SUNCOAST SEMINAR

Presented by the
Pinellas Optometric Association

Course Syllabus

Suncoast Seminar 2025
Schedule of Events

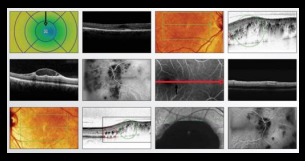
Saturday, April 26, 2025

7:45 am – 8:15 am	**Registration** - Exhibit Hall - Continental Breakfast *breakfast sponsored by Johnson & Johnson Vision*
8:15 am – 9:55 am	**Cataract Surgery Pre, Peri, and Post Op: Putting the Patient First (TQ) (COPE pending)** Pit Gills, M.D. and Andreas Zacharopoulos, O.D.
9:55 am – 10:40 am	**Break** - Exhibit Hall open *sponsored by Eye Institute of West Florida*
10:40 am – 12:20 pm	**Fuchs Corneal Dystrophy, Keratoconus, and Other Ectasias (TQ) (97310-TD)** Erin Greenberg, M.D.
12:20 pm – 1:10 pm	**Lunch** (included in registration) - Exhibit Hall Open *sponsored by St. Luke's Cataract & Laser Institute*
1:10 pm – 1:20 pm	**Lighthouse of Pinellas Update**
1:20 pm – 1:30 pm	**F.O.A. Update**
1:30 pm – 3:10 pm	**Our Top Topical Meds (TQ) (96194-PH)** Joseph Pizzimenti, O.D.
3:10 pm – 3:30 pm	**Break** *sponsored by Sight360*
3:30 pm – 5:10 pm	**Interprofessional Care of Retina Patients Using Multimodal Imaging (TQ) (96193-GO)** Joseph Pizzimenti, O.D.

Sunday, April 27, 2025

7:30 am – 8:00 am	**Registration** - Continental Breakfast *breakfast sponsored by Updegraff Laser Vision*
8:00 am – 9:40 am	**Emerging Trends in AMD (TQ) (96192-TD)** Joseph Pizzimenti, O.D.
9:40 am – 10:00 am	**Break** *sponsored by Pinellas Optometric Association*
10:00am – 11:40 am	**Prevention of Medical Errors (94908-EJ)** Joe Sowka, O.D.
11:40 am – 12:00 pm	**Lunch** – included in registration *sponsored by Newsom Eye*
12:00 pm – 1:40 pm	**Florida Jurisprudence (94437-EJ)** Joe Sowka, O.D.

Interprofessional Care of Retina Patients Using Multimodal Imaging



Joseph J. Pizzimenti, OD, FAAO

Financial Disclosures

- Proprietary Interests
  - None
- Consulting Fees
  - Zeiss
  - EyePromise/Zeavision
- Stockholder: Zeavision

All financial relationships have been mitigated.

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OptometricRetinaSociety.org

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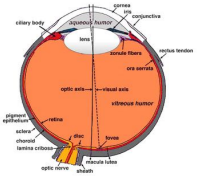
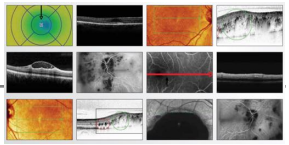


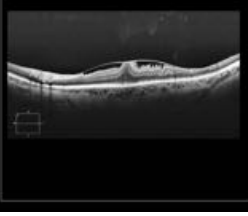
Questions and Answers?

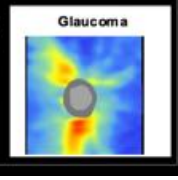
AUDIENCE



2-minute Stretch

- Click to add text



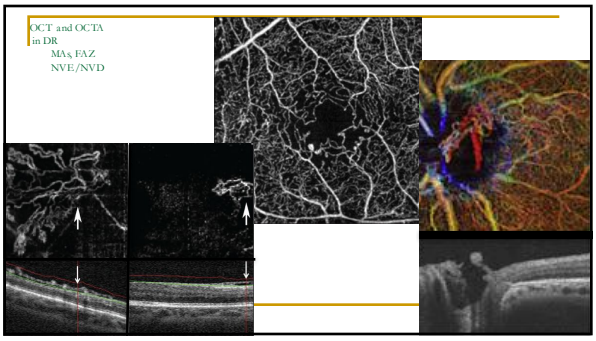


What is multimodal imaging (MMI)?

- MMI is the use of multiple technological systems to acquire images.
- These may include hybrid devices that can simultaneously perform more than one imaging modality.
- MMI does not replace, but rather it augments, traditional examination methods, such as DFE.

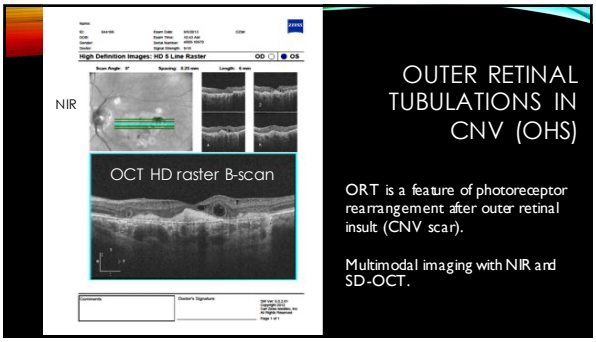
What is the purpose of MMI?

- Images acquired by MMI complement one another for the purpose of diagnosis, prognostication, management, and monitoring of disease.
- Common imaging modalities include:
  - color/multicolor fundus imaging
  - near-infrared reflectance (NIR)
  - fundus autofluorescence (FAF)
  - OCT and OCTA



Causes of CNV

- OHS



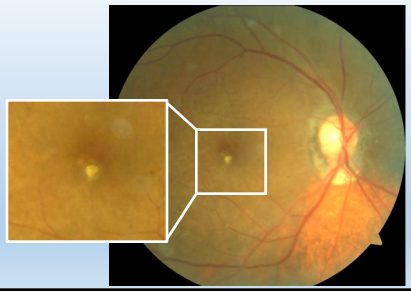
Non-Exudative (Quiescent) CNV

58yo HF

- OD: no symptoms
- Decreased vision OS x many years- no treatment
- DM type 2- History of NPDR
- VA OD 20/25, OS 20/100

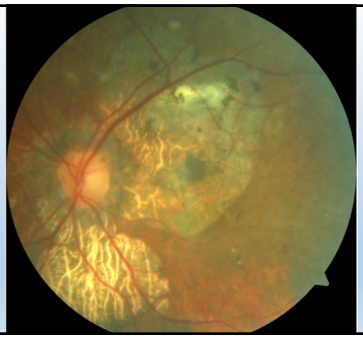
OD- 20/25

PPA
maculopathy
DR



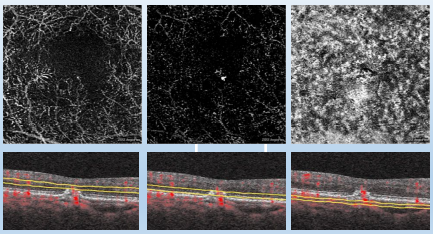
OS 20/100

atrophy
scar
DR

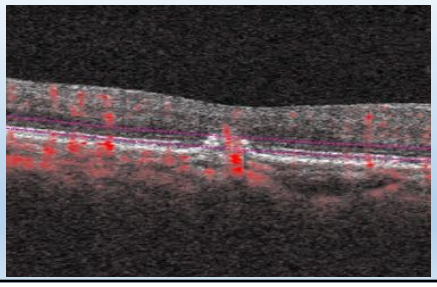


OD OCTA: NON-EXUDATIVE CNV

Deep Avascular Choroid

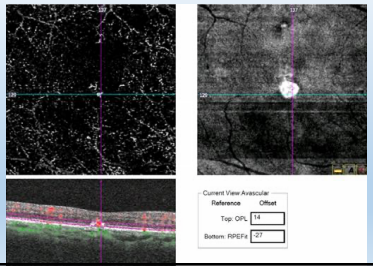


NON-EXUDATIVE CNV



NON-EXUDATIVE CNV

Avascular angio Avascular structure



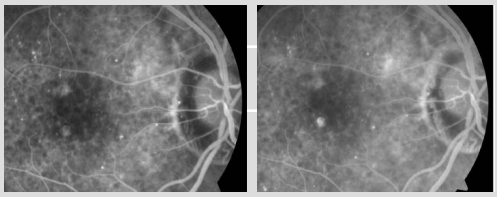
NON-EXUDATIVE (QUIESCENT) CNV

- A subset of patients with CNV have a membrane that is subclinical (ie. non-exudative).
- Historically, indocyanine green angiography (ICGA) has been used to characterize these lesions.
- The introduction of OCT-A has now given clinicians a rapid and reliable way to detect non-exudative CNV in patients with AMD, OHS, CSC and other conditions.

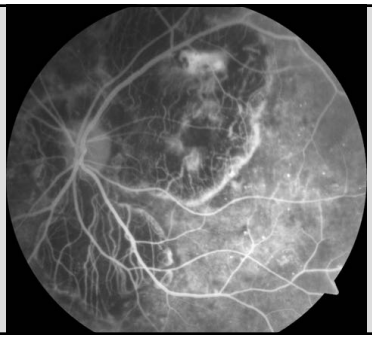
NONEXUDATIVE CNV

OD IVFA

1:20 6:09



OS IVFA (1:38)

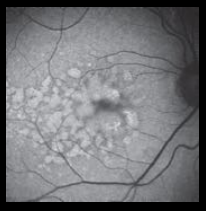


Non-Exudative (Quiescent) CNV: Plan

- These eyes have a higher risk of developing exudative disease than eyes without CNV detectable by OCTA.
- In one series, non-exudative CNV was identified in 14% of fellow eyes (intermediate AMD or geographic atrophy) of patients with unilateral exudative AMD, and these eyes were 15 times more likely to develop exudation within 1 year.
- We closely monitor these lesions; anti-VEGF therapy is not currently indicated in the absence of fluid leakage or clinical symptoms.

de Oliveira Dias JR, Zhang Q, Garcia JMB, et al. Natural history of subclinical neovascularization in nonexudative age related macular degeneration using sweptsource OCT angiography. Ophthalmology. 2018;125:255266.

Fundus Auto-fluorescence (FAF)

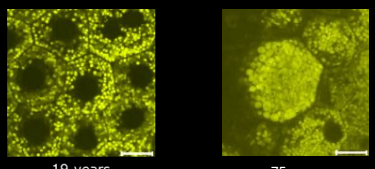


Joseph J. Pizzimenti, OD, FAAO

Lipofuscin

What is autofluorescence in the retina?

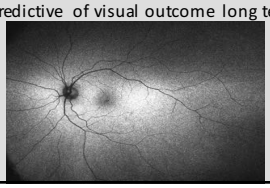
- It is the fluorescence of the lipofuscin molecule within the RPE cell layer that fluoresces with a certain wavelength.



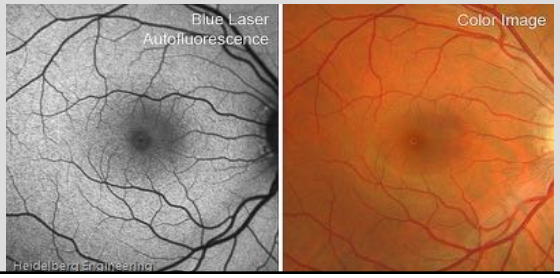
19 years 75 years

Clinical Value of FAF

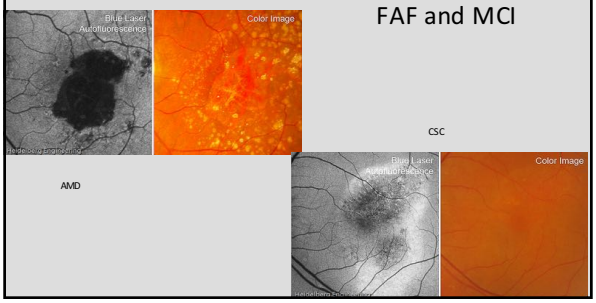
- Assessment or RPE damage and 'future' damage by identifying 'stressed' cells
- Amount of FAF damage correlates well with vision
- Somewhat predictive of visual outcome long term in AMD



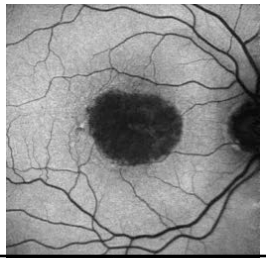
Blue-peak Laser FAF



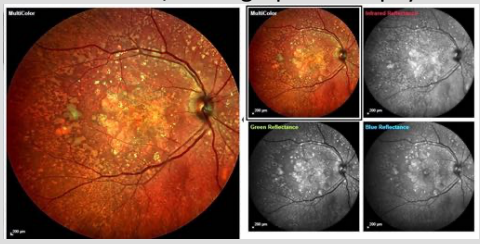
FAF and MCI



FAF and Progression-Geographic Atrophy

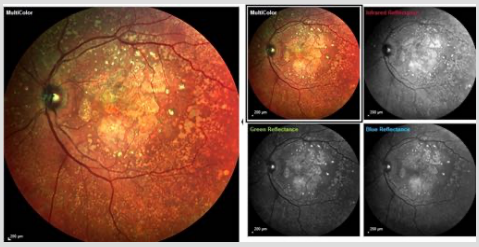


69 Y/O Geographic Atrophy



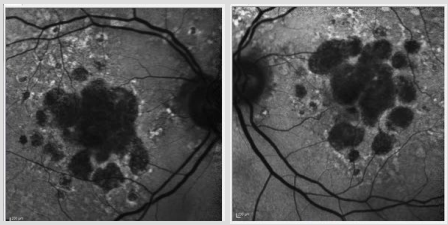
Which is the better seeing eye?

69 Y/O Geographic Atrophy



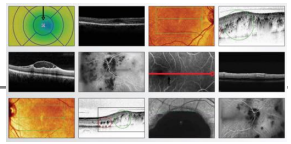
Which is the better seeing eye?

69 Y/O Geographic Atrophy



Which is the better seeing eye?

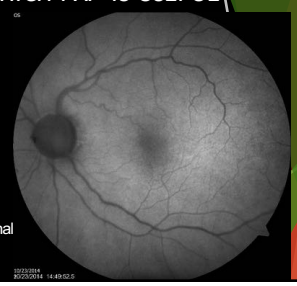
Questions and Answers?



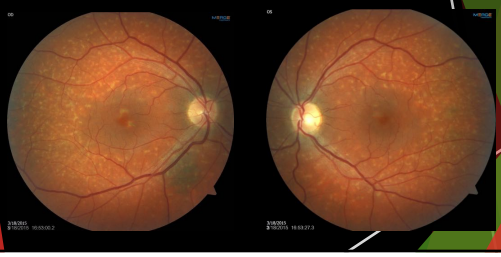
AUDIENCE

CONDITIONS IN WHICH FAF IS USEFUL

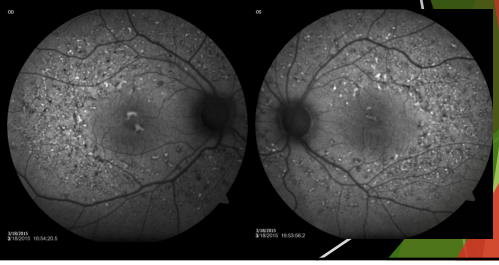
- AMD
- CSC (central serous chorioretinopathy)
- Plaquenil toxicity
- Nevi / melanomas, choroidal lesions
- White Dot syndromes
- ONH Drusen
- Inherited macular / retinal dystrophies



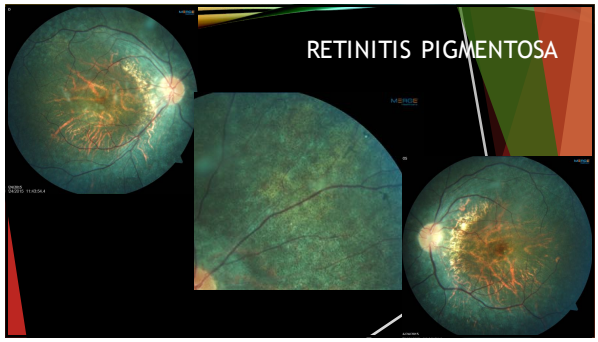
FUNDUS FLAVIMACULATUS OU + NEVUS OD



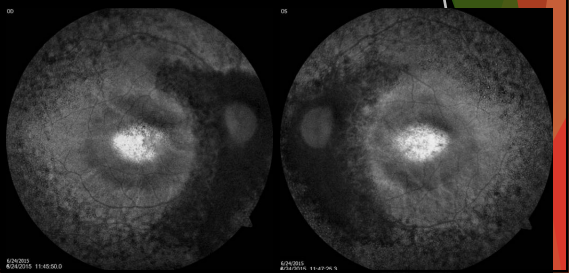
FUNDUS FLAVIMACULATUS - FAF

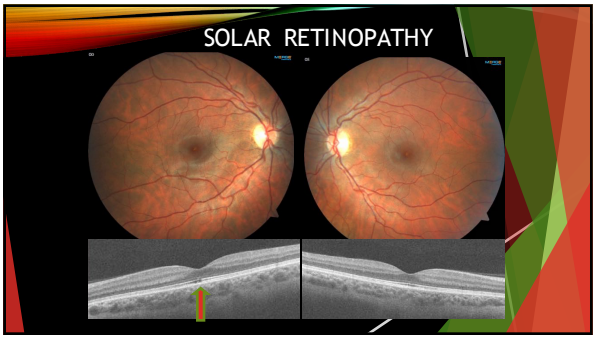


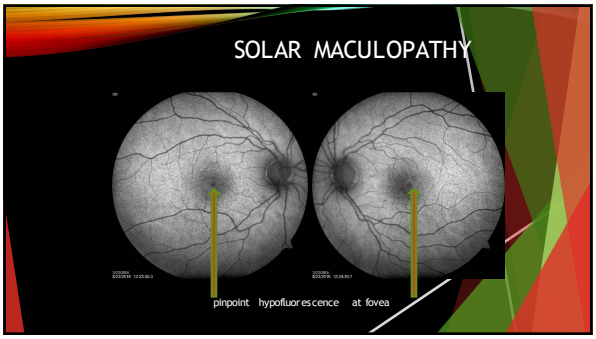
RETINITIS PIGMENTOSA

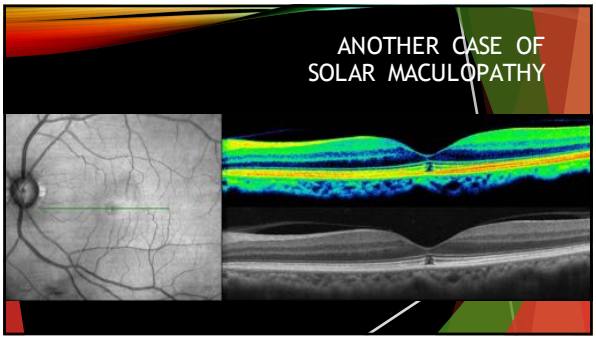


RP - FAF





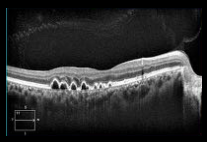




DISCUSSION

FAF and MCI: difference-makers or just fancy bells and whistles?

Tiny Bubbles



Joseph J. Pizzimenti, OD, FAAO

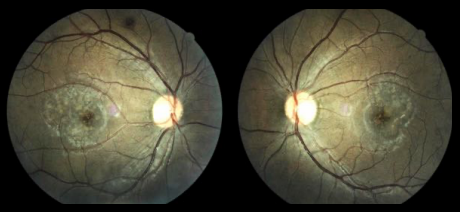
Case History and Clinical Findings

- A 30-year-old Hispanic male presented with a chief complaint of mild, bilateral central blur of one year's duration.
- Health history was positive for type 2 diabetes.
- Best corrected acuities were 20/25 in each eye.
- Amsler testing revealed central metamorphopsia in each eye.

Additional Clinical Findings

- Dilated funduscopy showed a honeycomb pattern of pigment epithelial changes within each central retina that resembled small, translucent bubbles.
- Moderate NPDR OD, mild NPDR OS
  - No DME
- Peripheral retina intact and unremarkable OU

Color Fundus Photography



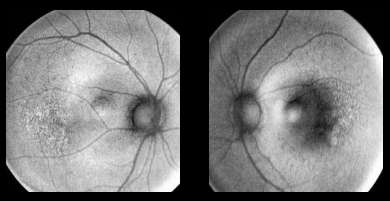
Special Testing

- Further investigation through multimodal imaging:
  - Fundus autofluorescence (FAF)
  - Infrared Imaging
  - OCT/OCTA
- MMI confirmed several serous RPEDs of various sizes within the maculae of both eyes.

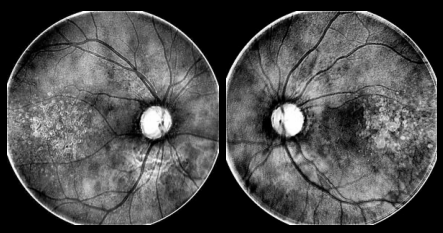
Differential Diagnoses

- Pattern Dystrophy of RPE
- Other dystrophic disease (CD, SD)
- Central Serous Chorioretinopathy
- Other Pachychoroidopathies
- Bilateral Idiopathic Multiple RPE Detachments
  - Appears in literature, though rarely

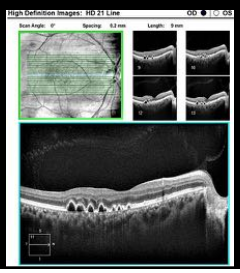
FAF



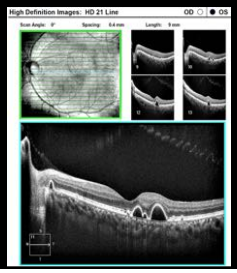
Infrared Imaging



OCT-OD: Multiple serous RPEDs of varied size. ILM, EZ band relatively intact OD/OS.

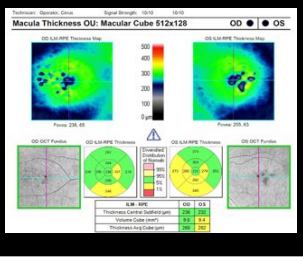


OCT OS: Multiple RPEDs of varied size. Choroid is of average thickness OU.

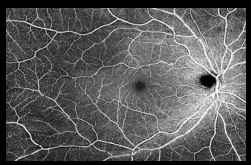


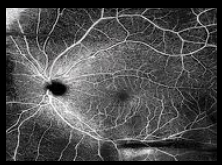
En Face Structural OCT Showing "Tiny Bubbles"

Retinal thickness maps show pattern of RPEDs. Sub-RPE fluid is underneath the dark blue areas.



Angioplex OCTA showed no evidence of CNV.



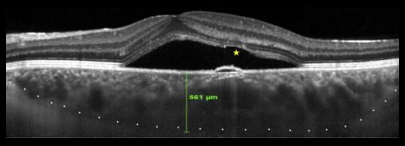


Genetic Testing

- We ordered the Blueprint Genetics Retinal Dystrophy Plus Panel and took a saliva sample.
- The panel included 266 genes with a known role in inherited retinal dystrophies.
- The genetic testing was sponsored via My Retina Tracker® genetic study program.
- The results were "negative for explaining the patient's phenotype" of bilateral multiple serous RPEDs.

Ruling Out CSC

- While an RPED may occur in CSC, its hallmark is a well-defined serous detachment of the sensory retina (star). Note also thick choroid.

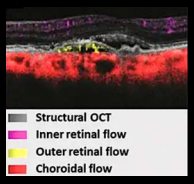


Discussion

- Bilateral Idiopathic Multiple RPED is rare.
- It may represent a precursor to CSC or other pachychoroid syndrome.
  - Pachychoroid pigment epitheliopathy?
- There is currently no preferred treatment, besides observation, as visual prognosis is typically good.
- Closely monitor for subretinal fluid and CNV.

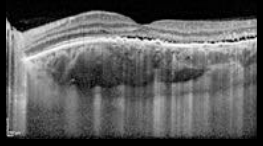
The Pachychoroid Spectrum

- Central serous chorioretinopathy (CSC)
- Pachychoroid pigment epitheliopathy (PPE)
- Pachychoroid neovasculopathy (PNV)
- Polypoidal choroidal vasculopathy (PCV)
- Focal choroidal excavation
- Peripapillary pachychoroid syndrome (PPS)



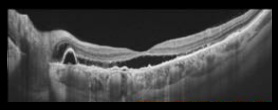
IMAGING THE CHOROID

PACHYCHOROID
AND SUBRETINAL FLUID IN CSC

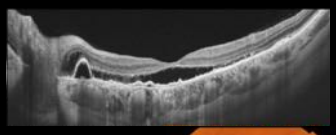


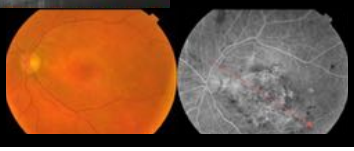
CSC

- Younger patients (not elderly)
- Steroids
- Type A
- "smoke-stack" hyperfluorescence on FA
- Metamorphopsia/blur
- Subretinal fluid
- Serous fluid leakage from CC

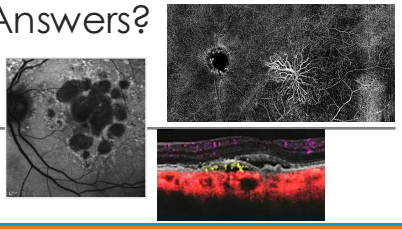


PACHYCHOROID
CNV IN CHRONIC CSC
EDI-OCT AND IVFA





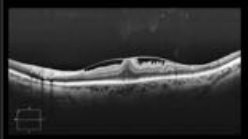
Questions and Answers?

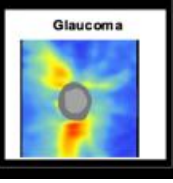


AUDIENCE

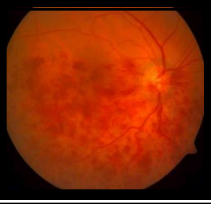
2-minute Stretch

- Click to add text





Case Study



69 year old Caucasian Woman

CC: Reduced central vision OD x 3 weeks @ distance and near

Ocular History: Unremarkable

Systemic History: Unremarkable ; Last PCP exam 15 years ago

Social History: Smokes ½ pack of cigarettes a day
Alcohol 5-6 drinks a day

Meds: Multivitamin

Allergies: +Penicillin

VA: s Rx 20/80 OD 20/20 OS

EOM: Smooth / Full

Pupils: PERRLA - APD

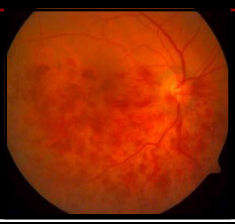
CF: Central blur OD Full Periphery OU

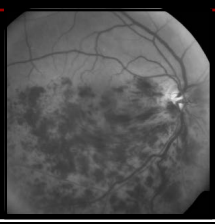
SLE: Unremarkable OU

TA : 20 mm Hg OU

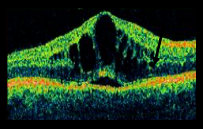
Vitreous: PVD OU

BP: 168 / 98 RAS





OCT Shows Cystoid Macular Edema, Sub-retinal fluid



What is your assessment?

Hemi-central RVO, perfused (aka non-ischemic) w/ME

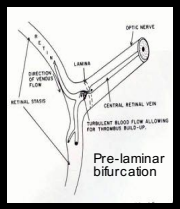
What is your plan?

Follow w/o treatment or co-manage with retina?

Hayreh's 6 Types of RVO

- Central retinal vein occlusion (CRVO)
  - Non-ischemic CRVO
  - Ischemic CRVO
- Hemi-central retinal vein occlusion (HCRVO)
  - Non-ischemic HCRVO
  - Ischemic
- Branch retinal vein occlusion (BRVO)
  - Major BRVO
  - Macular BRVO

CRVO Anatomy

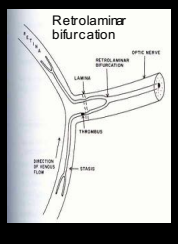


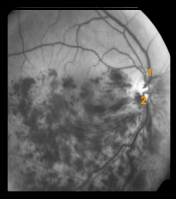
Pre-laminar bifurcation

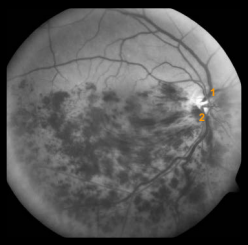
Hemi-central Retinal Vein Occlusion

- Uncommon type of hemispheric RVO
  - Occurs in "Dual Trunk" anomaly
- Same pathophysiology as CRVO.
- May affect either the superior or inferior CRV before they unite into common central retinal vein.
- Usually occurs at or near the optic disc.

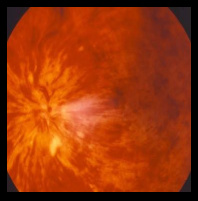
Anatomy of HCRVO







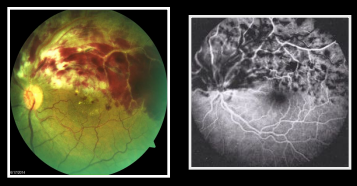
CRVO, non-perfused (ischemic)



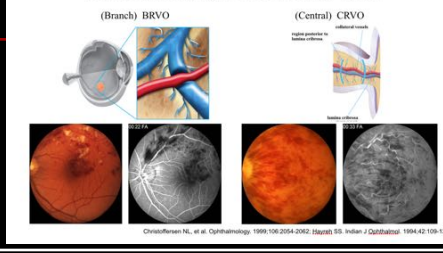
CRVO: Classification

Nonischemic	Ischemic
< 10DAs of NP via FA	~50% of all CRVOs
VA better than 20/200	≥10DAs of NP via FA
Usually no APD present	VA worse than 20/200
Limited hemes in all quadrants	Prominent APD
Limited VF defects	Severe hemorrhaging and CWSs in all quadrants ("blood and thunder")
<5% incidence of ant seg neo	Significant VF defects
	Abnormal ERG
	50-60% incidence of ant seg neo (most develop within 3-5 mo)!!!

Fluorescein Angiography HCRVO

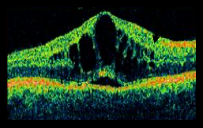


Pathophysiology of BRVO and CRVO

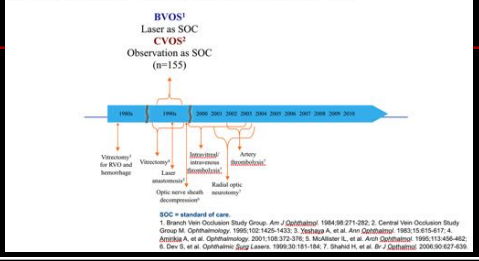


Christoffersen NL, et al. Ophthalmology. 1999;106:2054-2062; Hayreh SS. Indian J Ophthalmol. 1994;42:109-132.

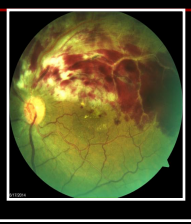
Treatment Options for ME in RVO



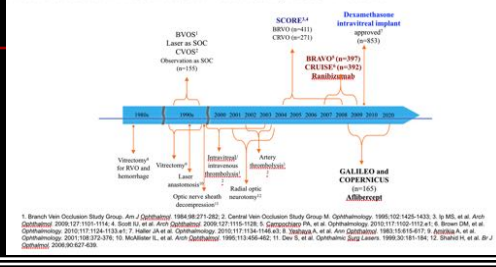
Interventions in Retinal Vein Occlusion, 1980-2005



Fast Forward



Interventions in Retinal Vein Occlusion, 2005-Present



1. Branch Vein Occlusion Study Group. Am J Ophthalmol. 1984;98:271-282; 2. Central Vein Occlusion Study Group M. Ophthalmology. 1995;102:1425-1433; 3. Ip MS, et al. Arch Ophthalmol. 2009;127:1101-1114; 4. Scott IU, et al. Arch Ophthalmol. 2009;127:1115-1128; 5. Campochiaro PA, et al. Ophthalmology. 2010;117:1102-1112.e1; 6. Brown DM, et al. Ophthalmology. 2010;117:1124-1133.e1; 7. Haller JA et al. Ophthalmology. 2010;117:1134-1146.e3; 8. Yeshaya A, et al. Ann Ophthalmol. 1983;15:615-617; 9. Amirikia A, et al. Ophthalmology. 2001;108:372-376; 10. McAllister IL, et al. Arch Ophthalmol. 1995;113:456-462; 11. Dev S, et al. Ophthalmic Surg Lasers. 1999;30:181-184; 12. Shahid H, et al. Br J Ophthalmol. 2006;90:627-639.

CRVO: Key Points

- A non-ischemic (perfused) CRVO can progress to an ischemic CRVO.
- When neovascularization develops in ischemic CRVO, it most often occurs in the anterior segment.
- 2/3 of patients with non-ischemic CRVO will recover to VA of 20/40 or better without any treatment.
- Up to 45% of eyes with ischemic CRVO develop neovascular glaucoma (NVG).**

	Non-ischemic CRVO	Ischemic CRVO
Visual acuity	>20/200	<20/200
RAPD (relative afferent papillary defect)	Mild or absent	present (>0.7 log units of neutral density filter)
Visual field defect	rare	common (use of Goldmann perimeter is suggested, as 30 degree field misses peripheral changes)
Fundus appearance	less disc/macular edema, hemorrhage, cotton-wool spot mild venous tortuosity and dilation	More disc/macular edema, hemorrhage, cotton-wool spot Severe venous tortuosity and dilation
Fundus fluorescein anglogram	less area of nonperfusion	retinal capillary nonperfusion more than 10 disc areas
ERG/electroretinogram	normal	Reduced b-wave amplitude (≤60% of the normal mean value of both photopic and scotopic ERG), and reduced b/a
Prognosis	good, less chance of anterior segment neovascularization/neovascular glaucoma	Poor, high chance of anterior segment neovascularization/neovascular glaucoma The visual prognosis may be worse than central retinal arterial occlusion

Co-manage RVO with:

Retina (non-perfused, or ME, or NV)

Internal Medicine/Cardiology

PCP

Ask the retina specialist:

When would you like to see RVO patients after initial diagnosis by the primary eye care clinician?

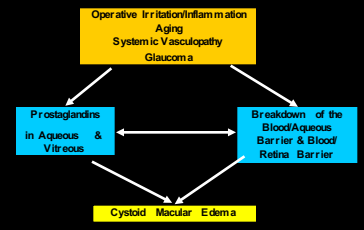
Questions and Answers

UWF FA of an ischemic CRVO.
Note extensive nonperfusion and diffuse blocking from retinal hemorrhages.

Irvine-Gass Syndrome

Post-operative Cystoid Macular Edema (CME)

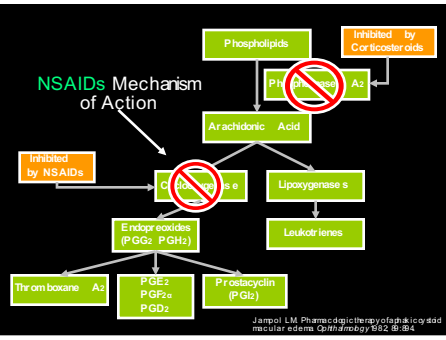
Pathogenesis



Adapted from Miyake K et al. *Jpn J Ophthalmol* 2000;44:58-67.

What is your plan?

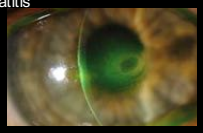
NSAIDs Mechanism of Action



Jampol LM. Pharmacologic therapy of aphakic cystoid macular edema. *Ophthalmology* 1982;89:384.

Adverse Events Associated With Conventional NSAID Therapy

- Mild/Moderate corneal side effects[1]:
  - Burning and irritation
  - Superficial punctate keratitis
  - Delayed wound healing
- Severe corneal issues[2]
  - Thinning
  - Perforation due to melts



1. Rich, AJ. Topical nonsteroidal antiinflammatory drugs in ophthalmology. *Int Ophthalmol Clin* 2002;42(1):1-11. 2. Mah et al. *AJOS*; 2005.
2. Prescribing Information: VOLTAREN ACULAR ACULAR LS

Treatment of Post-op CME

- Topical NSAID x 2-3 mon
- Topical steroid
- Topical NSAID + topical steroid

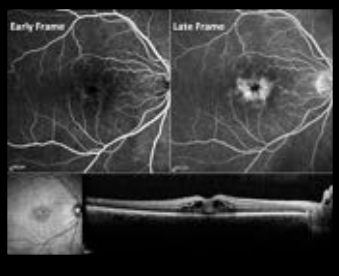
Ask the retina specialist:

what is your preferred treatment(s) for recalcitrant post-op CME?

Treatment of Recalcitrant Post-op CME

- Periocular anti-inflammatory meds
- Intravitreal anti-inflammatory meds

Questions and Answers



QUESTIONS?

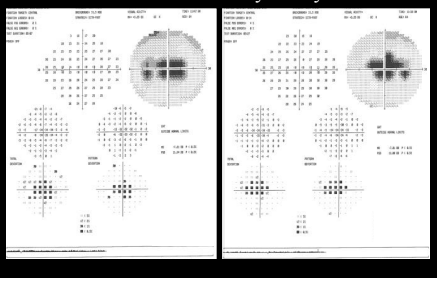
Case

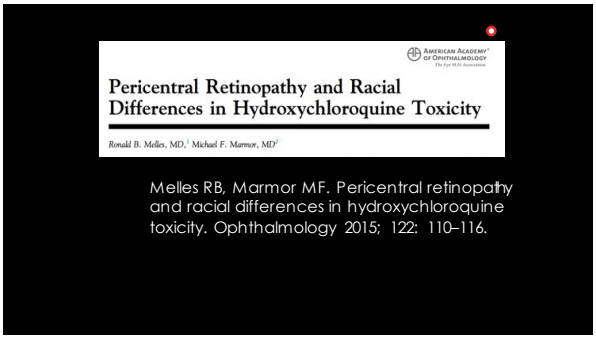
- 65 Year old Asian Female
- Comes in with complaints of blurred and dimmed vision
- PMH: Rheumatoid Arthritis x 15 years
- OcHx: S/P CE and IOL OU

Ophthalmic Exam

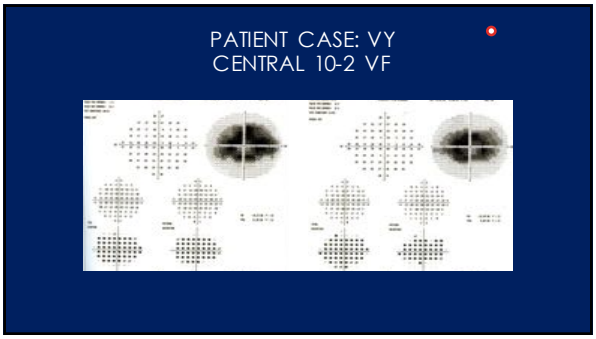
- VA:
  - OD: 20/60 OS: 20/70
- IOP
  - OD: 14 OS: 13
- SLE:
  - OD: PCIOL OS: PCIOL

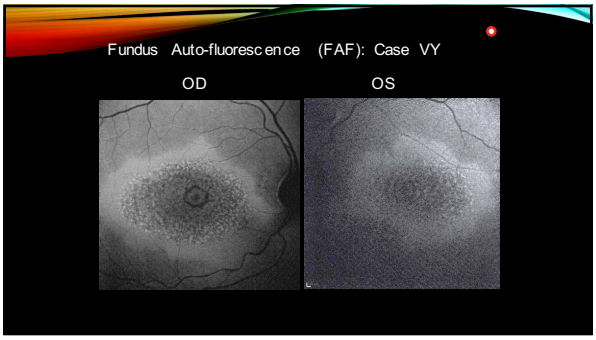
Patient Case: VY 65 y/o Asian Female Central Threshold Perimetry: Why 30-2?

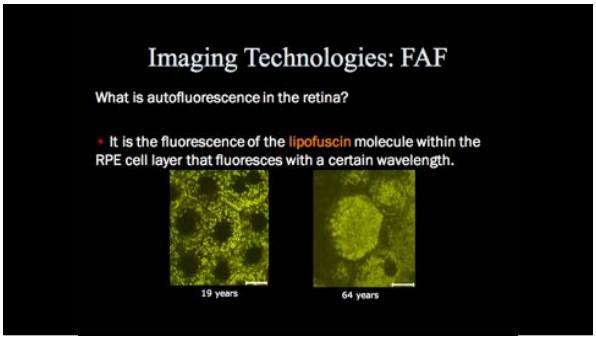




Melles RB, Marmor MF. Pericentral retinopathy and racial differences in hydroxychloroquine toxicity. Ophthalmology 2015; 122: 110–116.



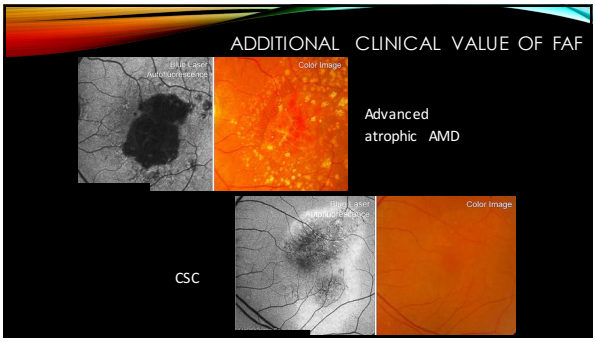




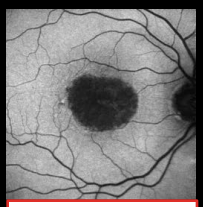
MULTIMODAL IMAGING:

FUNDUS AUTOFLUORESCENCE

While OCT assesses structure, and IVFA assesses BRB integrity, FAF captures **metabolic activity.**

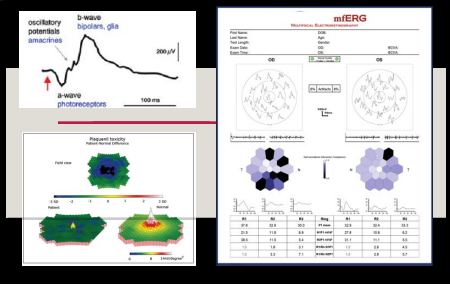


FAF SHOWS PROGRESSION - GEOGRAPHIC ATROPHY

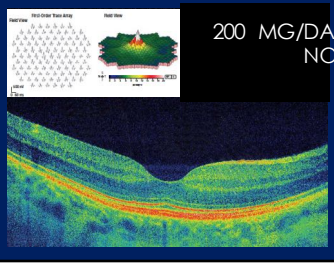


Progression of GA over an 18 month period

PLAQUENIL AND MF-ERG

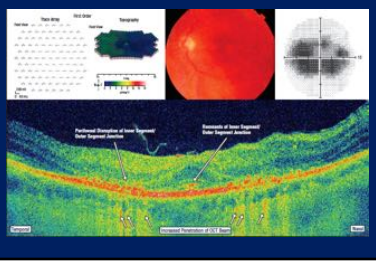


ANOTHER PATIENT ON PLAQUENIL



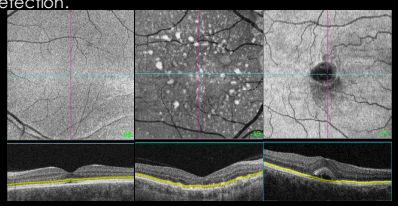
200 MG/DAY X 5 YRS
NO TOXICITY

PLAQUENIL TOXICITY- MFERG



PLAQUENIL TOXICITY

- By the time "flying saucer" or "bullseye" is detected, significant toxic damage has occurred.
- May progresses even if drug is stopped.
- Ganglion cell analysis and en face OCT may offer early detection.



What is the recommended maximum HCQ dose?

- Calculate Max Dose in mg/day
- 2.3 x weight (in lbs.) = Max dose
- At recommended dose, risk of toxicity is < 1% after 5 years, < 2% after 10 yrs.
- Risk rises to almost 20% after 20 years.**
  - Our patient VY (~110-120 lbs) was taking 400 mg/d for 20 yrs, or nearly double the MDD.
- Risk for HCQ maculopathy depends on daily dose, duration of use

AMERICAN ACADEMY OF OPHTHALMOLOGY

American Academy of Ophthalmology Statement

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

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

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

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

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

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

HCQ SCREENING FREQUENCY

- Baseline: DFE within 1 year of starting HCQ
- Visual field and SD-OCT if macular abnormalities are present at baseline
- Annual screening: Begin after 5 years of use
  - Sooner in presence of "major risk factors"

AMERICAN ACADEMY OF OPHTHALMOLOGY

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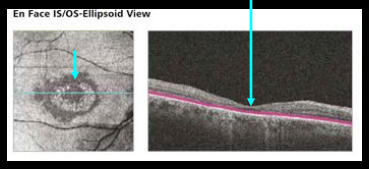
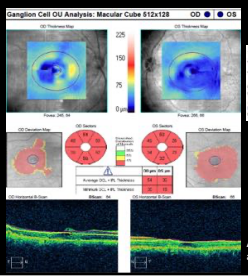
Michael F. Marmor, MD,[1] Ulrich Kellner, MD,[2] Timothy Y.Y. Lai, MD, FRCOphth,[3] Ronald B. Melles, MD,[4] William F. Mieler, MD,[5] for the American Academy of Ophthalmology

PLAQUENIL MACULOPATHY WITH CLASSIC BULL'S EYE DUE TO ANNULAR FOVEAL ATROPHY



GCL + IPL loss in HCQ maculopathy



Expanded spectral domain-OCT findings in the early detection of hydroxychloroquine retinopathy and changes following drug cessation

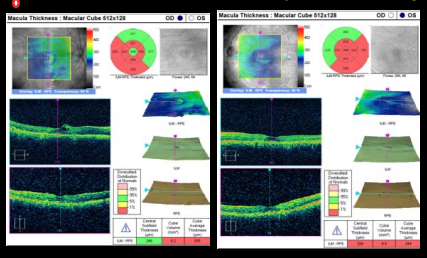
The Journal of Rheumatology

Hydroxychloroquine Ocular Toxicity: Lessons Learned

JEFF C. RABIN and KIRSTI RAMIREZ

Acknowledgement: Drs. K. Ramirez and J. Rabin, UIWRSO VNS clinic

Note significantly thin maculae and cystic retinal changes



Acknowledgement: Drs. K. Ramirez and J. Rabin, UIWRSO VNS clinic

FROM THE AUTHORS

- "(Real) weight-based dosage and early screening (DFE, central fields, OCT, FAF, mfERG) are essential to prevent HCQ toxicity,
- particularly with certain risk factors: small stature, high total dosage, diminished renal function, concomitant tamoxifen use, and/or existing retinal/macular disease.
- Interprofessional collaboration to optimize patient outcomes."

The Journal of Rheumatology

Hydroxychloroquine Ocular Toxicity: Lessons Learned

JEFF C. RABIN and KIRSTI RAMIREZ

Visual Neurophysiology Service

UNIVERSITY OF THE INCARNATE WORD

ROSENBERG SCHOOL of OPTOMETRY

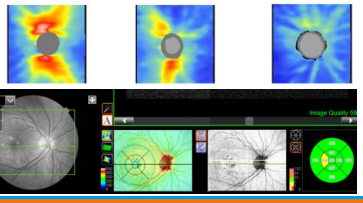
Plaquenil Maculopathy

- Testing for patients on Plaquenil
  - DFE
  - VF 10-2 W/W (add 24-2 or 30-2 in Asians)
  - SD or SS-OCT: raster and cube scans
  - FAF
  - mfERG
- Increase frequency of monitoring (2+ visits per year) w/degree of pathophysiology.

Summary and Case Outcome

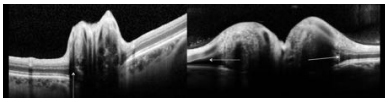
- MMI and other diagnostics are essential in evaluation of patients using CQ or HCQ on a chronic basis.
- Co-management team includes:
  - Optometry
  - Rheumatology
    - Other therapies: methotrexate, TNF inhibitors (our patient VY was switched to this drug class)

Questions and Answers?

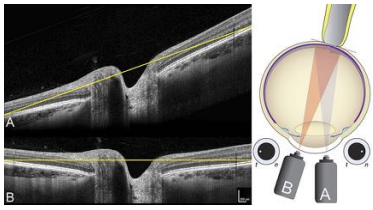


AUDIENCE

OCT Imaging in Differentiating Papilledema from Pseudopapilledema



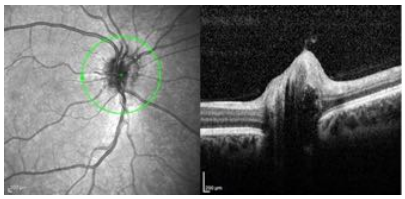
Ideal Imaging Technique



Pseudopapilledema-OCT Findings

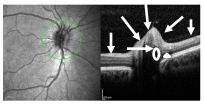
- Elevation of the optic nerve head with…..
- Minimal increase in RNFL thickness
- Minimal central cup
- Increased reflectance of hyaline
- Shadowing near hyaline
- Separation of deeper retina from RPE
- Neutral/Negative RPE and BM deflection

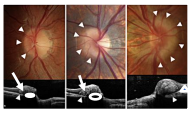
Pseudopapilledema-OCT Findings



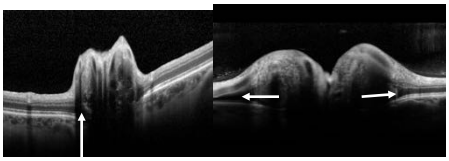
Disc Drusen-OCT findings

- Elevation
- Normal RNFL…then thin
- No/minimal cup
- Increased reflectance
- Shadowing
- Separation of outer retina

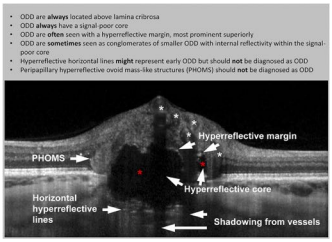




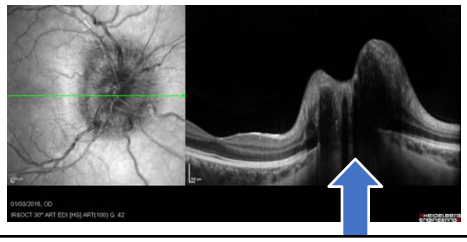
Disc Drusen- Shadowing & Separation of Outer Retinal Layers



Optic Disc Drusen Studies Consortium

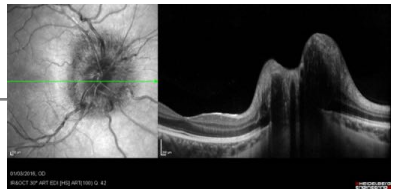


Forward Bowing of RPE/BM



Bilateral disc edema in IIH

AUDIENCE

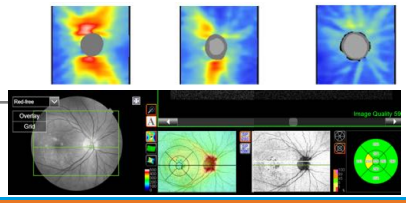


Key Points

- Not all elevated discs are swollen! (ODD)
- True optic disc edema has many causes.
- Not all disc edema is papilledema!!
- Clinicians must be adept at examining the optic nerve and associated structures.
- Physical examination together with patient history and other specialized testing (such as perimetry, OCT, echography, neuroimaging) should help differentiate true disc edema from pseudo-edema.

Questions and Answers?

AUDIENCE



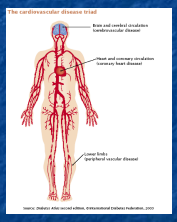
Conclusions

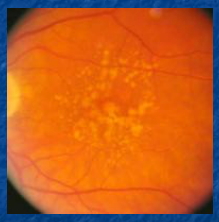
- Multimodal imaging technologies have enhanced our ability to visualize tissue microstructure, as well as assess risk for and detect early signs of disease.
- In addition to their diagnostic value, MMI methods enable clinicians to more accurately monitor patients for disease progression vs stability.
- Collaboration among health care professionals results in improved outcomes and better QOL!

Thank you for spending your precious time with me!

Joe

Emerging Trends in AMD





Joseph J. Pizzimenti, OD, FAAO

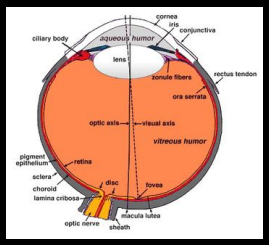
Financial Disclosures

- Proprietary Interests
  - None
- Consulting Fees
  - Zeiss
  - EyePromise/Zeavision
- Stockholder: Zeavision

ALL FINANCIAL RELATIONSHIPS HAVE BEEN MITIGATED.

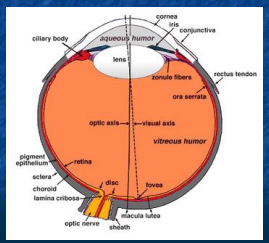
OptometricRetinaSociety.org

Check out our E-newsletter



OptometricRetinaSociety.org

Check out our E-newsletter



QUESTIONS AND ANSWERS

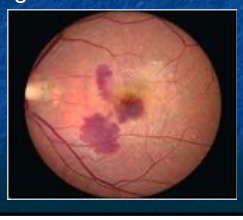
Email me at pizzimen@uiwtx.edu

Course Goals

- To provide clinically useful information about AMD
- Systemic approach
  - Prevention
    - Nutrition
  - Early diagnosis
  - Treatment and management

Statement of The Problem

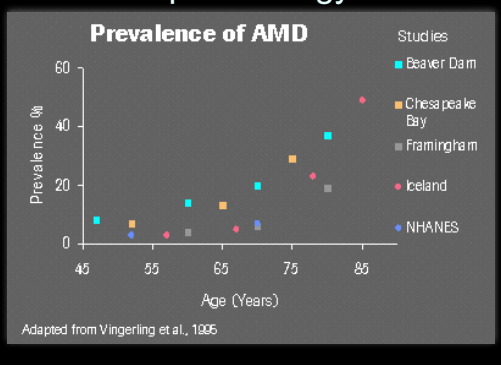
- The AMD "Epidemic"
- AMD is the leading cause of blindness in individuals over the age of 50 in the developed world.
  - Klein R, Klein BEK, Linton KLP. Prevalence of age-related maculopathy. Ophthalmology. 1992;99:933–943.



What is AMD?

- AMD is a heterogeneous disorder affecting the RPE/Bruch's membrane/choriocapillaris complex.
- Early disease is classically characterized by minor vision loss associated with focal or diffuse sub-RPE debris and changes in RPE pigmentation.
- Late, advanced disease is characterized by severe vision loss associated with extensive RPE atrophy (GA) with or without the sequelae of macular neovascularization (MNV).
  - Zarbin MA. Age-related macular degeneration: review of pathogenesis. Eu. J Ophthalmol. 1998;199–206.

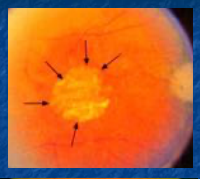
Epidemiology

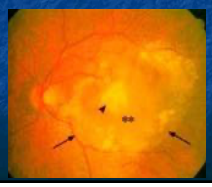


Adapted from Vingerling et al., 1995

Classification of AMD

- *Non-neovascular, aka "dry"*
  - Non-NV, non-exudative, atrophic
  - Can be performance-degrading
  - Majority of AMD cases
- *Neovascular (nAMD), aka "wet"*
  - Exudative, hemorrhagic
  - MNV –devastating to central vision
  - Minority of AMD cases
    - Majority of vision loss

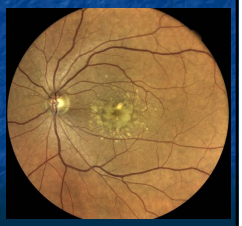




The Burden of Disease

The Burden of Severe Vision Loss in AMD

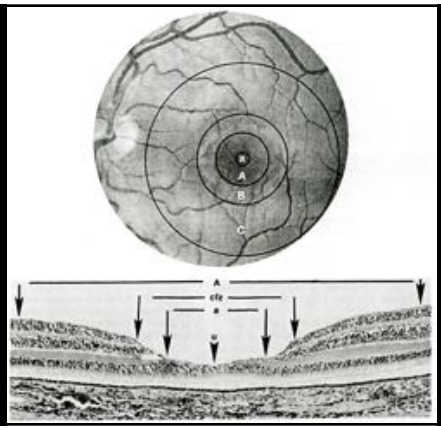
- Patients, loved ones, caregivers, medical community.
- Consequences may be:
  - Physical
  - Social- isolation
  - Economic
  - Psychological- depression



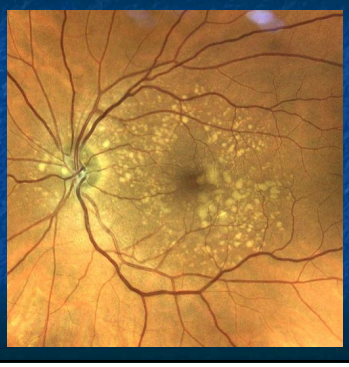
The AMD "Epidemic"

How should we as optometrists respond?

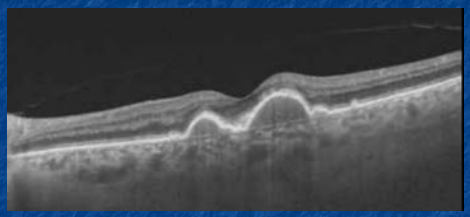
Prevention
Early Diagnosis
Early Intervention
Improved Visual Outcomes



Mixed Drusen



OCT of Soft Drusen



Current commercially available Spectral Domain OCT is capable of obtaining 3-5 um resolution.*

AMD Risk Factors

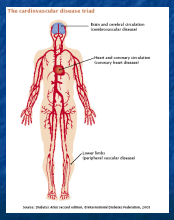
- Non-modifiable
  - Age
  - Heredity
  - Sex (F>M)
  - Pigmentation
  - Race
  - Iris color
- Modifiable
  - Smoking
  - Cardiovascular disease
  - Blood lipid status
  - Hypertension
  - Alcohol consumption
  - Light exposure (UV, blue)
  - Nutrition
  - Obesity
  - Low MPOD
  - Poor dark adaptation

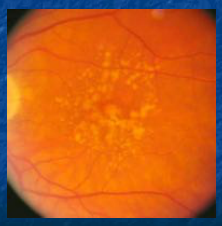
Macular Degeneration

Pathobiology of AMD

- Aging of the photoreceptors and RPE/Bruch
- Genetic component
- Environmental stress
  - Lifestyle/nutrition
  - Light-initiated oxidative damage

Emerging Trend: AMD as a Systemic Disease



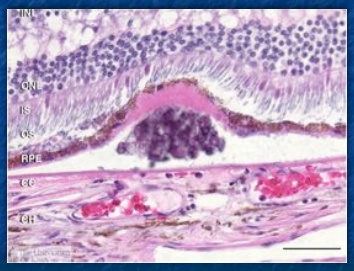


AMD and Drusen

- AMD is a disease resulting from poor "Waste Management".

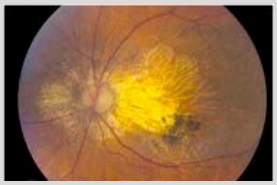
- Drusen are "pockets of inflammation"
  - Recent investigations show that proteins associated with inflammation and immune-mediated processes are prevalent in drusen.

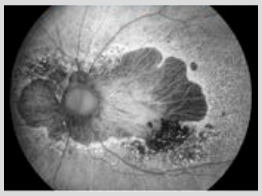
Drusen



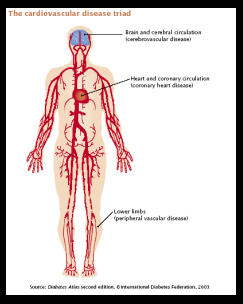
Drusen is the earliest clinically detectable feature of AMD.**

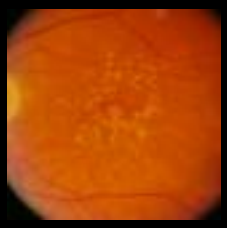
AMD: a sick eye in a sick body?





AMD and Cardiovascular (Heart) Disease

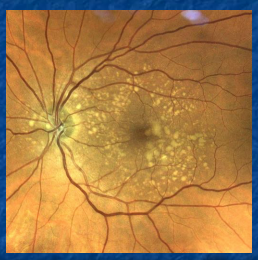




Parallel Worlds: Heart Disease and AMD

- Diet – Low fruit/vegetable consumption increases risk of AMD and CVD
- Obesity and physical inactivity
- C-reactive protein (elevated)
  - Inflammatory marker
- Homocysteine (elevated)
- Omega-3 EFA may be beneficial for AMD patients
- Cholesterol (elevated)
- Serum Iron – Increased amounts may increase AMD and CVD

QUESTIONS AND ANSWERS



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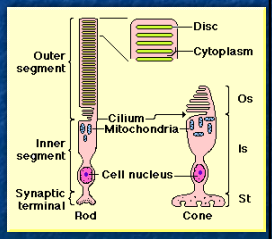
The 4 Seasons of AMD

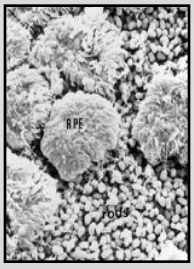
- Oxidation
- Inflammation/Ischemia
- Atrophy
- Neovascularization

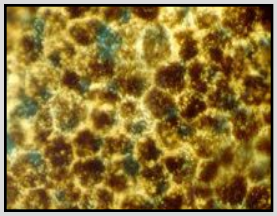
Normal Retinal Metabolism

- Outer segment discs of rods and cones are transported to RPE for metabolism
- Discs are engulfed into RPE and fuse with lysosomes, where they are digested
- Undigested residual bodies remain as lipofuscin
  - These are the real troublemakers!*



Abnormal Retinal Metabolism



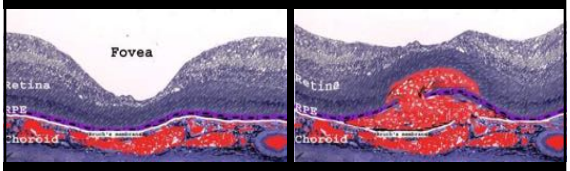


Lipofuscin accumulates in the aging RPE

Reactive Oxygen Species (ROS)

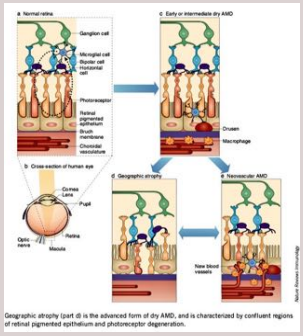
- ROS are the byproducts of oxygen metabolism.
  - Free radicals
  - Hydrogen peroxide
  - Singlet oxygen
- The retina/macula is particularly susceptible to oxidative stress because of its high O-2 consumption and exposure to visible light.

Wet AMD Pathology



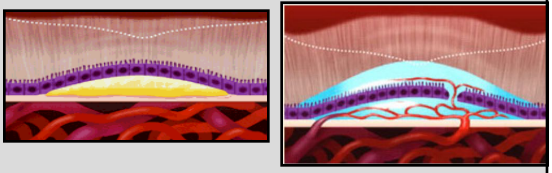
~20% of eyes w/dry AMD ultimately convert to wet AMD.*

Pathways in AMD Pathogenesis

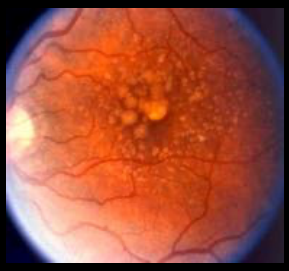


Pathogenesis of CNVM

- Breaks in Bruch's Theory
  - Diffuse thickening of Bruch's w/soft drusen
  - Predisposes Bruch's to breaks
  - New BV's from CC grow and proliferate



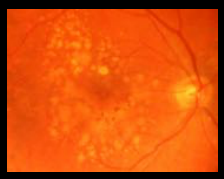
Advanced AMD starts out like this:



Large, ill-defined, and confluent soft drusen**

Intermediate Stage AMD

- AREDS Category 3



- Extensive intermediate drusen (63-124μ diameter)
- At least one large druse (>125μ)
- Geographic atrophy not involving the foveal center

Unfavorable prognostic signs leading to CNVM, GA:

- Soft, large, confluent drusen
- Reticular (pseudo) drusen*
- Focal hyperpigmentation
- Disciform lesion in the fellow eye
- Older age
- Poor dark adaptation*

Reticular (Pseudo)drusen (RPD)

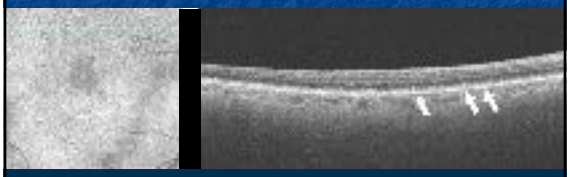
- Seen as a reticular pattern of small yellow-white lesions often in the superior macula, RPD are a high-risk sign for advanced AMD.

Reticular (Pseudo)drusen

Reticular (Pseudo)drusen

- Presence of RPD is a consistent risk factor for progression to both atrophy and CNV
- IS/OS C-scan

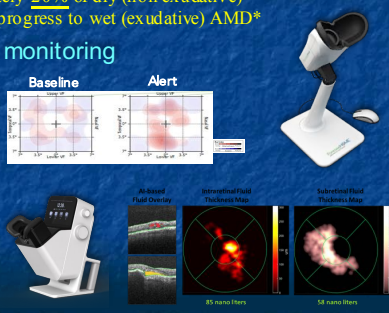
B-scan



Emerging Trend

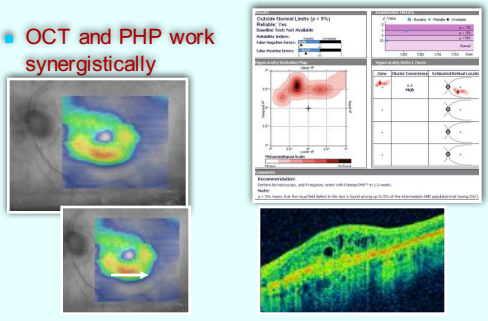
Approximately 20% of dry (non-exudative) AMD eyes progress to wet (exudative) AMD*

- Home monitoring
- PHP
- OCT



Structure and Function

- OCT and PHP work synergistically

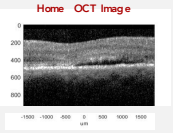


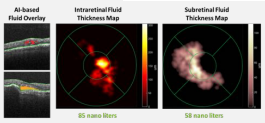
Home OCT for Monitoring Therapy of nAMD Between Visits

- Monitoring of intra- and subretinal fluid based on daily patient self-imaging
- Easy-to-use, patient-operated device
- Takes less than one minute per eye
- AI algorithm analyzes images on cloud
- Remote diagnostic clinic, provider of monitoring program, reports changes meeting physician-selected fluid volume thresholds to referring physician
- 24/7 physician access to all data

Home OCT Device

Home OCT Image





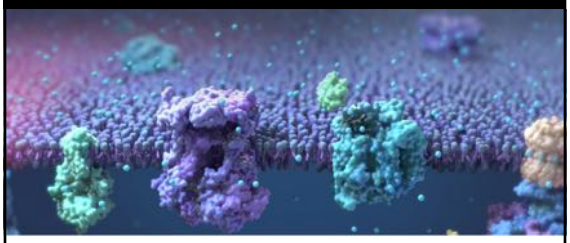
- Post-treatment AMD patients are monitored frequently because **there is a relatively high incidence of continued leakage from CNVM***

Photobiomodulation (PBM)

FDA Authorizes Valeda Treatment to Improve Vision in Dry AMD (November 04, 2024)

Valeda Light Delivery System

- First and only FDA-authorized treatment for dry AMD to improve vision
- U.S. LIGHTSITE III 24-month pivotal trial met BCVA primary endpoint and was used to support Valeda FDA submission
- CE Marked in Europe and available in select countries in Latin America
- Non–invasive treatment with a favorable safety profile with no signs of phototoxicity



Photobiomodulation is the medical application of low-level light wavelengths to stimulate cellular function leading to beneficial clinical effects.

Photobiomodulation

U.S. Indications for Use

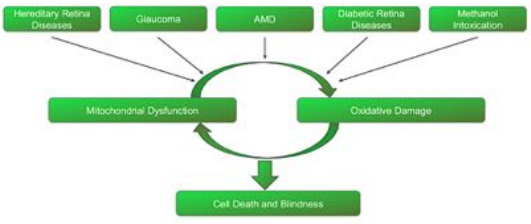
Indications for Use
The Valeda Light Delivery System is intended to provide improved visual acuity in patients with best corrected visual acuity (BCVA) of 20/32 through 20/70 and who have dry age-related macular degeneration (AMD) characterized by:

- The presence of at least 3 medium drusen (> 63 µm and ≤125 µm in diameter), or large drusen (> 125 µm in diameter), or non-central geographic atrophy, AND
- The absence of neovascular maculopathy or center-involving geographic atrophy

After about two years, the Valeda Light Delivery System treatment provides improved mean visual acuity of approximately one line of visual acuity (ETDRS) compared to those not receiving the treatment.

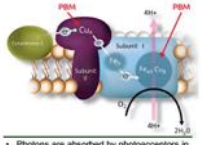
Contraindications
As a precaution, patients have not been tested and should not be treated with Valeda if they have any known photosensitivity to yellow light, red light, or near-infrared radiation (NIR), or if they have a history of light-activated central nervous system disorders (e.g., epilepsy, migraine). In addition, patients should not receive treatment within 30 days of using photosensitizing agents (e.g., topicals, injectables) that are affected by 590, 660, and/or 850 nm light before consulting with their physician.

Mitochondrial Dysfunction: An Important Role in Retinal Disease & Injury



Valeda Photobiomodulation Approach

Valeda uses low-level light to stimulate cells, restore energy production, and improve cellular health



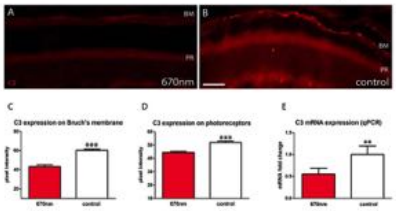
- Photons are absorbed by photoacceptors in the targeted tissue mitochondrial protein, cytochrome C oxidase (CcO) to restore energy production
- Sustained cellular changes also occur through activation of transcription factors

Valeda Wavelengths (nm)	Cellular Targets and Effect
590	Increases nitric oxide synthesis and vasodilation which can improve local oxygenation and nutrient delivery
660	Promotes O^2 binding (Cu_B), stimulates metabolic activity (ATP) and inhibits inflammation and cell death
850	Drives electron transfer (Cu_A) stimulates metabolic activity (ATP) and inhibits inflammation and cell death

Valeda wavelengths were selected based on their cellular targets and importance in AMD

Photobiomodulation Improves Inflammatory Responses

670 nm reduces outer retinal inflammation in a mouse model of AMD (CFH$^{-/-}$ Mice)



Following 670 nm treatment, C3 expression was significantly reduced on Bruch's membrane and photoreceptor outer segments

Valeda® Light Delivery System Treatment

- Treatment is straightforward with minimal training required
- No pupil dilation required
- A treatment series is nine (9) treatments delivered 3x/week over the course of 3-5 weeks
- A treatment series should be delivered every 4 months
- Implementation support available from LumiThera Customer Success

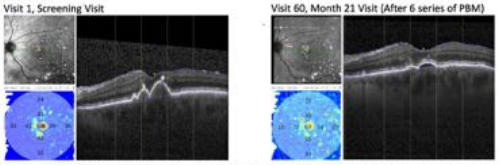
Photobiomodulation Delivery Specifications

- Valeda delivers eye-safe photobiomodulation treatment using LEDs
- The eye is uniquely accessible to PBM treatment. No other tissue or bone interferes with treatment directed to the eye
- Valeda is NOT a LASER. Valeda delivers a non-coherent, homogenized, light beam produced by LEDs
- Valeda meets all requirements set forth by ANSI Z80.36 and IEC 62471 for light exposure safety
- Valeda does not deliver thermal treatment or produce local cellular damage
- No phototoxicity or serious adverse events considered related to PBM treatment have been reported in Valeda clinical trials

LIGHTSITE III: US Pivotal 24-Month Trial

The LIGHTSITE III was an FDA, IDE-approved, prospective, double-masked, randomized, sham-controlled, parallel group, multi-center trial to assess the safety and efficacy of photobiomodulation (PBM) in subjects with dry age-related macular degeneration (AMD)

LIGHTSITE III: Macular Drusen Volume Reduction



Representative OCT imaging from a 77-year-old female subject showing a significant reduction in macular drusen volume after the final series of PBM treatment at Month 21 without visible loss of photoreceptor or retinal pigment epithelium.

Starting BCVA: 75 letters

Month 13 BCVA (4 series of PBM): 79 letters; 4 letter gain

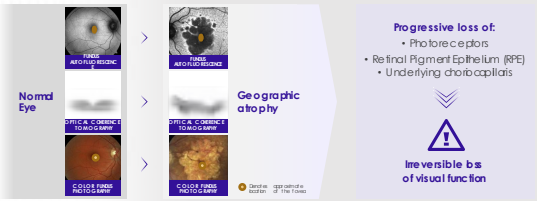
Month 21 BCVA (6 series of PBM): 84 letters; 9 letter gain

Month 24 BCVA (3 months after final PBM Tx): 82 letters; 7 letter gain

Questions and Answers

WHAT IS GEOGRAPHIC ATROPHY IN AMD?

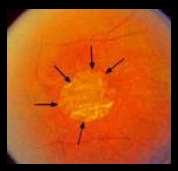
Geographic atrophy is defined by the presence of sharply demarcated atrophic lesions of the outer retina



Images: top left and right: Bogunović H, Bull N. Klein Optometrist 2013;72
Image: top middle: https://www.know-the-eyes.com/examinations/visual-examinations/
Image: bottom: Reckenstein M, et al. Ophthalmology. 2018;125:369-390.

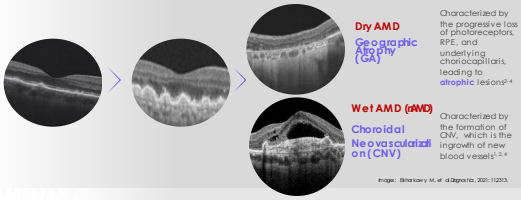
AMD, age-related macular degeneration; GA, geographic atrophy.
Reckenstein M, et al. Ophthalmology. 2018;125:369390.

Prevention and treatment of GA remains an unmet need.



This is changing thanks to innovations such as complement inhibition.

AMD is a disease spectrum ranging from early to late stages[1,2]

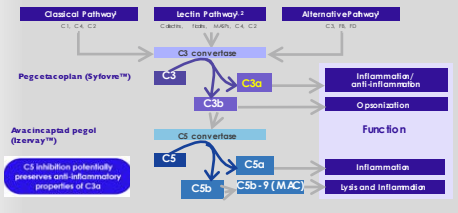


Images: Elsharkawy M, et al. Diagnostics. 2021;11:2313.

AMD, age-related macular degeneration; RPE, retinal pigmented epithelium.

1. Holz FG, et al. *J Clin Invest*. 2014;124:1430-1438; 2. Armento A, etal. *Cell Mol LifeSci*.2021;78:4487-4505; 3. Fleckenstein M, et al. *Ophthalmology*.2018;125:369-390 4. Elsharkawy M, et al.*Diagnostics*,2021:12313

Dysregulated activation of the complement system can lead to inflammation and cell death --→ GA[1]

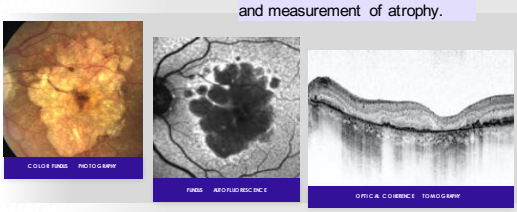


FB, factor B; FD, factor D; MAC, membrane attack complex; MASP, MBL-associated serineprotease; MBL, mannose-binding lectin

1. Xu H, et al. *Eur J Pharmacol*. 2016;787:94-104; 2. BajicG, et al. *EMBO J*. 2015;34(22):2735-2757.

MMI is used to visualize GA lesions[1,2]

Multimodal imaging is needed to obtain the most reliable detection and measurement of atrophy.



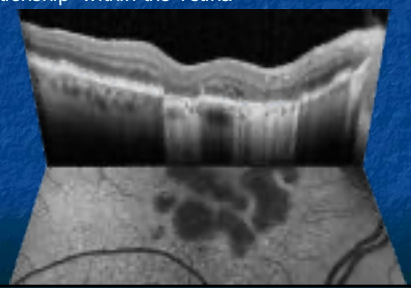
GA, geographic atrophy.

Images: Reckenstein M, et al. *Ophthalmology*. 2018;125:369-390

1. FleckensteinM, et al. *Ophthalmology*. 2018;125369-390; 2.Holz FG, etal. *Ophthalmology*. 2017;124:464-478

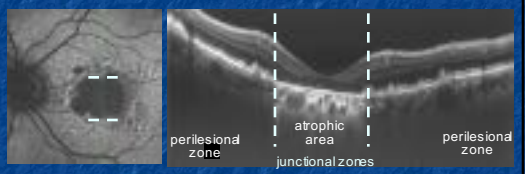
FAF + OCT in GA

Offers a new perspective of the structure-function relationship within the retina



Simultaneous FAF and OCT

Geographic Atrophy



- FAF shows areas of hypo-autofluorescence in GA
- OCT outlines the corresponding photoreceptor dropout

Nonfoveal (extrafoveal) GA lesions grow at a significantly greater rate than foveal lesions[1,2]

- GA is a progressive disease, with an average growth rate of 0.33 mm per year or 1.66 mm^2 per year[3]

Images: Reckenstein M, et al. *Ophthalmology*. 2018;125:369-390. Courtesy: Frank Holz, MD

GA, geographic atrophy.
1. Nassar, TD, et al. *Ophthalmology*. 2018;125:1913-1928. 2. Reckenstein M, et al. *Ophthalmology*. 2018;125:369-390. 3. Wang J, et al. *Ophthalmic Res*. 2021;64:205-215.

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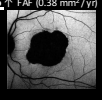
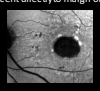
PROGNOSTIC VALUE OF GA PHENOTYPIC FAF PATTERNS

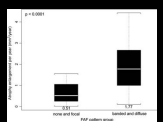
Slow Progression — Rapid Progression

No ↑ FAF (0.38 mm^2/yr)



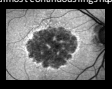
Focal (0.81 mm^2/yr)
Single or multifocal small spots of ↑ FAF adjacent directly to margin of GA



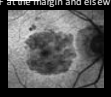


GA progression per year for the pooled data groups

Banded (1.81 mm^2/yr)
↑ FAF adjacent directly to margin of GA in an almost continuous ring shape



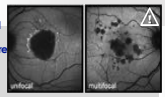
Diffuse (1.77 mm^2/yr)
↑ FAF at the margin and elsewhere



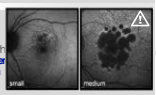
The GAIN Study. Am J Ophthalmol. 2015;160:345-353.e5.
Holz FG, et al (FAM-Study Group). Progression of GA and impact of FAF patterns in AMD. Am J Ophthalmol. 2007 Mar;143(3):463-72.

Other factors associated with GA progression

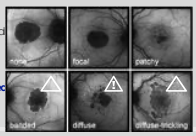
Lesion focality
Eyes with **multifocal lesions have GA growth rates that are significantly higher** than eyes with unifocal lesions[1]



Lesion size
Baseline GA lesion size has consistently been associated with progression; **smaller baseline GA area in mm^2 have a lower GA growth rate**[1,2]



Lesion characteristics and patterns
Lowest growth in eyes with no focal patterns; highest with banded or diffuse patterns. **Diffuse-trickling pattern associated with rapid progression**[1]



Bilateral GA (ie, GA in fellow eye)[1]

Images: Reckenstein M, et al. *Ophthalmology*. 2018;125:369-390

AMD, age-related macular degeneration; GA, geographic atrophy.

1. Fleckenstein M, et al. *Ophthalmology*. 2018;125369-390; 2. Wang J, et al. *Ophthalmic Res*. 2021;64:205215.

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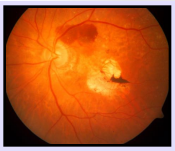
Advanced forms of AMD (GA and MNV), are not mutually exclusive



- MNV can occur in eyes with GA.
- A pt w/ GA in 1 eye and CNV in the fellow eye has a significant risk of developing CNV in the eye with GA[1]

MNV can occur in exudative or nonexudative forms[3]

Signs of exudation include IRF, SRF, and sub-RPE fluid

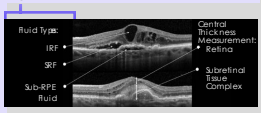


Image: Folgar FA, et al. *Ophthalmology*. 2014;121:1956-1965.

AMD, age-related macular degeneration; CNV, choroidal neovascularization; GA, geographic atrophy; IRF, intraretinal fluid; SRF, subretinal fluid; Sub-RPE, subretinal pigment epithelial.
1. Sunness JS, et al. *Ophthalmology*. 1999;106910-919; 2. Spaide RF, et al. *Ophthalmology*. 2020;127:616-636; 3. Sharma A, et al. *Graefes Arch Clin Exp Ophthalmol*. 2021;259:1881-1893.

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COMPLEMENT INHIBITION

- Pegcetacoplan (Syfovre™)
- OAKS
  - monthly injection resulted in a 22% reduction (P<0.0001), while EOM administration showed an 18% reduction (P=0.0002) in GA lesion growth rate at 24 months.
- DERBY
  - monthly administration led to a 19% reduction (P=0.0004), and EOM administration resulted in a 16% reduction (P=0.003) in GA lesion growth rate over 24 months.
- nAMD was 12% in the monthly administration group, 7% in the EOM administration group, versus 3% in the control group by month 24. These findings highlight the importance of closely monitoring patients
- Confirmed cases of occlusive (4 cases) and non-occlusive (3 cases) retinal vasculitis have emerged.

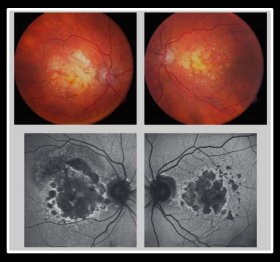
COMPLEMENT INHIBITION

- Avacincaptad pegol (Izervay™)
- GATHER1 study showed efficacy of avacincaptad pegol in reducing the progression of GA over 12 and 18 months in subjects with non-foveal GA.
- At 12 months, a reduction of 27.4% (P = 0.0072) was observed in the 2 mg cohort, and a similar reduction of 27.8% (P = 0.0051) was observed in the 4 mg cohort, compared to their respective sham treatment cohorts.
- The results, at 18 months, a similar decrease in mean GA growth, with a reported reduction of 28.1% (P = 0.0014) reported in the 2 mg and 30.0% (P = 0.0021) in the 4 mg cohort.
- A higher percentage of patients in the treatment groups developed MNV. Specifically, 11.9% in the 2 mg developed neovascularization and 15.7% in the 4 mg cohort, compared to 2.7% in the sham group.

- Avacincaptad pegol (Izervay™)
- In GATHER2, we saw a 14.3% reduction compared to sham.
- For Izervay dosed monthly (through 2 years) 14% statistically significant year-over-year reduction in the mean rate of GA growth at 2 years from baseline vs sham (p=0.0165)
- Note: this was the primary objective for year 2
- **For Izervay dosed EOM, after a year of monthly dosing, 19% reduction in the mean GA growth rate at 2 years vs sham** (nominal p-value=0.0015).

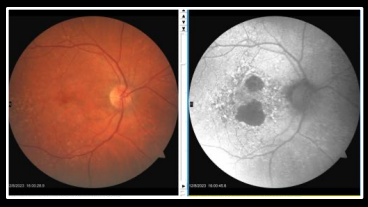
GOOD OR POOR CANDIDATE?

- 89 y/o F
- Prog GA
- OD = 10/400 FB W/EV
- OS = 10/400 FB W/EV



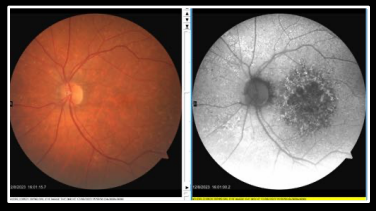
GOOD OR POOR CANDIDATE?

- 74 yo M
- Prog GA
- OD = 20/25



GOOD OR POOR CANDIDATE?

- 74 yo M
- Prog GA
- OS = 20/25



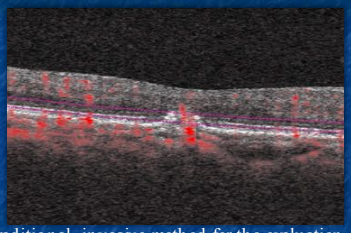
Summary of Treatments for DRYAMD

- At least one eye with intermediate dry AMD
  - AREDS 2-based formula
  - PBM
  - 3-6 mon follow up
- Advanced AMD in one eye (but not the other)
  - AREDS 2-based formula for the fellow (better) eye
  - PBM if criteria is met
  - 3-4 mon follow up
- Progressive GA, non-foveal centered or small foveal centered (< 1 disc area)
  - Complement inhibitors—intravitreal inj, 1-4 mon follow up, PBM?
- MNV
  - Anti-VEGF or Faricimab —intravitreal inj, 1-4 mon follow up

QUESTIONS AND ANSWERS

Email me at pizzimen@uiwtx.edu

Emerging Trend: OCTA

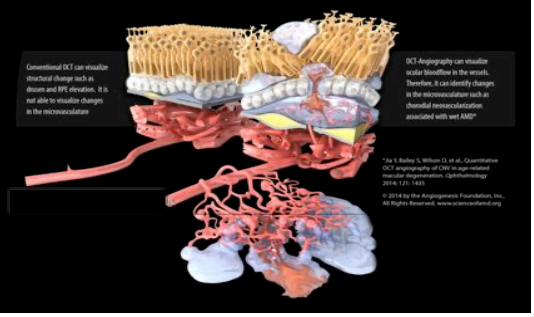


The traditional, invasive method for the evaluation of new onset choroidal neovascularization (CNV) in AMD patients is **fluorescein angiography (FA). ***

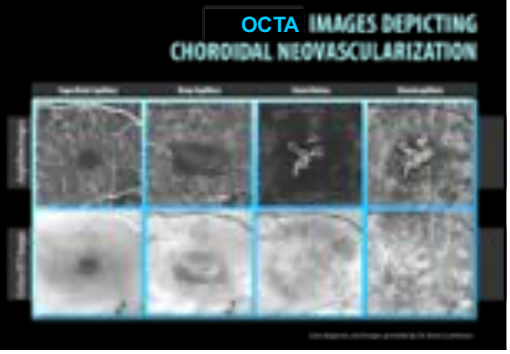
THE ARRIVAL OF OCT-ANGIOGRAPHY (OCTA)

A new way of visualizing ocular bloodflow in the vessels—identifies retinal microcirculation using the intrinsic motion of blood cells in the vessel

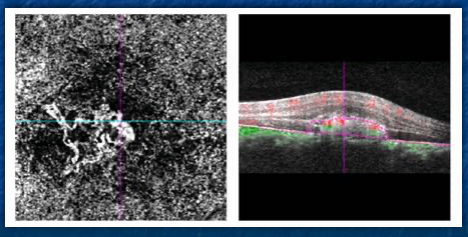
- Enables immediate assessment of microcirculation in ocular diseases with unprecedented microvascular detail

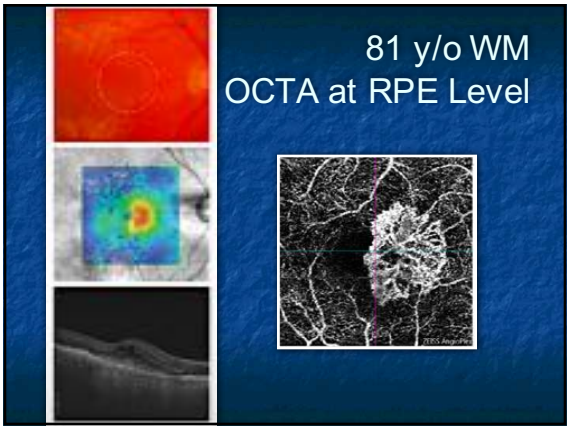


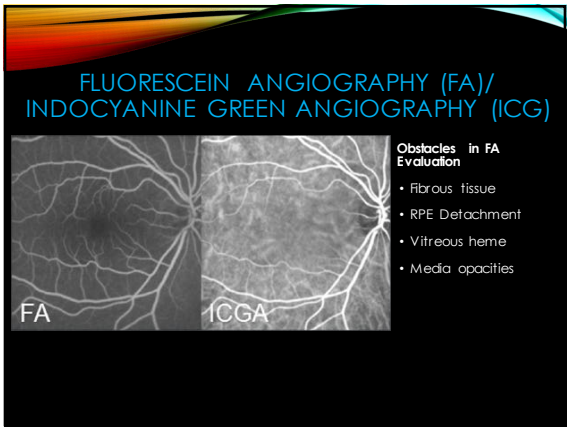
Imaging

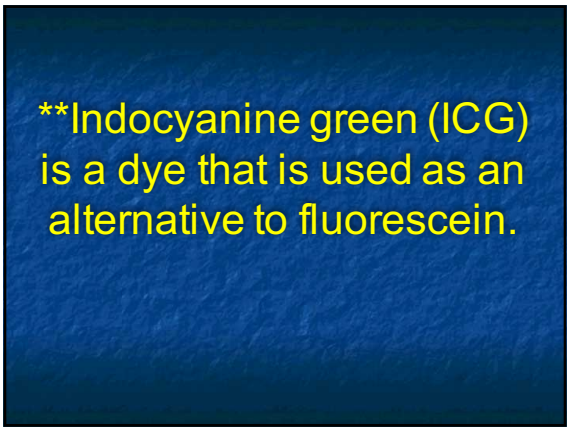


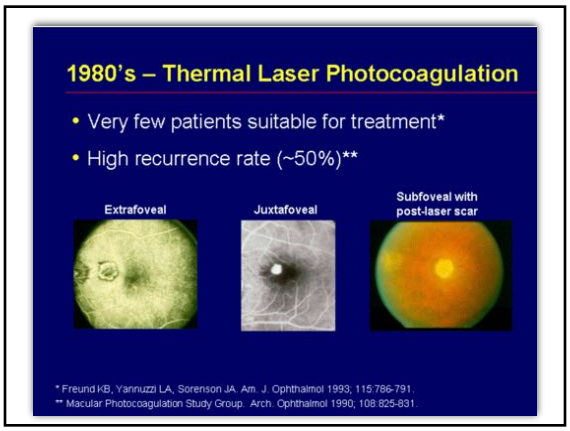
Cirrus Angioplex OCTA reveals CNV Lesion in nAMD

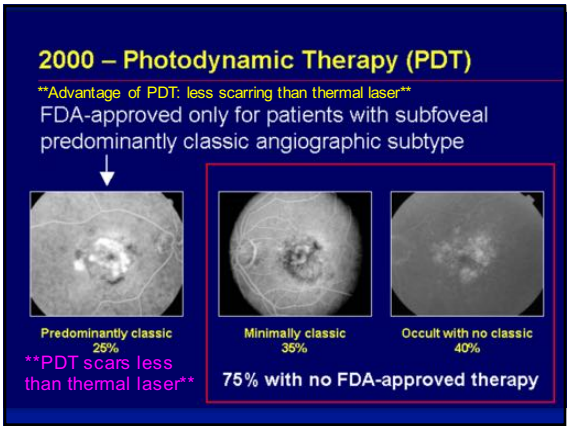


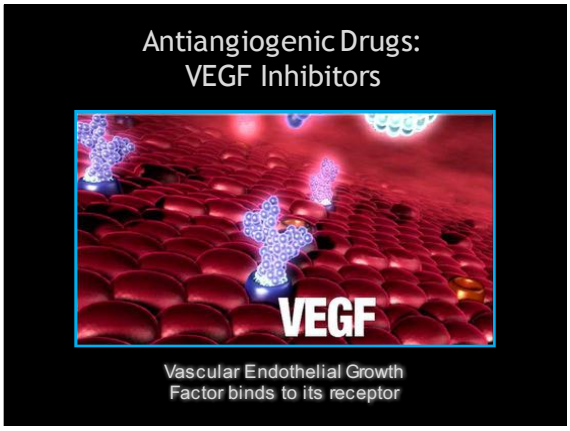

81 y/o WM
OCTA at RPE Level


FLUORESCEIN ANGIOGRAPHY (FA)/
INDOCYANINE GREEN ANGIOGRAPHY (ICG)
FA
ICGA
Obstacles in FA Evaluation
• Fibrous tissue
• RPE Detachment
• Vitreous heme
• Media opacities


**Indocyanine green (ICG) is a dye that is used as an alternative to fluorescein.


1980's – Thermal Laser Photocoagulation
• Very few patients suitable for treatment*
• High recurrence rate (~50%)**
Extrafoveal
Juxtafoveal
Subfoveal with post-laser scar
* Freund KB, Yannuzzi LA, Sorenson JA. Am. J. Ophthalmol 1993; 115:786-791.
** Macular Photocoagulation Study Group. Arch. Ophthalmol 1990; 108:825-831.


2000 – Photodynamic Therapy (PDT)
Advantage of PDT: less scarring than thermal laser
FDA-approved only for patients with subfoveal predominantly classic angiographic subtype
Predominantly classic 25%
Minimally classic 35%
Occult with no classic 40%
PDT scars less than thermal laser
75% with no FDA-approved therapy


Antiangiogenic Drugs:
VEGF Inhibitors
VEGF
Vascular Endothelial Growth Factor binds to its receptor

Angiogenesis

Environmental factors[1] (hypoxia,[2] pH) Growth factors, hormones[1] (EGF, bFGF, PDGF, IGF-1, IL-1α, IL-6, estrogen)

VEGF-A binding and activation of VEGF receptor[3]

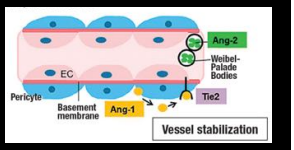
Endothelial cell activation[3]

VEGF-A = vascular endothelial growth factor A; EGF= epidermal growth factor; bFGF = basic fibroblast growth factor; PDGF = platelet-derived growth factor; IGF = insulin like growth factor; IL= interleukin.

1. Dvorak HF. *J Clin Oncol* 2002;20:4368-80. 2. Aiello LP, et al. *Arch Ophthalmol* 1995;113:1538.
3. Ferrara N, et al. *Nat Med* 2003;9:669-76. 4. Griffioen AW and Molema G. *Pharmacol Rev* 2000;52:237-68.

Faricimab

- Bi-specific Ab that targets the VEGF and angiopoietin pathways.
  - VEGF and Ang-2 inhibitor
- There are 2 ligands, Ang-1 and Ang-2, and they both affect the Tie2 receptor. This receptor is critical for the stability of vascular tissue.
- In nAMD, Ang-2 is upregulated. This competes with the Ang-1-Tie2 signaling, causing vascular endothelial tight junction breakdown, as well as increased inflammation and MNV.



Faricimab

- Phase 3 studies TENAYA and LUCERNE evaluated faricimab in nAMD.
- Both studies achieved visual outcomes with faricimab that were non-inferior to those of aflibercept (Eylea, Regeneron) injections q8wks.
- Also approved for DME.

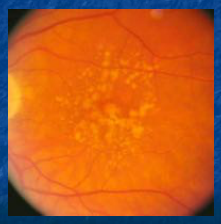
Pharmacologic Treatments for MNV

- Intravitreal agents used for the treatment of MNV include:
  - Pegaptanib sodium (Macugen®)- seldom used
  - Ranibizumab (Lucentis®)
  - Bevacizumab (off-label Avastin®)
  - Aflibercept (Eylea®)
  - Brolucizumab (Beovu®)
  - Faricimab (Vabysmo®) **VEGF and Ang-2 inhibitor

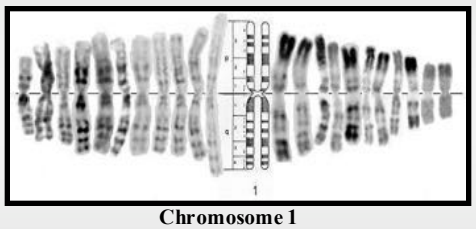
Other Treatment Approaches

- Laser photocoagulation
- Photodynamic therapy
  - Uses light-activated drugs (eg, verteporfin) and non-thermal light to achieve selective destruction of CNV
  - May be combined with intravitreal agents

Emerging Trend: Genetics and Genomics



Genetics: ARMD-1



Chromosome 1

Region Displayed: 1q25-q31

Genetics and AMD

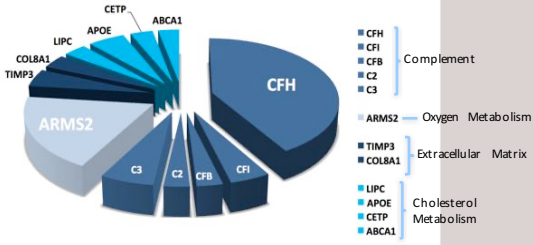
- Inherited variation in the complement factor H gene is a major risk factor for drusen.
- A single-nucleotide polymorphism (SNP) in the promoter region of HTRA1 (a serine protease gene on chromosome 10q26) is a major risk factor for nAMD.
  - DeWan, A. Science, November 2006:Vol. 314. no. 5801, pp. 989 - 992

Genetics and AMD

Naturally occurring variations conferring AMD risk

Marker	Allele	Odds Ratio	Freq
CFH	H1+H3 (risk)	>15	0.202
	Average		0.495
	(H2+H4)		0.303
C3 rs2230199	G (risk)	2.6	0.18
	C		0.83
ARMS2 rs10490924	T (risk)	8.2	0.17
	G		0.83
Smoking	Current (risk)	3.14	0.17
	Never		0.55
mt A4917G	G (risk)	2.2	0.09
	A		0.90

Key AMD-associated Genes



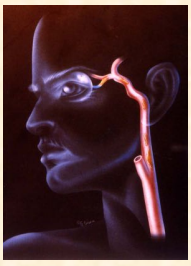
Example of Genomics

Smoking interacts with CFH Gene variants to increase AMD risk by 5X compared with genetically similar nonsmokers.

Am J Epidemiol. 2009 March 1; 169(5): 633–641.

Cigarette Smoking, Ocular & Vascular Disease

- Increased arteriolar stiffness (sclerosis)
- Increased Vascular Endothelial Growth Factor (VEGF) production
- Development/worsening of DR
- Development/worsening of AMD



AMD Gene Associations

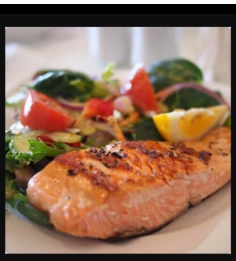
- Mutations in the TIMP3 gene
  - Metalloproteinase inhibitor 3 gene
- Two variants involved in the HDL cholesterol pathway.
  - Human hepatic lipase (LIPC) and cholesterol ester transfer protein (CETP).
  - Proceedings of the National Academy of Sciences (4/2010)

Example of Genomics

A BMI over 30 increases AMD risk by 2.5X.

Clinical & Experimental Ophthalmology

Celebiler et al., J Clin Exp Ophthalmol 2012, 3:5



IS AMD A NUTRITION-RESPONSIVE DISEASE?

AMD and Nutrition

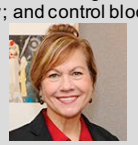
AREDS
Age-Related Eye Disease Study

"The AREDS 1 Study resulted in a formulation of vitamin C, beta carotene, zinc, and vitamin E that reduced the risk of progression of advanced disease by 25% at 5 years."

Emily Chew, MD, from the National Eye Institute in Bethesda, Maryland

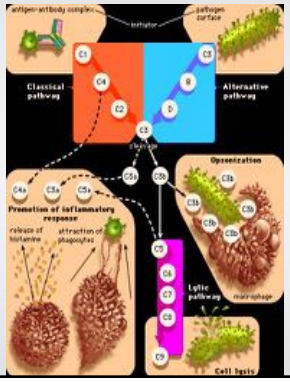
Johanna Seddon, MD (Tufts U)

" Don't smoke; follow a healthful diet rich in dark green leafy vegetables and low in fat; eat fish a few times a week; maintain a normal weight and waist size; exercise regularly; and control blood pressure and cholesterol."



"Anyone with signs of intermediate-level macular degeneration in both eyes or advanced macular degeneration in one eye should also take dietary supplements that contain lutein, zeaxanthin, vitamin C, vitamin E, and zinc."

The Complement Cascade: Inflammation



AREDS 2

AREDS 2

AREDS 1 and 2 Formulations

- Vitamin C: 500 mg*
- Vitamin E: 400 IU*
- Beta-carotene: 15 mg (May be listed on the label as "25,000 IU vitamin A as beta-carotene") (eliminated)
  - Why?
- Zinc oxide: 80 mg (40 mg)
  - Why?
- Copper: 2 mg (needed to prevent Cu deficiency caused by high dosage of zinc)*
- Lutein & Zeaxanthin (10 mg & 2 mg)
- Omega-3 fatty acids (1 gram)

Study Subjects: AREDS 1 vs AREDS 2

- All stages of AMD
- Average age = 69
- 67% took Centrum (no L)
- Varied diets
- Varied serum L and Z

- More advanced stage
- average age = 74
- 89% taking Centrum Silver (w/minimal L)
- diet high in carotenoids and vegetables
- higher serum L and Z

These differences could impact the ability to detect a more significant reduction in progression!

Evidence-based Advice for Patients

AREDS-Established Risk Factors to Advanced AMD

- Increased risk for NV AMD: smokers, Caucasians
- Increased risk for CGA: smokers, those with a higher body mass index (AREDS-19)
- Higher intake of omega-3 long-chain polyunsaturated fatty acid (LCPUFA) and fish: associated with decreased likelihood of having NV AMD (AREDS-20)
- Higher dietary intake of lutein/zeaxanthin: associated with decreased likelihood of having NV AMD and GA (AREDS-22)
- Omega-3 LCPUFA intake: associated with a decreased risk of progression from bilateral drusen to CGA (AREDS-23)

Age-Related Eye Disease Study Research Group. Control Clin Trials. 1999;20(6):573-600.

QUESTIONS?

pizzimen@uiwtx.edu

It would be naïve to assume that only 6 vitamins/nutrients are important in retinal health

Emerging Trend: "Superfoods"

In AMD Prevention and Management

Dietary Sources of Lutein/Zeaxanthin

Dietary Lutein and Zeaxanthin: Eggs have high bioavailability

Lutein

Lutein

Zeaxanthin

Dietary Zeaxanthin: Gogi Berry

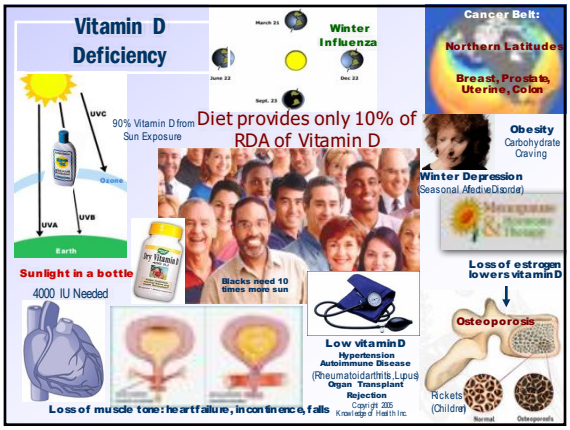
Benefits of Supplementation with Dietary Xanthophyll Carotenoids for People WITH OR WITHOUT AMD at Any Age

- Ocular structural and visual function development
- Ocular health and visual performance enhancement
- Brain development/health and cognitive performance
- Preserve retinal/macular health by improving MPOD, physiology
- Preserve cognitive health
- Preserve systemic vascular health (DM, CV)
- Blue light protection

Essential Fatty Acids (AMD, CVD, Stroke)

Dietary Vitamin D: Cod Liver Oil, Sockeye Salmon

- Modulation of cell growth
- Neuromuscular and immune function
- Reduction of inflammation

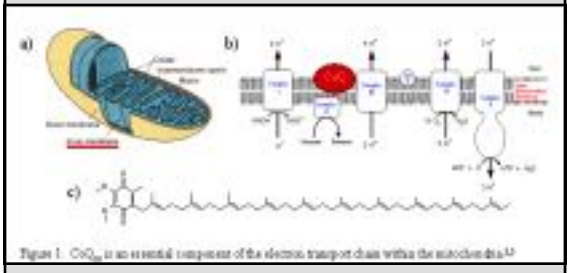


- For people aged one to 70 years, the RDA is at least 600 IU.
- For people over 70, RDA is at least 800 IU

Phototrop Study

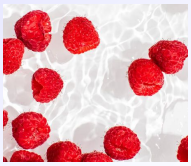
- Improvement of Visual Function and Fundus Alterations in Early AMD Treated With a Combination of Acetyl-L-Carnitine, n-3 Fatty Acids, and CoQ10
  - Feher, et.al.
  - *Ophthalmologica:2005;219:154-166*
- 160 early AMD subjects randomized to Tx and controls
- 12 months
- VFMD, foveal sensitivity
- ETDRS VA, fundus exam
- All 4 parameters showed statistically significant improvement
- Principle: improved mitochondrial lipid metabolism

CoQ10



Flavonoids are Anti-oxidants, CA Fighters

B-carotene, L, and Z



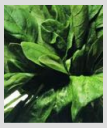
Not-so-guilty Pleasures

- Walnuts favorably affect cholesterol levels, reduce risk of heart disease.
- Dark chocolate, red wine are rich in antioxidants.
- Resveratrol enhances circulatory health (blood flow) and may have benefits in certain types of cancer.

Folic Acid, B_6, B_{12}

- Folic Acid, Pyridoxine, and Cyanocobalamin Combination Treatment and Age-Related Macular Degeneration in Women: The Women's Antioxidant and Folic Acid Cardiovascular Study
  - William G. Christen, ScD; Robert J. Glynn, ScD; Emily Y. Chew, MD; Christine M. Albert, MD; JoAnn E. Manson, MD
  - *Arch Intern Med.* 2009;169(4):335-341.

Folic Acid, B_6, B_{12} in Foods

Folic Acid, B_6, B_{12}

- 5442 female health care professionals 40 years or older with pre-existing CV disease
- Randomly assigned to receive a combination of folic acid (2.5 mg/d), pyridoxine hydrochloride (50 mg/d), and cyanocobalamin (1 mg/d) or placebo.
- After an average of 7.3 years of treatment and follow-up, there were 55 cases of AMD in the combination treatment group and 82 in the placebo group (relative risk, 0.66; 95% confidence interval, 0.47-0.93 [*P* = .02]).

Behavior Modification

- Physical activity
- Fish consumption
- Greens
- Smaller portions
- Alcohol in moderation (or none)
- Nutritional supplements
- Blocking blue light from reaching retina

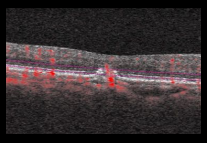
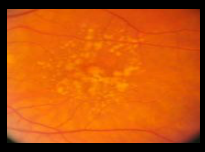
Behavior Modification

- Sedentary lifestyle
- Smoking
- Excess Alcohol
- Excess weight
  - High BMI/waist circ.
- HTN, Cholesterol
- Poor diet

Conclusions

- AMD is on the rise, and it has systemic comorbidities and implications.
- Diet, nutrition, lifestyle matter.
- We must take proactive steps on behalf of our patients.

Questions and Answers

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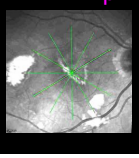
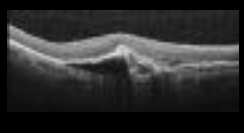

Thank you!

Joe