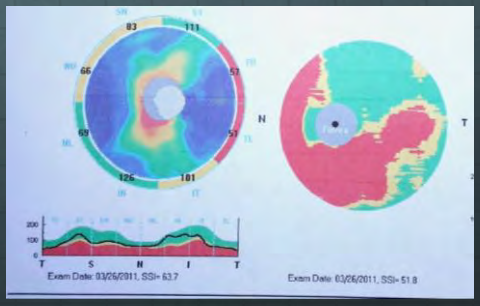
Additional testing

- Contrast sensitivity
- VEP
- OCT: RNFL and Optic Discs



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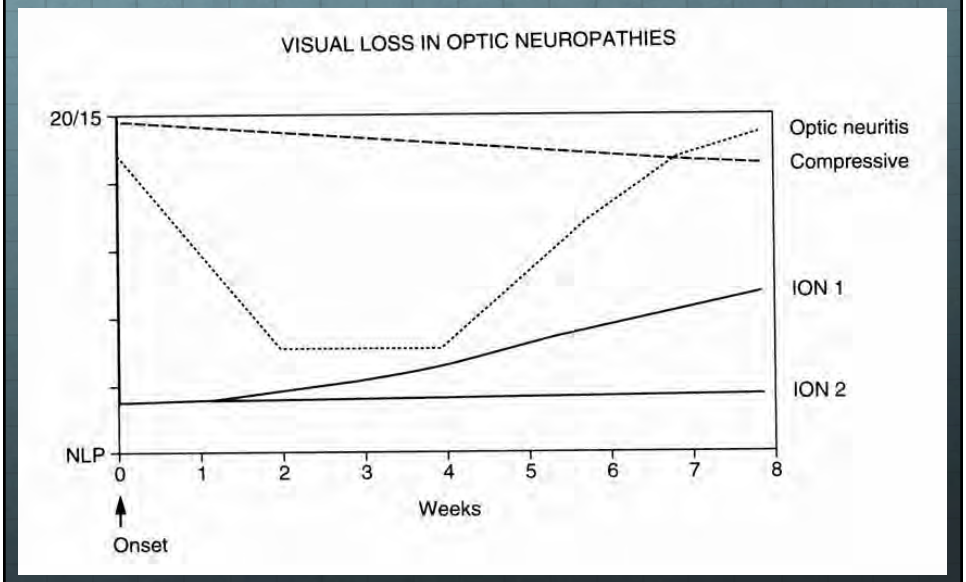

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OCT and Optic Neuropathy

- RNFL loss has been documented in all optic neuropathies.
  - May see thickening or thinning of RNFL based on stage of presentation
  - Can be used to track resolution
  - May be predictive of visual outcomes
  - Can be useful in differential diagnoses
- Ganglion cell/ Macular scans
  - Many optic neuropathies can involve the papillomacular bundle
  - Some present with sub-retinal fluid

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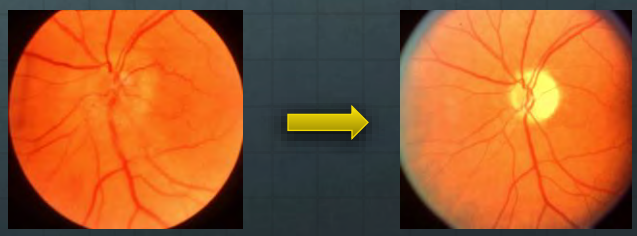
Optic Atrophy or Pallor

- Atrophy can be a sign of chronic compression by neoplastic process
- Atrophy follows injury to the optic disc
  - AION, Traumatic optic neuropathy, Optic neuritis
  - Nutritional optic neuropathy
  - Hereditary optic neuropathy



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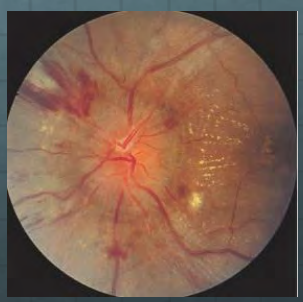
Disc Edema by Age

Young

Older

- Neuroretinitis
- Optic Neuritis
- Pseudotumor Cerebri
- Malignant hypertension
- Anterior Ischemic Optic Neuropathy
- Giant Cell Arteritis



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Unilateral *	Bilateral
Papillitis	Hypertension
AION	Papilledema
Diabetic Papillopathy	Pseudotumor
Compressive/ Sarcoid	Infections
CRVO	Leber's (separated in time)
Fistulas	Toxic
Neuroretinitis	Infilltrative

* More likely to be unilateral than bilateral

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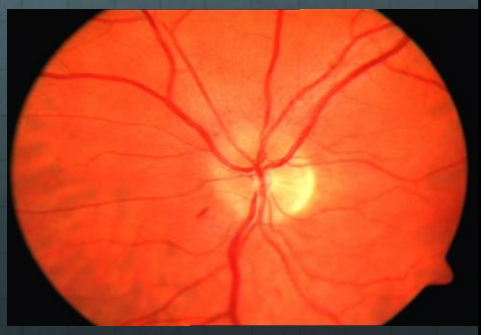
"I need to sing in the Xmas pageant"

- 39 year old WF with headaches x 4 months
  - Tinnitus, transient loss of vision
  - VA's: 20/20, 20/20



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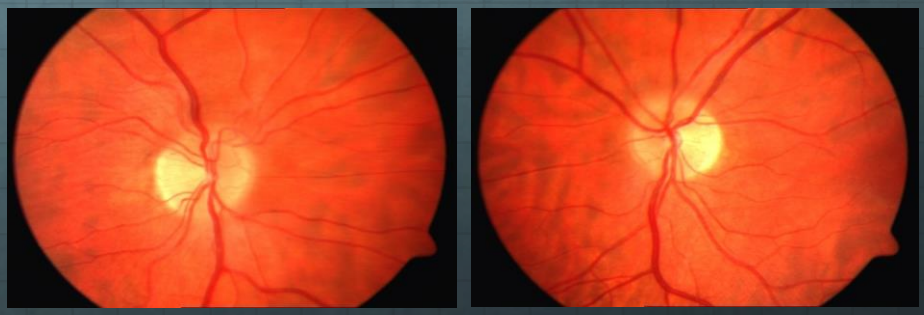
Sang in the show, got an MRI!

- Dx: Sagittal sinus meningioma
- Photos: 4 months following surgery



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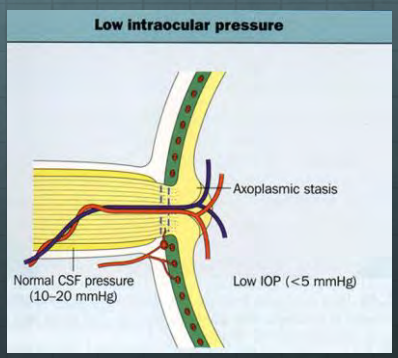
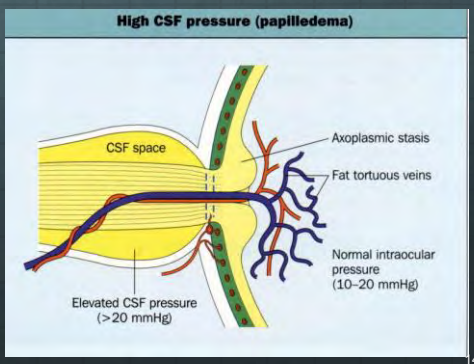
Papilledema

- Increased intracranial pressure leads to swelling of the optic nerve head
- Disc swelling can occur due to translaminar gradient (CSF pressure > IOP)





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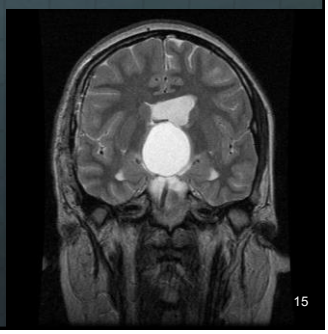
Causes of Papilledema

- Hydrocephalus
- Intracranial Mass
- Increased Venous pressure
- Cerebral Venous Thrombosis
- Meningeal Disorder
- Idiopathic
- Increased ICP production
- Malignant Hypertension
- Spinal Cord Tumor



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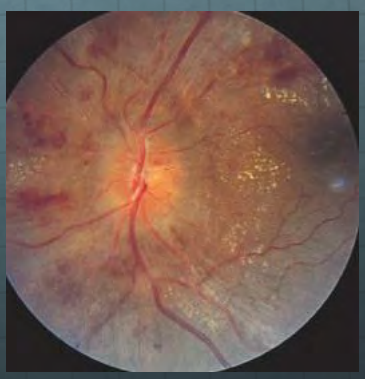
Malignant Hypertension



ALWAYS MEASURE BLOOD PRESSURE!

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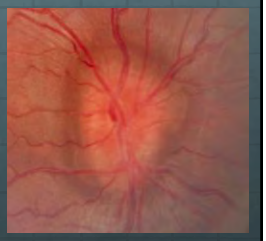
Idiopathic Intracranial Hypertension (IIH)

- Often used interchangeably with Pseudotumor Cerebri
  - First reported in 1897
- Incidence: .9- 2/100,000 persons
  - 3.5/100,000 in women 15-44 yrs old
  - Mean age of diagnosis is 30
  - Obesity: 10 fold risk factor
    - NORDIC study: Ave BMI of 39
  - Associated with rapid weight gain
  - Women: Men 9:1
    - Men: Consider sleep apnea or malignant HTN



Wall,2014

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Modified Dandy Criteria for IIH

- Signs and symptoms of increased intracranial pressure
- No neurological deficits except abducens palsy
- The patient is awake and alert
- Normal MRI and MRV (no venous sinus thrombosis)
- Increased ICP but normal CSF composition
  - Opening pressure
  - Greater than 250 mm H20
- No secondary causes

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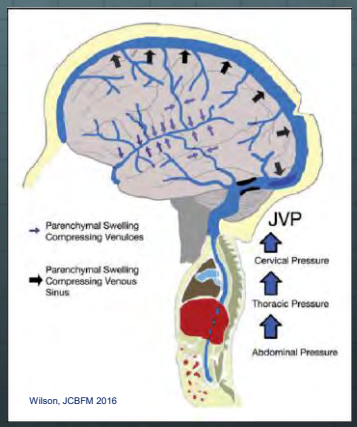
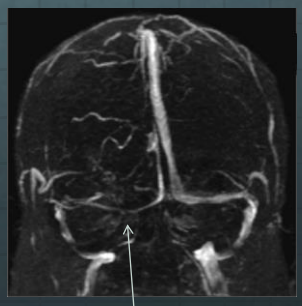
Pathophysiology of IIH

- Adipose tissue in the intrathoracic cavity reduces venous outflow from the brain
- Dural venous sinus stenosis: 94% of cases (Morris, 2016)
  - Bilateral





Narrowed Transverse Sinus on MRV

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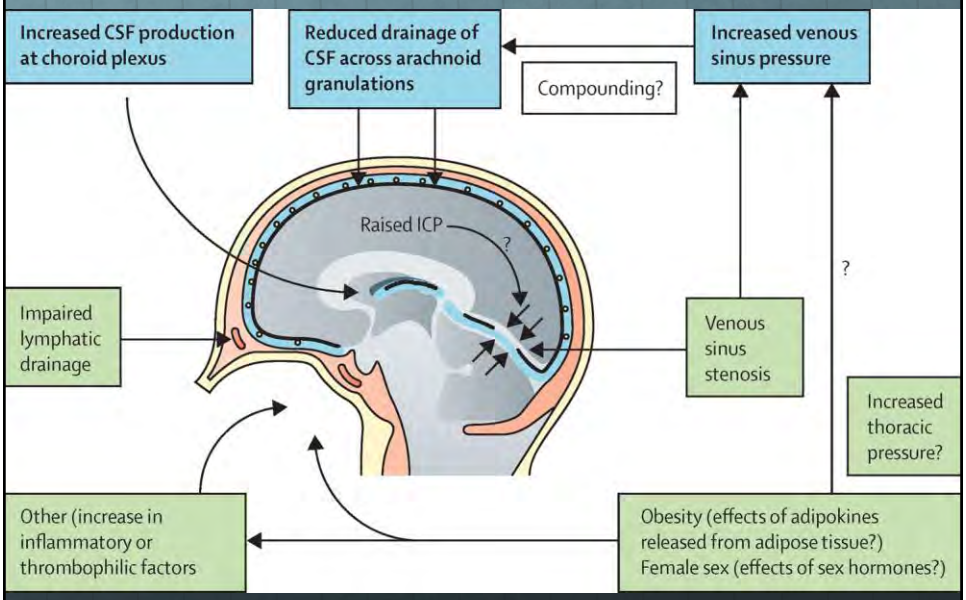
Mechanisms of IIH



From Markey, Lancet, 2016

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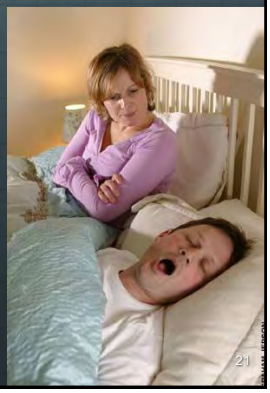
Secondary Causes of Papilledema

- Medications: Tetracycline, lithium, retinoids, growth hormone, steroids
- Excess Vitamin A? – IIH treatment trial disproved this
- Endocrine disorders
- Sleep apnea
- Oral contraceptives* - Thrombosis
- Iron deficiency
- Uremia



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Signs and Symptoms of Papilledema

- Headaches (94%)
  - Continuous, pulsatile headache
  - May awaken patient
  - Increases with Valsalva
  - Neck and shoulder pain
- Transient Visual obscuration (68%)
  - Seconds up to 1 minute
  - "Rheostat"
- Pulse synchronous Tinnitus (58%)
- Retrobulbar pain (44%) on eye movement
- Abducens paresis (38%) – eso posture
- Nausea and Vomiting

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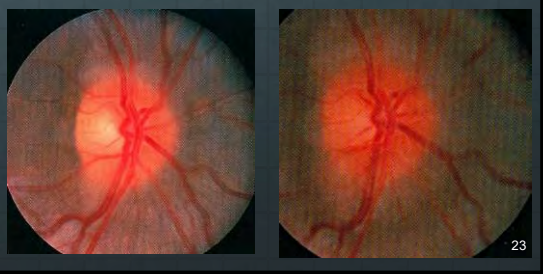
How quickly does Papilledema develop?

- 1-7 days following rise in CSF pressure
  - Speed of ICP rise is important
    - Sub-arachnoid heme vs.Concussion
    - Brain tumor
- Look at the "poles"



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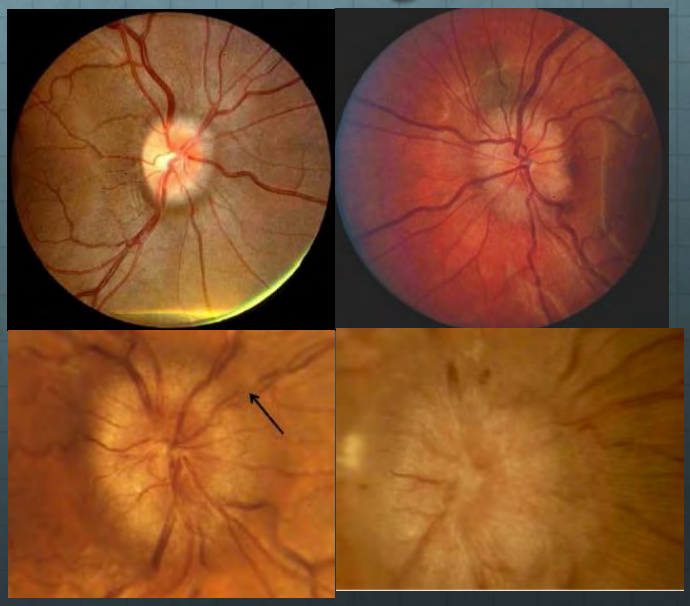
Frisen Grading criteria

Stage 1

Stage 2



Stage 3

Stage 4

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The Stages of Papilledema

- **Incipient (early):**
  - Mild hyperemia, loss of SVP, blurred margins at 12 and 6 oclock
- **Acute:**
  - Blurred, elevated disc margins, NFL
  - Disc hyperemia, loss of SVP
  - Hemorrhages
  - Paton's lines
- **Chronic:**
  - Less hyperemia, pseudodrusen
- **Atrophic:**
  - Pale optic disc

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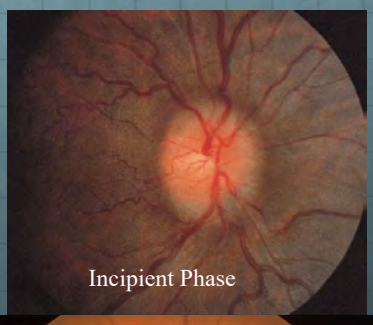
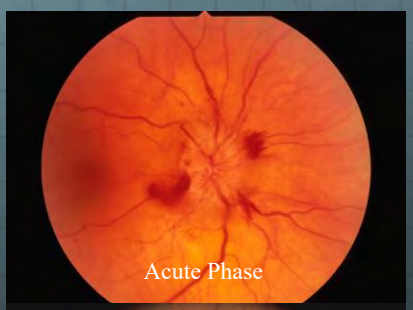
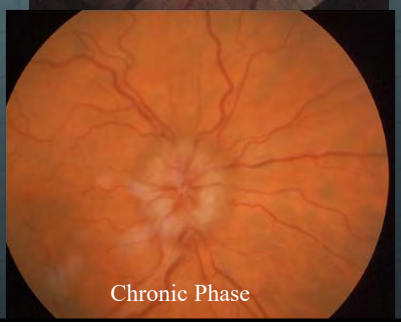
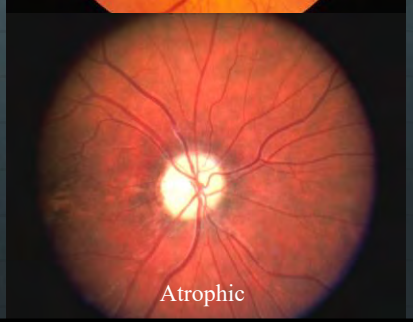
Stages of Papilledema









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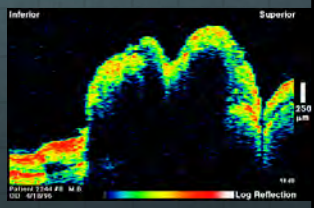
OCT for disc edema

- Does not replace MRI
- Asssessment of Peripapillary NFL and disc parameters
  - Peripapillary NFL is thicker
    - Ave: 122 microns vs 91 for controls
  - Cross sectional imaging
    - Subretinal Fluid accumulation
    - Tissue thickening



- Johnson et al, Arch Ophthalmol, 2009
- Menke et al, IOVS, 2005

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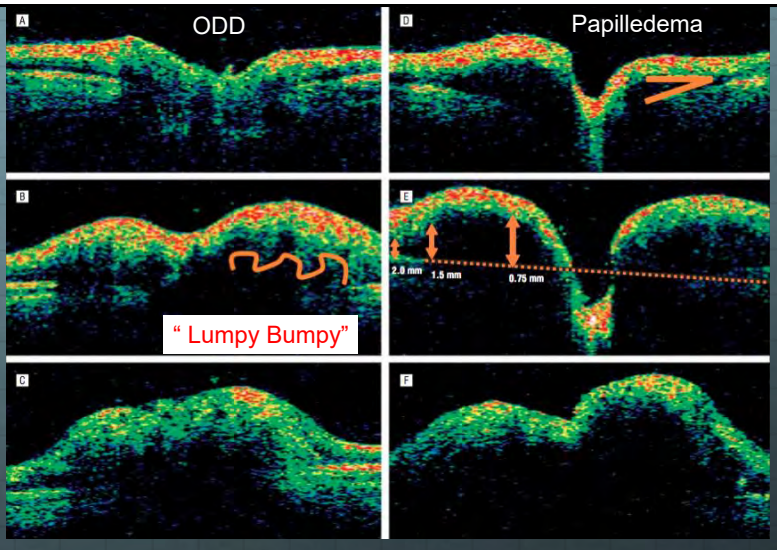

- Differentiation of Optic Disc Edema from Optic Nerve Drusen
  - Internal contour and separation of sub-retinal hyporeflective space can differentiate the two
    - Johnson et al, Arch Ophthal, 2009

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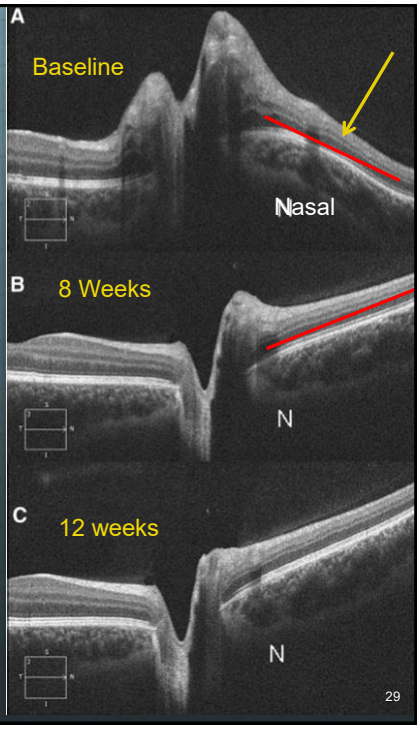
28

- Deformation of the RPE/ Basement Membrane in Swollen Optic Discs
  - 67% had Positive slope in early phases
    - Observed in about 10% of AION or Optic Neuritis cases
  - Angulation did not correlate with amount of disc swelling
  - Resolves over time
    - Kupersmith et al, IOVS, 2011



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28 year old East Indian Female

- Headaches x 2 months
- Transient Visual Obscurations – 2 secs
- No medical problems or medications
- VA's: 20/20, 20/20
- Pupils: No APD
- BP: 118/78
- Anterior seg: unremarkable

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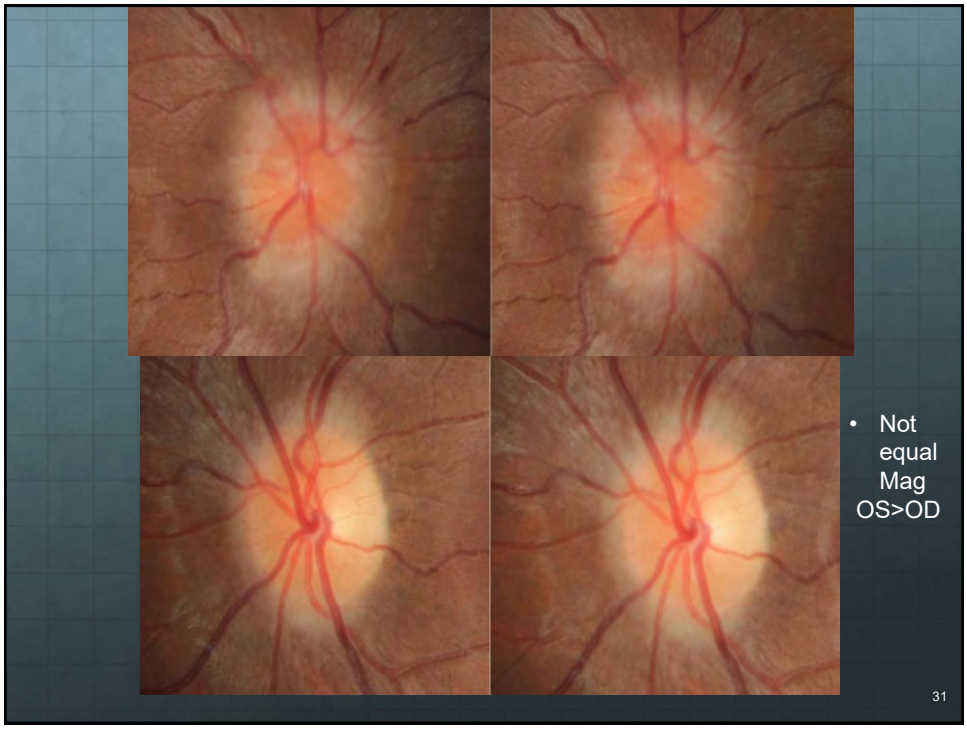
• Not equal Mag OS>OD
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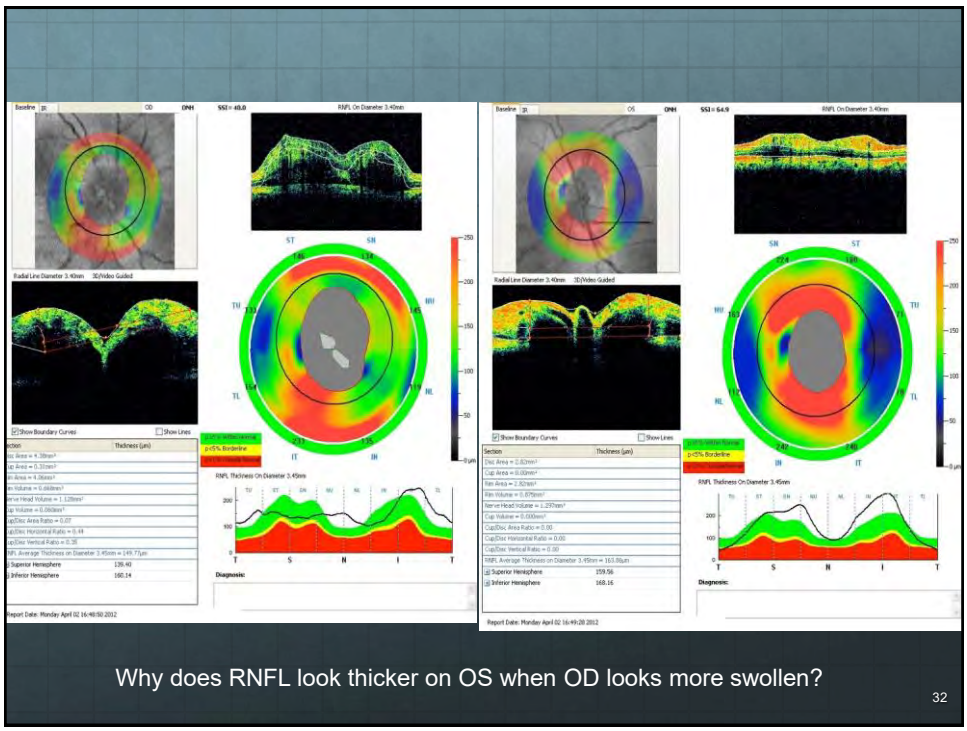
Why does RNFL look thicker on OS when OD looks more swollen?
32

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32 year old female

- CC: Intermittent flashes of light, blurred vision x 2 days.
- Recently diagnosed with viral meningitis. Polycystic ovarian syndrome, elevated cholesterol.
- Meds: Metformin, Amoxicillin, Lyrica, Hydrocortisone, Clarythromycin, Flexiril, Flonase
- BVA: OD: 20/60-, OS: 20/200
- BP: 117/76
- Pupils: 3+ reaction to light OU.

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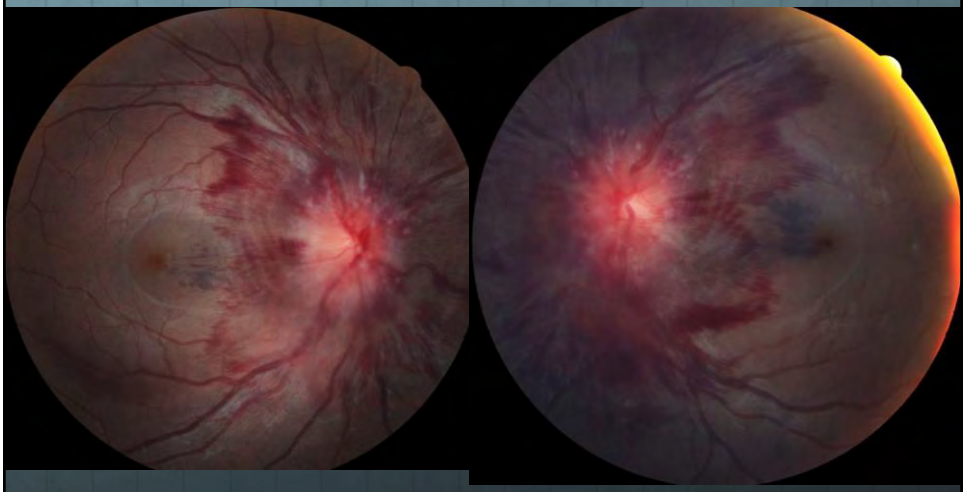
Baseline photos



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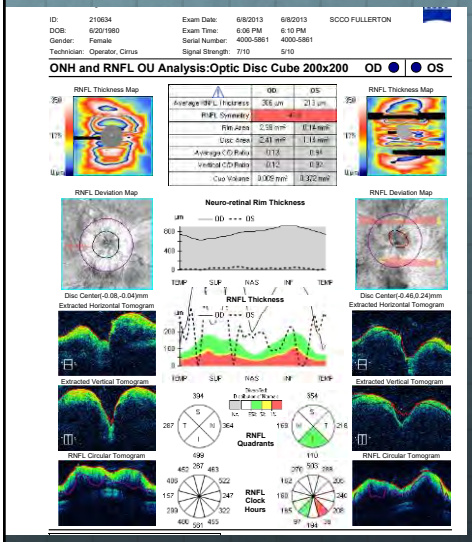
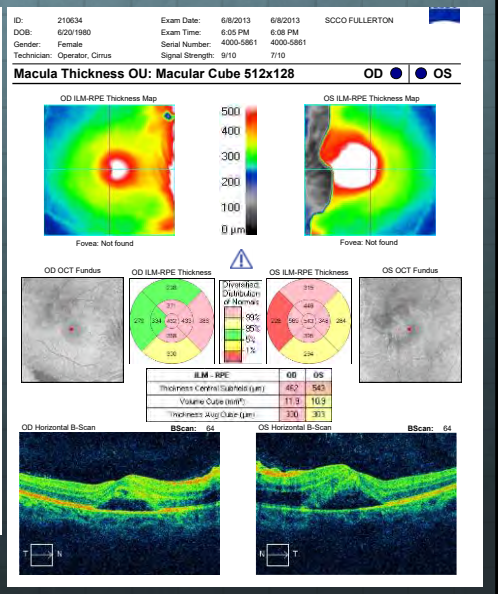
OCT of ONH/RNFL and Macula





Tx: Started the patient on Diamox

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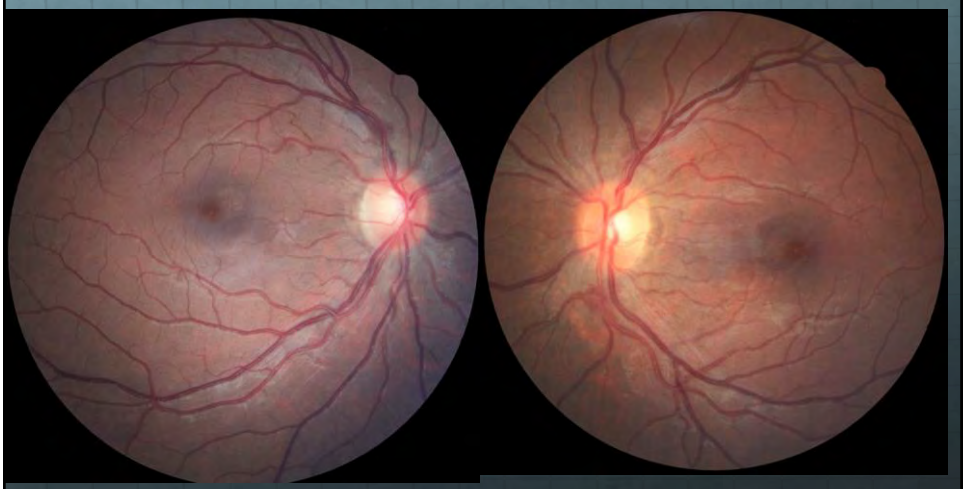
2 months later



VA: OD: 20/20, OS: 20/40

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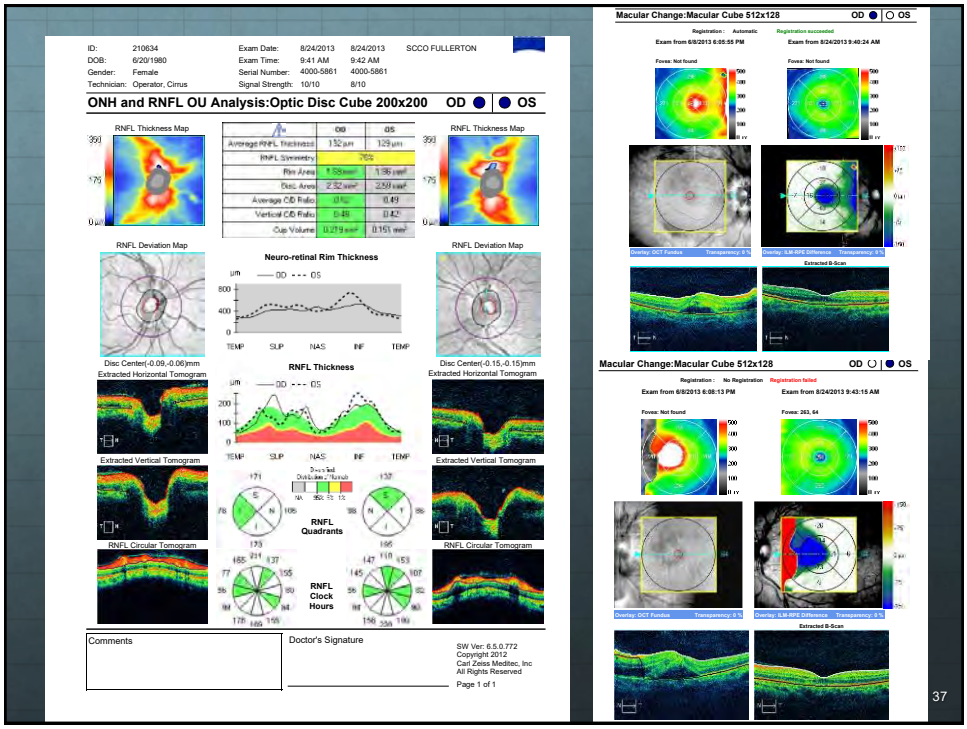
ONH and RNFL OU Analysis:Optic Disc Cube 200x200 OD OS
RNFL Thickness Map
RNFL Deviation Map
Neuro-retinal Rim Thickness
RNFL Thickness
Extracted Horizontal Tomogram
Extracted Vertical Tomogram
RNFL Circular Tomogram
RNFL Quadrants
RNFL Clock Hours
Comments
Doctor's Signature
Macular Change:Macular Cube 512x128 OD OS
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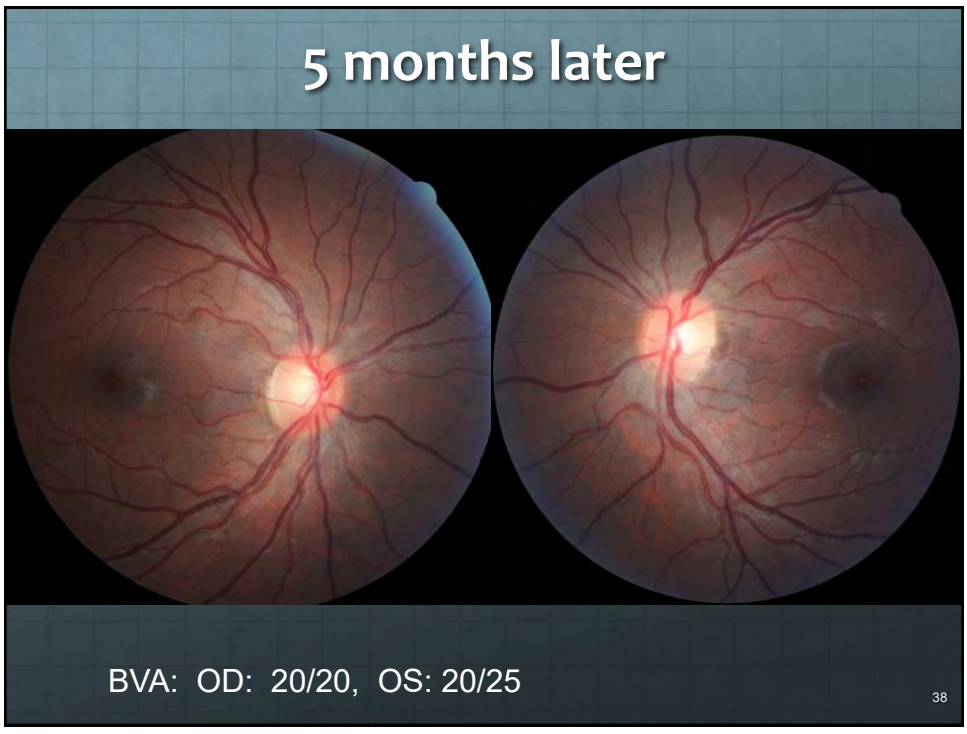
5 months later
BVA: OD: 20/20, OS: 20/25
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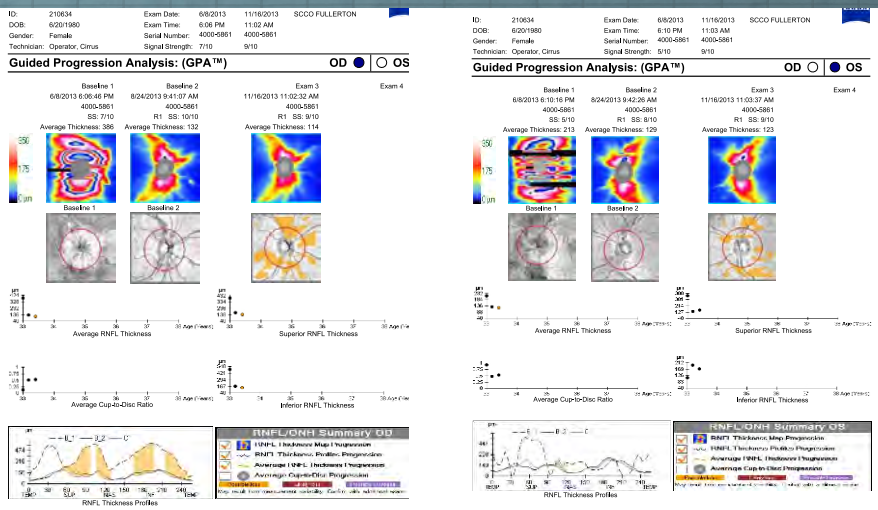
Progression analysis



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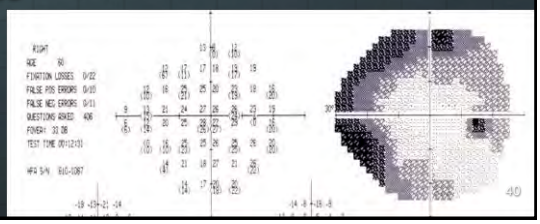
Vision loss in Papilledema

- VF loss from compression of visual pathways
- Enlarged blind spot
- Glaucomatous VF defects
  - Arcuate bundles
  - Blindness
  - Reversible upon treatment
    - Unless axonal loss



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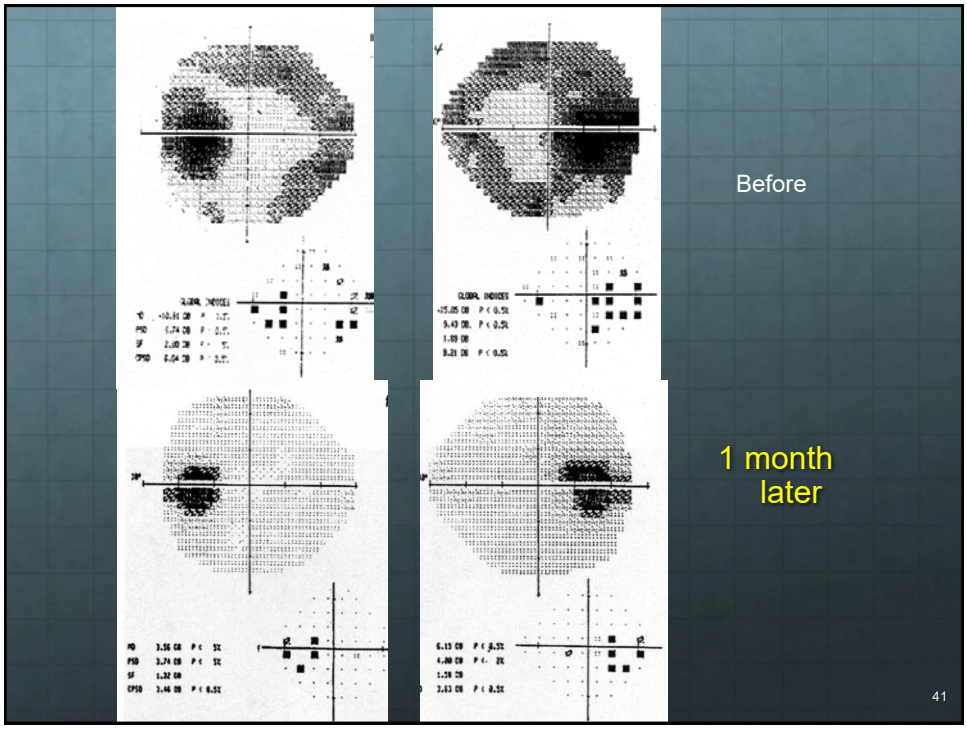

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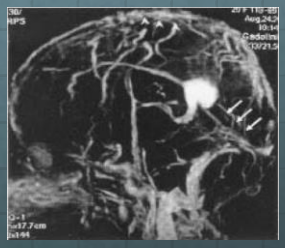
Management of IIH

- Neuroimaging: MRI/MRV
- Lumbar puncture with opening pressure
- Lab tests to rule out coagulopathies
  - Cerebral Venous Sinus Thrombosis
- Serial VF and OCT



Treatment of IIH

No Visual Loss	Mild Visual Loss	Severe Visual Loss
Low Na⁺ diet 10% weight loss consider Acetazolamide	⇄ Low Na⁺ diet 10% weight loss Acetazolamide	⇄ Low Na⁺ diet 10% weight loss Acetazolamide ONSF – visual loss Shunt - headache

optic nerve sheath fenestration
or CSF diversion procedure

24 hour blood pressure monitoring
and sleep study

Wall, 2014 42

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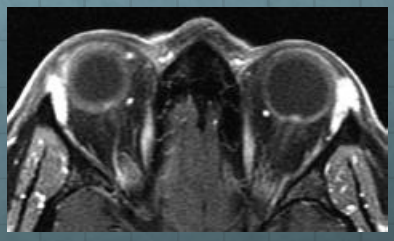
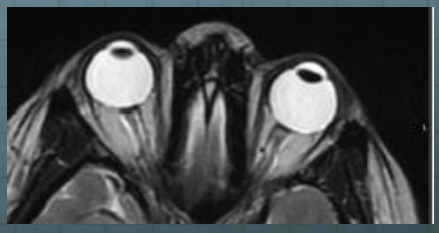
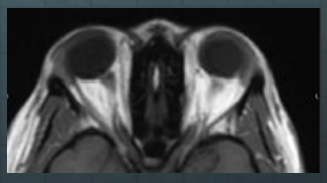
Orbital findings on MRI



Elevated ONH



Flattened Posterior Sclera



Hyperopic shift?

Tortuosity of the Optic Nerve

Passi, Degnan, Levy, 2013 43

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Follow-up OCT

- **Subsequent macular thinning: De-swelling vs. optic atrophy?**
  - **GCC is important for this distinction**
- **Rebolleda and Munoz-Negrete found that higher grades of papilledema at baseline had a worse visual outcome**
  - **Every 10 microns of increased RNFL thickening = a lowering of 0.6 dB on a VF at 1 year.**

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43 year old Female

- Chief Complaint:
  - Decreased acuity OD x 2-3 weeks
  - Slight pain on eye movement
- Occupation: Pet Groomer
- Medical history: DM, HTN, Elev. Cholesterol
- Vas: 20/80, 20/20 with current Rx
- Pupils: 2+ APD OD, color desaturation
- No restrictions of motility
- Anterior seg unremarkable

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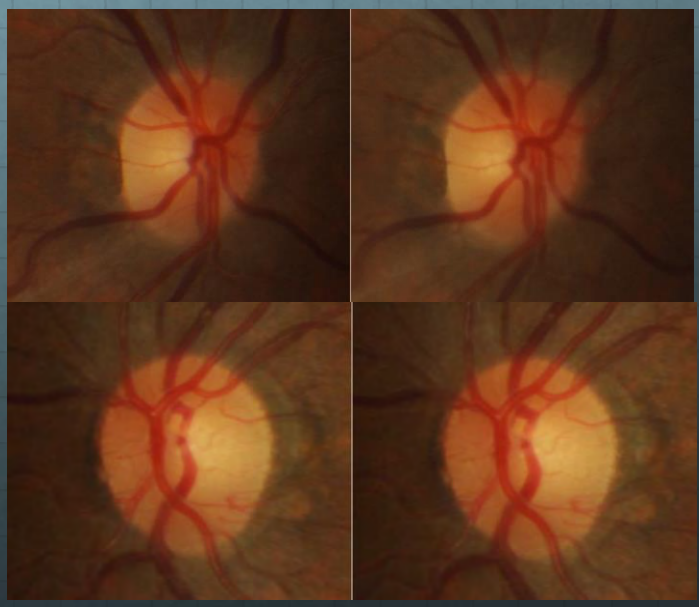

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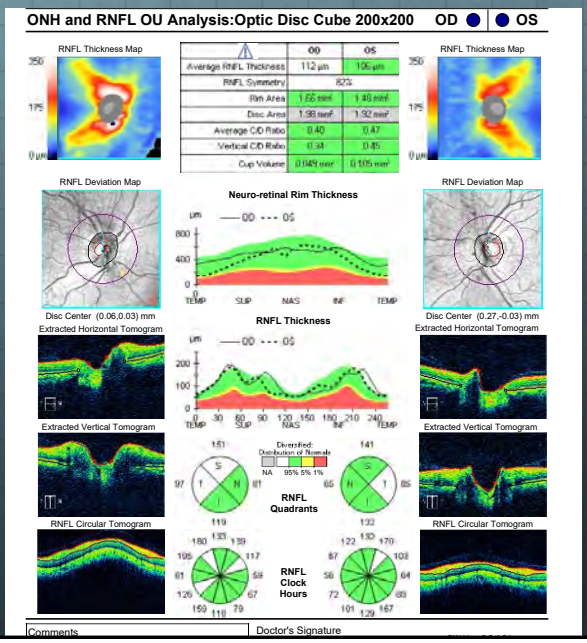
OCT



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Optic Neuritis

- **Patient profiles**
  - Young to middle age adults (16-55 yrs of age)
  - Female to male: 2:1
  - Annual incidence: 1-5/100,000
  - 20% of MS patients – ON is the initial symptom
  - 50% of MS patients have evidence of having ON
- **Symptoms:**
  - 90% have loss of vision, pain on eye movement, orbital pain, loss of peripheral vision, loss of color and contrast

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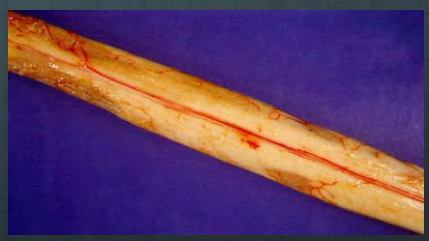
Pathophysiology

- Demyelination
  - CNS white matter, optic nerve
  - Acute phase: Perivascular cuffing of T and B cells on the myelin sheath
  - Macrophages engulf products and glial cells proliferate resulting in permanent conduction deficits



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37th Parallel

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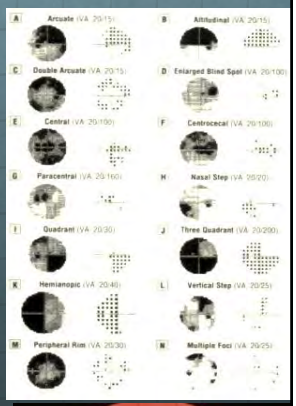
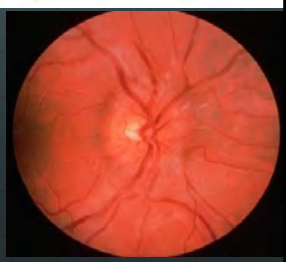
Signs of Optic Neuritis

- Visual Acuity: 20/20 to LP
- Color vision: B-Y initially
- Contrast sensitivity
- Pupils: (+)APD
- Visual fields (Keltner, Arch Ophth, 1994)
  - Diffuse loss - 48%
  - Localized - 20%
  - Central - 8%
- Fundus appearance
  - 3:1: Retrobulbar optic neuritis: Papillitis





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DDx of Optic Neuritis

- Differential Diagnosis from Demyelination:
  - Infectious
  - Post-vaccination
  - Inflammatory disease
  - Medications
- Neuromyelitis Optica (Devic's Diseease)
  - NMO is a rare disorder
  - Characterized by Optic neuritis and acute myelitis
    - Negative brain MRI
    - Abnormal spinal cord MRI
    - Seropositive NMO- IgG
      - NMO criteria, 2006

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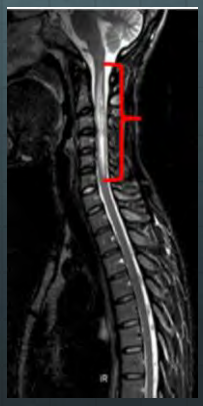
Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Optic Neuritis – Unilateral or bilateral
- Preceded by or followed within days or weeks by Transverse Myelitis
  - Spinal Cord involvement (greater than 3 vertebral segments)
- VA tends to be worse than MS optic neuritis
  - Patients are usually older than MS type
    - Can be older than 60
  - Women tend to have recurrent/relapsing type
  - Higher rates than MS in Asia and Caribbean



Asgari, 2013

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Neuromyelitis Optica Spectrum

	Antibodies	Response to steroids
NMO- AQ4 Neuromyelitis Optica Aquaporin-4	Antibody against water channel protein Aquaporin 4 found in cell membranes in astrocyte foot plates found in serum and CSF	Poor response Can relapse after taper
NMO - MOG Myelin Oligodendrocyte Glycoprotein	Antibodies against the myelin	Rapid response Good recovery

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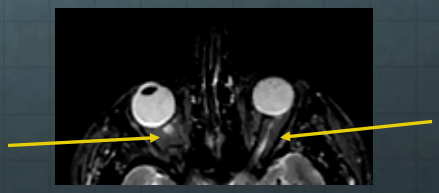
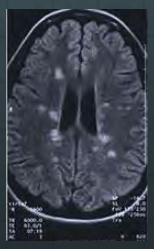
Contrast enhanced MRI

- MRI is not routinely utilized to diagnose optic neuritis
  - Contrast enhanced MRI of the orbit with fat suppression.
- Value of MRI is to identify the presence of clinically silent demyelinating lesions
  - Periventricular white matter lesions on T2 scans





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Utility of OCT in Optic Neuritis

- OCT of the RNFL
  - Allows quantification of unmyelinated axons in eyes with and without a history of Optic Neuritis in MS patients
  - It can be used to follow recovery of optic neuritis over 12 months

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RNFL and acute optic neuritis

- Pro et al (2006) - HRT2 and OCT3
  - RNFL was slightly thicker in RON pts (no ophthalmoscopically evident swelling) at baseline.
  - HRT2 showed smaller mean cup size vs fellow eye and did not correlate to the MRI –demonstrated lesion
  - RNFL thinned temporally (46.8 microns vs. 57.8 – fellow eye)
  - Cup normalized at the follow-up (1 and 3 mos)

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Optic Neuritis

- Evolution of RNFL loss
  - RNFL thinning most often occurs between 3 and 6 months in 85% of patients
    - Ave RNFL of 78 microns vs. 100 microns
  - First inter-eye difference is seen at 2 mos
  - Stabilized between 7-12 months
  - No change between 1 and 2 years
    - Costello et al, 2006, 2008, 2009
  - Also noted that below 75 microns was when persistent visual dysfunction was predicted.

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OCT and MS

- Cohorts of MS patients across the US display similar findings of ave RNFL thickness vs. controls (90-93 microns vs. 103-105 microns) with OCT3
  - RNFL Thinning:
    - MS with ON> MS pts > Controls
- OCT findings differ among MS subtypes
  - Secondary progressive MS vs. Relapsing MS or primary progressive types
    - Secondary progressive shows more thinning

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OCT and MS

- Annals of Neurology, 2016
- 107 MS patients followed for 4 years
- Aim: to determine if OCT changes mirror changes on MRI in MS patients
- Conclusions:
  - Rate of tissue thinning in the eye (ganglion cell and IPL) mirrored that of MRI degeneration in specific brain regions (whole brain, white matter, gray matter, thalamus)

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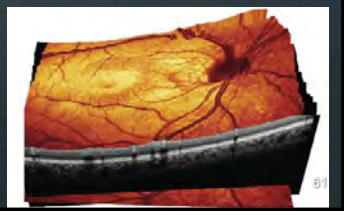
Predictors based on OCT?

- Progressive disability in MS is associated with axonal loss, not demyelination.
- For every 10 microns of RNFL loss, the odds of being ambulatory are decreased 2.5 fold
  - Costello, NANOS, 2009
  - But conflicting data is also reported
- Future risk of developing MS or progression??
  - Linear vs. Non-linear forms



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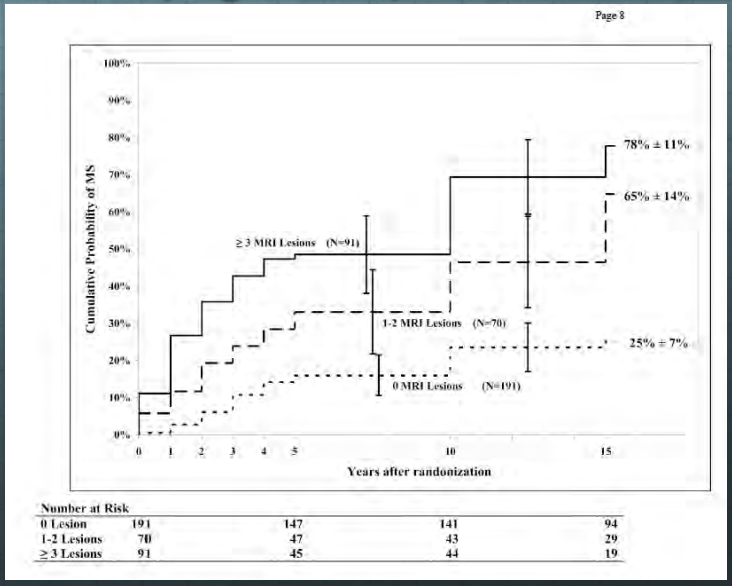
Baseline MRI findings vs. risk of developing clinically definitive MS



ONTT – 15 year, Arch, Neurology, 2008

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To treat or not to treat ON

- Optic Neuritis Treatment Trial
  - Oral vs. IV steroids
  - Showed no of Baseline MRI lesions was a predictor to development of CDMS
  - Clinical outcomes are the same.
- Early treatment delays conversion to CDMS but does not show any benefit in improving neurological disability.
- Neurological evaluation for management of global demyelinating disease
  - Treatment of the MS

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Case : Dimming of Vision

- 61 year old East Indian Male
- Blurred vision x 1 month.
  - Dimming of vision, thinks it may be related to a red eye he had
- Ocular Hx: Cataract Sx 2 yrs prior OU
- Med Hx: Type II DM x 5 yrs, HTN, hypercholesterolemia
- Meds: Tricor, Metformin, Lisinopril

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Patient Data

- Corrected VA's: OD: 20/40-, OS: 20/25
- Pupils: (+) +2 APD OD
- EOM's: Unrestricted
- Anterior Segment: Unremarkable OD, 1+ PCO OS
- GAT: 15, 18
- BP – 120/70
- Visual fields: See slides
- Post Segment: See slides

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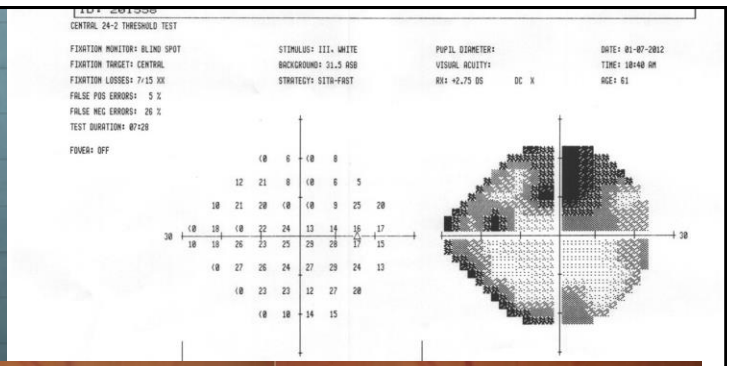
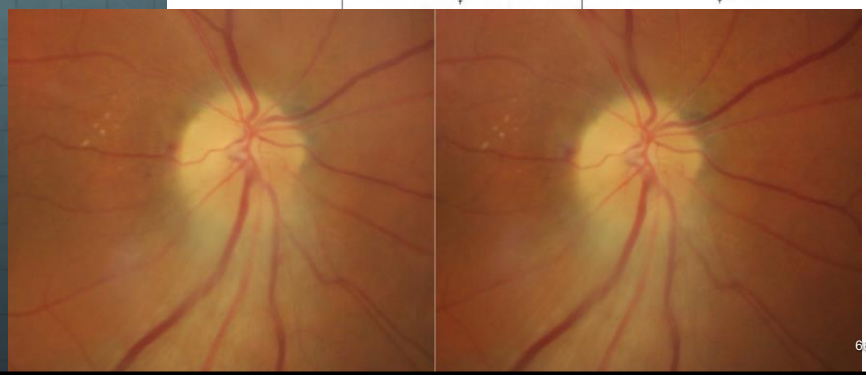
VF
OD





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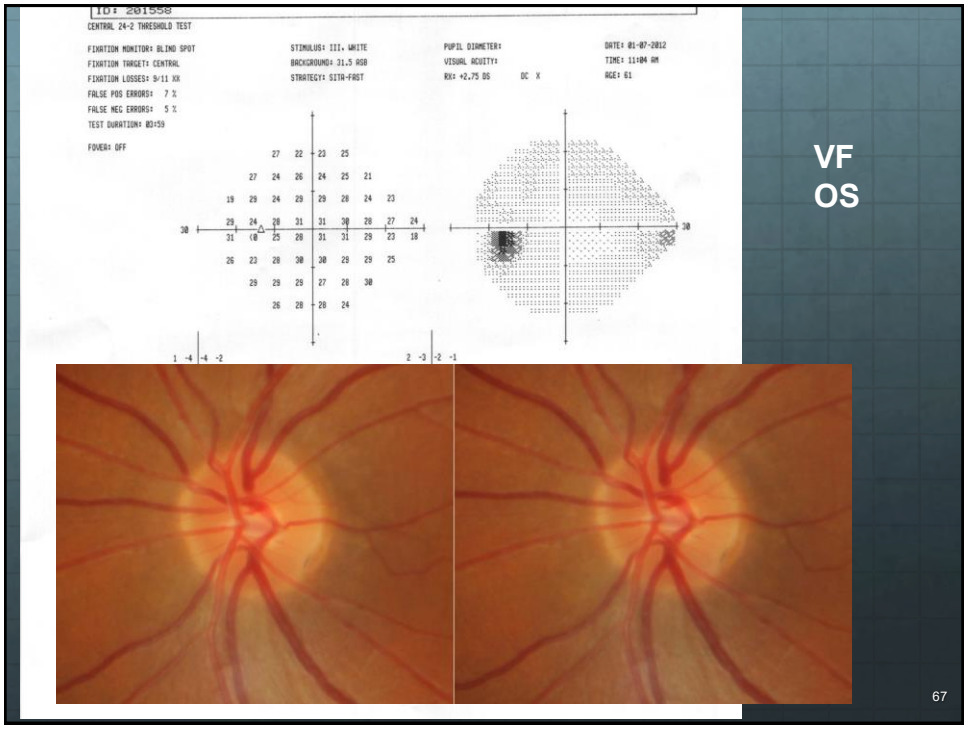

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Considerations?

- Swollen Optic Disc – Sectoral - OD
- Afferent pupillary defect OD
- Dimming of Vision
- History of Vascular Disease

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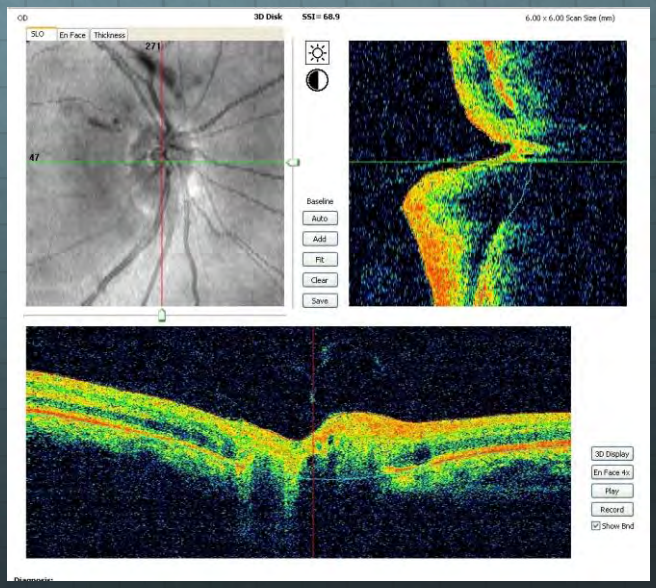
OCT of the OD ONH



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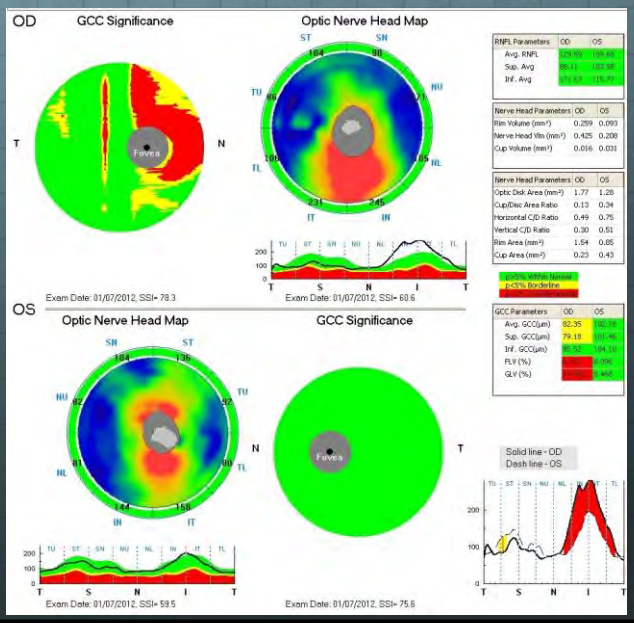
OCT OU



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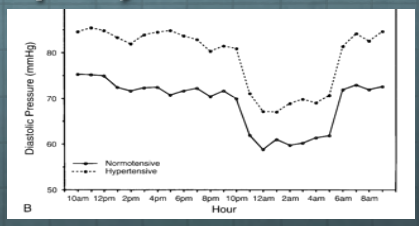
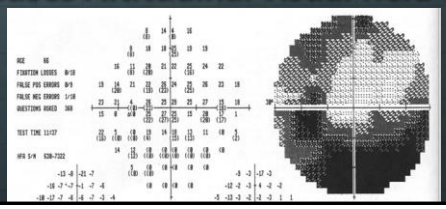
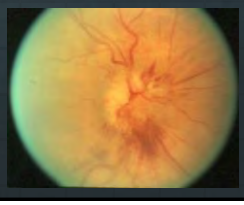
What about Anterior Ischemic Optic Neuropathy?

- **What we remember:**
  - Disk at risk
  - Unilateral ON swelling
  - Poor disc perfusion
  - Two types:
    - **Arteritic – AION: Giant Cell or Temporal Arteritis**
    - **NA-AION: everything else**
  - Causes Altitudinal visual field defect







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Is it Arteritic or Non- Arteritic?

	Artertic - AION	Non Arteritic AION
% of cases of AION	12.5%	87.5%
Mean Age	73	60
VA loss	75% are worse than 20/200	Better than 20/60 in 50%
Systemic Symptoms	75%. of patients	None
ESR	75 or greater	30-40 (normal)
Amaurosis Fugax	75% - within 1-2 weeks before	25% of patients
Disc Appearance	50% edema, 50% pale	Sectoral or full edema
Bilateral Involvement	75% within a week, if no tx	11-43% within 2 years
Treatment	Corticosteroids	None proven
Improvement	Rare	16-43%

RULE OF 75

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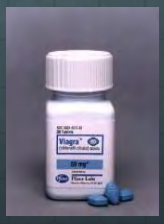
Risk factors of Non-arteritic AION

- Small optic nerve
- Diabetes (Heyreh, 1990, Feldon, 1999)
- Hypertension/ Hypotension
  - Aggressive management/ QHS Dosing (Hayreh)
- Sleep Apnea (Arch Ophthal, May, 2002)
- Viagra, Cialis (J Neuroophth, Ophthalmol, Arch Ophthal)
- Carotid artery disease, Ischemic heart disease
- Hyperlipidemia (Ophthalmology, 2003)
- Smoking
- Migraine(Heyreh, 1997)
- Sticky Platelet syndrome (BJO, 2008)
- High altitude(Ind J Ophthal, 2002)
- Ocular surgery(AJO, 2003) , Spinal/Cardiac surgery(Surv Ophthal, 1998)
- Disc Drusen (NANOS, 2002)
- Shock induced or blood loss (Brown, 1994, Chun, 1997)



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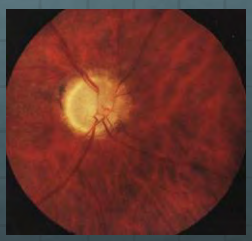
But… are A-AION and NA-AION even more Different?

- **A-AION: Arterial disease**
  - VA/ Visual loss is more profound
  - Complete excavation of the disc
  - Less hemorrhages
- **NA-AION: Is it a Venous disorder?**
  - Can accompany CRVO
  - Hemorrhages are more common
  - Visual loss/ structural changes are more similar to venous occlusion in CRVO vs. arterial infarction
  - Assoc w/ low rate of large vessel occlusive dz and CVA
  - FANG shows mildly delayed arterial filling, normal choroidal circulation



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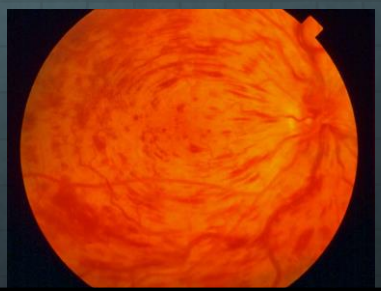
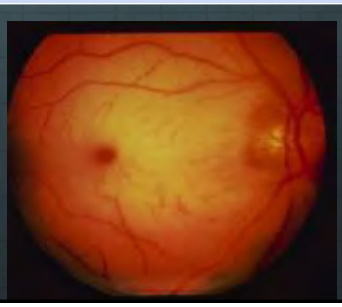
CRVO	CRAO
Hypertension	Hypertension
Diabetes	Diabetes
Bleeding /Clotting Disorders	Giant Cell Arteritis
Vasculitis	Embolism
Cardiovascular Disorders	Patent Foramen Ovale
ED drugs	Cardiac valve disease
Oral contraceptives	Atherosclerosis
Sleep apnea?	Hypercoagulable state
Hypotension	Collagen Vascular Dz





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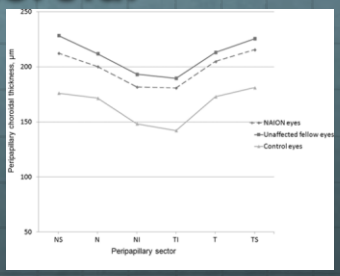
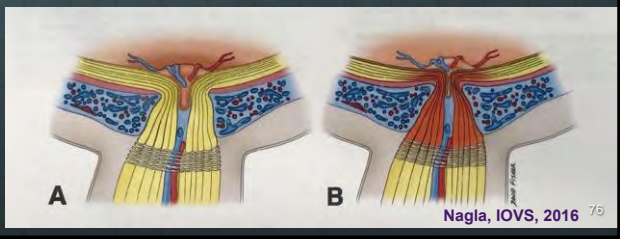
Impact of the choroid?

- Peripapillary choroid is thicker in NA-AION eyes and fellow eyes vs. Control eyes. (121-143%)
  - Perez – Sarregui, 2018
  - Fard, IOVS, 2015



- Creates the "Disc at risk"
  - Bruch's membrane opening is not smaller in NA-AION eyes
- Peripapillary choroid thickens with PDE use in normal young subjects,
  - Moschos, JCEO, 2016



Nagla, IOVS, 2016

76

76

Giant Cell Arteritis

- Chronic vasculitis of the Medium and large extracranial arteries
- What is new?
  - Color Doppler/Duplex ultrasound of temporal arteries
  - Higher incidence of occlusions in the axillary and and subclavian arteries
  - Marked increase in developing aortic aneurysms/aortic dissection
    - MRA of these large vessels

77
Cleveland Clinic

77

ACR Revised Criteria for GCA 2016

Table A: 2016 ACR revised criteria for early diagnosis of Giant Cell (Temporal) Arteritis [a]

❖ **Entry Criteria**:	
• Age at onset ≥ 50 years old	
• Absence of exclusion criteria [b]	
❖ **Domain I criteria**	
• New onset localized headache [c]	1.p
• Sudden onset of visual disturbances [c]	1.p
• Polymyalgia Rheumatica (PMR)	2.p
• Jaw Claudication [c]	1.p
• Abnormal temporal artery [d]	Up to 2.p
❖ **Domain II criteria**	
• Unexplained fever and/or anemia	1.p
• ESR ≥ 50 mm/hour [e]	1.p
• Compatible pathology [f]	Up to 2.p

a. In the presence of 3 points or more out of 11 with at least one point belonging to domain I along with all entry criteria, the diagnosis of Giant cell arteritis can be established.

b. Exclusion criteria are including : ENT and eye inflammation, kidney, skin and peripheral nervous system involvement, lung infiltration, lymphadenopathies, stiff neck and digital gangrene or ulceration

c. No other etiologies can better explain any one of the criteria

d. Enlarged and/or pulseless temporal artery : 1.p. / tender temporal artery: 1.p

e. It must be ignored in the presence of PMR

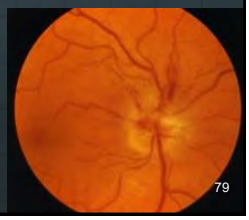
f. Vascular and/or perivascular fibrinoid necrosis along with leukocyte infiltration: 1.p. /and granuloma: 1.p

Salehi- Abari, 2016 [78]

78

OCT and ION

- Contreras (Ophthal, 2007) demonstrated in eyes with NA-AION that the mean RNFL would increase 96% in the affected eye in the acute phase.
  - Then at 6 months, the RNFL was thinnest superiorly, inferiorly, temporally, then nasally
- Hedges et al, noted the presence of sub-retinal fluid in 8 patients.
  - Not from the choroid or retinal vessels based on FANG of one patient
  - Acuity improved as fluid resolved



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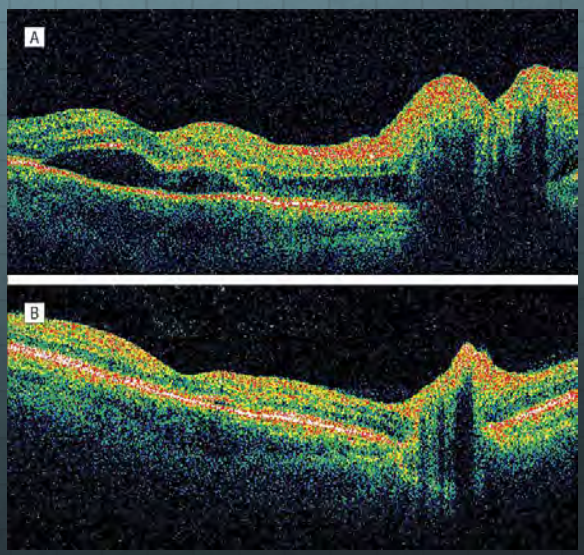
Baseline and 7 weeks later

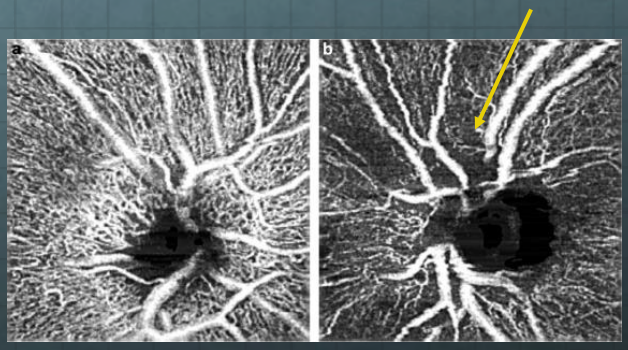


Hedges et al, Arch Ophthalmol, 2008 80

80

OCT - Angiography

- OCT-A shows diffuse loss of peripapillary microvascular cuff
  - Also Sectoral loss that correlates w VF defect



Normal AION

Rougier, 2017

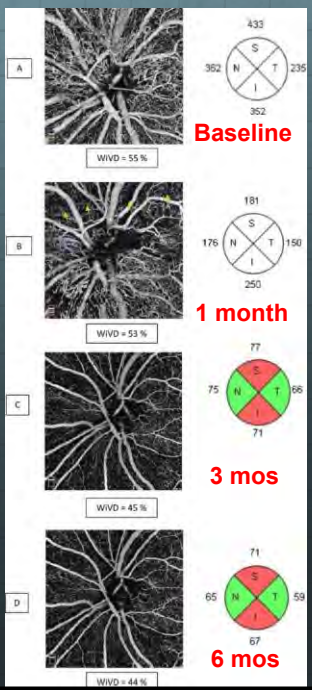
81

81

OCT-A

Augstberger, IOVS 2021

Found that Widefield Vessel Density reduced between baseline and 3 months and did not change afterwards



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82

Management of A-AION

- Arteritic: Giant Cell Arteritis
  - Based on the presumptive diagnosis of GCA-AION, initiate immediate treatment of corticosteroids
    - Goal is to reduce profound VA loss in fellow eye
    - 75% of untreated cases can go bilateral in one wk
  - Then STAT ESR and C-Reactive Protein
  - Temporal artery biopsy
  - Doppler of temporal arteries
  - MRA of the aorta to rule out dissection/aneurysm
  - Prognosis of patients: Fair to poor
    - Recovery of vision
    - Cupping of the optic disc

83

Management of NA-AION

- No proven treatments
  - Aspirin, high dose steroids, Avastin
- Rule out GCA in older patients
- Manage systemic disorders
- Sleep Apnea?
- Avoid hypotension – night time
  - Issues with perfusion pressure
    - Diastolic BP – IOP: Less than 30

84

84

Management of AION

- Non-Arteritic
  - Control of underlying vascular disorder
  - Visual Prognosis: Can see visual improvement up to 43% of patients

  - Phase III Quark Study
    - Intravenous injection of Neuroprotection agent
    - Vision loss in the last 14 days

85

85

Management of this Patient

- One month out - less efficacy with any Tx
- Sent to PCP for lab testing and better control of DM and HTN
- Take BP meds in the Morning, not the PM
- Monthly follow-ups

86

86

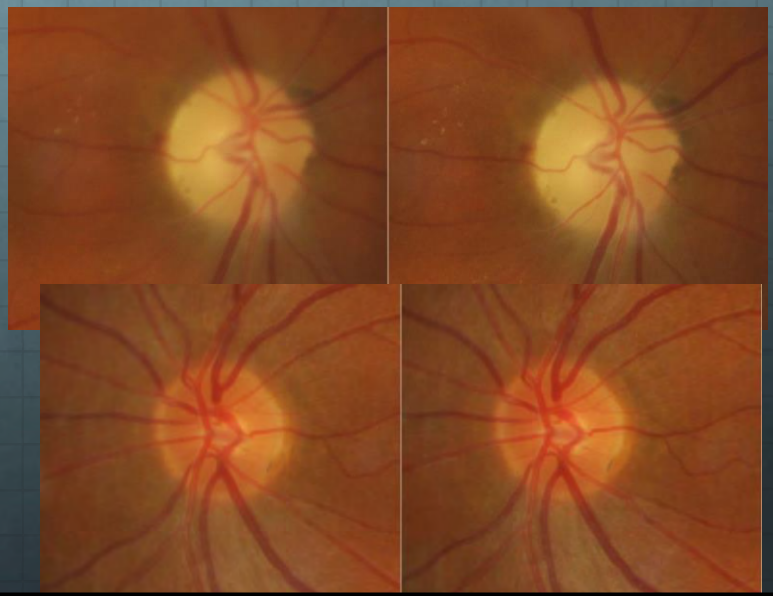
Follow –up of patient

- One month follow-up
- CC: Vision seems to be about 10-20% better
- VAs: OD: 20/40+, OS: 20/25
- See Imaging and VF

87

87

Follow-up 1 month



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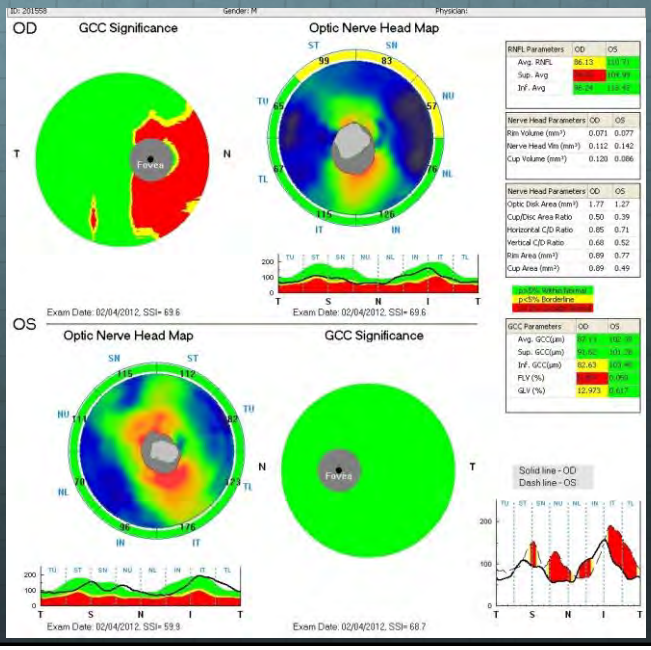
OCT – 1 month



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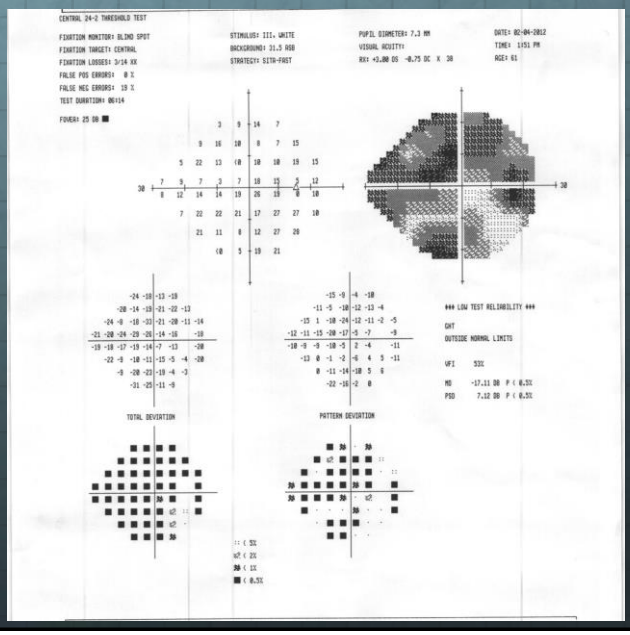
VF - OD



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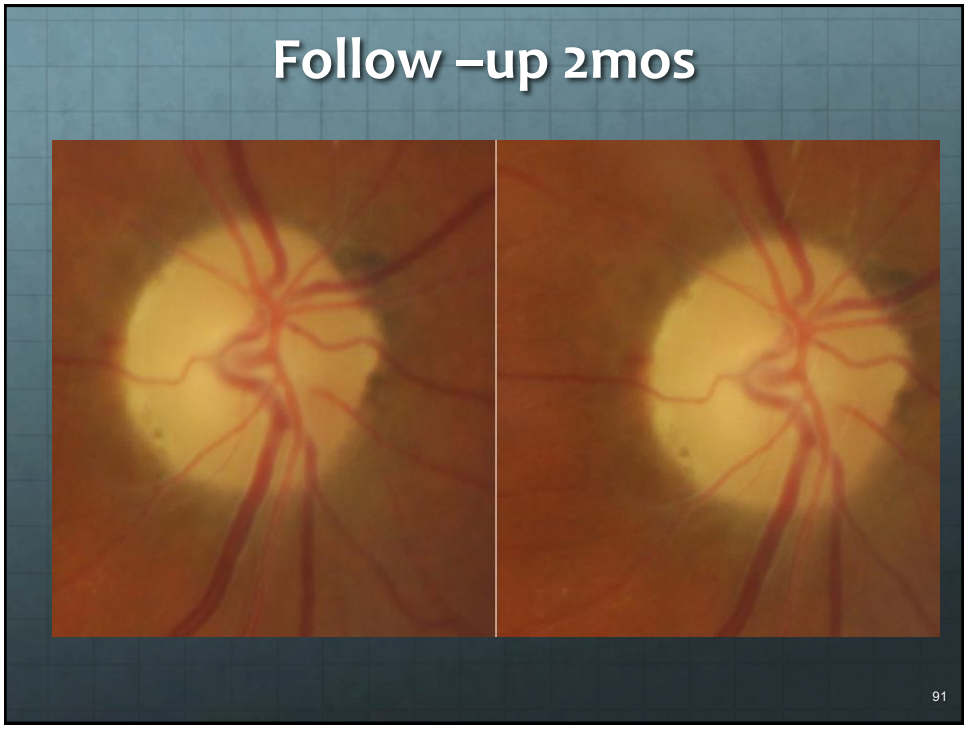

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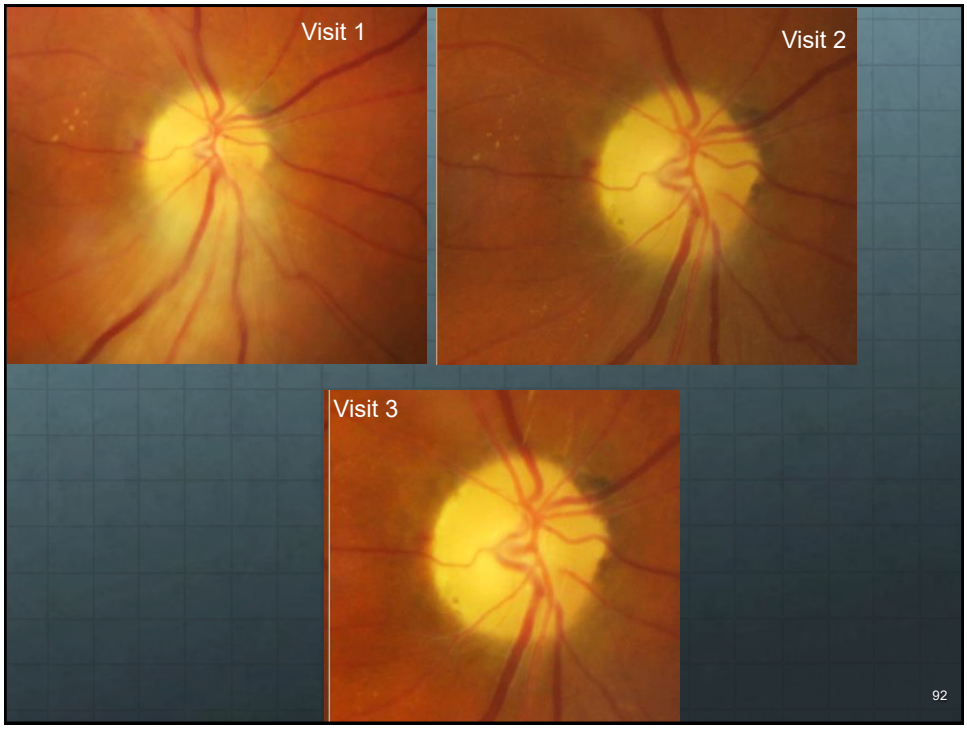

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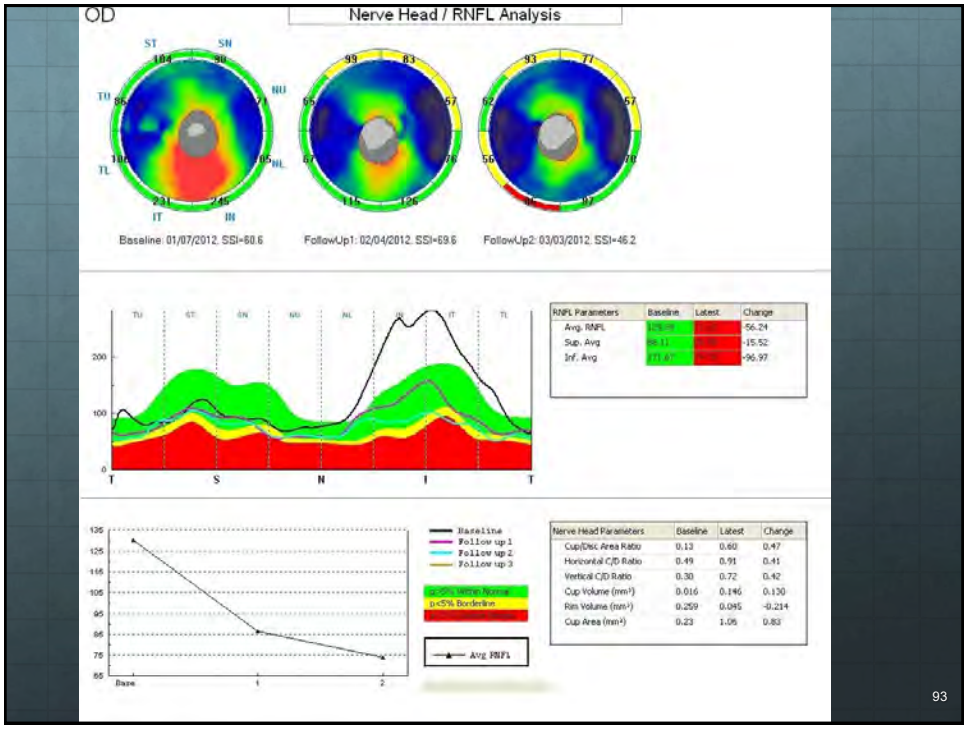
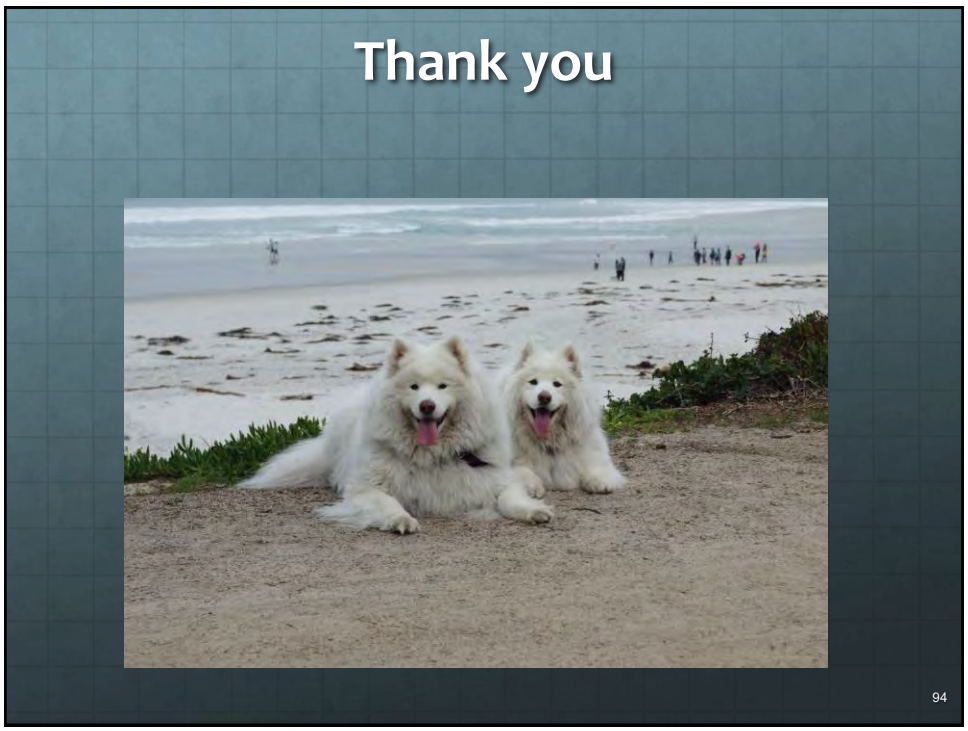

OD
Nerve Head / RNFL Analysis
Baseline: 01/07/2012, SSI=60.6
FollowUp1: 02/04/2012, SSI=69.6
FollowUp2: 03/03/2012, SSI=46.2
RNFL Parameters | Baseline | Latest | Change
Avg. RNFL | | | -56.24
Sup. Avg | | | -15.52
Inf. Avg | | | -96.97
Nerve Head Parameters | Baseline | Latest | Change
Cup/Disc Area Ratio | 0.13 | 0.60 | 0.47
Horizontal C/D Ratio | 0.49 | 0.91 | 0.41
Vertical C/D Ratio | 0.30 | 0.72 | 0.42
Cup Volume (mm³) | 0.016 | 0.146 | 0.130
Rim Volume (mm³) | 0.259 | 0.045 | -0.214
Cup Area (mm²) | 0.23 | 1.06 | 0.83
Baseline
Follow up 1
Follow up 2
Follow up 3
Avg RNFL
93

93


Thank you
94

94

PAMM, Plagues, and RAM: Uncommon Retinal Manifestations from Common Systemic Diseases

Presented by Xiao Xi Yu, OD

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Southern California College of Optometry
Department of Continuing Education
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PAMM PLAQUES AND RAM:

Uncommon Retinal Manifestations from Common Systemic

Shawn X. Yu, OD, FAAO
Chief of Low Vision, VA West LA
Assistant Professor
MBKU College of Optometry

No Financial disclosures

1

CONDITIONS

- HTN Related
  - PAMM**
    - Also caused by many other conditions
  - Macro-aneurysm
- Vascular abnormalities of DM?
- Retinal Emboli

2

HYPERTENSION

- Currently defined as 130/80 or higher in adults
  - (2019 American College of Cardiology & American Heart Association guidelines)
- Only 10% of patients with HTN have identifiable secondary cause
  - Renal disease
  - Adverse drug effect
  - Aortic disease
- **Emergency** referral if diastolic is over **120 mmHg**

3

SYMPTOMS (ACUTE ELEVATED BP)

- Difficulty breathing
- Chest pain
- Headache
- Blurry vision
- Nausea/vomiting
- Confusion
- Seizures
- Somnolence
- Focal neurological symptoms

4

CLASSIFICATIONS OF HYPERTENSIVE RETINOPATHY

Keith-Wagener-Barker Classification (1939)

- Grade 1: Generalized arteriolar narrowing
- Grade 2: Focal narrowing and arteriovenous nicking/nipping
- Grade 3: Grade 2 plus exudates, hemorrhages, and cotton–wool spots
- Grade 4: Grade 3 plus optic disc swelling

5

CLASSIFICATIONS OF HYPERTENSIVE RETINOPATHY

Mitchell-Wong Classification (2004)

- Mild: generalized and/or focal arteriolar narrowing, arteriovenous nicking/nipping, opacity of arteriolar wall (copper/silver wiring)
- Moderate: retinal hemorrhages (flame, dot, blot), exudates, cotton–wool spots
- Malignant: moderate plus optic disc swelling

6

Table 1. Classification of Hypertensive Retinopathy on the Basis of Recent Population-Based Data.

Grade of Retinopathy	Retinal Signs	Systemic Associations*
None	No detectable signs	None
Mild	Generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacity ("copper wiring") of arteriolar wall, or a combination of these signs	Modest association with risk of clinical stroke,[41,43] subclinical stroke,[43] coronary heart disease,[48,49] and death[45]
Moderate	Hemorrhage (blot, dot, or flame-shaped), microaneurysm, cotton-wool spot, hard exudate, or a combination of these signs	Strong association with risk of clinical stroke,[41,43] subclinical stroke,[43] cognitive decline,[42] and death from cardiovascular causes[45]
Malignant	Signs of moderate retinopathy plus swelling of the optic disk†	Strong association with death

* A modest association is defined as an odds ratio of greater than 1 but less than 2. A strong association is defined as an odds ratio of 2 or greater.
† Anterior ischemic optic neuropathy, characterized by unilateral swelling of the optic disk, visual loss, and sectorial visual-field loss, should be ruled out.

7

CASE

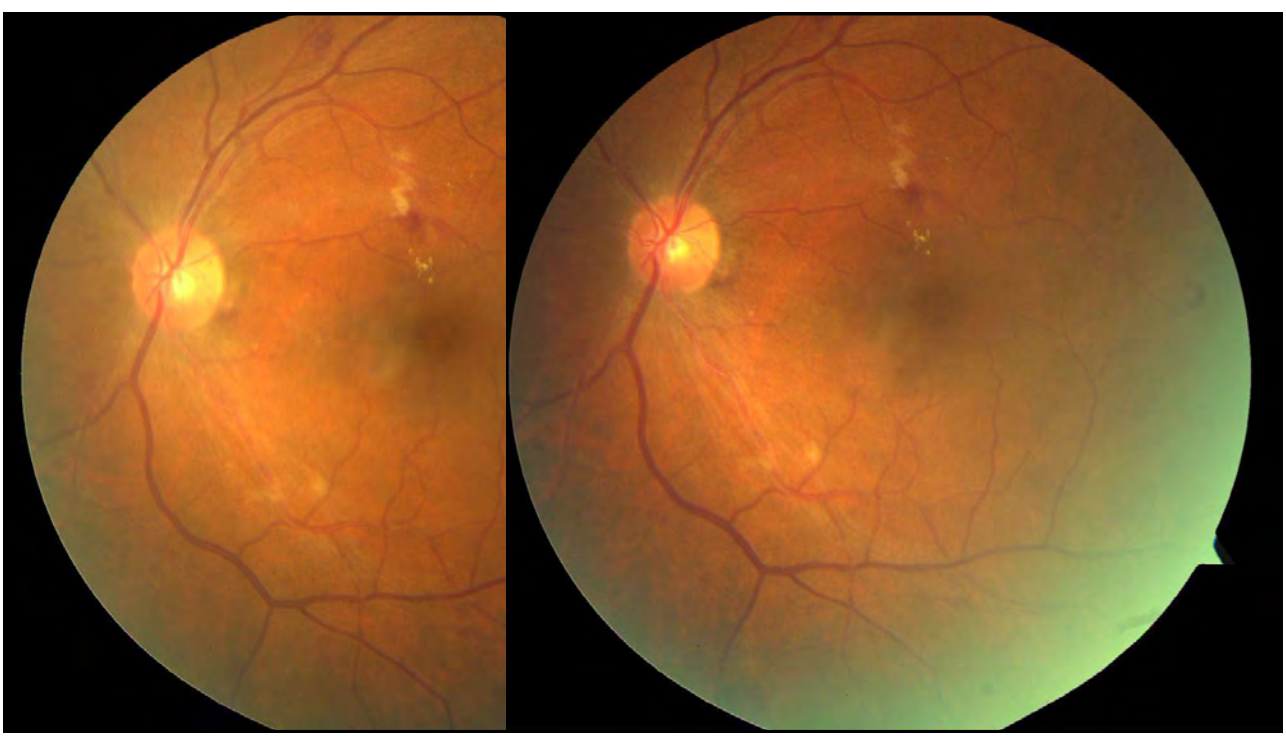
- The day before Christmas eve, we had a walk in patient.
- 66 year old AA male who was a inpatient presented to clinic.
- He complained about an amorphic spot close to the center of his vision
  - It stays in the same spot
  - Changes color and has amoeba like shape
  - Constantly present for past week or so.
- Drug abuse?
- He tried to give me stock investing advice…

8

CASE CONT

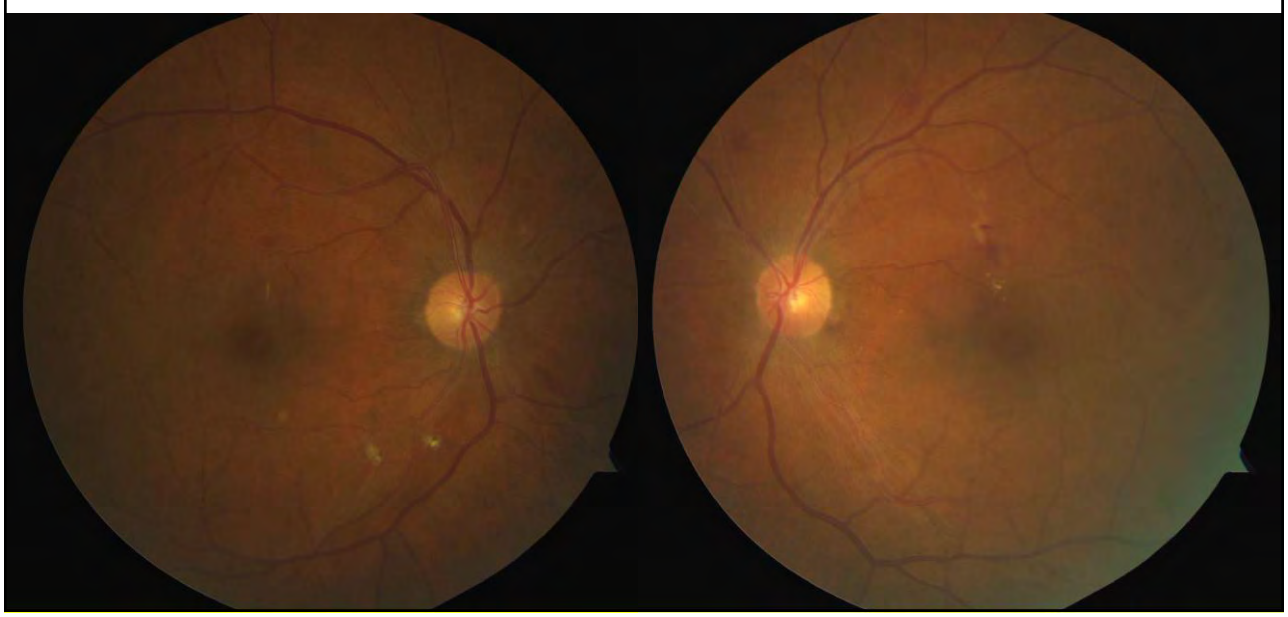
- More Hx: currently hospitalized for Malignant HTN,
  - BP 250/150
  - Renal Failure
- BCVA 20/20 OD, OS
- EOM: full/smooth
- Pupils: PERRL-APD
- FDT: had some misses sup temp and inf temp field.
- Ant Seg: unremarkable

9



10

POSTERIOR POLE 1 WEEK F/UP



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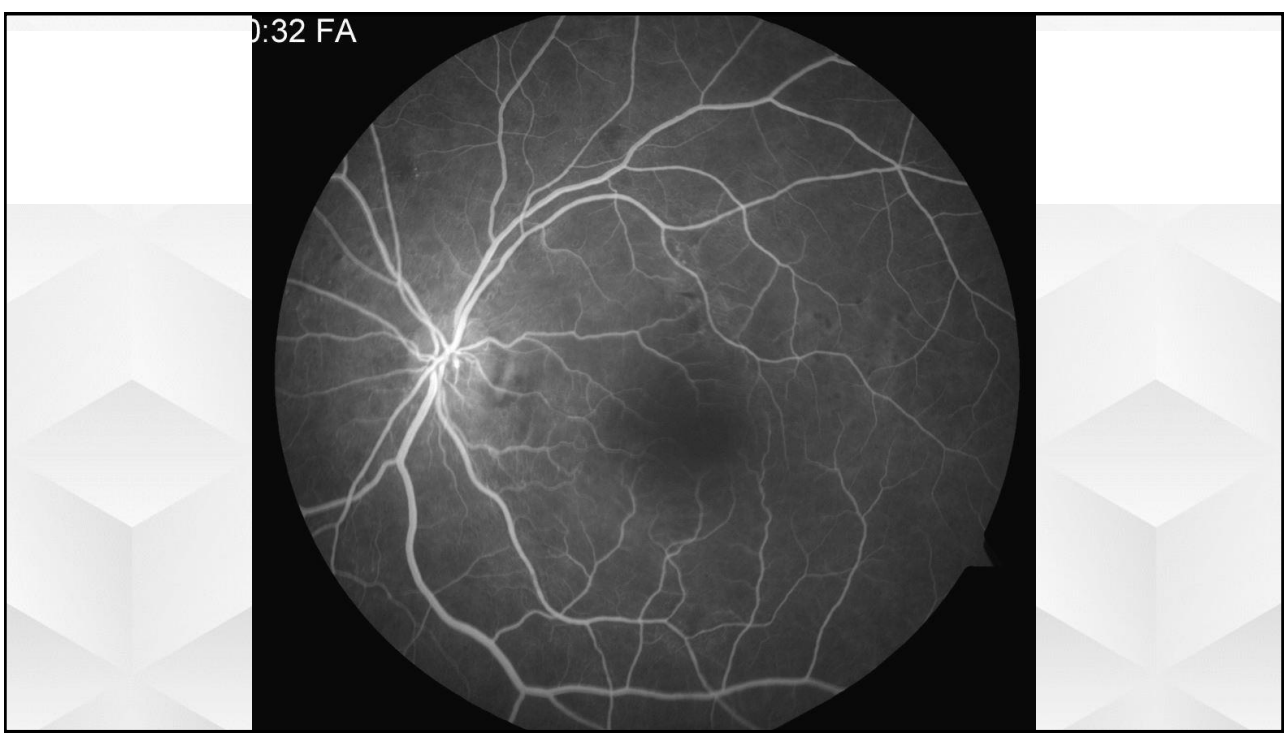

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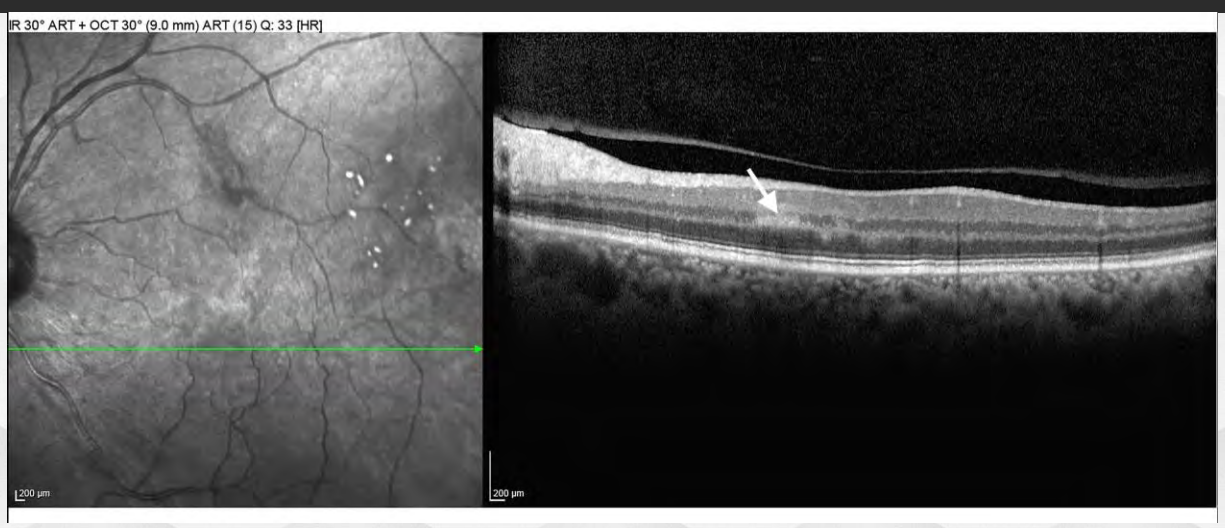
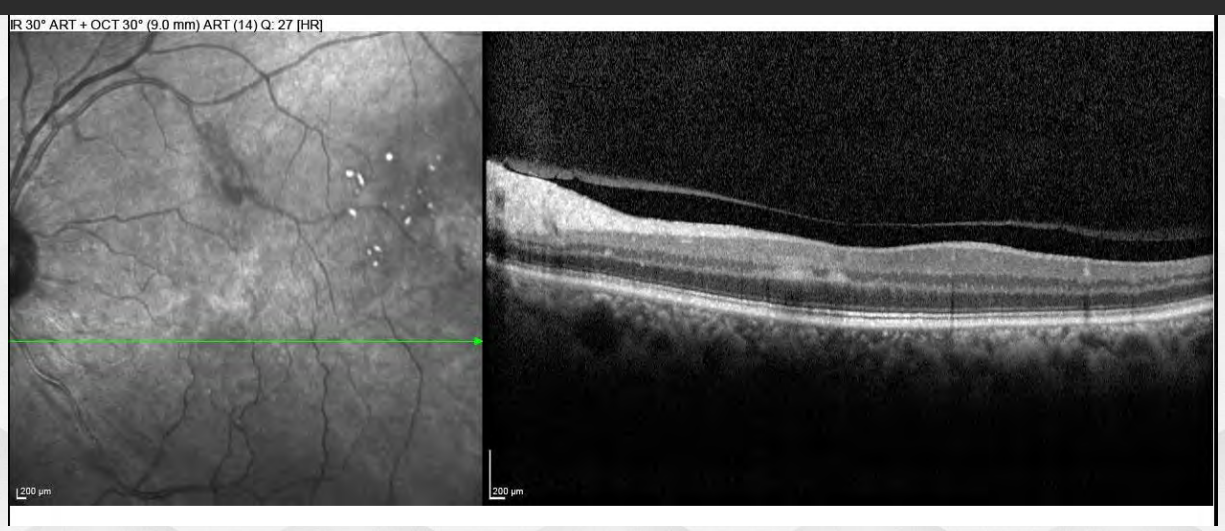
OCT


IR 30° ART + OCT 30° (9.0 mm) ART (15) Q: 33 [HR]
200 µm
200 µm

13

OCT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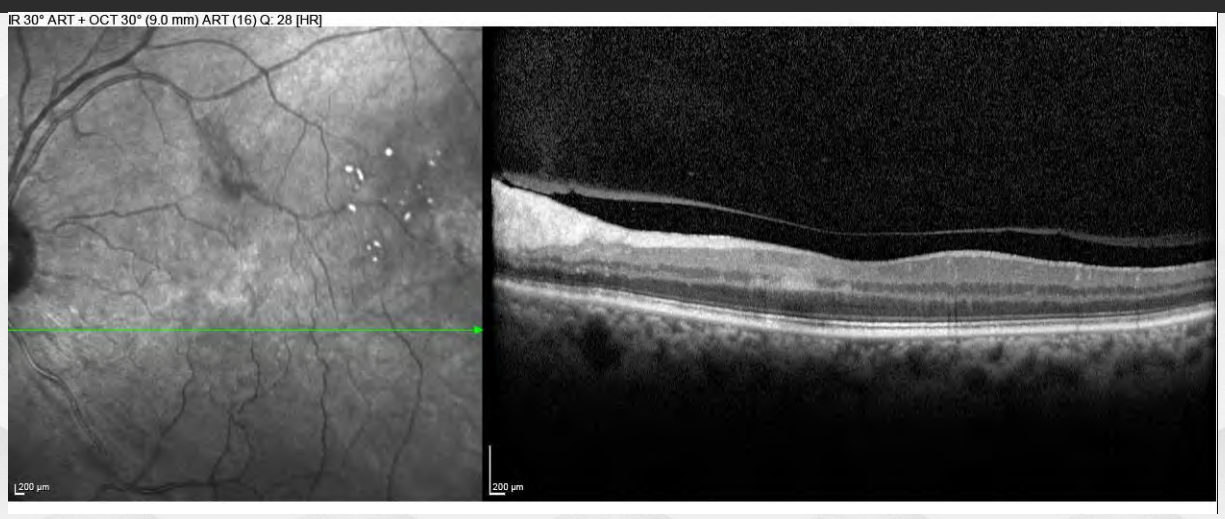
200 µm
200 µm

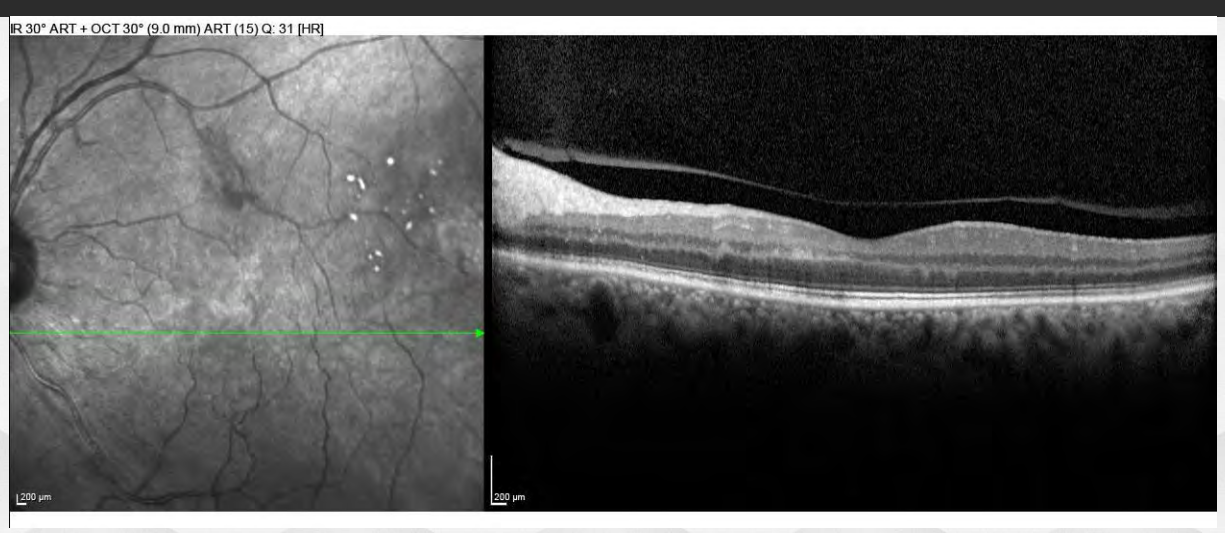
14

OCT

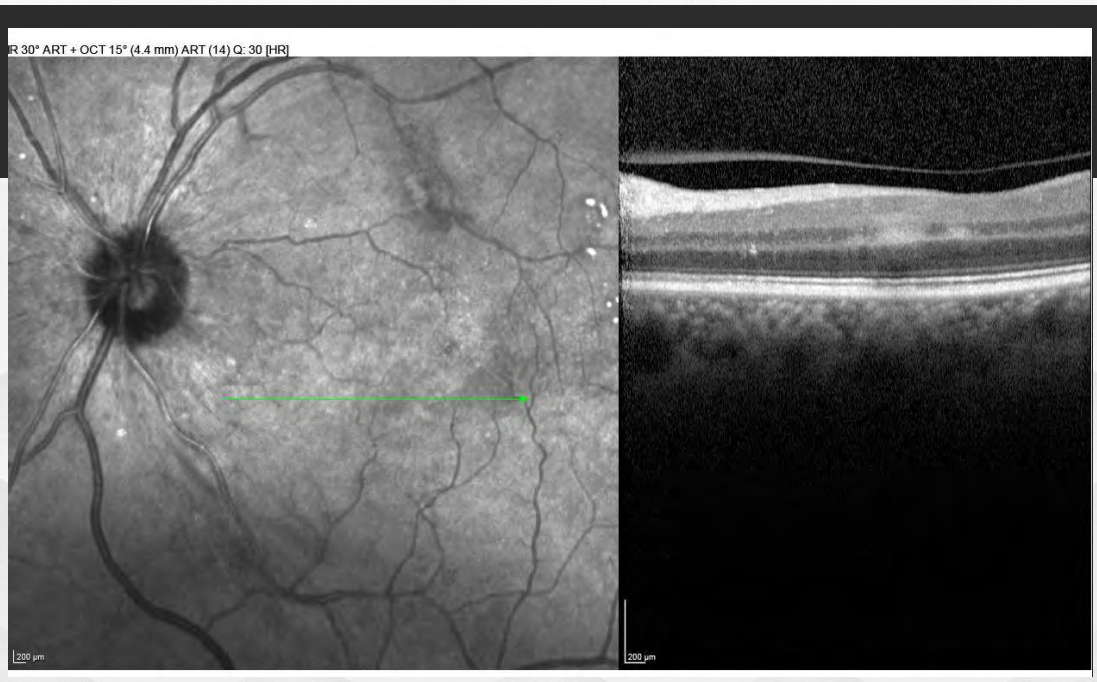

IR 30° ART + OCT 30° (9.0 mm) ART (16) Q: 28 [HR]
200 µm
200 µm

15

OCT


IR 30° ART + OCT 30° (9.0 mm) ART (15) Q: 31 [HR]
200 µm
200 µm

16



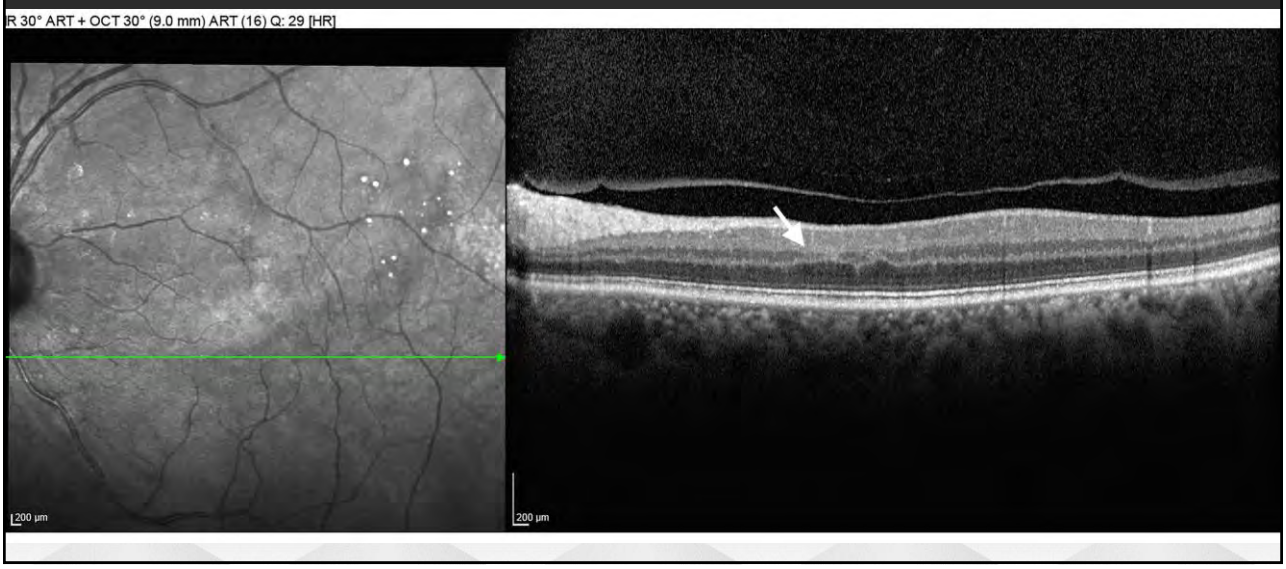
17

PARACENTRAL MIDDLE ACUTE MACULOPATHY

- First described in 2013, (Sarraf et al.)
- Paracentral hyper-reflective band-like lesion of inner nuclear layer (INL)
  - Theorized to be CWS of deeper retina.
- Arises from deep capillary retinal plexus ischemia.
- Difficult to observe in SL funduscopy, usually more visible on OCT.
- Usually resolves with INL atrophy/loss.

18

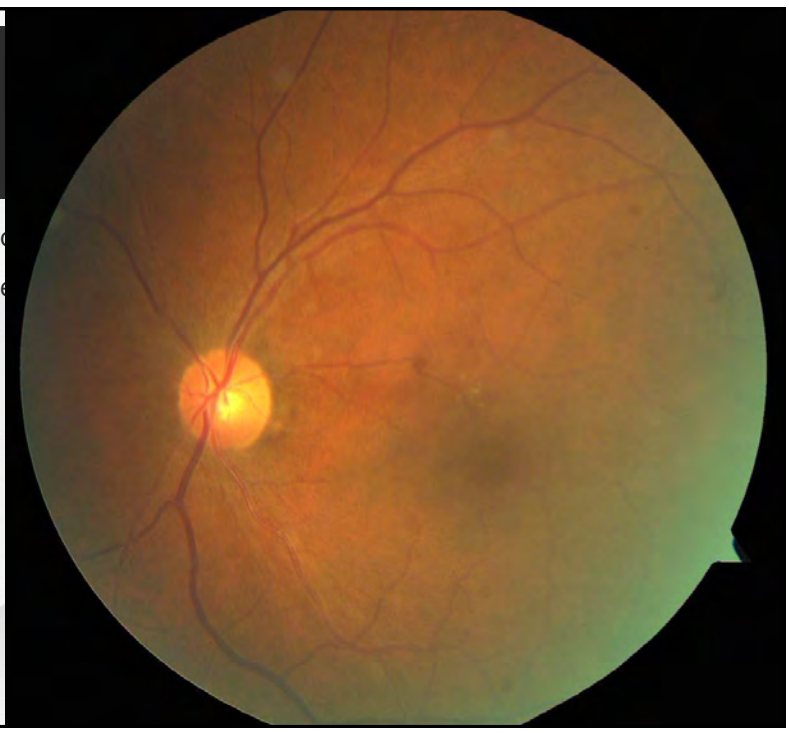
2 MONTH F/UP



19

2 MONTH F/UP

- Symptoms improved, occasi
- CWS, PAMM lesion and heme

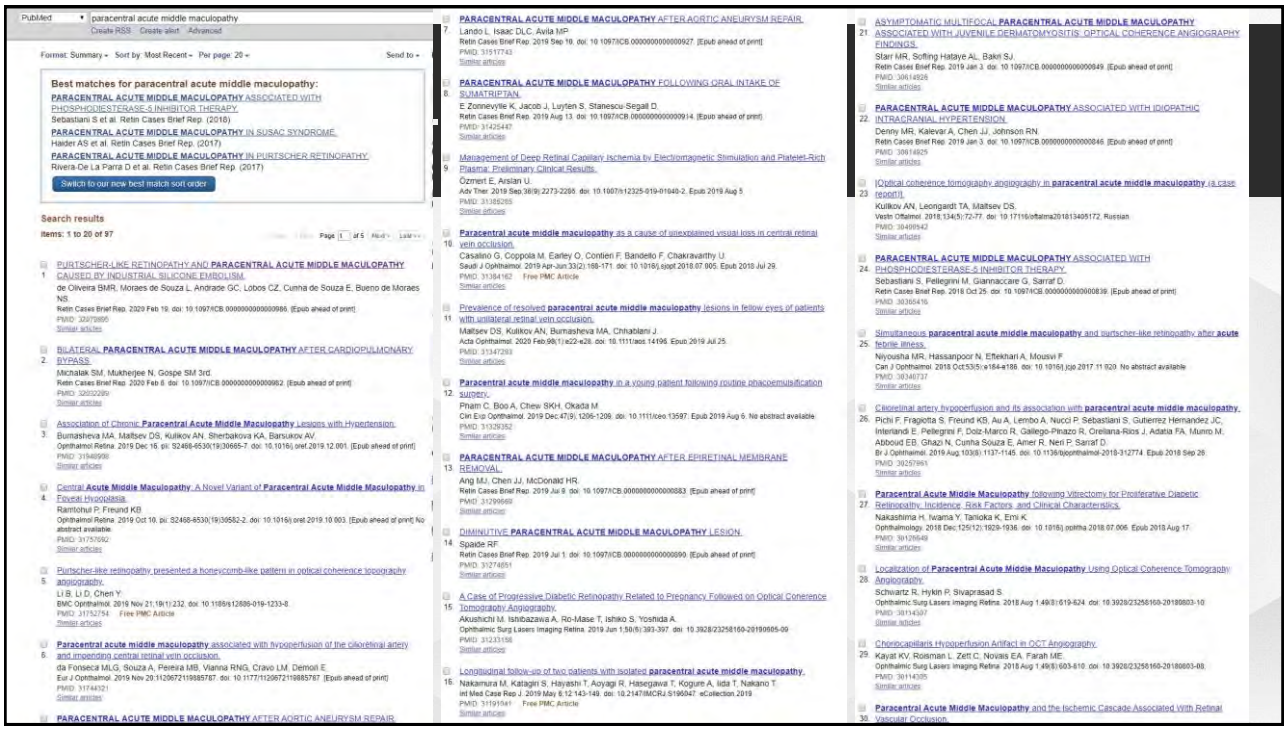


20

CAUSES OF PAMM

- Idiopathic
- Vascular diseases such as HTN/DM
- CRVO, CRAO, BRAO, sickle cell
- Purtscher / trauma
- Birdshot retinopathy
- Retinal vasculitis
- Excessive coffee consumption
- Amphetamines
- Vasopressors
- Oral birth control
- Hypovolemia
- Upper respiratory infection, (H1N1), new COVID-19?

21



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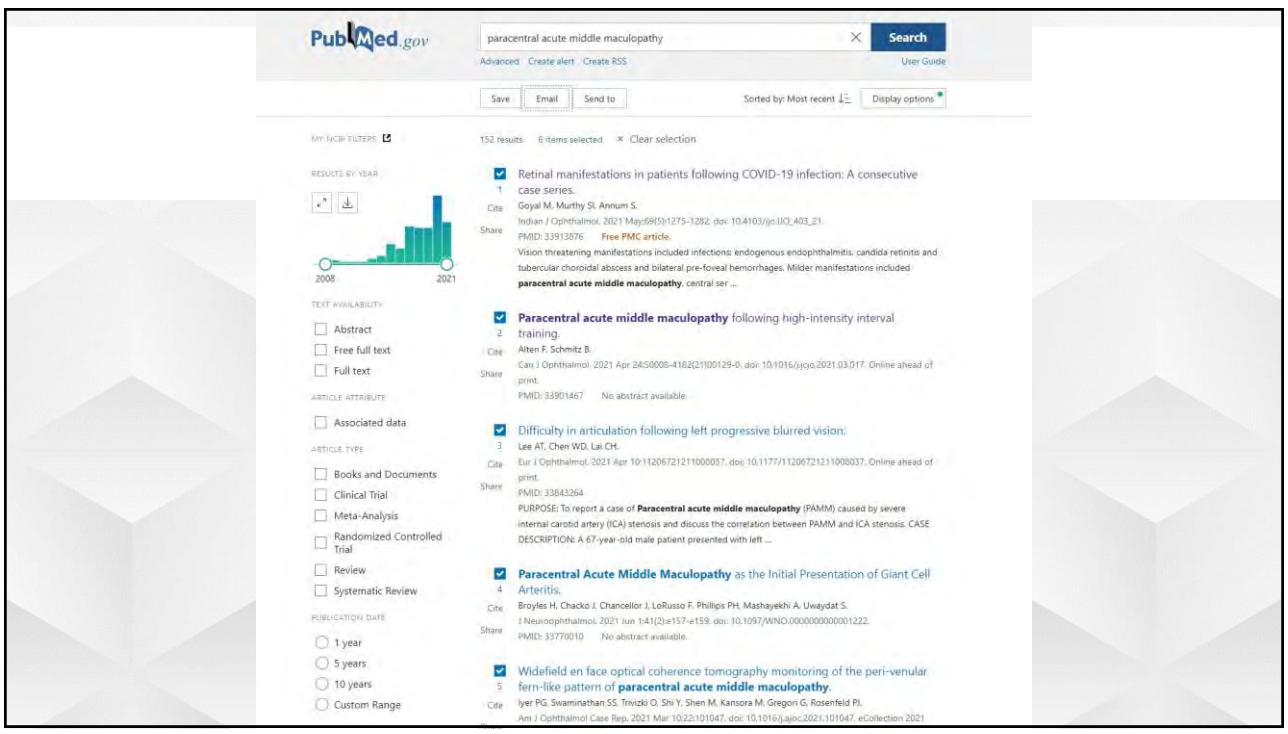
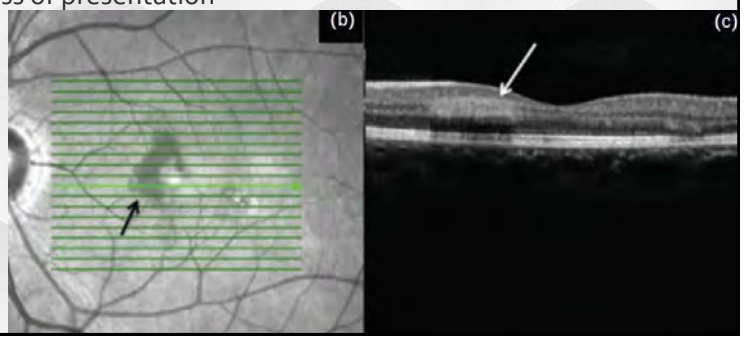


23

TESTING FOR PAMM

- Difficult to observe on Slit-lamp unless in very acute stage
- Does not show up on fluorescein angiography
- Best observed on OCT and near-infrared (NIR) reflectance.
- NIR will vary depend on acuteness of presentation



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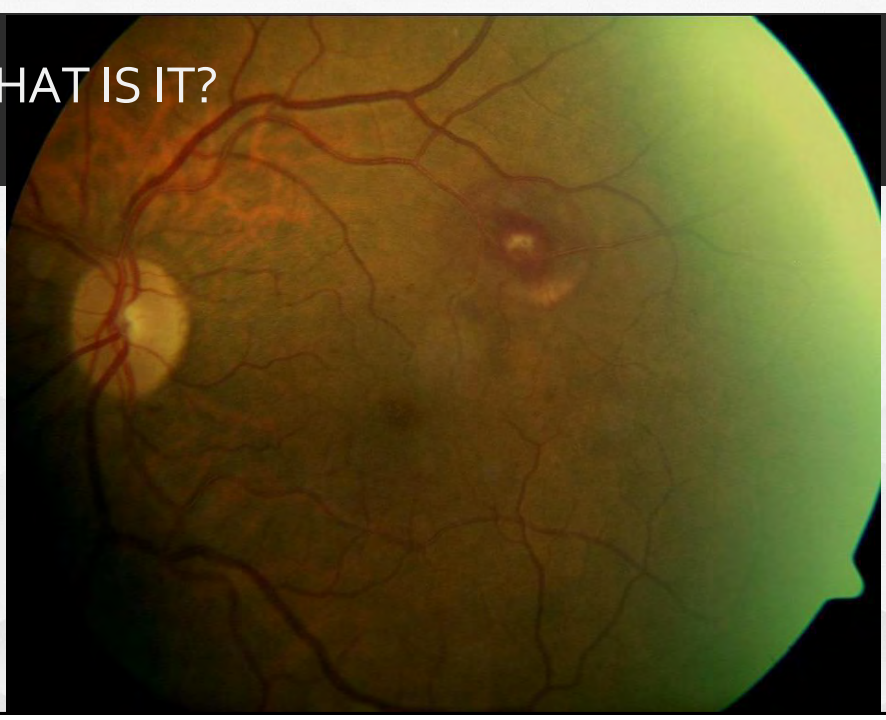
TREATMENT

- PAMM will typically resolve in several weeks
- Can have impact on vision if located in critical area
- Expect thinning of INL in area of PAMM
- Treatment should focus on underlying cause and referral to appropriate specialist or PCP. (some causes are worthy of emergency)
- Can monitor till resolution.

25

WHAT IS IT?



26

RETINAL ARTERIAL MACROANERURYSM

- Described as an arterial aneurysm typically located within the first 3 bifurcations.
- Results of arteriosclerosis and HTN, mechanism not fully understood.
  - 75% of patients with RAM have HTN
  - Theorized due to focal weakening of arterial wall, more susceptible to pressure.
  - Localization of RAM lesion is not well understood, but suggested due to emboli lodged in wall or local thrombosis.
  - Histology backs this theory (both thrombus and cholesterol plaques have been found in RAM)
- Most RAM can spontaneously resolve over months.
- Depending on location, with leakage or hemorrhaging can cause vision loss.

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RAM

- Careful observation of patients, especially if located in sup arcade above Macula
- Consider referral if appears leaky and ready to rupture.
- Treatments typically involve anti-VEGF

Intravitreal Bevacizumab for Macular Complications From Retinal Arterial Macroaneurysms

FRANCESCO PICHI, MARIACHIARA MORARA, CARLO TORRAZZA, GIANLUIGI MANZI, MICOL ALKABES, NICOLE BALDUCCI, LUCIA VITALE, ANDREA LEMBO, ANTONIO P. CIARDELLA, AND PAOLO NUCCI

28

ANTI-VEGF STUDY

- 37 patients, 38 total RAMs treated.
- First Study to demonstrate treatment which can improve vision and outcome

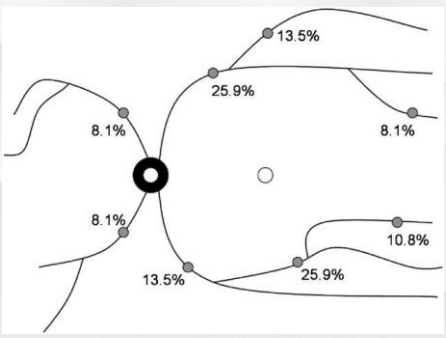


TABLE 3. Progression of Best-Corrected Visual Acuity and Central Retinal Thickness in the Retinal Arterial Macroaneurysm Groups With Hemorrhagic and Exudative Complications, After Each of the 3 Injections of Intravitreal Bevacizumab

	Hemorrhagic Retinal Arterial Macroaneurysms (n = 18) (mean ± SD)	Exudative Retinal Arterial Macroaneurysms (n = 19) (mean ± SD)	*P* (Mann-Whitney Test)
BCVA (logMAR)			
Baseline	0.60 ± 0.21	0.53 ± 0.2	.51
Week 2	0.36 ± 0.13	0.46 ± 0.14	.04
Week 6	0.22 ± 0.15	0.23 ± 0.09	.81
Week 12	0.06 ± 0.08	0.10 ± 0.10	.28
CRT (μm)			
Baseline	543.53 ± 203.50	495.94 ± 179.49	.38
Week 2	412.63 ± 142.86	378.94 ± 130.56	.49
Week 6	290.26 ± 76.80	277.11 ± 67.79	.47
Week 12	213.95 ± 25.41	215.78 ± 29.03	.81

BCVA = best-corrected visual acuity; CRT = central retinal thickness; logMAR = logarithm of minimal angle of resolution.

29

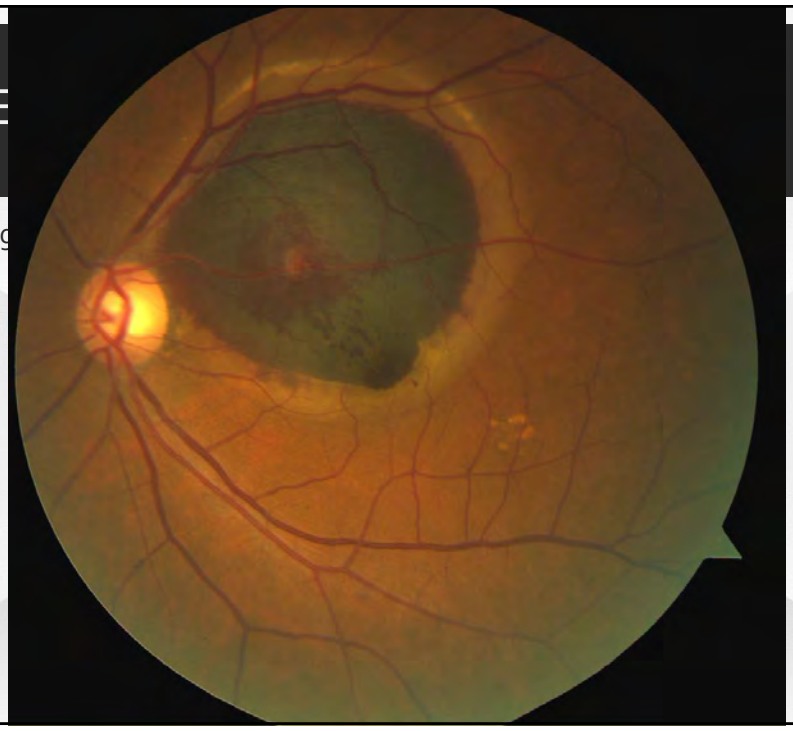
RAM CASE

- 68yr old Asian male with established hx and regularly followed for glaucoma suspicion.
- Last seen 2 months ago, walked in today complaining of grey blob in center of vision left eye. Started last night when watching TV. Symptom is constant.
- Laundry list of vascular conditions:
  - A-fib
  - Atrial flutter
  - Hx of stents
  - Tabaco smoker
  - Hyperlipidemia
  - HTN
  - Obesity

30

CASE

- Entering



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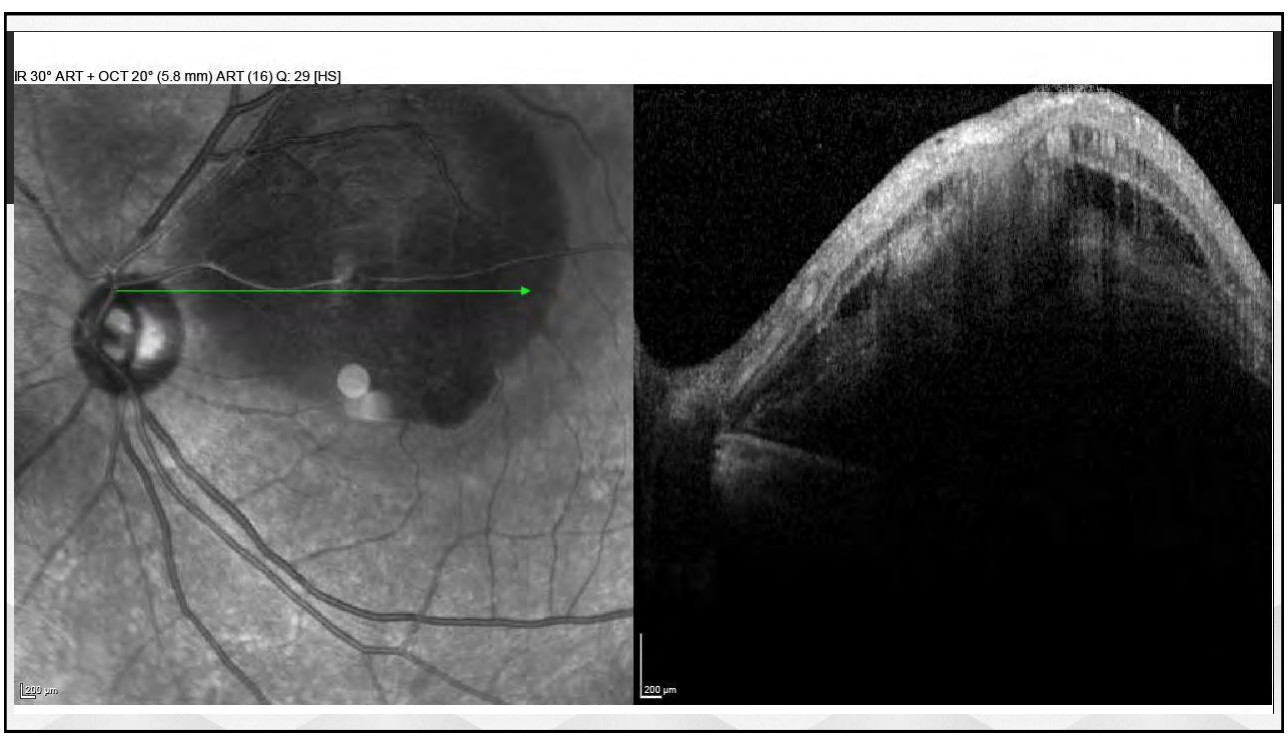
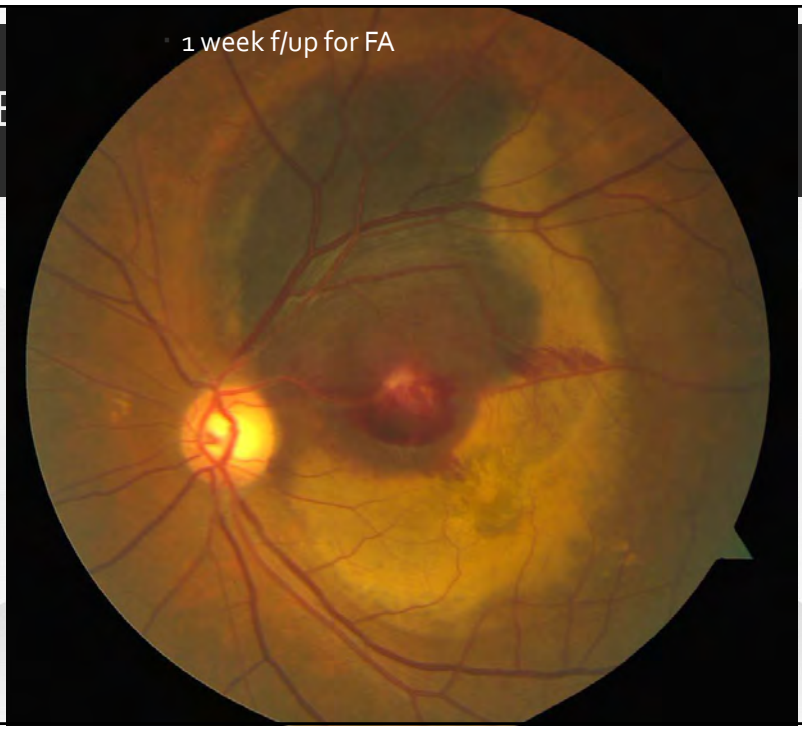


32

CASE

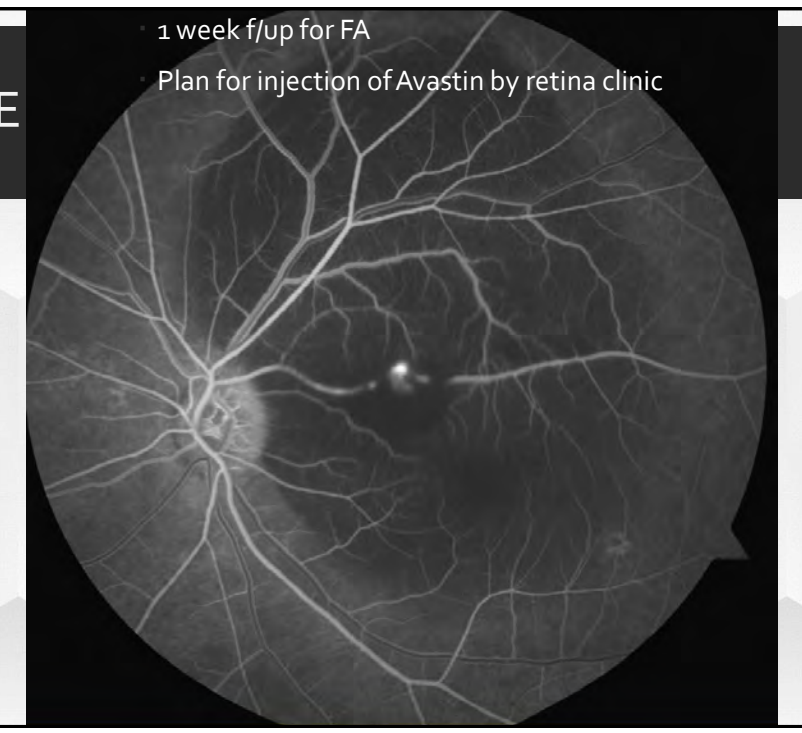
- 1 week f/up for FA



33

CASE

- 1 week f/up for FA
- Plan for injection of Avastin by retina clinic



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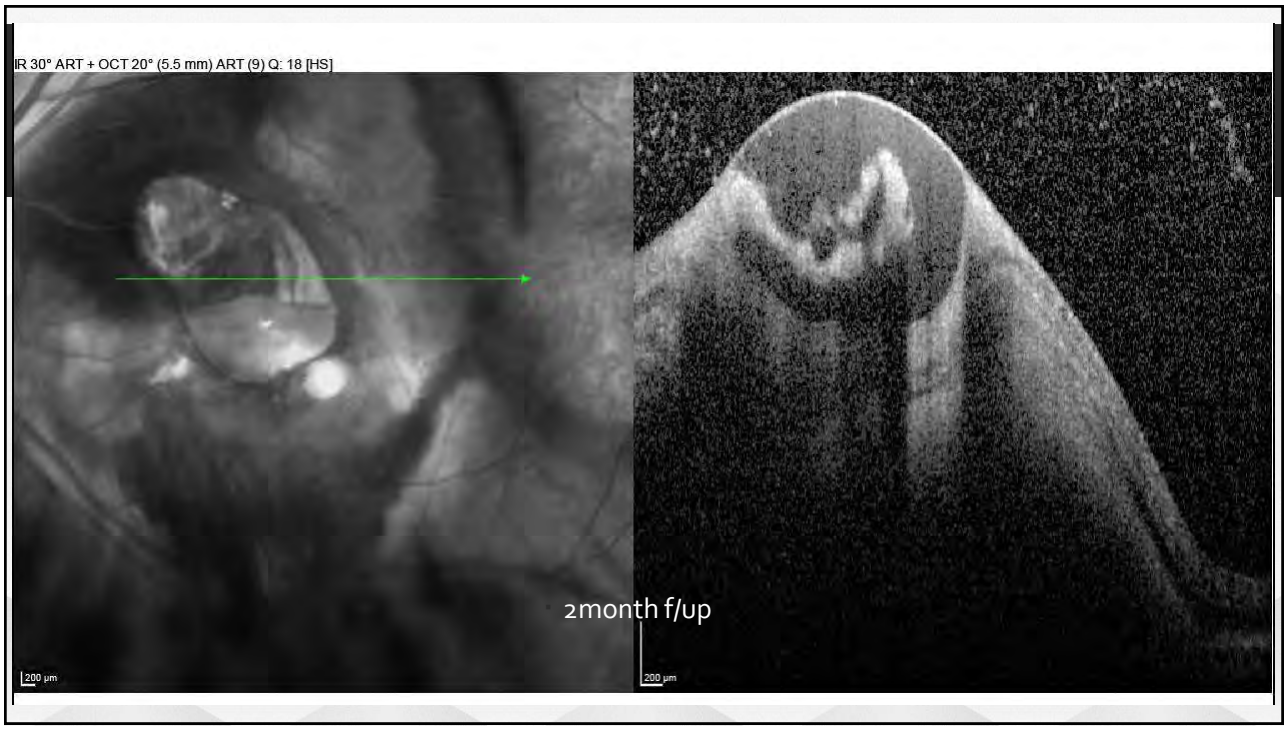
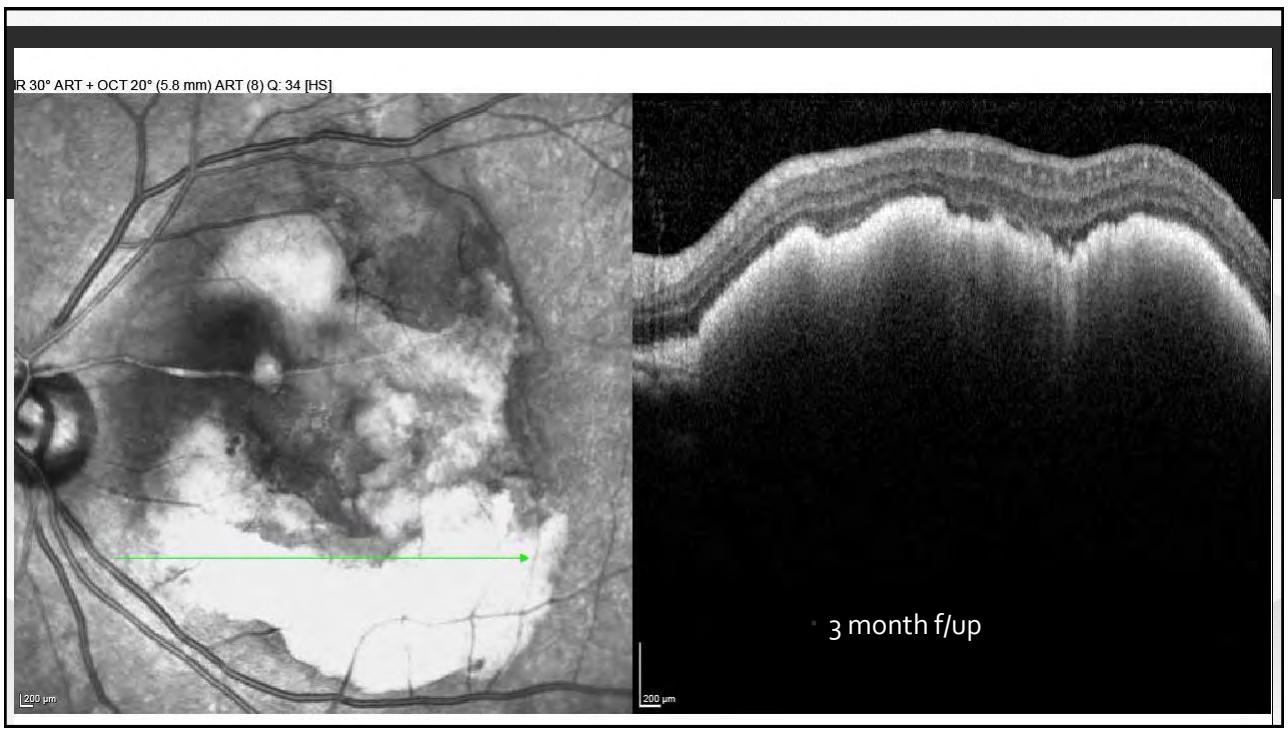
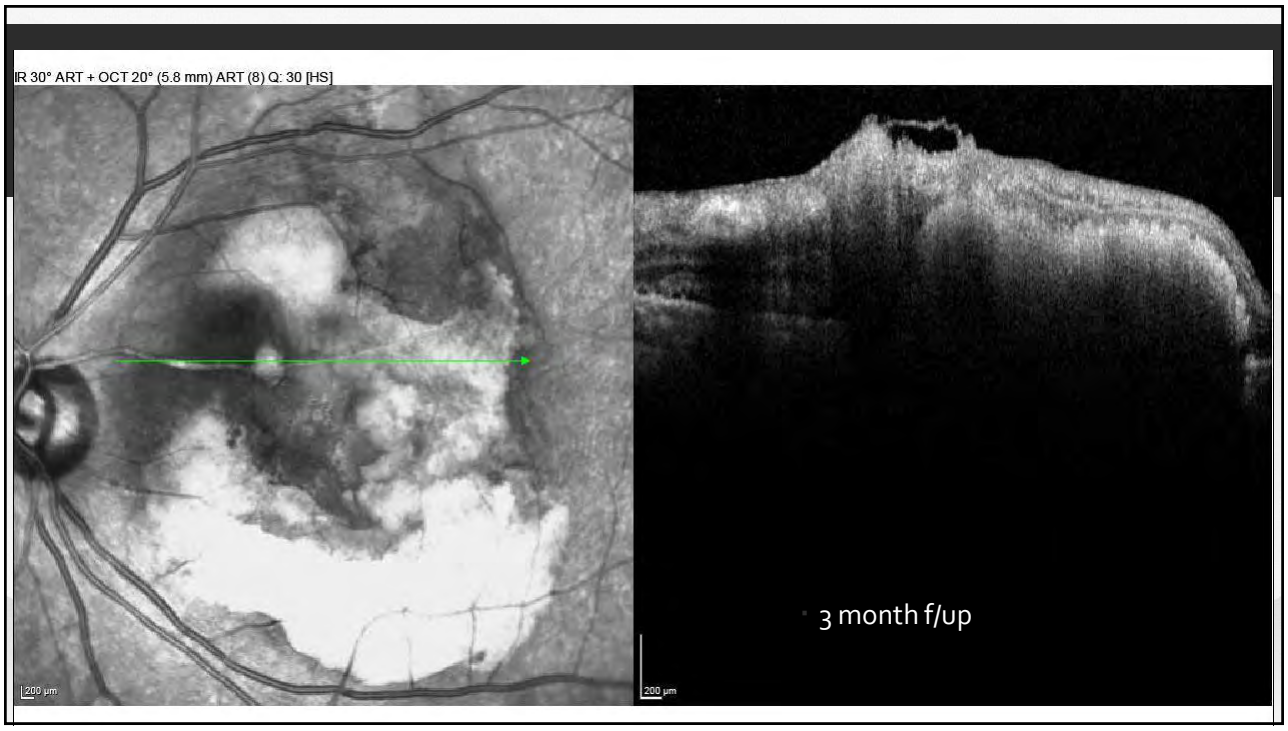

IR 30° ART + OCT 20° (5.5 mm) ART (9) Q: 18 [HS]
2month f/up
200 µm
200 µm

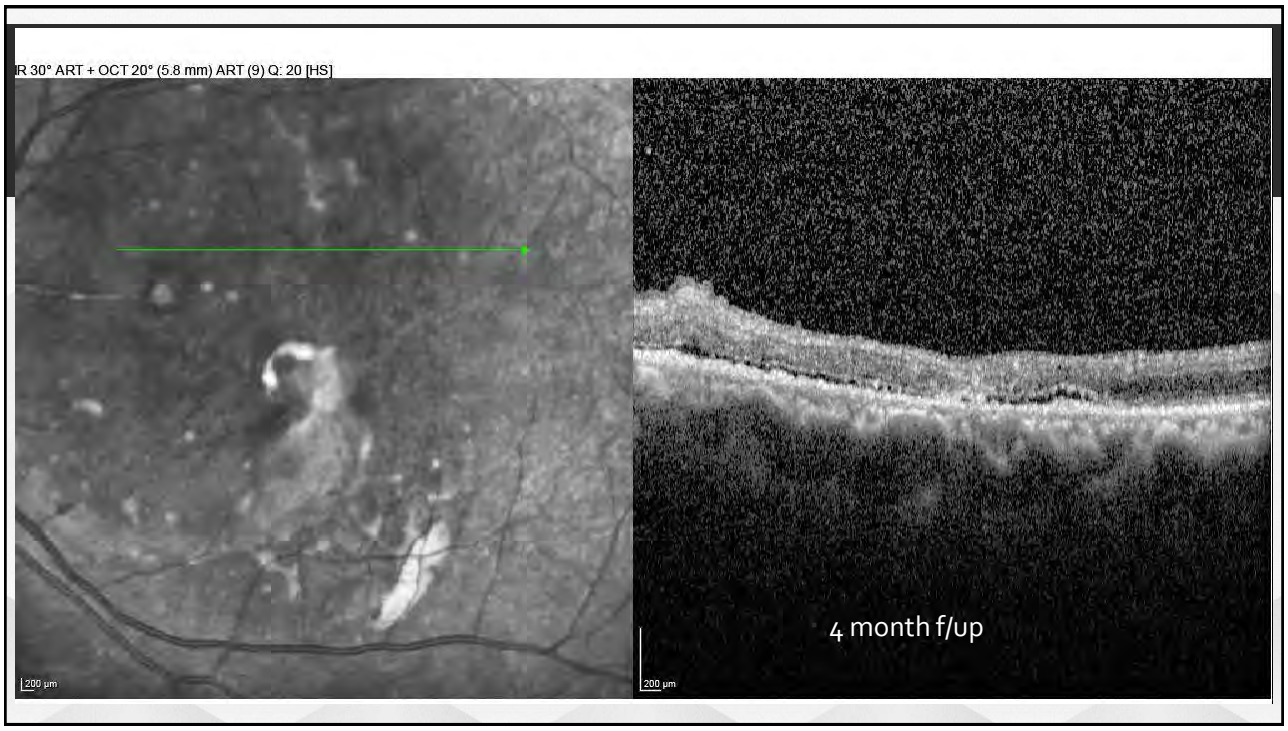
35


IR 30° ART + OCT 20° (5.8 mm) ART (8) Q: 34 [HS]
3 month f/up
200 µm
200 µm

36

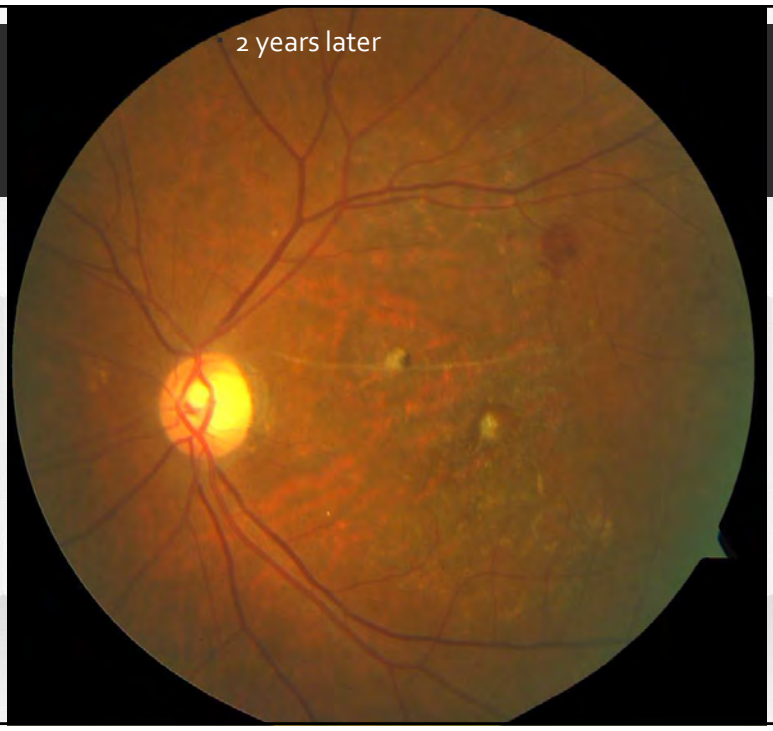

IR 30° ART + OCT 20° (5.8 mm) ART (8) Q: 30 [HS]
3 month f/up
200 µm
200 µm

37


IR 30° ART + OCT 20° (5.8 mm) ART (9) Q: 20 [HS]
4 month f/up
200 µm
200 µm

38

- 2 years later



39

DIFFERENTIAL TO CONSIDER

- Aneurysms of a venous nature can look very similar in size.
- Less likely to break or leak as much less pressure in venous system.
- More likely to form in DM retinopathy, poorly resolved venous occlusions.

40

CASE 2

- 85 year old Caucasian male with long standing hx of Hollenhorst plaque along superior arcade OS
- Plaque first discovered in 10/27/2016. Carotid ultrasound results: "Minimal plaque, no evidence of hemodynamically significant stenosis."
- Per Hematology-Oncology department: "no indication for noval oral anticoagulant". Pt should be routinely screened for medical disease.

41

CASE 2 CONT

- 85 year old Caucasian male with long standing hx of Hollenhorst plaque along superior arcade OS
- Plaque first discovered in 10/27/2016. Carotid ultrasound results: "Minimal plaque, no evidence of hemodynamically significant stenosis."
- Per Hematology-Oncology department: "no indication for noval oral anticoagulant". Pt should be routinely screened for medical disease.
- Pt has been followed for multiple issues such as few episodes of amaurosis fugax and GL suspect.
- Last seen 2 months ago for comprehensive exam, presented to clinic because of fluctuating vision and "a film" over his right eye.

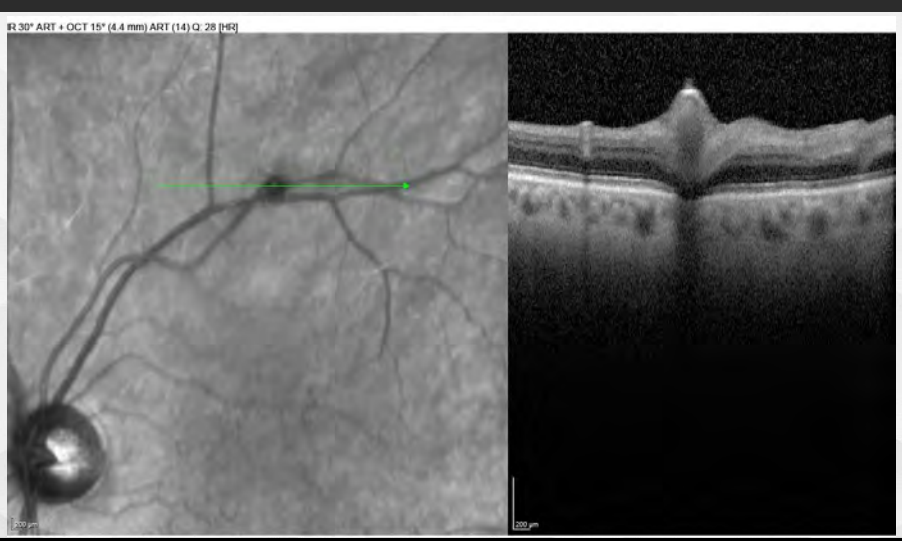
42

CASE 2 CONT

- BCVA 20/25 OD, 20/25 OS
- Ant seg findings remarkable for blepharitis/MGD and visually significant cataracts OU
- Post seg: Retinal aneurysm at location of hollenhorst plaque.

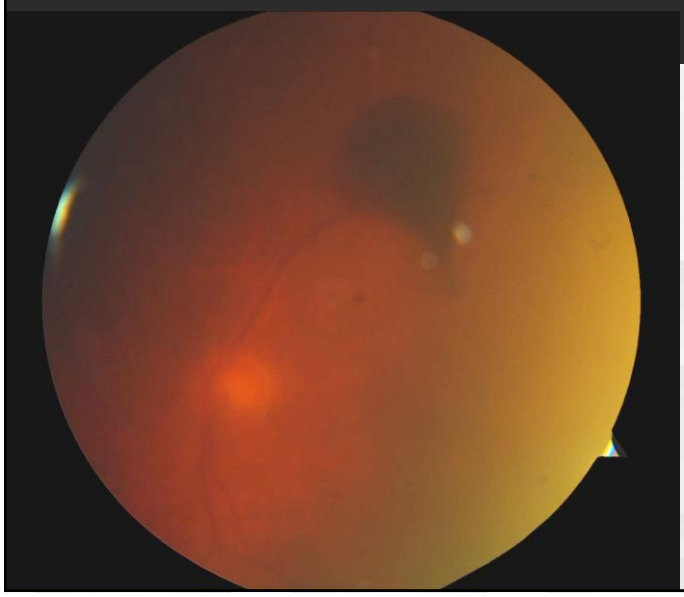
43

OCT



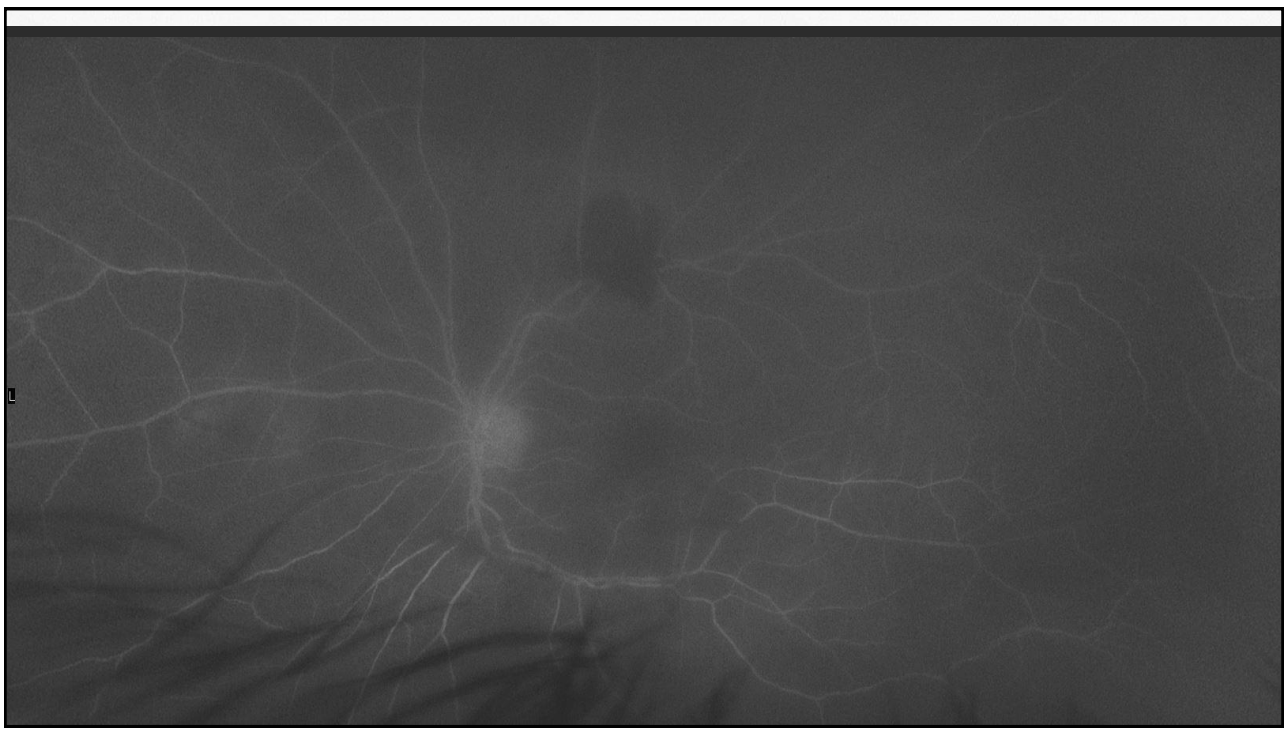
44

PHOTO 1 MONTH LATER



Pt had dense cataracts
Sorry for poor quality photos.

45

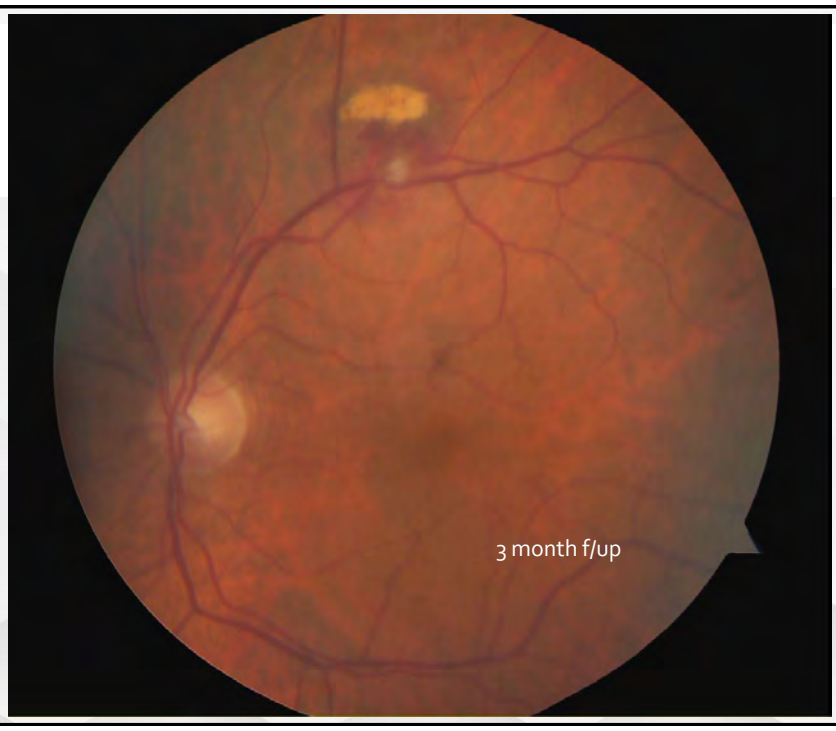


46

CASE 2 CONT

- Pt decided to have CEIOL done at JSEI in between f/up.
- vitrectomy simultaneously performed with CEIOL OS.

47



48

RETINAL PLAQUES

- Age related:
  - 0.8% visible in 49 to 60
  - 1.4% in ages 60 to 69
  - 2.1% in ages 70 to 79
  - 1.5% in the population over 80 years old
- Retinal emboli men > women
- single embolism (88%)
- multiple emboli (12%) -> referral to ER
- cholesterol (80%)
- platelet-fibrin (14%)
- calcific (6%).

49

RETINAL PLAQUES DDX

- Calcific emboli
  - White (non-refractile), larger size usually close to the optic disc.
  - originating from heart valve calcifications.
- Platelet-fibrin emboli
  - White/gray (non-refractile), elongated.
  - From cardiac and carotid disease
- Talc emboli
  - Small, white/yellow, highly refractile, typically located in the macular region.
- Lipid/fat emboli
  - Usually cannot visualize the emboli, cotton wool spots are often seen.
- Tumor cells
  - Originating from main source and expanding through adjacent arteries.
- Septic emboli
  - Ganulomatous in nature, r/o bacterial endocarditis

50

PLAQUE CONT

Prevalence of Retinal Emboli and Acute Retinal Artery Occlusion in Acute Ischemic Stroke

Robert A. Egan, MD,* and Helmi L. Lutsep, MD†

- 65 patients with stroke enrolled in study
- 11/65 had retinal emboli (16.9%)
- All emboli were hollenhorst.

51

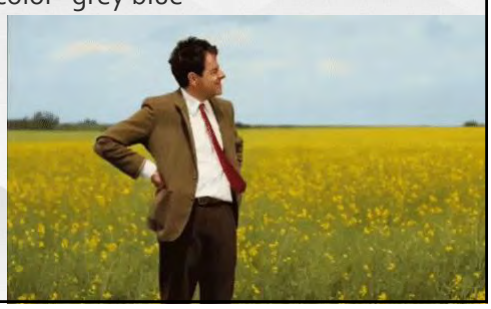
MANAGEMENT

- Typically cholesterol plaques (Hollenhorst) does not obstruct blood flow
- If obstructive, may require treatment depending on severity.
- F/up testing:
  - Lipid Panel
  - Carotid Ultrasound to r/o carotid stenosis
  - Transthoracic echocardiography? Vs Transesophageal echo?

52

LAST CASE

- 87 year old Caucasian male referred from ER to eye clinic for vision loss OS x 3 days.
- Pt was sent in the morning, didn't arrive till 4:30pm!
- Reports lost vision without pain upon waking.
- Additionally, pt sees large central spot that is light in color "grey blue"
- Spot may have gotten bigger in the last few days.

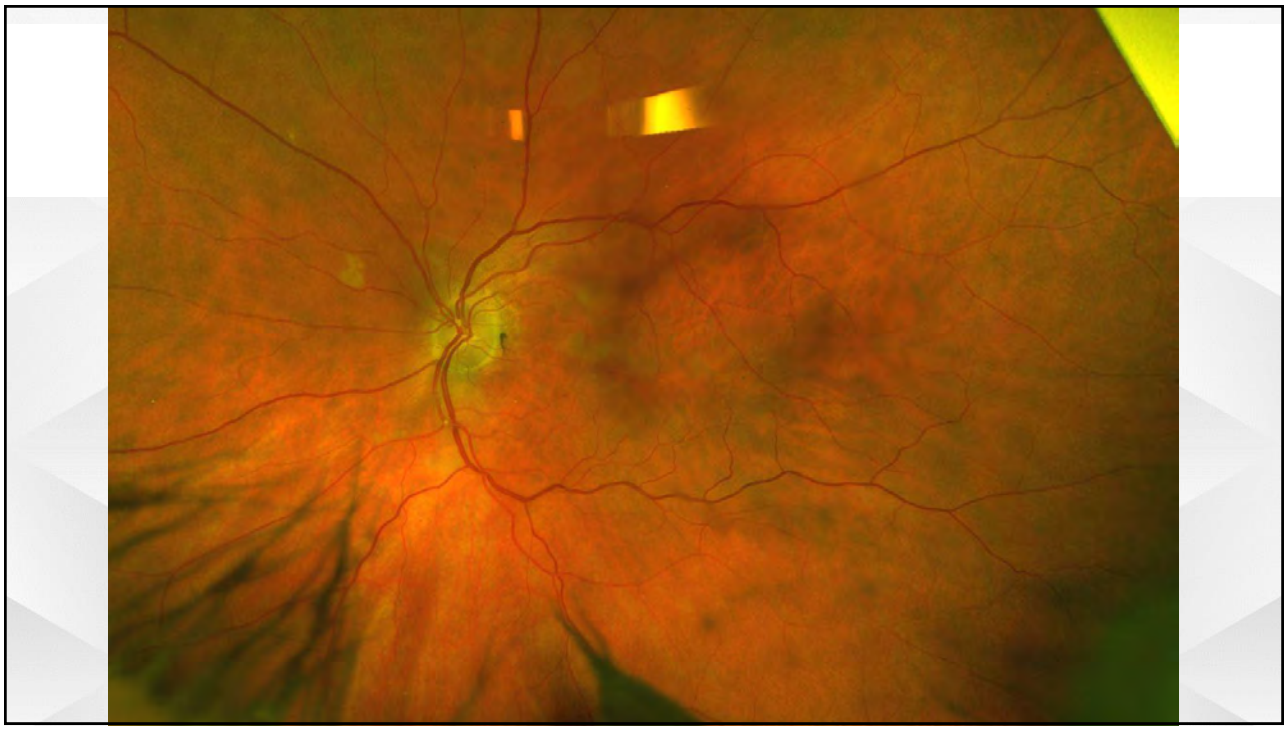


53

TESTING

- Systemic Hx:
  - HTN, hx of stroke, Stage 3 kidney disease, basal cell carcinoma.
- BCVA: 20/30 OD, 20/100 OS
- PERRL –apd
- Confrontational field: FTFC OD, OS
- SL: remarkable for PCIOLs OU, ectropion, floppy lids, MGD OU

54



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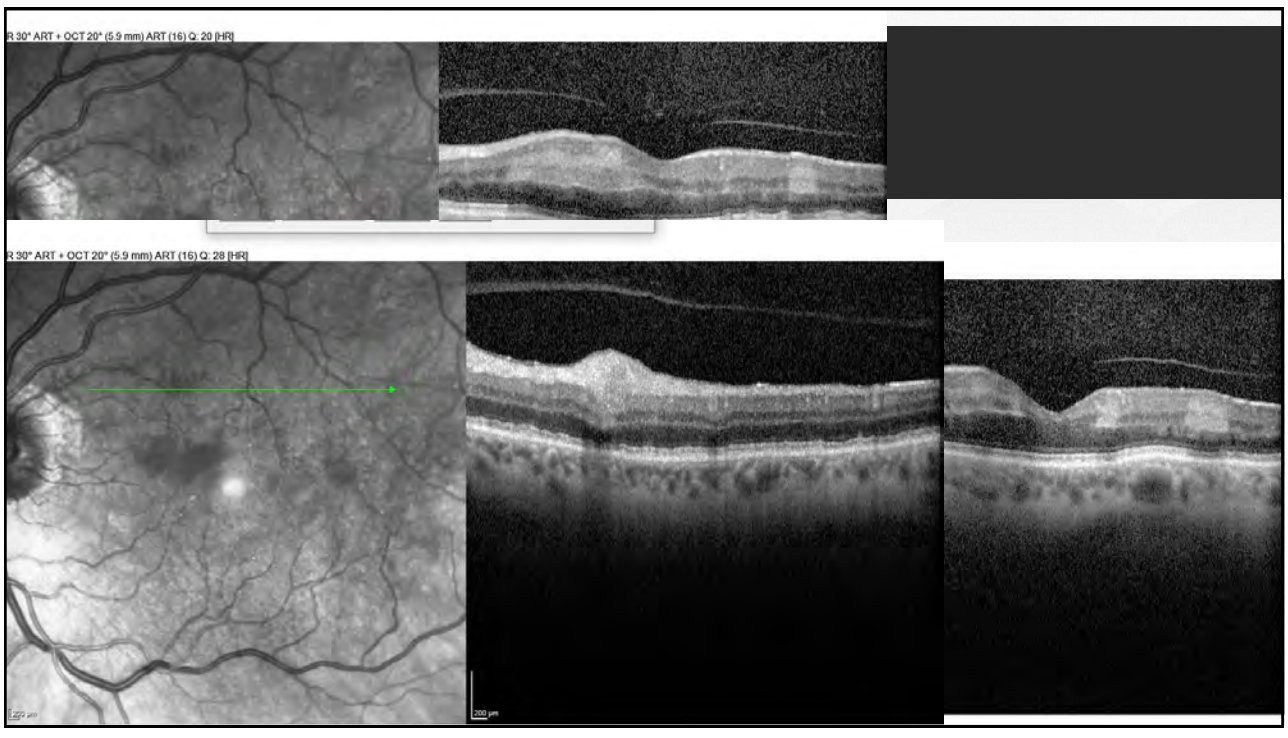
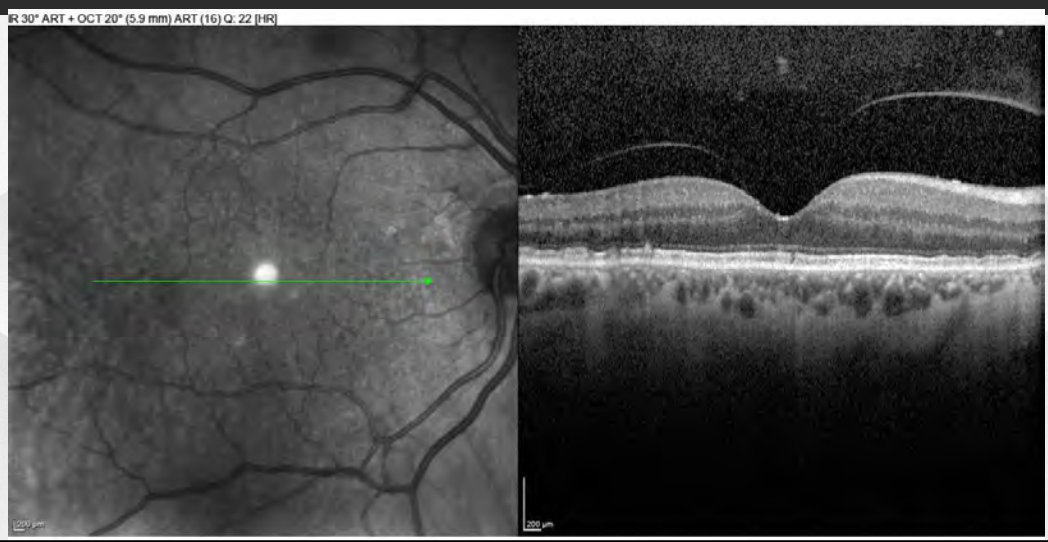

R 30° ART + OCT 20° (5.9 mm) ART (16) Q: 20 [HR]
R 30° ART + OCT 20° (5.9 mm) ART (16) Q: 28 [HR]

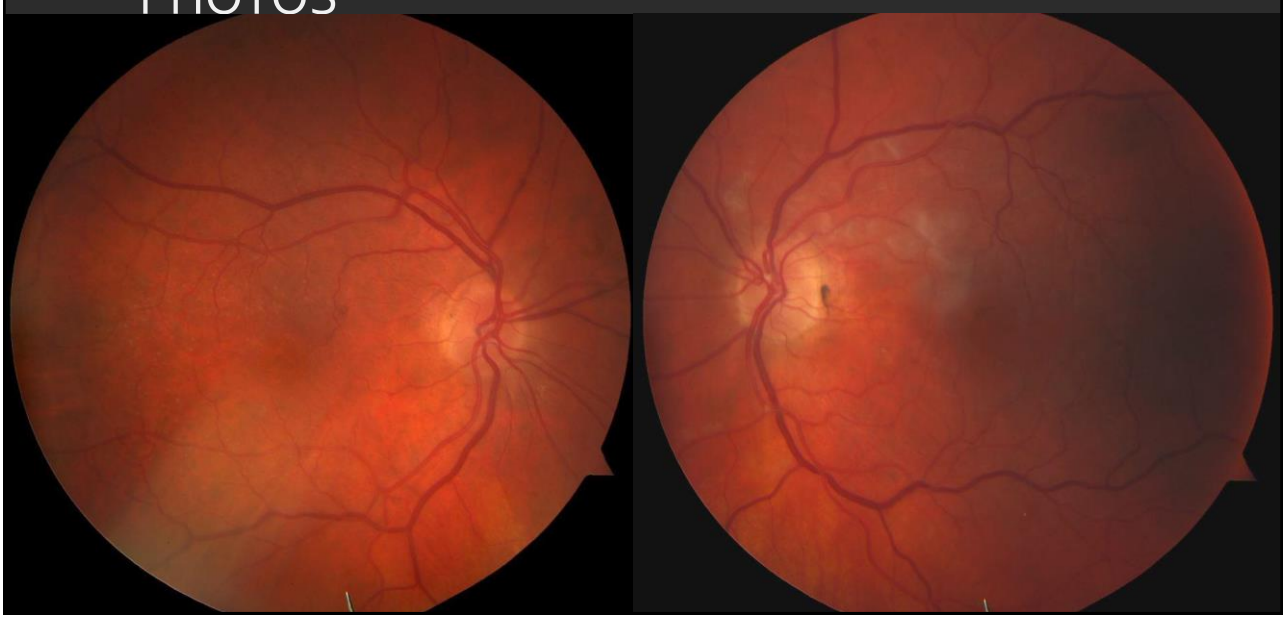
56

OCT



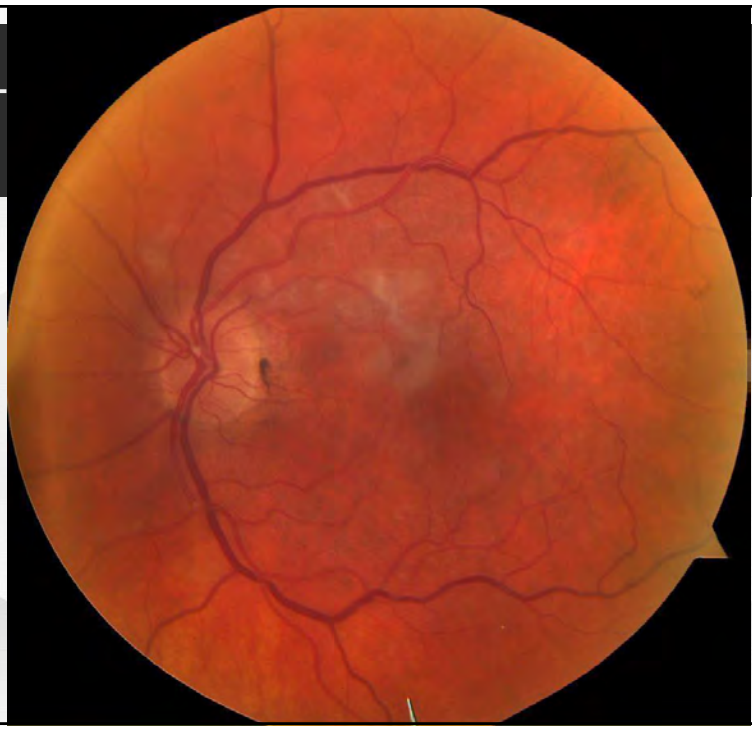
57

PHOTOS



58

PHOT



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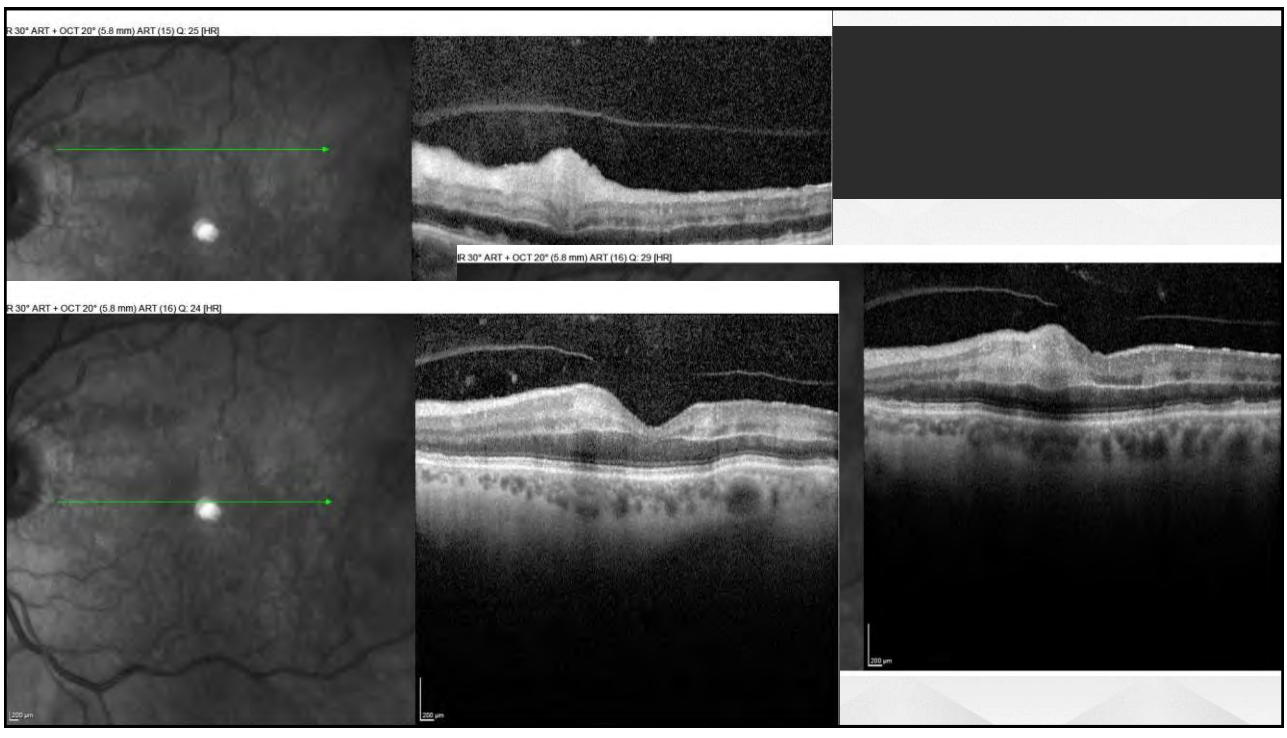
R 30° ART + OCT 20° (5.8 mm) ART (15) Q: 25 [HR]
R 30° ART + OCT 20° (5.8 mm) ART (16) Q: 29 [HR]
R 30° ART + OCT 20° (5.8 mm) ART (16) Q: 24 [HR]

60

CASE CONT

- Evolving BRAO OS, multiple Emboli
- Referred back to ER for stroke work up.
- Carotid ultrasound: 75% stenosed on ipsilateral side
- MRA/MRI:
  - "Multiple small punctate foci of diffusion positive recently completed ischemic injuries along the left middle cerebral artery territory, involving predominately the frontal, parietal and temporal cortex."

61

CASE CONT

- Patient was offered vascular surgery on left carotid. Pt refused intervention.
- Has been following up with neurology, now 76% stenosed since 6months ago.
- Still refusing treatment.

62

TAKE AWAYS

- Vascular disease has many serious implications, important to recognize other forms/manifestations and comorbidities.
- Appropriate referrals to neurology, ER, PCP etc. can be crucial in the overall health outcome of your patient.
- Look for subtly and detail in your exams, think beyond the immediate and think beyond vision.

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BR

BRAZILIAN BOOTY RETINOPATHY: PURTSCHER-LIKE RETINOPATHY WITH PARACENTRAL ACUTE MIDDLE MACULOPATHY ASSOCIATED WITH PMMA INJECTION INTO BUTTOCKS

Azadeh Khatibi, MD, MS, MPH

Purpose: To report a case of Purtscher-like retinopathy with paracentral acute middle maculopathy preceded by febrile illness after filler injection into the buttock muscles bilaterally for cosmesis to achieve a "Brazilian booty."

Methods: Retrospective case report.

Results: A 35-year-old female presented with febrile illness and then decreased vision after repeat polymethyl methacrylate injections into her buttock muscles in Mexico. Examination was significant for retinal whitening, especially in the perifoveal areas, and intraretinal hemorrhages. Optical coherence tomography and fluorescein angiography imaging were consistent with small-vessel ischemic disease in the retina and choroid. Once systemic infection was ruled out, patient was treated with high-dose intravenous and then oral steroids. Vision recovery was good, with retinal atrophy on optical coherence tomography in the previous areas of retinal whitening.

Conclusion: A Purtscher-like retinopathy with paracentral acute middle maculopathy and loss of vision may occur after filler injection below the neck, not just the face. This is the first report of vision loss caused by filler injected outside the face.

RETINAL CASES & BRIEF REPORTS 12:17–20, 2018

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BRAZILIAN BOOTY RETINOPATHY!?

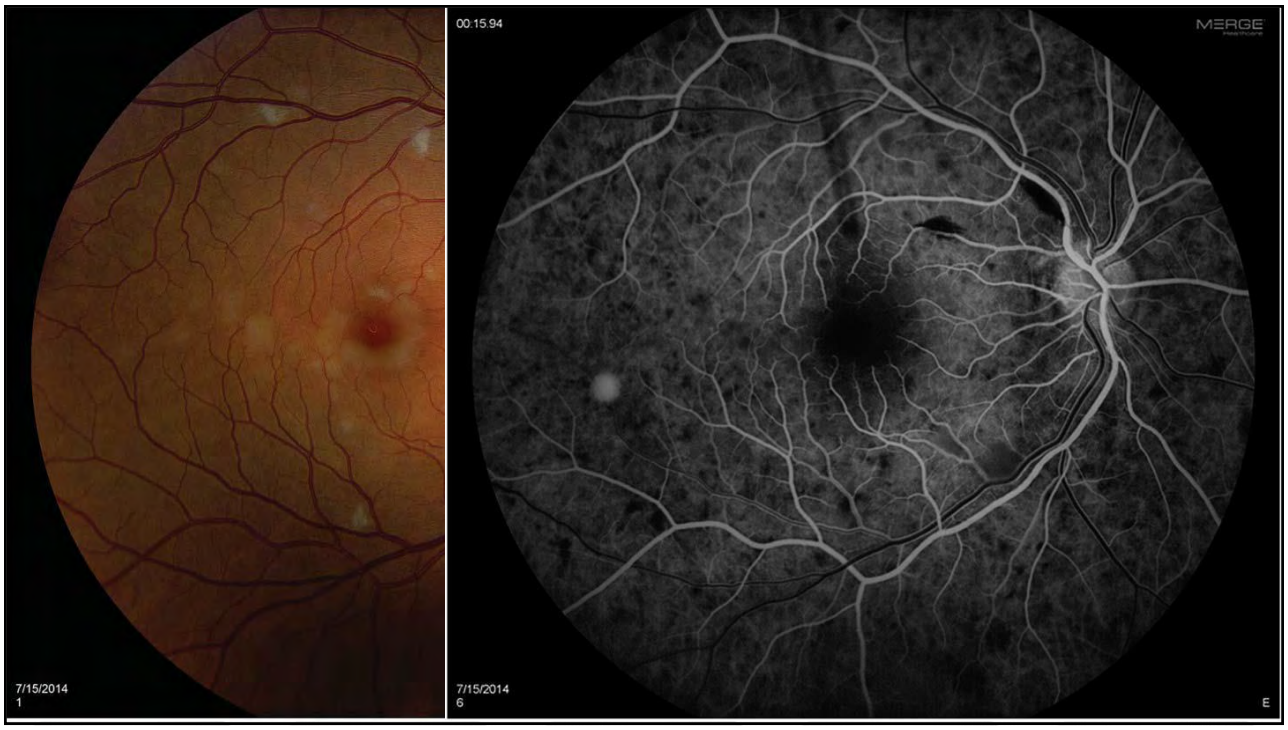
- 35 year old female with hx of depression
- Hx of liposuction and PMMA (Polymethylmethacrylate) injection in the buttocks bilaterally without incident.
- She returned 2 weeks later for round 2.
- Day 5: later she developed
  - HA, fever, body aches, nausea and vomiting.
- Day 8: Chest tightness and decreased vision OU.
- She was admitted to the hospital, extensive workup!

65

BRAZILIAN BOOTY RET CONT

- Lab Results:
  - Mild anemia
  - Elevated CRP, elevated ESR
  - Normal Lumbar puncture results
  - CT/MRI with and without contrast normal
  - Cardiac echo WNL
- BCVA 20/40 OD, 20/100 OS

66



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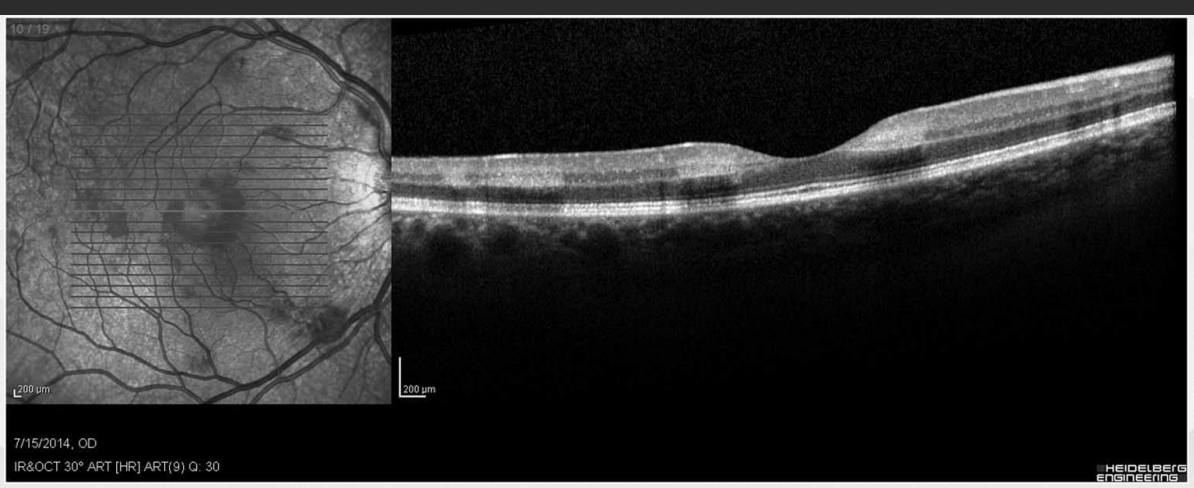
BRAZILIAN BOOTY RET CONT



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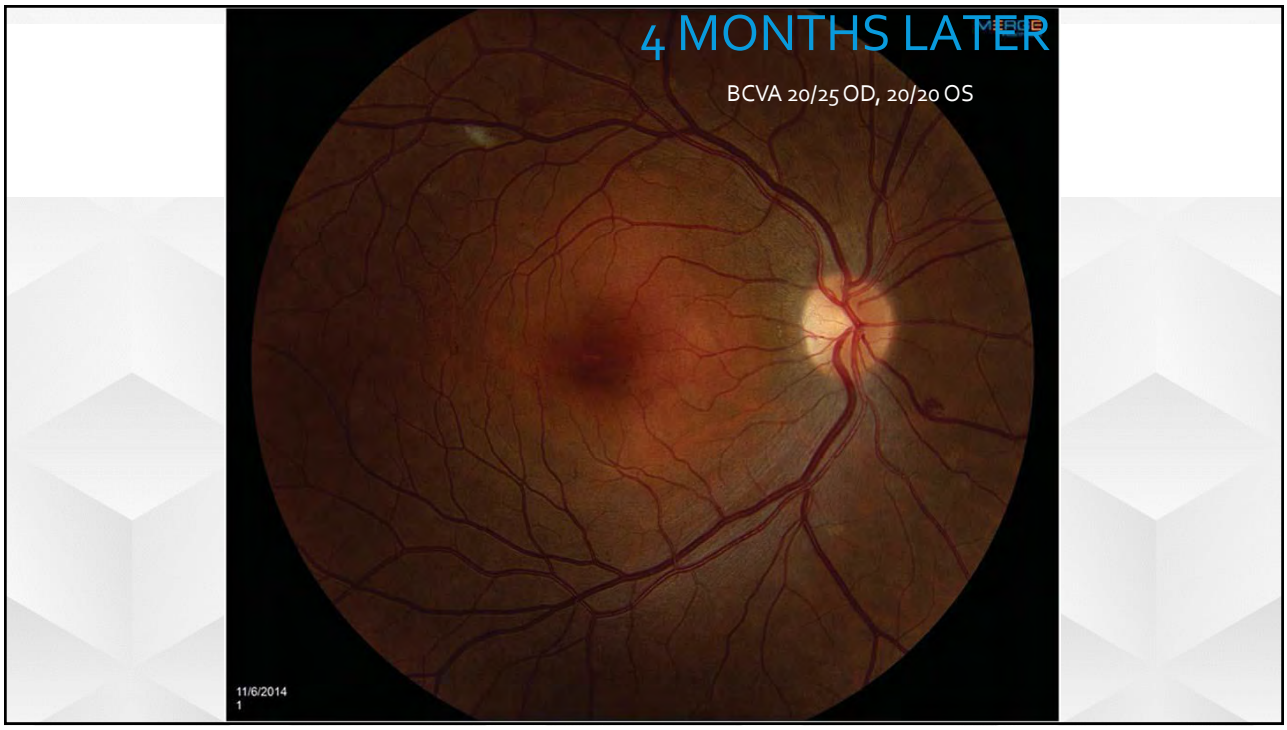
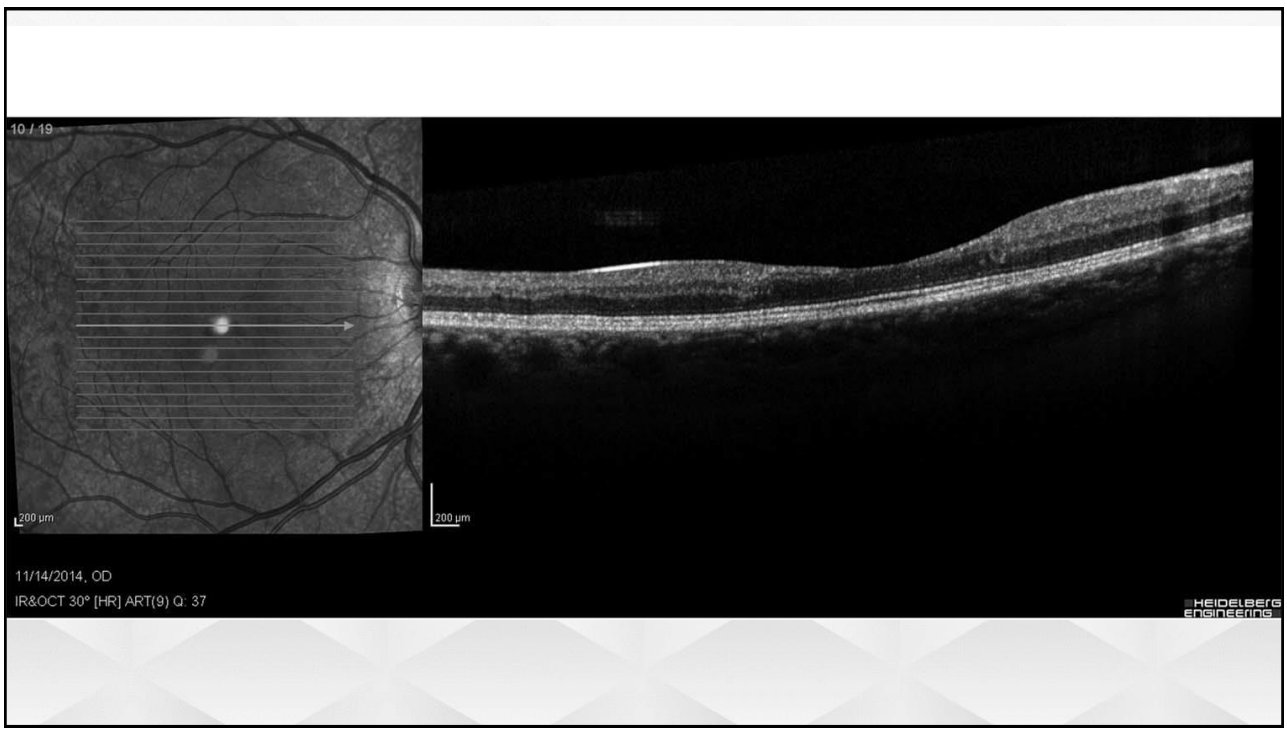

4 MONTHS LATER
BCVA 20/25 OD, 20/20 OS
11/6/2014
1

69


10 / 19
200 µm
200 µm
11/14/2014, OD
IR&OCT 30° [HR] ART(9) Q: 37
HEIDELBERG ENGINEERING

70

BRAZILIAN BOOTY RET CONT

- Author speculates PMMA travelled from injection site back to eyes.
- Causes a ischemic and inflammatory response that presented with Purtscher-like retinopathy and PAMM.
- Author questions whether large quantity PMMA vs Additives may have causes presentation. Pt's should be warned about possibility of vision loss with PMMA use.

71

REFERENCES

- Walsh JB: Hypertensive retinopathy. Description, classification, and prognosis. Ophthalmology 1982; 89: pp. 1127-1131
- Wong TY, and Mitchell P: Hypertensive retinopathy. N Engl J Med 2004; 351: pp. 231-2317
- Chawluk JB, Kushner MJ, Bank WJ, Silver FL, Jamieson DG, Bosley TM, Conway DJ, Cohen D, Savino PJ. Atherosclerotic carotid artery disease in patients with retinal ischemic syndromes. Neurology. 1988 Jun;38(6):858-63.
- Rahimy, E., Sarraf, D. "Paracentral acute middle maculopathy spectraldomain optical coherence tomography feature of deep capillary ischemia." Curr Opin Ophthalmol 2014, 25:207–212

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Stargardt's Macular Dystrophy: A Family Affair

Presented by Ashley Deemer, OD

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Stargardt's Macular Dystrophy: A Family Affair

Ashley Deemer, OD, FAAO
Assistant Professor
Marshall B. Ketchum University
Southern California College of Optometry

1

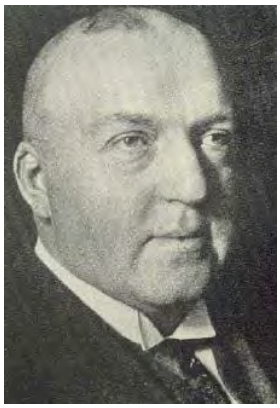
Disclosures

- No financial disclosures

2

Stargardt's Macular Dystrophy

- Most common autosomal recessive juvenile onset macular dystrophy
- Atrophic macular lesions with varying yellowish retinal flecks
  - Also known as fundus flavimaculatus



Weleber RG. *Arch Ophthalmol*. 1994.

3

Genetics

- Majority of cases caused by mutation in ABCA4 gene (STGD1)
  - Autosomal recessive
  - ABCA4 protein clears away vitamin A byproducts in photoreceptors
  - Mutation causes accumulation of lipofuscin

Avoid Vitamin A supplements!

4

Other Mutations

- Mutation in *ELOVL4* (STGD3)
  - Autosomal dominant
- Mutation in *PROM1* (STGD4)
  - Autosomal dominant
  - Some cases inherited in autosomal recessive manner

5

Presentation

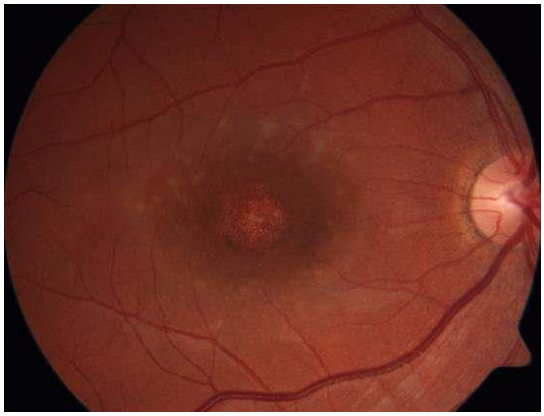
- Estimated prevalence 1:8000-10000
- Reduced VA in 1st or 2nd decade of life
- Later age of onset <20 years associated with better visual prognosis

Walia S, Fishman GA. Ophthalmic Genetics. 2009.

6

Clinical Presentation

- Lesions with beaten-metal appearance, yellow-white flecks
- Majority of patients have presence of "dark choroid"



American Academy of Ophthalmology Disease Review

7

Stage 1

- Presence of variable pigmentary changes: faint, irregular pigment mottling; beaten-metal appearance
- Flecks within 1DD of fovea
- Normal ERG and EOG
  - *Possible reduced cone ERG*

Fishman GA. *Arch Ophthalmol*. 1976
Lois N, et. al. *Arch Ophthalmol*. 2001.

8

Stage 2

- Flecks beyond 1DD of fovea
- May have partial resorption of flecks
- Relative central scotoma

- ERG and EOG most of the time normal
  - *Subnormal cone and rod responses may be observed*
  - *Some take longer to reach normal scotopic ERG amps, prolonged dark adaptation*

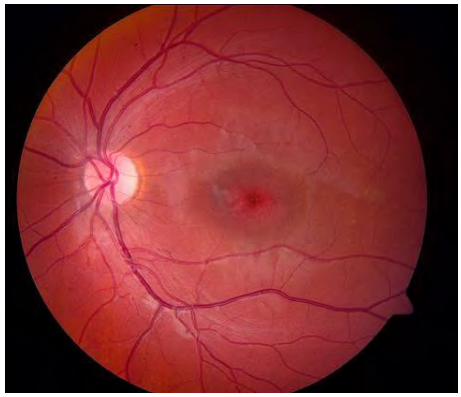
9

Stage 3

- Diffusely resorbed flecks
- Atrophy of choriocapillaris
- Abnormal electrophysiology testing

10

Stage 4



American Academy of Ophthalmology Disease Review

- Diffusely resorbed flecks and extensive atrophy of choriocapillaris and RPE
- ERG notably reduced; elevated cone and rod thresholds on dark adaption

11

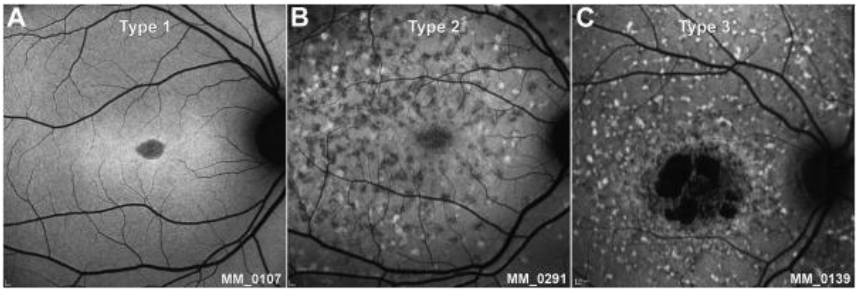
Fundus Autofluorescence

- Type 1:
  Localized low FAF signal at the fovea surrounded by a homogeneous background with or without perifoveal foci of high or low signal
- Type 2:
  Localized low FAF signal at the macula surrounded by a heterogeneous background and *widespread foci of high or low FAF signal extending anterior to the vascular arcades*
- Type 3:
  Multiple areas of low FAF signal at posterior pole with heterogeneous background and/or *foci of high or low signal*

Fujinami K, et. al. Invest Ophthalmol. 2013.

12

FAF

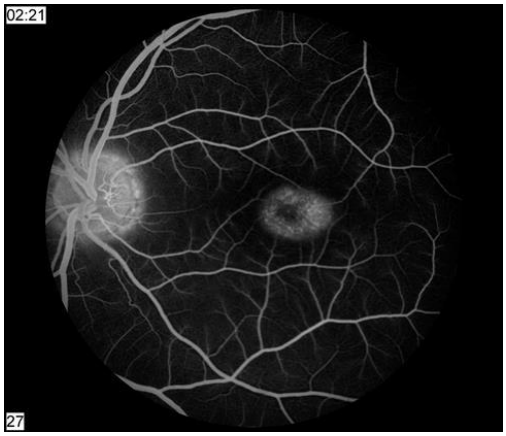


Georgiou M, et. al. American Journal of Ophthalmology. 2020

13

Fluorescein Angiography

- "Dark" or "silent choroid" sign present in 60-87% of patients
- Lipofuscin deposits block choroidal fluorescence

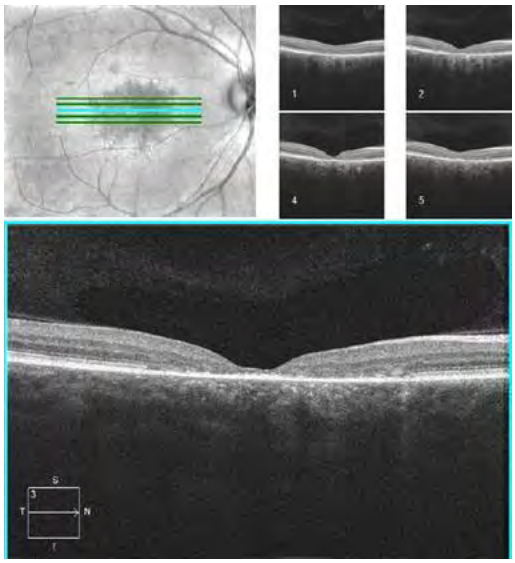


Lambertus S, et. al. Ophthalmology 2015.
Fishman GA, et. al. Ophthalmology. 1987.

14

OCT

Earliest OCT finding is thickening of the external limiting membrane prior to outer retinal atrophy



Lee W, et. al. IOVS. 2014.

15

Phenotypes

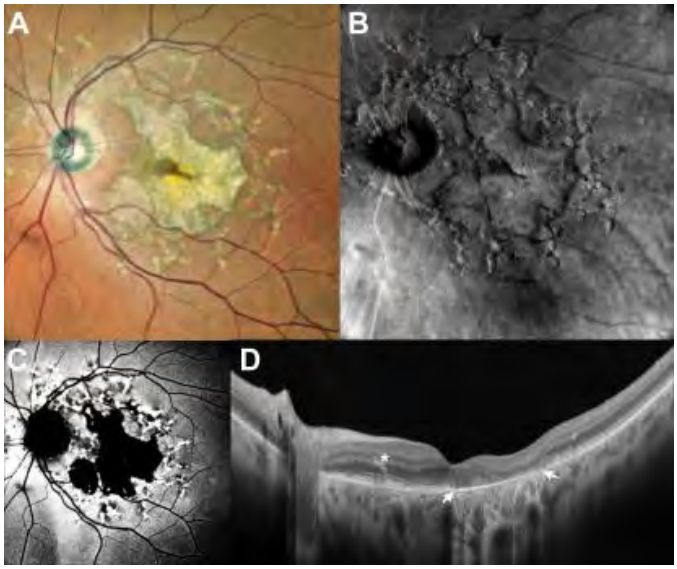
Phenotype	Description
I	Patients exhibiting clinically apparent disease changes confined to the macula (defined as the region bound by the temporal arcades)
II	Patients exhibiting any flecks (yellow or pigmented) outside the temporal arcades, regardless of how mild
III	Patients exhibiting RPE atrophy, choroidal atrophy, or bone spicules that extend outside of the macula

RPE = retinal pigment epithelium.

Variations in ABCA4 can be associated with cone, cone-rod, or rod-cone phenotypes

Oh KT, et. al. Retina. 2004.
Sparrow JR, et. al. Prog Retin Eye Res. 2012

16



Corradetti G, et. al. Ophthalmology. 2021.

17

Natural History and Prognosis

- VA usually declines to 20/200 and stabilizes after reaching 20/200 to 20/400
- Probability of VA of 20/40 or better:
  - 52% by age 19
  - 32% by age 29
  - 22% by age 29
- Median time to decline from 20/40 to 20/200:
  - 7 years if presenting within first 2 decades of life
  - 22 years within 2nd-4th decades of life
  - 29 years within 4th-6th decade of life
- No clinically observed atrophic lesion can maintain VA of 20/40 or better

Walia S, Fishman GA. Ophthalmic Genetics. 2009.
Fishman GA, et. al. Ophthalmology. 1987.

18

Stargardt's Macular Dystrophy vs AMD

- Evidence to support a common inflammatory etiology of AMD and STGD1 maculopathy

(Radu RA, et.al. Membrane attack complex induces RPE cell death in Stargardt Disease. ARVO, 2021)

- No transition zone of GA unlike AMD

19

Fixation

- Bivariate contour ellipsoid area (BCEA)
  - Stargardt's patients: 4.98 (mean SD 7.37) degrees^2
  - Normal: 0.08 - 0.45 degrees^2
- Preferred Retinal Loci
  - 6.45 (mean SD 4.52) degrees from the fovea in Stargardt's patients
  - PRL tends to be above the central retinal lesion but its location is also contingent on the task and stimulus

Schonbach E. ARVO 2021.
Reinhard. Vis Res. 2007.
Sullivan. Ophthalmic Physiol Opt. 2008

20

Treatment

- Dark glasses and hats when out in bright light (??)
- Avoid cigarettes and vitamin supplements
- Low Vision Rehabilitation

21

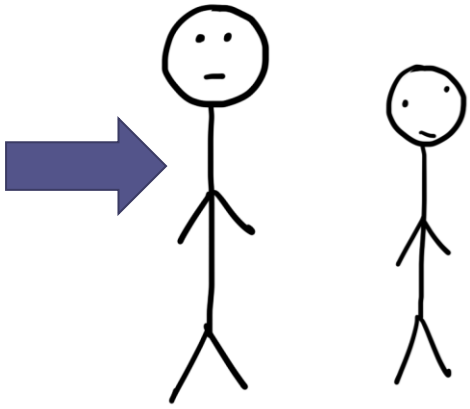
TBD Treatment

NIH U.S. National Library of Medicine
ClinicalTrials.gov

- Gene Therapy
  - Adeno-associated viral vector delivered gene therapy
  - CRISPR gene editing and RNA targeted therapy
- Stem Cells
  - iPS and RPE cells
- Emixustat
- Zimura™ (Complement C5 Inhibitor)
- ALK-001 (modified form of Vitamin A)
- Metformin

22

Case Study: A Family Affair



23

Low Vision Clinic Visit

- 15 yo white male
- Follow-up to update school accommodations
- CC:
  - Hard to see what the teacher is writing on the board
  - Difficulty seeing print on his phone
  - Difficulty reading books

24

Case History

- POHx: Stargardt's maculopathy both eyes
- No significant PMHx

- 9th grade honors student
- Doing great in school but feels like his vision limits his efficiency
- Hopes to attend Virginia Tech or MIT and eventually work for NASA

25

Current School Accommodations

- Large print
- Preferential seating
- iPad
- Large computer monitor (min 24 inch)

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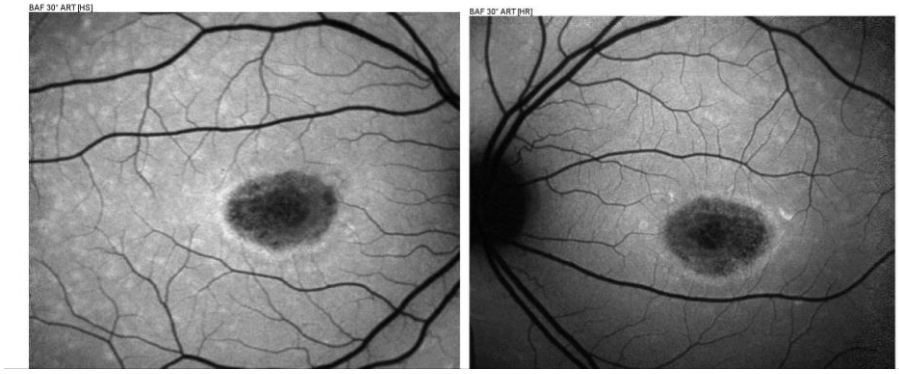
Low Vision Exam

- BCVA
  - Right Eye: 20/80, using superior EV
  - Left Eye: 20/80, using superior EV
- Mars Contrast Sensitivity
  - 1.72 log units

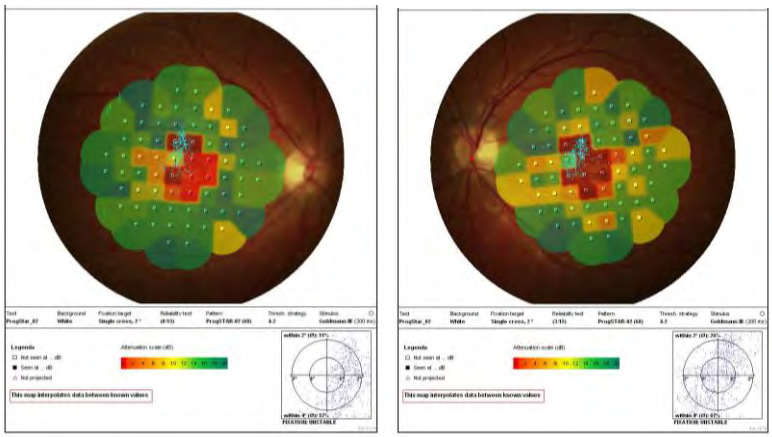
27

Fundus Autofluorescence



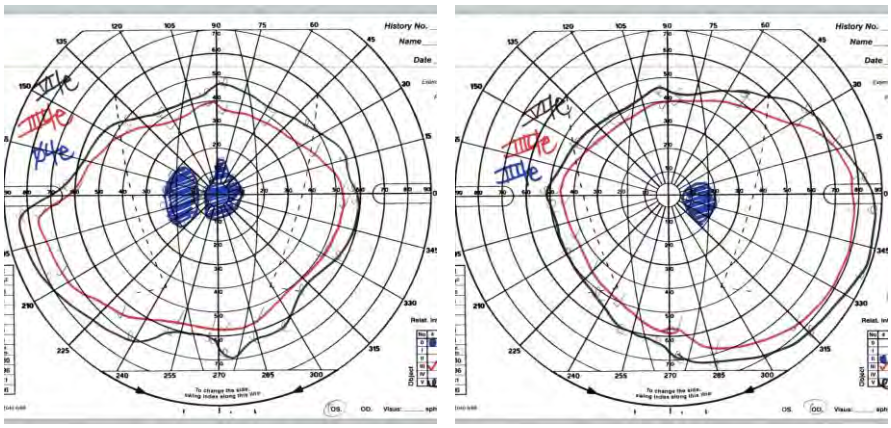
28

Microperimetry



29

Goldmann Visual Fields



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Low Vision Evaluation

- Distance VAE Evaluation:
  - 4x monocular telescope
    - Right eye preference : 20/20-
- Reading Evaluation:
  - Comfortable with 3.2M print @ 30cm
  - Slows at 2.5M
  - Moves page closer starting at 1.6M
  - Threshold 0.8M @18cm

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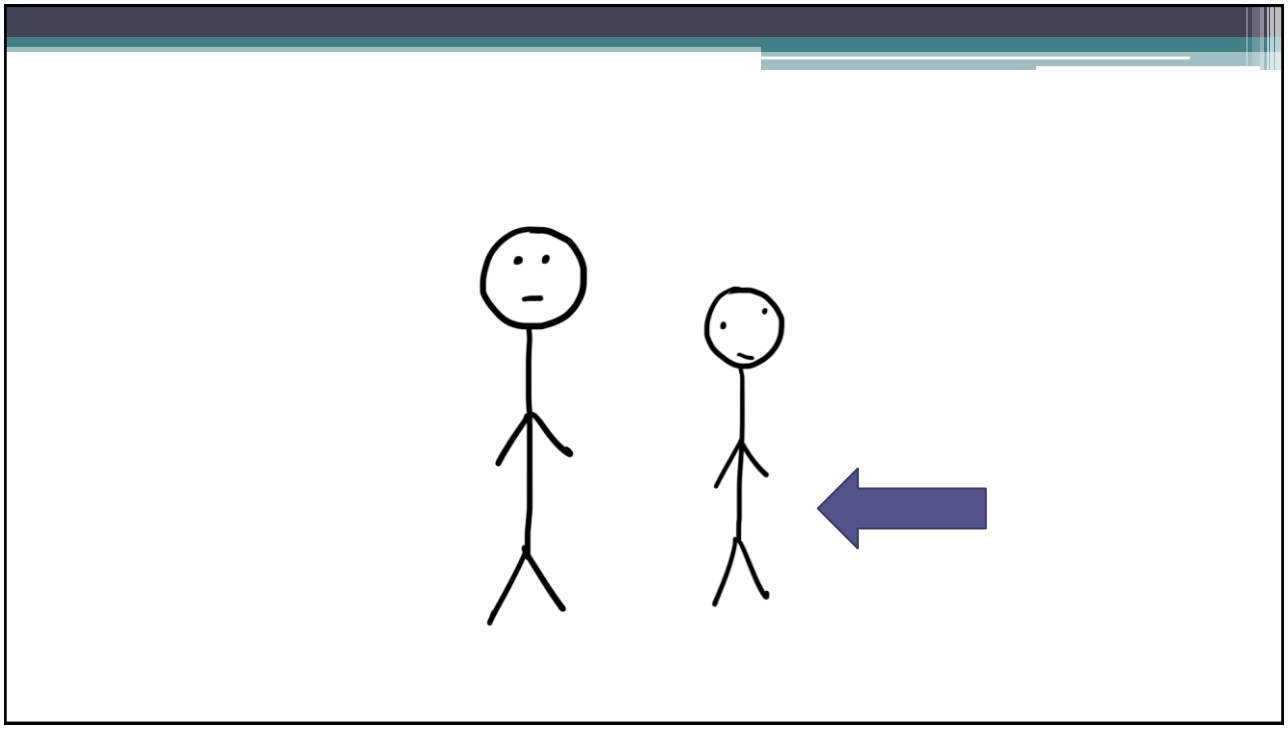
Low Vision Evaluation

- Near VAE Evaluation:
  - +4w/6BI
    - Comfortable at 1.3-1.0M
    - Threshold 0.6M-

32



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Low Vision Clinic Visit

- 13 yo white male
- Follow-up to evaluate school accommodations
- CC:
  - Feels like his vision continues to get worse

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Case History

- POHx: Stargardt's maculopathy both eyes
- No significant PMHx

- 7th grade student
- Longstanding established school accommodations
- Interested in new technology; saw a tablet with text-to-speech

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Current School Accommodations

1. Tablet – iPad and Nook to manage language arts work
2. Large print
3. Large button calculator
4. Laptop with digital textbooks
5. Monocular telescope
6. Bookshare – audiobooks and Braille books
7. Allowed to wear baseball cap and sunglasses inside to reduce glare
8. Extra time on tests
9. Allowed to put his head down and rest during class
10. Vision teacher visits 2x per week

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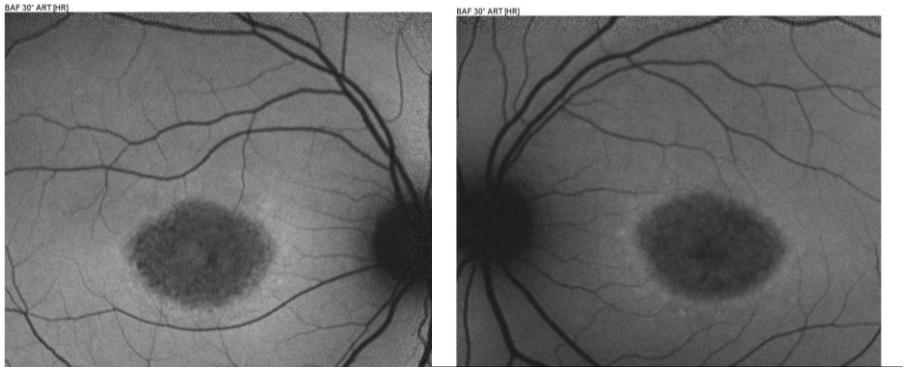
Low Vision Exam

- BCVA
  - Right Eye: 20/250
  - Left Eye: 20/250
  - Both Eyes: 20/160
- Mars Contrast Sensitivity
  - 0.92 log units

37

Fundus Autofluorescence



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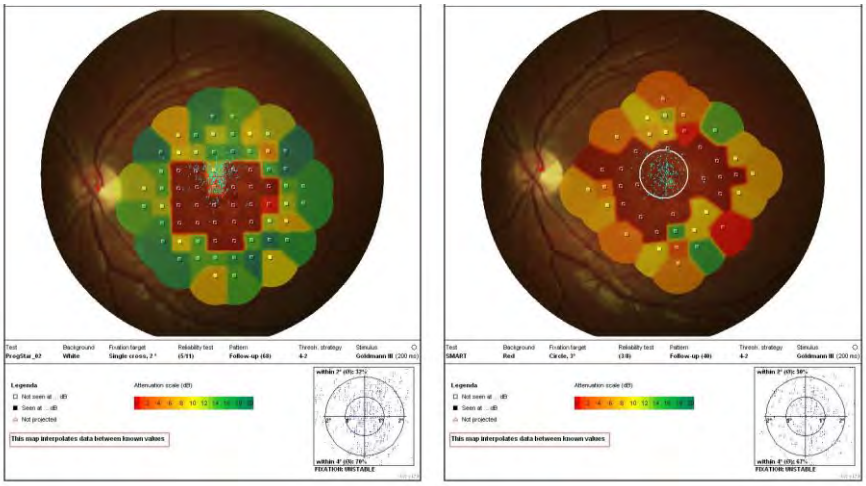
Microperimetry



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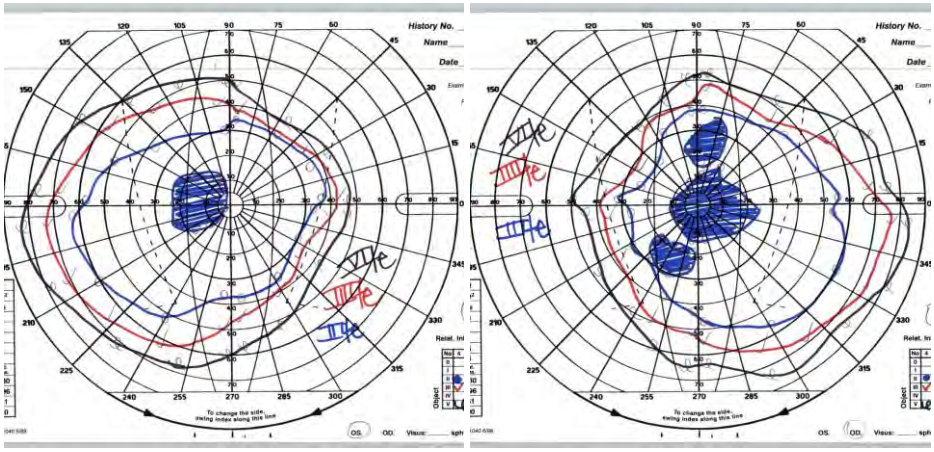
Goldmann Visual Fields



40

Low Vision Exam

- Reading Evaluation:
  - Comfortable with 4.0M print @ 30cm
  - Slows at 3.2M
  - Threshold 2.5M
- Near VAE Evaluation:
  - +4w/6BI
    - Threshold 0.8M
  - +6w/8BI
    - Threshold 0.6M
  - 2.2x MBSM
    - Threshold 0.5M
    - Prefers over HMs

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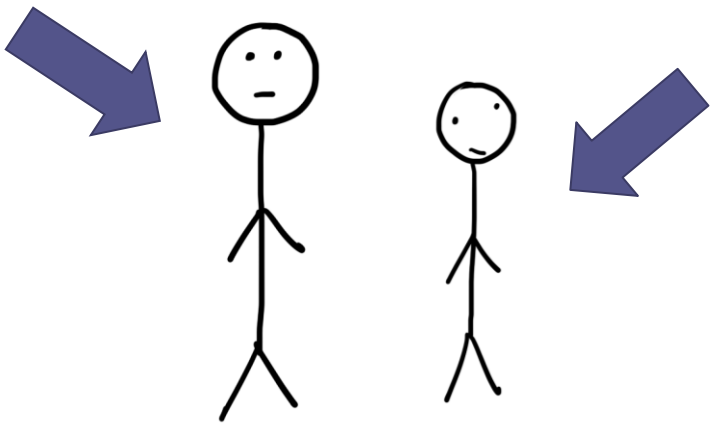

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Video magnification

- Able to optimize magnification and contrast
  - Closed Circuit Television (CCTV)
  - Head-mounted devices

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CCTV

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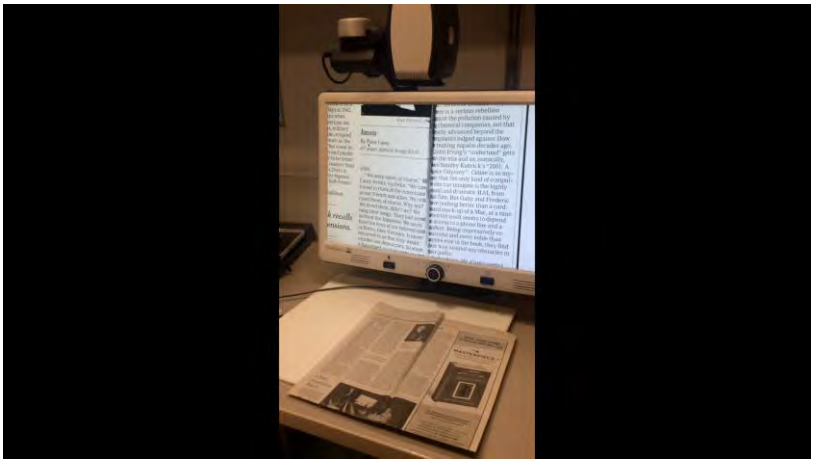
Optical Character Recognition (OCR)



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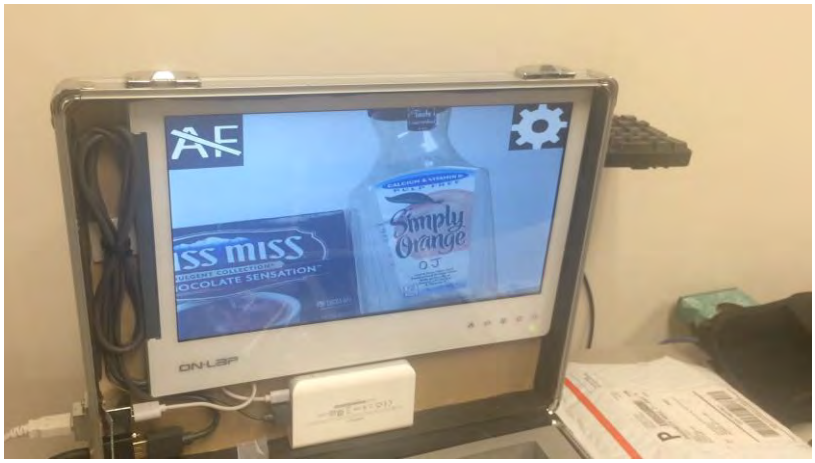
E-Sight



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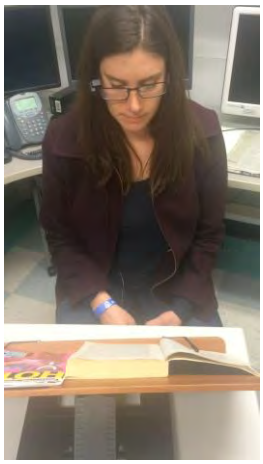
OrCam – Portable Text-to-Speech



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Plan of Care - Brother #1 (15 yo)

- Recommend meeting with vision teacher to establish an IEP
  - Central scotomas and reduced visual acuity cause significant challenges in keeping up with course load
  - Visual acuity over-estimates visual function

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Plan of Care - Brother #1

- Recommendations for school accommodations:
  - Large print (18pt or larger) handouts and for tests
  - Copies of presentations and lectures ahead of time
  - Prismatic NVO to reduce visual fatigue
  - Preferential seating in classroom
  - Extra time (1.5x) on tests including standardized tests
  - Video magnification in classroom, at home, and for testing
  - 4x bioptic telescope system
  - Books in digital format and access to tablet
  - 24+ inch larger computer monitor
  - Access to text-to-speech

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Plan of Care - Brother #2 (13 yo)

- Encourage current IEP accommodations and continuation with vision teacher
  - Bookshare Program / Audio books
  - Books in digital format and access to laptop/tablet
  - Large print for all classwork, homework, and tests
  - Stand magnifier or prismatic NVO to use with large print
  - 6x16 monocular telescope for distance spotting and viewing classroom board
  - Allow use of brimmed hat and tinted lenses
  - Allow for visual breaks as needed
  - Large button calculator
  - Extra time (1.5x) on tests including standardized tests
  - Video magnification in classroom, at home, and for testing
  - Access to text to speech

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School Accommodations

- What is a 504 Plan?
  - Developed for students with disabilities who do not require specialized instruction but need the assurance that they will receive equal access to public education and services
- What is an IEP?
  - For students with disabilities who do require specialized instruction
  - More involved and requires documentation of measurable growth

Both should be updated annually

52

Take Home Points

Same condition
Same genetic background

Two different clinical and functional presentations

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Take Home Points

- Central scotomas can severely impact visual function
- Important to follow-up with school aged patients to update school accommodations
- Video magnification and text-to-speech accessibility can aid in reduced visual fatigue

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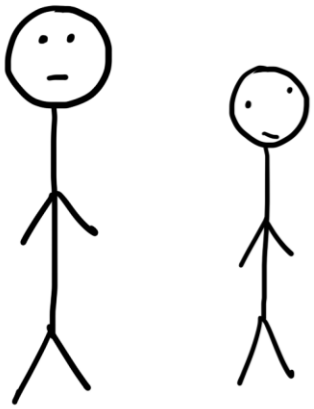
Thank you

adeemer@ketchum.edu

KETCHUM HEALTH



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Minimally Invasive Glaucoma Surgery (MIGS) Updates and Options

Presented by Igor Bussel, MD

Marshall B.
KETCHUM UNIVERSITY
Southern California College of Optometry
Department of Continuing Education
ketchum.edu/ce | ce@ketchum.edu

Minimally Invasive Glaucoma Surgery (MIGS) Updates and Options

Igor Bussel, MD, MS, MHA
Glaucoma, Cataract, Advanced Anterior Segment Surgery

Currently: UCI Gavin Herbert Eye Institute
STARTING JULY 2021:
Terry & Kim Eye Institute in Fullerton, CA

Gavin Herbert Eye Institute
UCI Health

1

Disclosures

- None

UCI Health
Gavin Herbert Eye Institute

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Overview

- Glaucoma
- Glaucoma Treatment Spectrum
- What is MIGS?
- Why do we need MIGS?
- When to use MIGS?
- Which MIGS to use?
- Brief summary of MIGS efficacy and risk

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Glaucoma can be devastating…

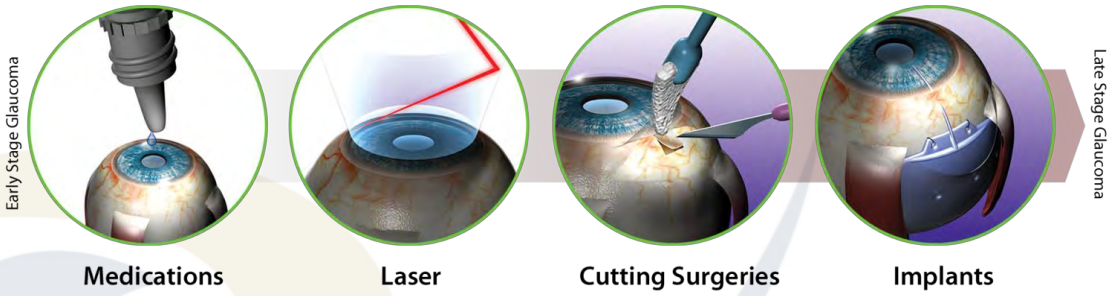
Leading cause of irreversible blindness

Glaucomatous optic neuropathy = The silent thief of sight

The only modifiable risk-factor remains intraocular pressure (IOP)

4

Glaucoma Treatment Spectrum



5

What is MIGS?

Micro-invasive glaucoma surgery: current perspectives and future directions

Hady Sahab[a,b] and Iqbal Ike K. Ahmed[a,c]

- Ab interno clear corneal approach
- Potential Advantages
  - Minimal tissue trauma (conjunctiva, angle)
  - Biocompatibility
  - Neutral refractive state
- Efficacy – “modest”
- Safety
- Rapid Recovery

6

Why MIGS?

- Topical drops are benign…

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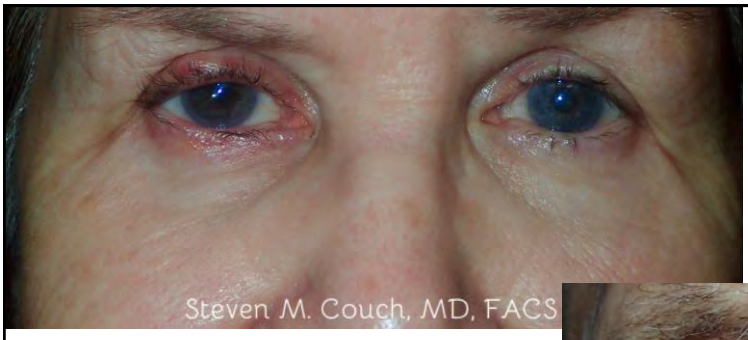

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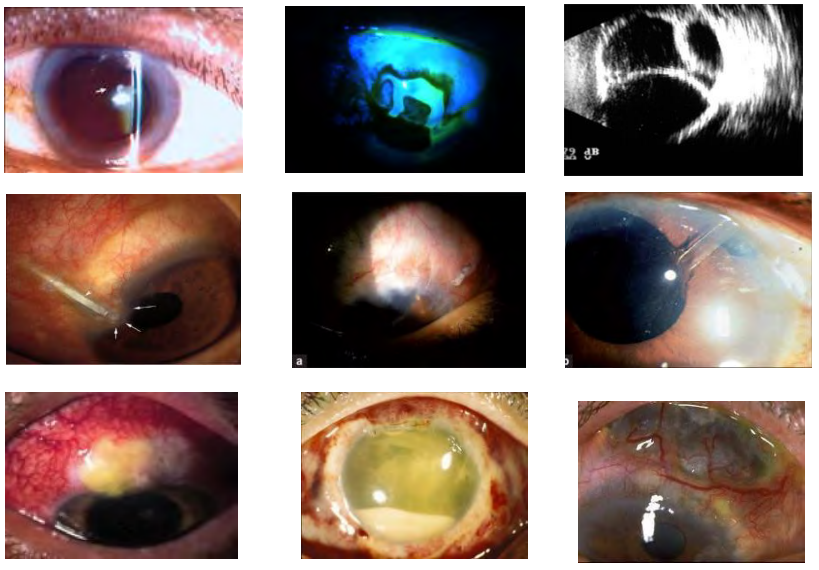
Why MIGS?

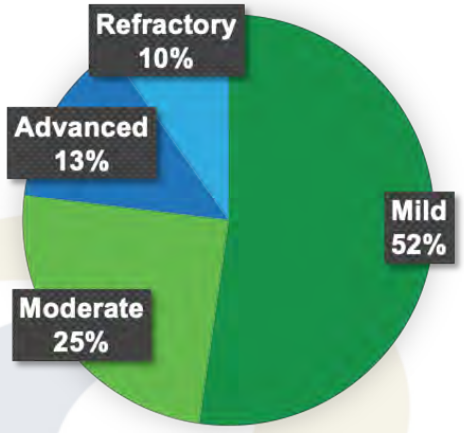
- Poor adherence
  - a well-established problem in glaucoma
  - multifactorial and complex
- Cost burden to patient and system

Trabeculectomy and Tube Shunt Complications

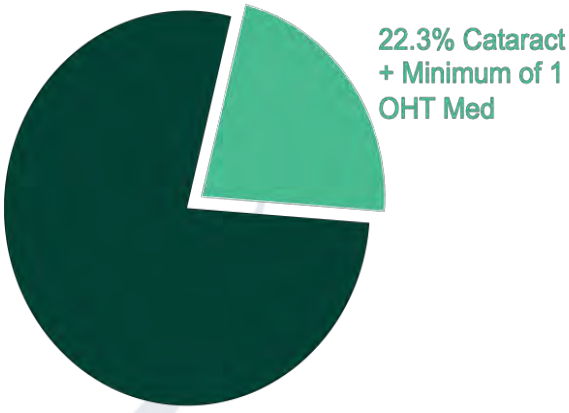


When MIGS?

Patients with Glaucoma



4.3M US Cataract Procedures



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When MIGS?

- Combined with cataract surgery vs stand-alone procedure?
- Progression of glaucoma?
- IOP above goal?
- Medication reduction?

- What is the patient's goal? What is the doctor's goal?
  - Manage expectations

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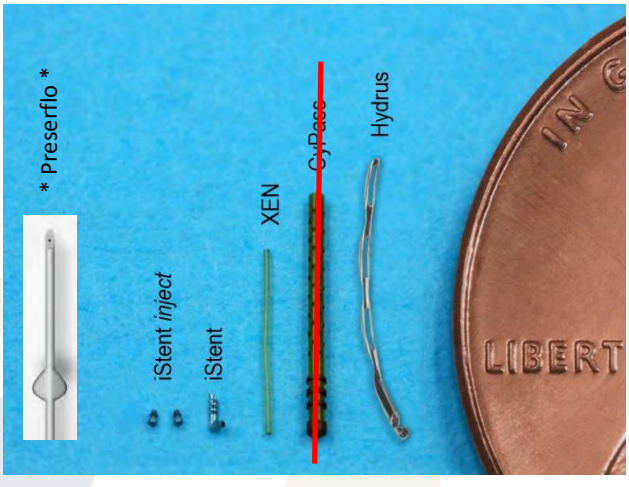
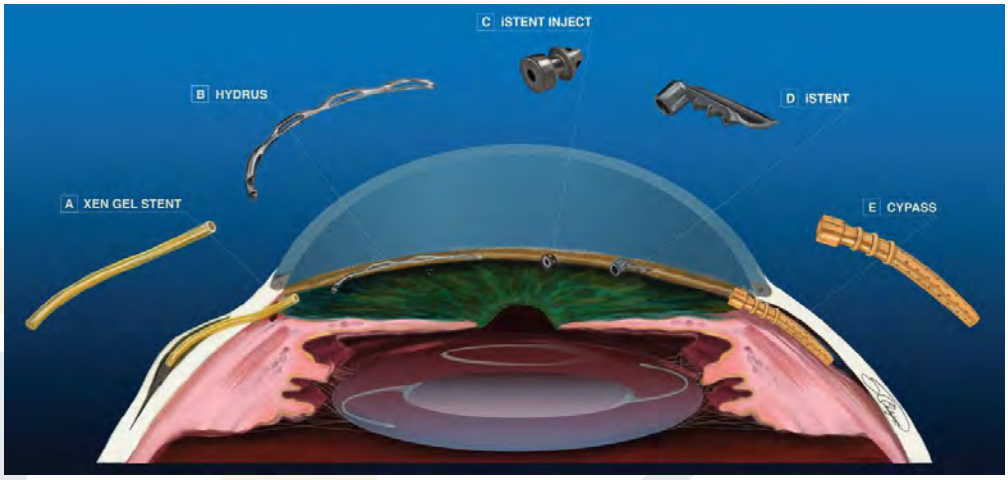
Which MIGS?

- **Trabecular Meshwork / Schlemm's Canal**
- ***Suprachoroidal (on hold, TBD, Cypass ECL story)***
- **Transcleral / Subconjunctival**

Which MIGS?



Device Implants:
Trabecular vs Suprachoroidal vs Subconj/Transcleral



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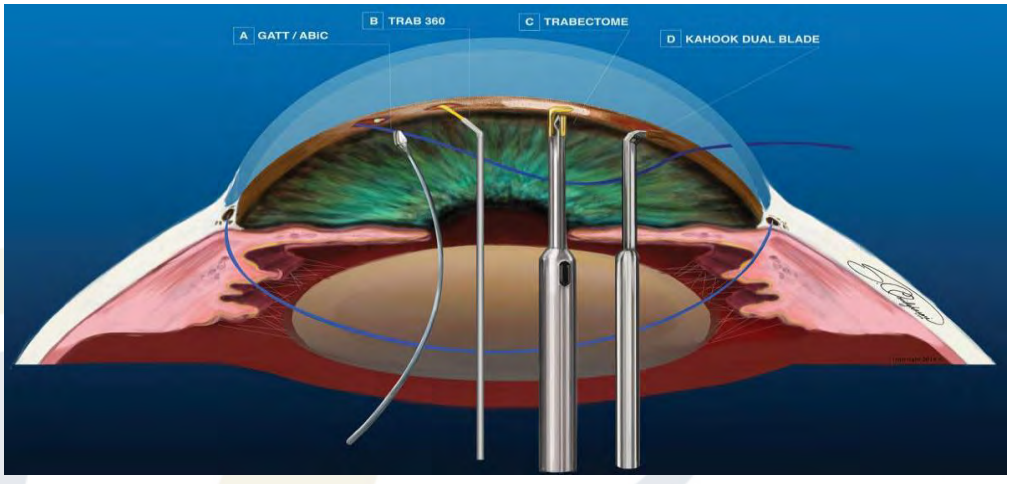
Non-implant Procedures:
Degree of TM manipulation



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Summary of MIGS since 2000s

- More effect with higher pre-operative baseline IOP
- Episcleral venous pressure limits post-op effect regardless of baseline to mid-teens
- Effect wanes, medication reliance
- IOP ⇩ with Subconj >> TM/SC MIGS

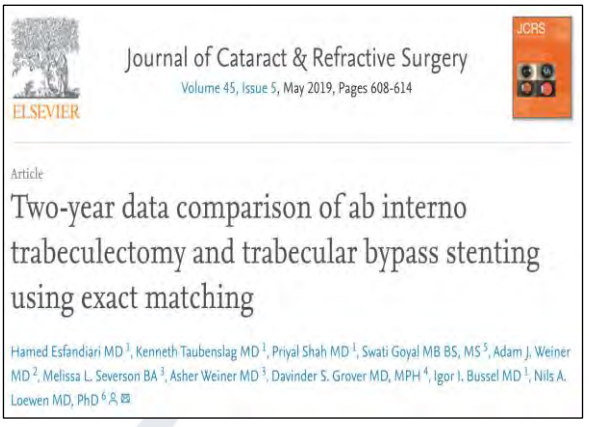
MIGS Updates

- Too little time for comprehensive data update
- Phaco alone can lower IOP
- Phaco + MIGS lowers IOP more (20-30%) and on less medications (decrease 1-2 classes)
- More TM/SC tx = More IOP lowering
- Fibrosis and failure w/ and w/o implant device
- They are not without risk...

MIGS Risks

- Hyphema (More TM/Canal tx = More Risk)
  - less hyphema with device vs tissue removal
- IOP spikes
- Implant-related complications
- Descemet's tear, cyclodialysis, iridodialysis, IOL-bag complex injury
- ECL, corneal decompensation

Comparison Studies Are Lacking...



Conclusion

- Every Eye/Patient and MIGS is unique
- Consider degree of advantage/effect vs real-world risk probability in each patient
- Manage patient expectations

What do glaucoma patients want?

- Preserve vision
- Reduce burdens of therapy
- Avoid post-op complications
- Convenience

Thank you!

Questions?

Emergency Consults?

Presentations?

- **MIGS management**

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Mobile: (310) 801-1829

Starting July 2021

T&KEI

TERRY & KIM EYE INSTITUTE

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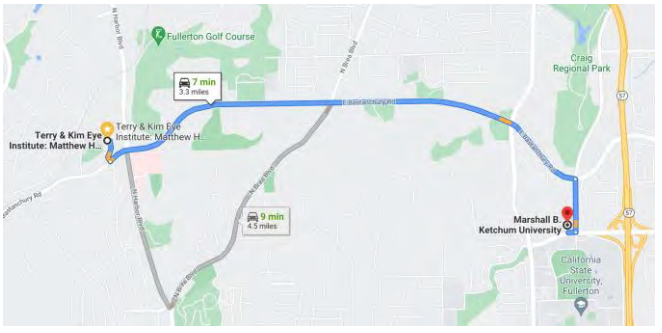

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SOUTHERN CALIFORNIA COLLEGE OF OPTOMETRY

CONTINUING EDUCATION COURSE SCHEDULE

2021 COURSE SCHEDULE

DATE	LOCATION	COURSE TOPIC	CE UNITS
July 10 & 11	**SCCO	MBKU** *Live Webinar*	**Ocular Disease Part II** *COPE Approval Pending*	16
September 19	**SCCO	MBKU** *Live Webinar*	**Joint SCCO I USC I VA Symposium** *COPE Approval Pending*	8
December 12	**SCCO	MBKU** *Live Webinar*	**Contemporary Topics in Optometry** *COPE Approval Pending*	8

GENERAL INFORMATION

MBKU CAMPUS LOCATIONS

SCCO I FULLERTON CAMPUS
2575 Yorba Linda Blvd. Fullerton, CA 92831

LEARN MORE & REGISTER *ketchum.edu/ce*

CONTACT US

email: ce@ketchum.edu

Marshall B. KETCHUM UNIVERSITY
Southern California College of Optometry

Neurotrophic keratitis is a degenerative disease that warrants immediate attention[1]

oxervate®
(cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

OXERVATE is the first FDA-approved pharmacologic treatment that targets the root pathogenesis of neurotrophic keratitis (NK)[2]

Cenegermin-bkbj, the active ingredient in FDA-approved OXERVATE, is structurally identical to the human nerve growth factor (NGF) protein made in ocular tissues.[3]

Endogenous NGF is a protein involved in the differentiation and maintenance of neurons and is believed to support corneal integrity through three mechanisms (in preclinical models): corneal innervation, tear secretion, and epithelial cell growth.[3-5]

In clinical studies, with a single 8-week course of therapy:

- Up to **72%** of patients with NK achieved complete corneal healing*†[2]
- **80%** of patients who achieved complete corneal healing remained completely healed at 1 year (REPARO trial)[6]

OXERVATE is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis.

Important Safety Information

WARNINGS AND PRECAUTIONS

Patients should remove contact lenses before applying OXERVATE and wait 15 minutes after instillation of the dose before reinsertion.

ADVERSE REACTIONS

The most common adverse reaction in clinical trials that occurred more frequently with OXERVATE was eye pain (16% of patients). Other adverse reactions included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation, and increase in tears (1%-10% of patients).

Please see additional Important Safety Information on accompanying page and full Prescribing Information, including patient information, at OXERVATE.com/prescribing-information.

You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Dompé at 1-833-366-7387 or Usmedinfo@dompe.com.

TREAT NK TODAY
OXERVATE.com/HCP

*Study NGF0212 (REPARO): 52 patients per group; European patients with NK in one eye; 72% of patients completely healed; key findings were after 8 weeks of treatment; 6 times daily; vehicle response rate 33.3%.[2] Study NGF0214: 24 patients per group; US patients with NK in one or both eyes; 65.2% completely healed; vehicle response rate 16.7%[2,7]

†Complete corneal healing was defined as the absence of staining of the corneal lesion and no persistent staining in the rest of the cornea after 8 weeks of OXERVATE treatment.[2]

References: 1. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol.* 2014;8:571-579. **2.** OXERVATE (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) [US package insert]. Boston, MA: Dompé U.S. Inc.; 2019. **3.** Voelker R. New drug treats rare, debilitating neurotrophic keratitis. *JAMA*. 2018;320:1309. **4.** Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. *J Cell Physiol*. 2017;232:717-724. **5.** Muzi S, Colafrancesco V, Sornelli F, et al. Nerve growth factor in the developing and adult lacrimal glands of rat with and without inherited retinitis pigmentosa. *Cornea*. 2010;29:1163-1168. **6.** Data on file. Dompé U.S. Inc.; 2021. NGF0212. **7.** Pflugfelder SC, Massaro-Giordano M, Perez VL, Hamrah P, Deng SX, Espandar L, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy. *Ophthalmology*. 2020;127:14-26.

Dompé

US-OXE-1900180.02 02/21

oxervate™
(cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

Brief Summary of Safety

Consult the full Prescribing Information for complete product information.

INDICATIONS AND USAGE

OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% is indicated for the treatment of neurotrophic keratitis.

DOSAGE AND ADMINISTRATION

Contact lenses should be removed before applying OXERVATE and may be reinserted 15 minutes after administration.

If a dose is missed, treatment should be continued as normal, at the next scheduled administration.

If more than one topical ophthalmic product is being used, administer the eye drops at least 15 minutes apart to avoid diluting products. Administer OXERVATE 15 minutes prior to using any eye ointment, gel or other viscous eye drops.

Recommended Dosage and Dose Administration

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

ADVERSE REACTIONS

Clinical Studies Experience Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

In two clinical trials of patients with neurotrophic keratitis, a total of 101 patients received cenegermin-bkbj eye drops at 20 mcg/mL at a frequency of 6 times daily in the affected eye(s) for a duration of 8 weeks. The mean age of the population was 61 to 65 years of age (18 to 95). The majority of the treated patients were female (61%). The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

Administration of cenegermin-bkbj to pregnant rats or rabbits during the period of organogenesis did not produce adverse fetal effects at clinically relevant doses. In a pre- and postnatal development study, administration of cenegermin-bkbj to pregnant rats throughout gestation and lactation did not produce adverse effects in offspring at clinically relevant doses.

Animal Data

In embryofetal development studies, daily subcutaneous administration of cenegermin-bkbj to pregnant rats and rabbits throughout the period of organogenesis produced a slight increase in post-implantation loss at doses greater than or equal to 42 mcg/kg/day (267 times the MRHOD). A no observed adverse effect level (NOAEL) was not established for post-implantation loss in either species. In rats, hydrocephaly and ureter anomalies were each observed in one fetus at 267 mcg/kg/day (1709 times the MRHOD). In rabbits, cardiovascular malformations, including ventricular and atrial septal defects, enlarged heart and aortic arch dilation were each observed in one fetus at 83 mcg/kg/day (534 times the MRHOD). No fetal malformations were observed in rats and rabbits at doses of 133 mcg/kg/day and 42 mcg/kg/day, respectively. In a pre- and postnatal development study, daily subcutaneous administration of cenegermin-bkbj to pregnant rats during the period of organogenesis and lactation did not affect parturition and was not associated with adverse toxicity in offspring at doses up to 267 mcg/kg/day. In parental rats and rabbits, an immunogenic response to cenegermin-bkbj was observed. Given that cenegermin-bkbj is a heterologous protein in animals, this response may not be relevant to humans.

Lactation

There are no data on the presence of OXERVATE in human milk, the effects on breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for OXERVATE, and any potential adverse effects on the breastfed infant from OXERVATE.

Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in this population is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in pediatric patients from 2 years of age and older [*see Clinical Studies (14)*].

Geriatric Use

Of the total number of subjects in clinical studies of OXERVATE, 43.5 % were 65 years old and over. No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis and Mutagenesis Animal studies have not been conducted to determine the carcinogenic and mutagenic potential of cenegermin-bkbj.

Impairment of fertility Daily subcutaneous administration of cenegermin-bkbj to male and female rats for at least 14 days prior to mating, and at least 18 days post-coitum had no effect on fertility parameters in male or female rats at doses up to 267 mcg/kg/day (1709 times the MRHOD). In general toxicology studies, subcutaneous and ocular administration of cenegermin-bkbj in females was associated with ovarian findings including persistent estrus, ovarian follicular cysts, atrophy/reduction of corpora lutea, and changes in ovarian weight at doses greater than or equal to 19 mcg/kg/day (119 times the MRHOD).

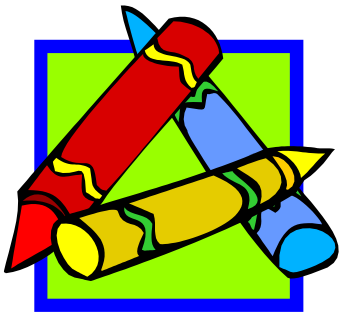
Dompé

Amblyopia Treatment Study

RECRUITMENT UNDERWAY FOR NIH-SPONSORED STUDY

Amblyopia is the most common cause of monocular visual impairment in children. The choice of a sequential approach versus a simultaneous approach to "optical treatment (glasses) plus patching treatment" remains unresolved, with some existing data supporting one approach and some data supporting the other. There is a reasonable rationale for either approach. This unresolved controversy results in a dichotomy of current clinical practice, with some care providers favoring one approach and others favoring the opposite approach. In addition, the influence of adherence to patching on treatment response is not well understood.

The Pediatric Eye Disease Investigator Group (PEDIG) is conducting a clinical trial to evaluate if treating amblyopia with glasses and patching at the same time improves vision as well as treating amblyopia first with glasses and then with patching, if needed. This study will also use occlusion dose monitors (ODMs) to record adherence with prescribed patching treatment, to study dose-response. The study is supported through funding from the National Eye Institute of the U.S. National Institutes of Health and is being coordinated by the Jaeb Center for Health Research in Tampa, Florida.



Study Specifics

- 544 children are expected to be enrolled
- Children must be between 3 to < 13 years old
- Visual acuity in the amblyopic eye must be between 20/40 and 20/200
- Random assignment to either:
  - **Sequential treatment**: full-time glasses first, with subsequent patching for 2 hours per day/7 days per week if there is no further improvement in amblyopic eye visual acuity with glasses alone and there is residual amblyopia, OR
  - **Simultaneous treatment:** full-time glasses and part-time patching for 2 hours per day/7 days per week
- Occlusion dose monitors (ODMs) will be used to record actual patch wear time during prescribed patching
- Follow-up visits every 8 weeks for 56 weeks
- No previous treatment for amblyopia is allowed, including glasses or contact lenses.

How Can You Help?

- Your assistance is needed in referring children who may qualify.
- Referrals can be sent to the investigator listed below, or for more information, visit the PEDIG website at http://pedig.net/ or call the PEDIG Coordinating Center toll free at 1-888-797-3344

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NATIONAL INSTITUTES OF HEALTH

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Pediatric Eye Disease Investigator Group