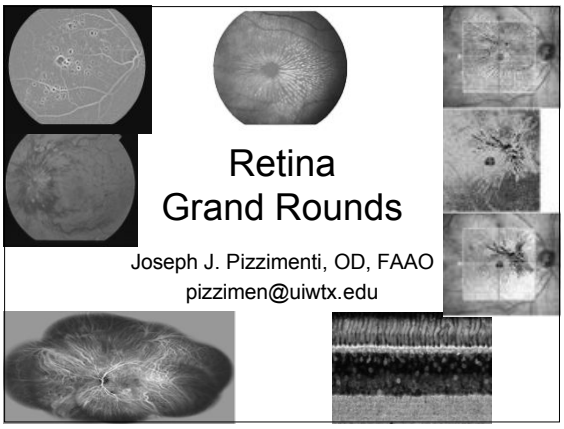


Retina Grand Rounds

Joseph J. Pizzimenti, OD, FAAO
pizzimen@uiwtx.edu

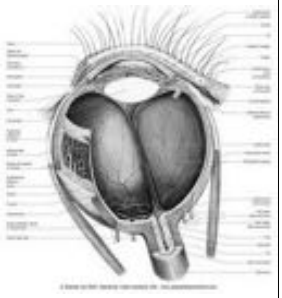
Financial Disclosures: JP

- Honoraria
  - Review of Optometry
  - Optometric Management
- Paid Scientific Advisory Board Member
  - Thrombogenics
  - Genentech
  - EyePromise
- Consulting Fees
  - Zeiss
  - Annidis
- Stockholder
  - EyePromise

Questions and Comments?

Goal

- To provide clinically relevant information about posterior segment disease using cases and topical discussion.



Statement of the Problem

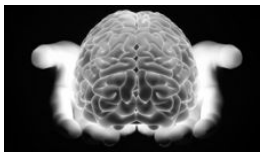
Posterior segment diseases impose an enormous burden on optometrists and ophthalmologists, office staff, caregivers, and above all, patients and their loved ones.

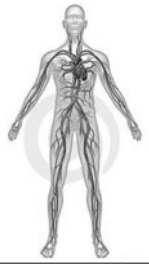
Global Retina Concerns

- AMD
- DR
- RVO, RAO
- Melanoma and other PS Tumors
- ROP
- Infectious PS Dx
- Myopia??

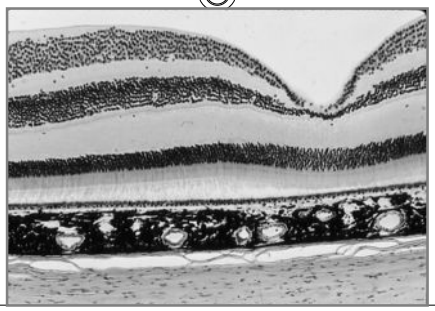
Prevention
Early Diagnosis
Early Intervention
Improved Visual Outcomes
Enhanced Quality of Life!

The eye is the only part of the body where neurological and vascular tissues can be viewed directly.

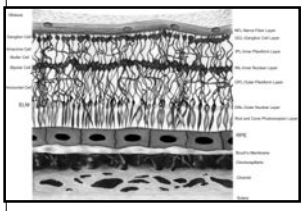




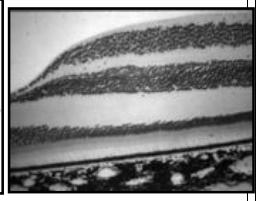
Retinal and Choroidal Anatomy



Retinal and Choroidal Anatomy

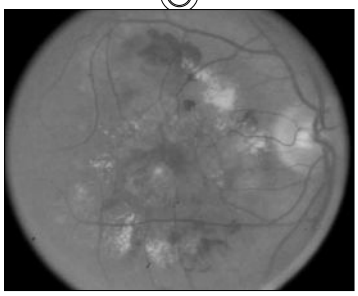


Inner and Outer Blood Retinal Barriers



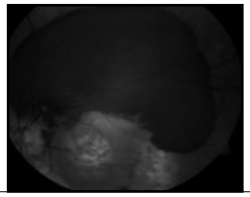
Retina/RPE, Choroidal Pigmentation

The AMD Epidemic



The Problem

- The AMD "Epidemic"
- AMD is the leading cause of blindness in individuals over the age of 50 in the developed world.



AMD - The Growing Numbers

- 15 – 17 million Americans affected
- Our population is aging
- Prevalence expected to triple by 2025
- Leading cause of significant vision loss in adults over the age of 50
- 1 in 3 over age 65 diagnosed with AMD

AMD is a Multi-etiological Disease

- Genetics
- Inflammatory response
- Oxidative damage
- Harmful light damage

The Problem
Patients don't understand what these things mean.

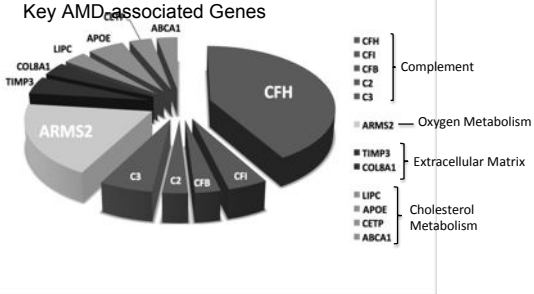
The Opportunity
We can help save vision.

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



Nutrigenomics

- Nutrigenomics refers to the application of genomics in nutrition research.
- Analogous to pharmacogenomics.
- Enables associations to be made between specific nutrients and genetic factors
  - e.g. Food ingredients may influence gene expression.

International Journal of Pharmaceutical Sciences Review and Research
Available online at www.globalresearchonline.net

Gene-Nutrients-Lifestyle

- Genotype is NOT an immutable prescription for disease (phenotype).
- Multiple external and internal factors (dietary, nutritional & lifestyle) strongly influence phenotype.
- Nutritional & lifestyle modification can counter a disease-promoting genome.
  - Kaput & Rodriguez, 2004

Can nutritional therapy reduce the genetic risk of early AMD?

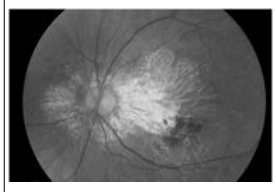
Rotterdam Study

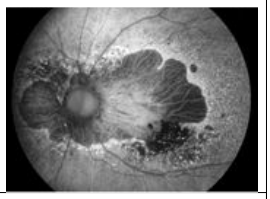
- 2167 subjects 55 and over tested + for genetic variants CFH and/or LOC
  - High genetic risk
- Dietary intake assessment
- Exam for early AMD
  - Baseline
  - 3 follow-up visits
  - Mean total follow-up was 8.6 years

Rotterdam Study

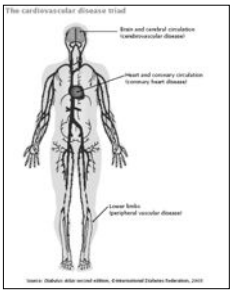
- Results
  - 517 developed early AMD
  - Biological interaction between CFH and: Zn, B-carotene, Lutein, Zeaxanthin, EPA/DHA
  - Interaction between LOC and DHA
  - Risk reductions
- Conclusions
  - High dietary L&Z, antioxidants, DHA reduced risk of early AMD in those with high genetic risk

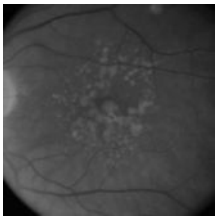
AMD: a sick eye in a sick body?





Is AMD a Systemic Disease?





Johanna Seddon, MD (Tufts U)

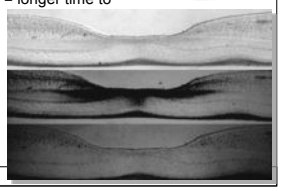
" Don't smoke; follow a healthful diet rich in dark green leafy vegetables and low in fat; eat fish a few times a week; maintain a normal weight and waist size; exercise regularly; and control blood pressure and cholesterol."

"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."

Measurement of Macular Pigment Optical Density (MPOD)

HFP works on the principle that:

- Macular pigment absorbs blue light (not green light)
- Dense or thicker macular pigment = longer time to see the target begin to flicker
- Results are quantified in density units (du) via software



- Macular Pigment Optical Density
  - –MPOD Score is analagous to IOP

1. AMD risk assessment
   - along w/heredity, smoking, age, etc.
2. Establish a baseline before nutritional therapy
3. Monitor response to nutritional therapy

QUESTIONS AND COMMENTS?

Xanthophyll Carotenoids and AMD

- Zeaxanthin, lutein, and their metabolites form macular xanthophyll pigment.
- Dietary sources include green leafy vegetables, eggs, and orange-yellow fruits.
- Act as antioxidants and blue light screening compounds.

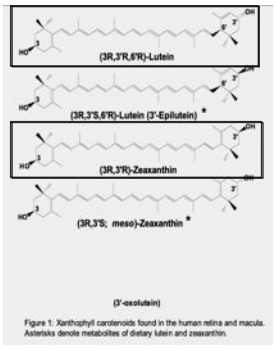


Figure 1: Xanthophyll carotenoids found in the human retina and macula. Asterisks denote metabolites of dietary lutein and zeaxanthin.

The Importance of Xanthophyll Macular Pigment

- Filters blue light
- Acts as an antioxidant by quenching free radicals
- Provides support to sensory retina
- MPOD is a biomarker of retinal and systemic health (DM, cognition)

Heterochromatic Flicker Photometry

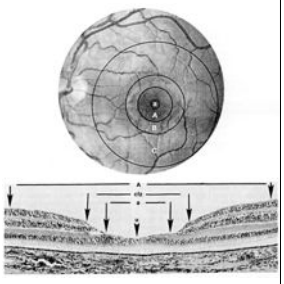
Test Results

Macular Pigment Optical Density (du)

Low	Average	High
0.10- 0.30	0.30- 0.50	> 0.50

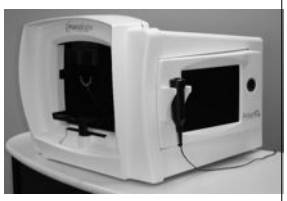
A Rod-centric Model of AMD

- In healthy, young adults, rods outnumber cones in the macula by 9:1.
- Therefore, the macula may be described as cone-enriched but rod-dominated.
- In the entire retina, rods outnumber cones 20:1.

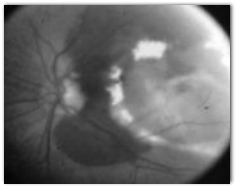


Dark Adaptometry in the Clinic Setting

- AdaptDx™ is an AC powered, automated adaptometer (biophotometer) that measures the time for retinal adaptation after exposure to a light stimulus.
- Functional biomarker of early disease.

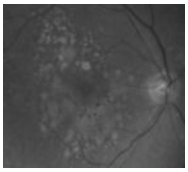


Case Studies:
Age-related macular degeneration



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

**Soft drusen: Large, ill-defined, and confluent

The Beckman Committee: 4 Stages

Classification of AMD	Definition (lesions assessed within 2 disc diameters of fovea in either eye)
No apparent aging changes	No drusen and No AMD pigmentary abnormalities*
Normal aging changes	Only drupelets (small drusen ≤63 μm) and No AMD pigmentary abnormalities*
Early AMD	Medium drusen >63 μm and ≤125 μm and No AMD pigmentary abnormalities*
Intermediate AMD	Large drusen > 125 μm and/or Any AMD pigmentary abnormalities*
Late AMD	Neovascular AMD and/or Any geographic atrophy

Ferris et al. Ophthalmology 2013; 120(4):844-851

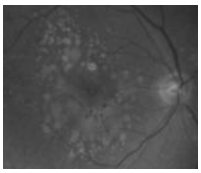
Determining Management Plan Through Diagnostic Criteria

Type Of Patient	Frequency Of Evaluation	Management Plan
Patient With Two or More Risk Factors for AMD, Over Age 55	Annual examination	Patient education; recommend UVR protection, antioxidant supplementation, home Amsler weekly
Patient with Hard Drusen and/or Pigmentary Degeneration	6-12 months depending on risk	Patient education; recommend UVR protection, antioxidant supplementation, home Amsler twice each week
Patient with Geographic Atrophy, VA 20/30-20/70	6-12 months depending on extent of atrophy	Patient education; recommend UVR protection, antioxidant supplementation, home Amsler every other day; monitor for CNV
Patient at High Risk with Soft Confluent Drusen and Granular Pigmentary Degeneration	4-6 months	Patient education; recommend UVR protection, antioxidant supplementation, home Amsler daily; low vision consultation and evaluation
Patient with CNV within 2500 Microns of Center of Foveal Avascular Zone	2 weeks after fluorescein angiography (FA) laser photocoagulation; at 6 weeks, then every 2-3 months after repeat FA	Patient education; recommend UVR protection, antioxidant supplementation, home Amsler daily; immediate consultation for signs of recurrent CNV; low vision consultation and evaluation
Patient with Disciform Scar in Both Eyes	6-12 months	Review; low vision consultation and evaluation
Patient with Large Drusen, VA 20/60, No Advanced AMD, and at Risk for Wet AMD	Each day by patient at home	Practitioner will be alerted when there is change in patient vision from ForeseeHome®

American Optometric Association, Care of the Patient with Age-Related Macular Degeneration; http://www.aoa.org/documents/optometrists/ORG-6.pdf. Published 2004. Accessed: November 21, 2016
The AREDS2-HOME Study Research Group. Randomized Trial of a Home Monitoring System for Early Detection of Choroidal Neovascularization HOme Monitoring of the Eye (HOME) Study. Ophthalmology. 2014;121(2):535-544. doi:10.1016/j.ophtha.2013.10.027

Intermediate Dry AMD OD/OS

- AREDS Category 3

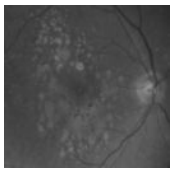


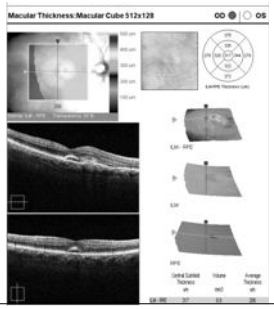
Baseline OCT showed no evidence of CNV in either eye *

Follow or Co-manage?

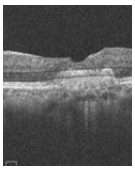
MPOD
Dark Adaptometry
OCT/OCTA
Treatment?

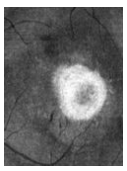
On 3 mon f/u, OCT Shows Change

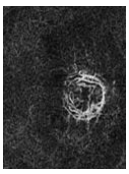




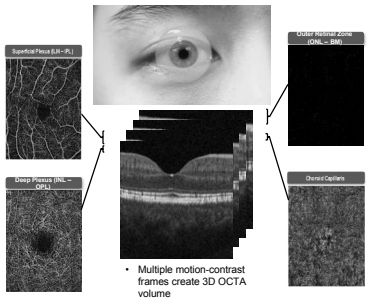
Another case: OCTA of CNV







How do you acquire an OCT Angiogram?



- Multiple motion-contrast frames create 3D OCTA volume
- Enface visualization of layers obtained by slicing and projecting slabs from 3D OCTA data

Co-manage Wet AMD with:

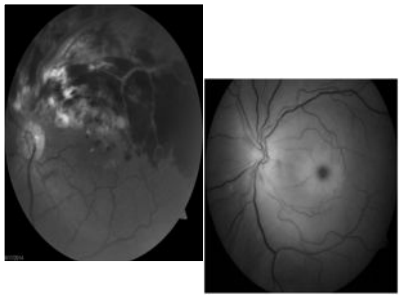
Retina

Internal Medicine/Cardiology if there are CV risk factors

Low Vision Optometrist

Questions and Comments?

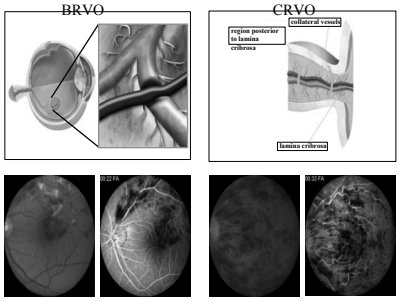
Case Studies:
Retinal vascular occlusion



Pathophysiology of BRVO and CRVO

(Branch) BRVO

(Central) CRVO



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

69 year old Caucasian Female

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

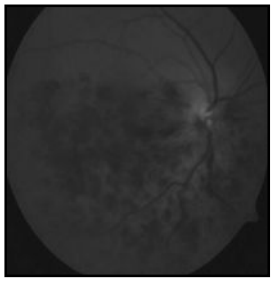
CF: Central blur OD Full Periphery OU

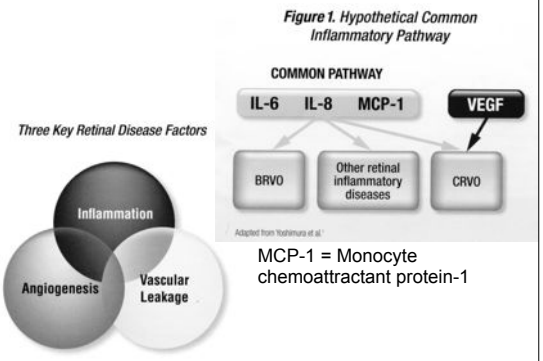
SLE: Unremarkable OU

TA: 20 mm Hg OU

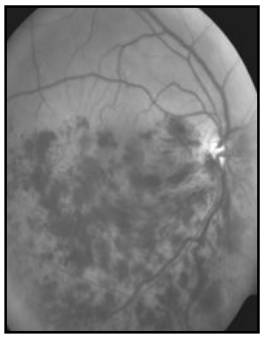
Vitreous: PVD OU

BP: 168 / 98 RAS

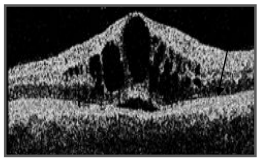




MCP-1 = Monocyte chemoattractant protein-1



Macular Edema in RVO



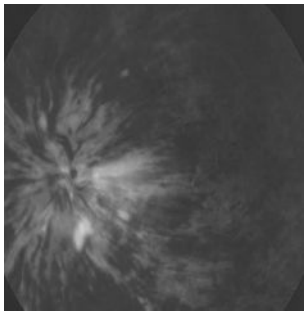
What is your assessment?

Hemispheric Retinal Vein Occlusion (perfused) w/ME

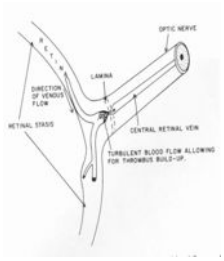
What is your plan?

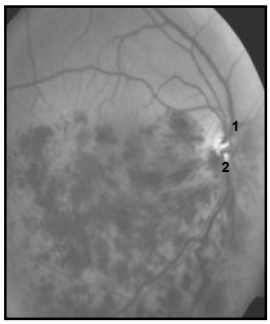
Follow or Co-manage?

CRVO

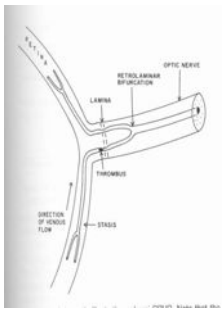


CRVO Anatomy



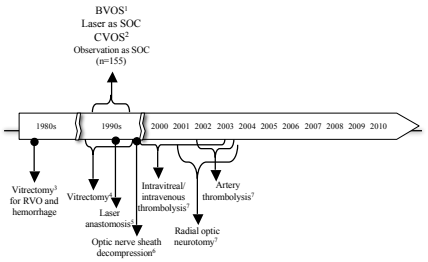


Anatomy of HCRVO



Treatment Options
for ME in RVO

Interventions in Retinal Vein Occlusion

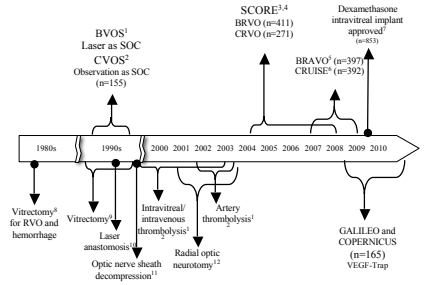


SOC = standard of care.

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. Yeshaya A, et al. *Ann Ophthalmol*. 1983;15:615-617; 4. Amirikia A, et al. *Ophthalmology*. 2001;108:372-376; 5. McAllister IL, et al. *Arch Ophthalmol*. 1995;113:456-462; 6. Dev S, et al. *Ophthalmic Surg Lasers*. 1999;30:181-184; 7. Shahid H, et al. *Br J Opthalmol*. 2006;90:627-639.

Fast Forward to 2018

Interventions in Retinal Vein Occlusion



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 Opthalmol*. 2006;90:627-639.

Co-manage RVO with:

Retina

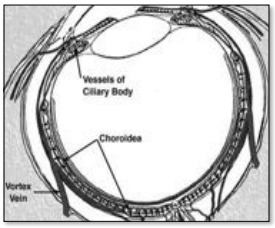
Internal Medicine/Cardiology

PCP

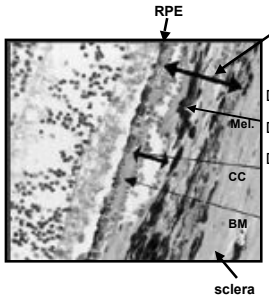
Questions and Comments?

The Choroid

- Located between the sclera and the RPE
  - Extends from ora serrata to optic nerve
- Pigmented/vascular tissue .75mm thick
- Nourishes the RPE
  - Choroiocapillaris designed to leak
- Absorbs light that passes through retina



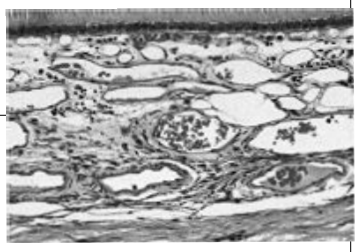
The Choriod

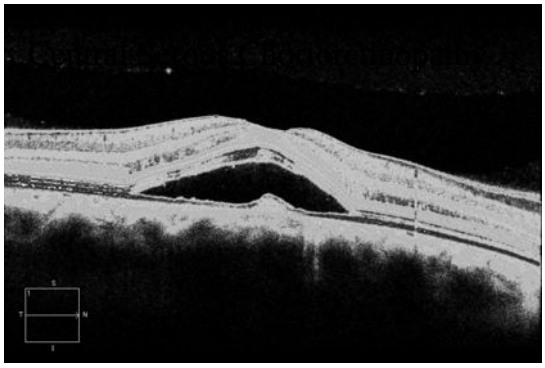


- Loose connective tissue
- Melanocytes
- Choriocapillaris
  - Fenestrated endothelium allows diffusion of proteins
  - S_____ regulation
  - High blood flow
  - Very little O-2 extracted, so high venous O-2

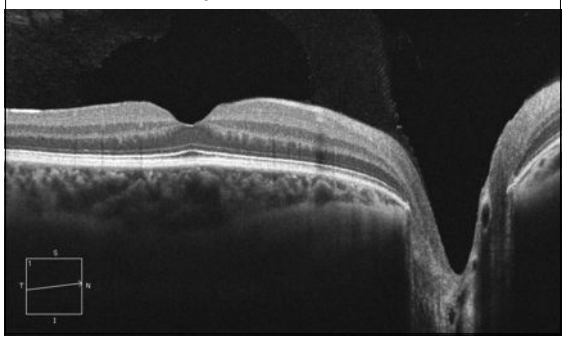
Choroid Microstructure

- Choriocapillaris
- Sattler's layer
- Haller's layer
- Supra - choroid

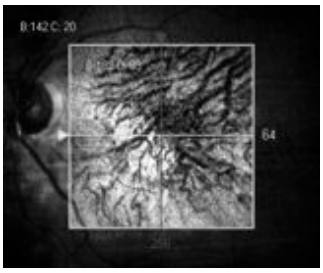




Vascular Layers of the Choroid

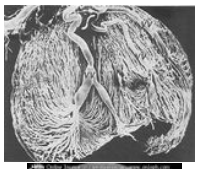


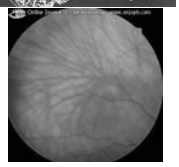
Vascular Layers of the Choroid



Choroidal Vasculature

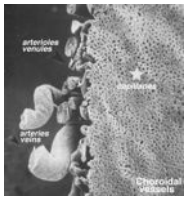
- SPCAs provide blood flow to choroid posterior to equator
- ACA and LPCA supply anterior choroid
- Vortex veins drain the choroidal veins
- V.V. drain into sup, inf ophthalmic vein

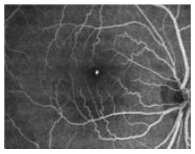




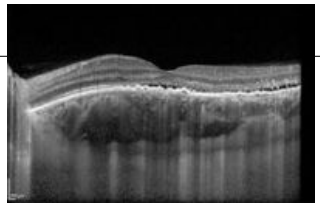
Retinal Vasculature

- 2 sources of blood supply:
- Choroidal BV
  - Supply outer retinal layers, including PRs
- CRA
  - 4 branches nourish inner retina
  - Run radially toward fovea



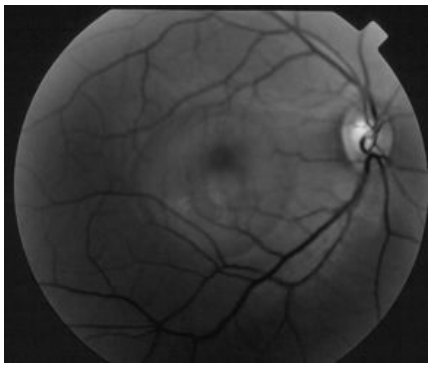


Imaging the Choroid

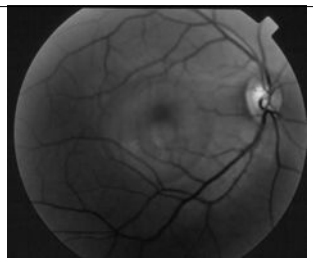


Mystery Macula

- Subjective
  - 35 y/o WM
  - sudden, unilateral blur OD
  - no pain or trauma
  - "Type A"
- Objective
  - VA
    - OD 20/60
    - OS 20/20
  - Hyperopic shift



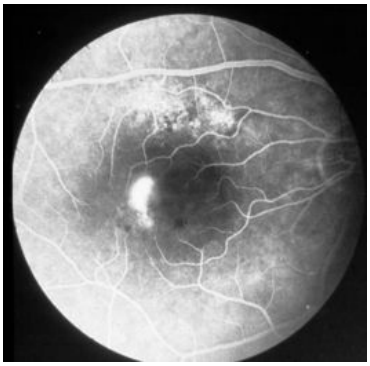
Describe That Fundus!



- DFE shows large, serous elevation
- Focal detachment of sensory retina

What other tests would you like to perform?

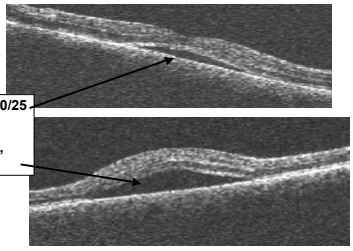
OCT



(Idiopathic) Central Serous Chorioretinopathy

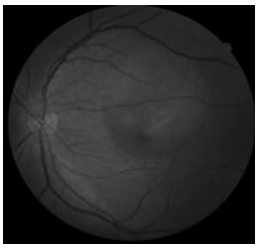
(ICSC)

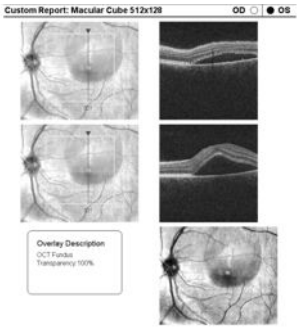
Patient Outcome



Central Serous Chorioretinopathy

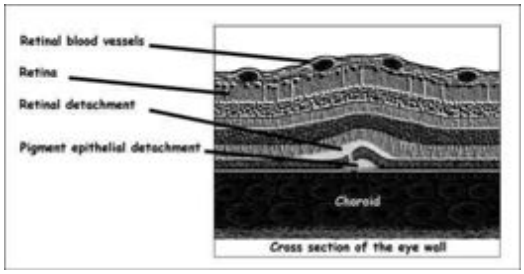
- 36 y/o WM
- CC: Sudden central blur OS
- VA OD 20/20
- VA OS 20/200



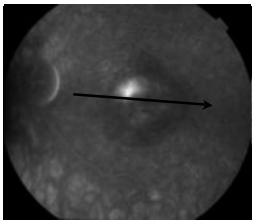


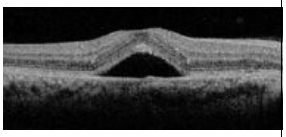
ICSC

- Objective
  - Breakdown of outer blood-retina barrier
  - FA shows classic "smoke-stack"
    - Pooling beneath RPE detachment
    - Dye ascends vertically, then laterally in SRS
- Differential Diagnosis
  - Tumor
  - RPE detachment/CNVM
  - Steroid-induced CSC

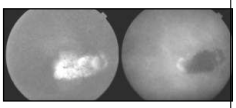


CSC

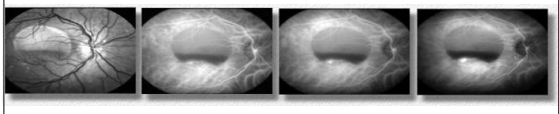




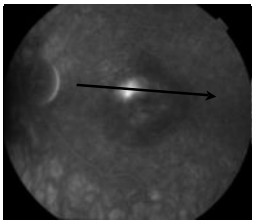
Indocyanine Green Angiography (ICGA)

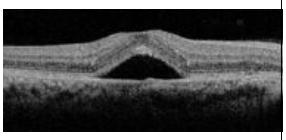


- Uses digital imaging
- Dye properties
- "Sees through" blood
- Delineates choroidal circulation better than fluorescein angiography
- Boundaries of occult membranes imaged

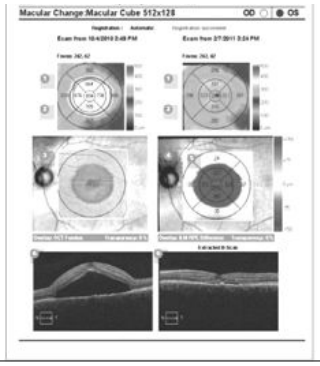


Central Serous Chorioretinopathy

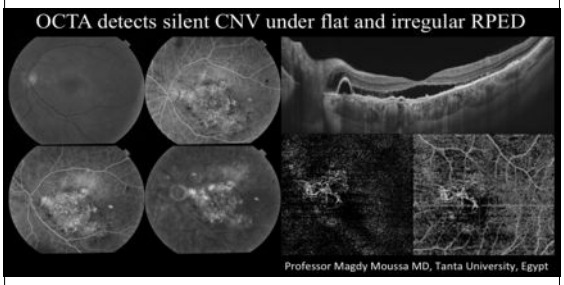




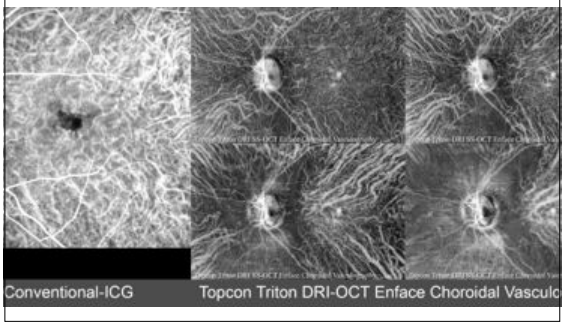
Macular Change Analysis in resolving CSC



Multimodal Imaging of CNV in CSC



Central Serous Chorioretinopathy

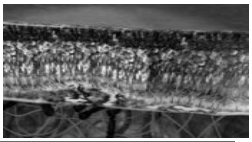


Plan

- Observation
  - 60% regain 20/20 w/no intervention
  - monitor q4wks for 6 mon
- Focal Laser
  - Unresolved after 4-6 mon
  - Recurrent
  - Focal, direct treatment
  - Leak must be outside FAZ (500 um)

Treatments for CSC

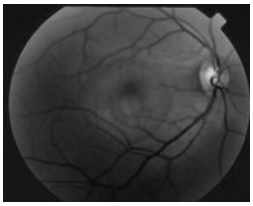
- Thermal laser



- Photodynamic Therapy
  - Visudyne (Verteporfin)
  - A light-activated drug

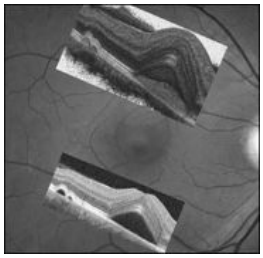
What's new in CSC Treatment?

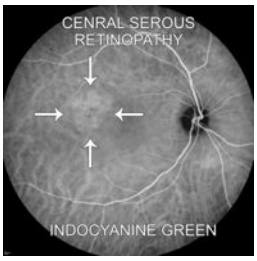
- Intravitreal bevacizumab (Avastin) has shown some benefit in small case series.



Low-fluence PDT

ICGA-guided, lower flow, lighter dosage resulted in less hypoperfusion of the choriocapillaris





Questions and Comments?

Case of the FLM

Joseph J. Pizzimenti, OD, FAAO

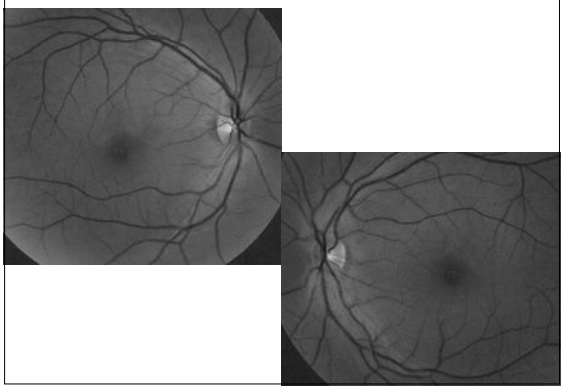
pizzimen@uiwtx.edu

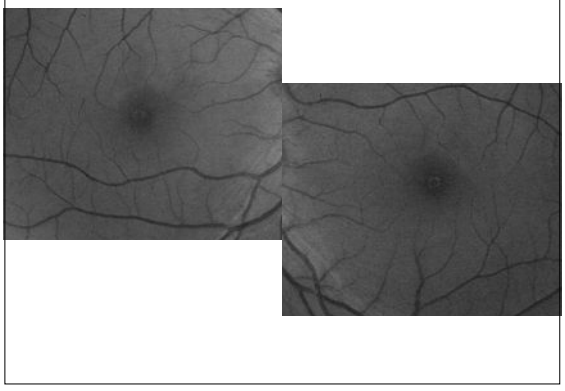
Case History

- A 32 year-old black female presented with bilateral complaints of gradually reducing central vision, photophobia, and poor color discrimination.
- Ocular history positive for previous episodes of pars planitis and anterior uveitis OD/OS.
- Health history positive for mitral valve prolapse dx 10 years ago, occasional migraines.
- She was taking no medications at the time of visit.
- Her moderate myopia was corrected with soft daily wear disposable contact lenses.

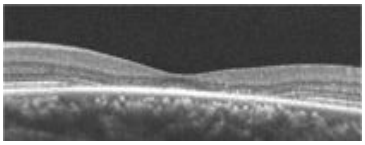
Case Report

- Best-corrected VA: 20/25 OD, 20/30 OS
- Amsler testing revealed a central ring-shaped defect OD and inferotemporal distortion OS.
- Unable to identify shapes and numbers with either eye on Ishihara CV testing
- DFE revealed an extremely subtle bilateral, irregular, "bull's eye" maculopathy.
- Automated threshold 10-2 perimetry revealed paracentral defects OD and OS.



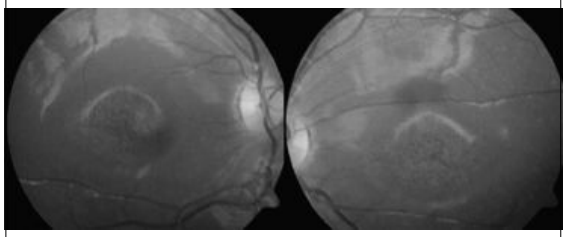


Additional Workup: OCT and Full-field ERG



- OCT revealed central foveal disruption of the photoreceptor inner-segment/outer-segment junction, external limiting membrane and RPE.
- Note thin central fovea with enhancement of choriocapillaris.
- FF ERG showed only a slightly low b-wave amplitude

Hereditary Dystrophic Disease



Severe Cone Dystrophy

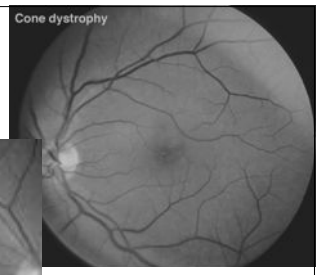
What is Retinal Dystrophy?

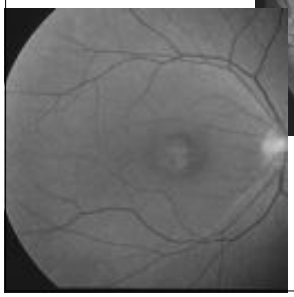
- A general name given to a wide range of conditions.
- 'Dystrophy' means a condition that a person is born with.
- Associated with reduced or deteriorating vision in both eyes.
- Most are genetic.
- Some are diagnosed early in life, but sometimes symptoms do not develop until adulthood.
- Occasionally a retinal dystrophy can be part of a pattern of particular problems which affect other parts of the body ('Syndromic' retinal dystrophies).

What is a Degeneration?

- Deterioration of a tissue or an organ in which its vitality is diminished or its structure impaired:
  - specialized cells are replaced by less specialized cells (as in fibrosis or in malignancies)
  - cells are functionally impaired (as by deposition of abnormal matter in the tissue)
- May be unilateral or bilateral
- May or may not have a genetic component.

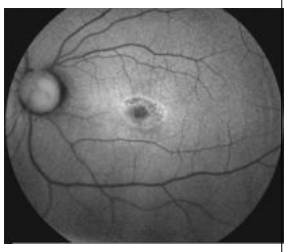
Early CD

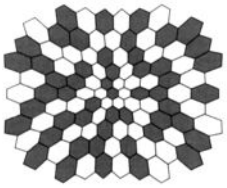




Imaging Early CD with FAF

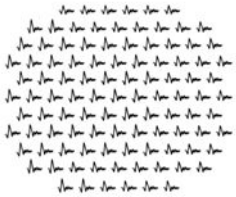
- Fundus autofluorescence may demonstrate a hyper-AF ring and central spots in the fovea.

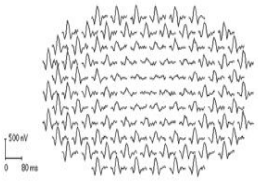




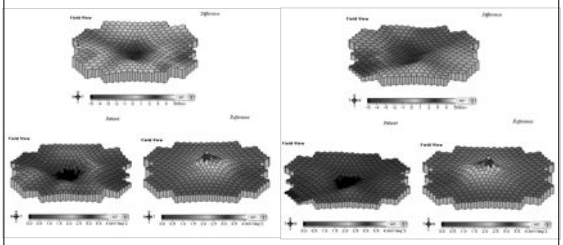
Left (Top & Bottom):
Normal multifocal ERG showing the 103 hexagons in the visual field that are tested

Right-bottom: Multifocal ERG in a CD patient with a central scotoma





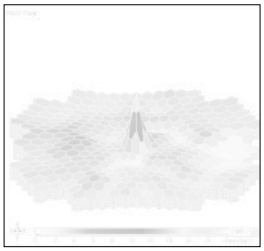
OD OS



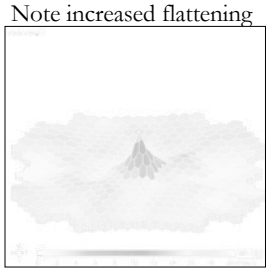
Mf-ERG revealed a central "ring-depression" in each eye.

Mf-ERG revealed a "ring-depression" surrounding a small central peak in each eye.

OD 10/2005



OD 4/2006:
Note increased flattening



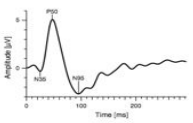
Cone Dystrophy

At right, another patient with full presentation of cone dystrophy. Note minimal central peak. (20/100 VA)

Visual Function Tip

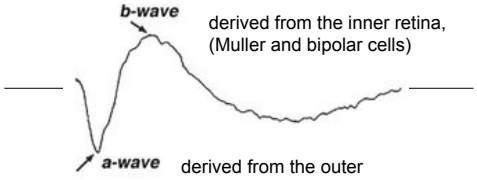
In patients with cone dystrophy, quality of vision often depends on lighting situations. In bright light, vision might be blurry and washed out. However, the same person might feel quite comfortable in darker settings, such as at dusk, or inside with the curtains drawn.

Flash ERG (fERG)



- Pros
  - both eyes tested at same time
  - measures both rods and cones
  - characteristic patterns for certain diseases
  - fixation/eye movement has small amount of effect on testing compared to mfERG
- Cons
  - Gives overall retinal potential, a ***gross retinal response*** (no mapping of responses)
  - ***Patients with a small area of retinal disease can have normal response***
  - Greater cooperation needed to perform test

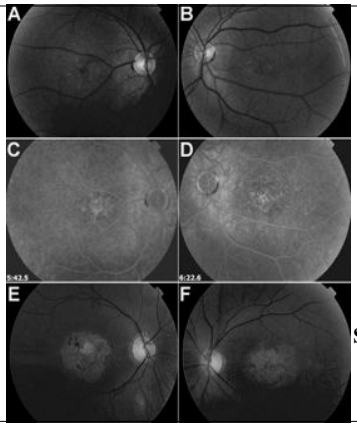
Normal Flash ERG



derived from the inner retina, (Muller and bipolar cells)

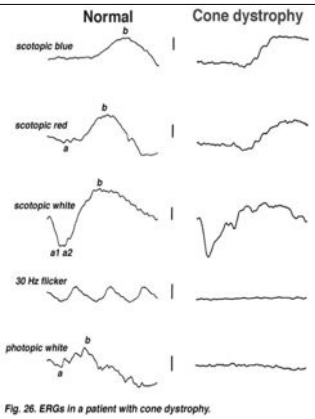
derived from the outer photoreceptor layers

Fig.1 The biphasic waveform of the ERG of a normal patient.



Moderate CD color photos and IVFA

Severe CD



(moderate/ severe)

Fig. 26. ERGs in a patient with cone dystrophy.

Our info thus far is consistent with CD vs. CRD

Let's go to the literature.

A subset of CD patients have been described in whom the full-field ERG appears normal, and involvement of only the foveal or central cones has been documented.

Carr RE . Cone dystrophies. In: Guyer DR, Yannuzzi LA, Chang S, Shields JA.Retina–Vitreous–Macula. Philadelphia: Saunders; 1999:942–948.

Michaelides M , HardcastleAJ, HuntDM, MooreAT. Progressive cone and cone-rod dystrophies: phenotypes and underlying molecular genetic basis.Surv Ophthalmol.2006;51:232–258.

CD and CRD

Cone dystrophy (CD) and cone–rod dystrophy (CRD) are the most common hereditary cone disorders with a frequency of 1:30 000 to 40 000 worldwide.[1–3] Both diseases are characterized by loss of cone photoreceptors and progressive visual decline, but CD and CRD are also distinct disease entities with considerable variability in genetic causes and clinical consequences.

1. Michaelides M, Hunt DM, Moore AT. The cone dysfunction syndromes. Br J Ophthalmol 2004;88:291–7.
2. Michaelides M, Hardcastle AJ, Hunt DM, Moore AT. Progressive cone and cone-rod dystrophies: phenotypes and underlying molecular genetic basis. Surv Ophthalmol 2006;51: 232–58.
3. Berger W, Kloeckener-Gruissem B, Neidhardt J. The molecular basis of human retinal and vitreoretinal diseases. Prog Retin Eye Res 2010;29:335–75.

Pathophysiology

- Mutations of various genes have been identified in CD and CRD.
- Proteins of these genes are involved in phototransduction, retinoid metabolism, transport along the connecting cilium, intercellular signaling or synaptic interaction, interphotoreceptor matrix, gene regulation, and phagocytosis.

CD and CRD: Inheritance

- A/R
- Sporadic*
- A/D
- X/L - less common
  - * Sporadic genetic disease is not inherited from parents, but arises via a mutation. However, a sporadic disease becomes inheritable to children of the person who has acquired the disease via mutation.

CD and CRD: Similarities

- Onset within first 2 decades
- Gradual visual decline
  - Legal blindness by middle age
  - Central visual field deficits
  - Show diminished cone amplitudes on ERG
    - EOG may also be subnormal
- *ABCA4* associated with very poor outcome

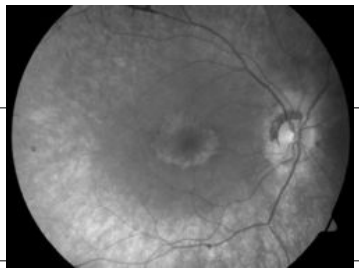
CD and CRD: Similarities

- Symptoms
  - Photophobia
  - Hemeralopia: "day blindness"
  - Central vision loss
  - Poor color discrimination
- Signs
  - Bull's eye macula common
  - Diffuse macular pigment changes
  - Reduced VA, color vision
  - Acquired nystagmus in some cases

Cone-Rod Dystrophy

- May be part of the retinitis pigmentosa spectrum.
- Cones are affected first and more so than rods.
- Night vision problems

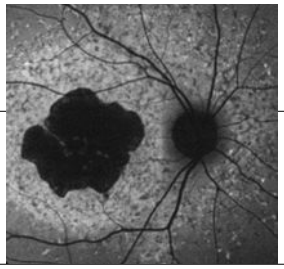
Cone-Rod Dystrophy



CD and CRD: Differences

- CRD may have an **earlier onset** by ~5 years
- CRD may progress **more rapidly** and to a fuller extent; therefore a more severe disease
- CRD has some early involvement of **rods**.
- This is reflected in symptoms (nyctalopia) and clinical signs (central + peripheral VF loss, BV attenuation, periph pigment, ERG shows reduced cone and rod responses with cone loss > rod loss).

Severe Cone-Rod Dystrophy FAF



CD and CRD

- No treatment
- Some animal studies have shown that antioxidant vitamins may slow progression.
- Mice with cone dystrophy have been effectively treated with gene therapy, but it is unknown if the approach will work in humans.
- Low Vision Rehabilitation
- Genetic counseling

Outcome

- Our patient is currently being followed with periodic DFE, mf-ERG, central threshold perimetry, contrast sensitivity, OCT, FAF, color vision.
- She continues to enjoy successful contact lens wear.
- This case underscores the importance of electrodiagnostic testing when photoreceptor disease is suspected.
- Mf-ERG may be of significant value in detection of CD/CRD in patients that develop symptoms later in life.

What is the future?

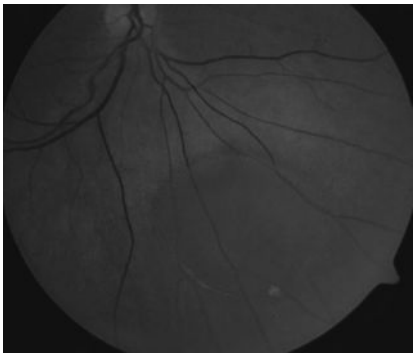
- Electrophysiological testing and autofluorescence imaging help diagnose and predict course of disease.
- Better phenotyping can contribute to better-directed, cost-efficient genotyping.
- Combining fundoscopy, FAF, and electrophysiological testing is essential in approaching patients with retinal dystrophies.
- Emerging are new gene-based treatments for these devastating conditions.

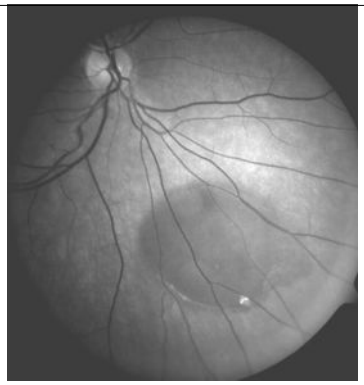
Issues to consider...

- How to break the news to the family due to the severity/potential severity of this disease?
- LVR of the patient with CD or CRD?
- Intra-professional referral

QUESTIONS AND COMMENTS?

Pigmented Retinal Lesions





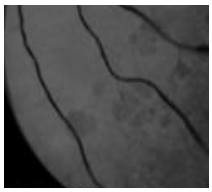
Outcome:

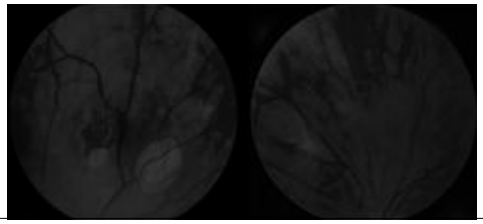
- Congenital Hypertrophy of Retinal Pigment Epithelium (CHRPE)
- Photos taken
- Patient referred back to Optometrist
- Monitor 1 year

The Real Deal on CHRPE

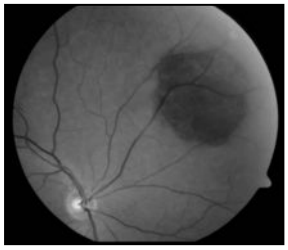
- Dark black, only slightly raised
- No malignant potential
- When present in multiple locations, investigate for Gardner's Syndrome
  - This is familial polyposis coli, which can lead to colorectal carcinoma.
  - Autosomal dominant condition
  - Probe family history, patient GI symptoms
  - Consider gastroenterology consult if symptomatic or + family history

CHRPE





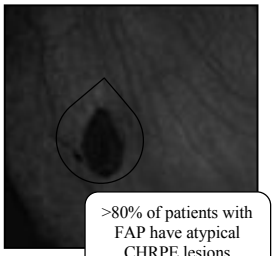
- **Common benign lesion**
- **Focal area in which the RPE cells are taller and more densely packed with melanosomes**



Congenital Hypertrophy of the Retinal Pigment Epithelium

Familial Adenomatous Polyposis (FAP)

- **AD inheritance**
- **Adenomatous polyps throughout rectum & colon**
- **Starts to develop in adolescence (15-40 yrs)**
- **If untreated – all pts will develop <u>colorectal cancer</u>**

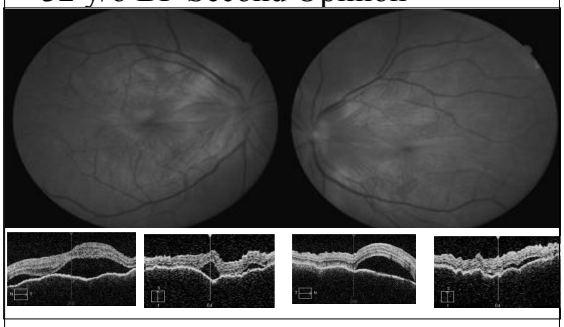


>80% of patients with FAP have atypical CHRPE lesions

Systemic Association

Infection and Inflammation

32 y/o BF Second Opinion



Diagnostic Criteria for VKH	
1	No history of penetrating ocular trauma or surgery
2	No evidence of other ocular or systemic disease
3	Bilateral ocular disease Early manifestation Late manifestation
4	Neurologic and auditory findings
5	Dermatologic findings

Most types of anterior uveitis are sterile inflammatory reactions. Many of the posterior uveitic syndromes are caused by infections.

Case Hx:

A 16 year old Caucasian male presented with a chief complaint of blurred vision and floaters in both eyes for a one month duration.

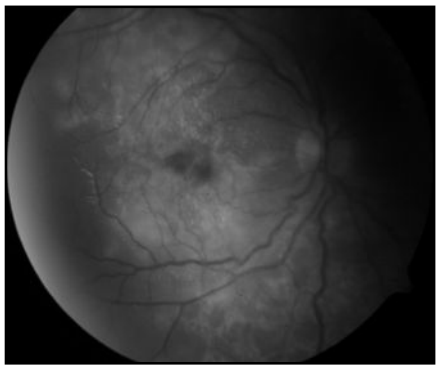
Floaters began immediately following a viral prodrome with mild headache. He then noticed progressive blur OS > OD.

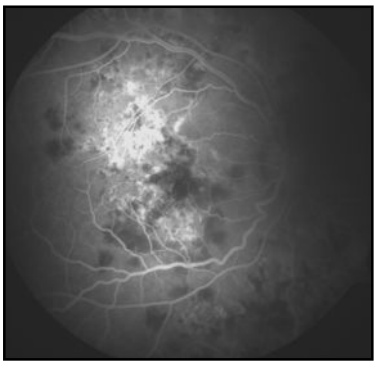
Visual field defects were also noted in both eyes.

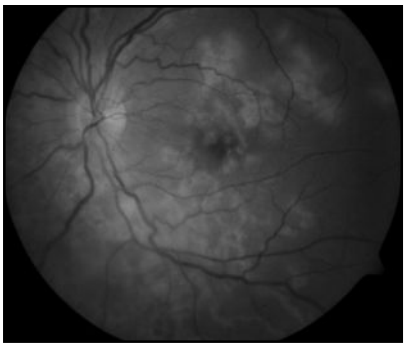
No other ocular complaints.

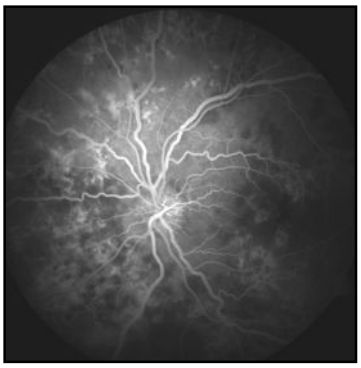
Medical history: negative Medications: none

Allergies: None to environment/medications









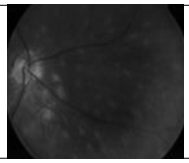
Inflammatory "White Dot Syndrome" - APMPPE

- Occurs in healthy men or women between 20 – 50 years old
- Acute bilateral vision loss
- Prodromal viral illness in about 30 % of patients

Symptoms:
- Central or paracentral scotomas/hotopsia/floaters
- Reduced visual acuity

Signs:
- Mild vitreous cells are usually present
- Yellow/white placoid lesions located in the posterior pole/midperiphery
- Located at the level of the retinal pigment epithelium/choriocapillaris
- Lesions start to fade within 2 weeks
- Lesions are replaced with atrophy and hyperpigmentation

The White Dot Syndromes are characterized by bilateral choroidal infiltrates and retinal vasculitis.



White Dot Syndromes

- Multifocal Choroiditis/Panuveitis (MCP)
- Acute retinal pigment epitheliitis (ARPE)
- APMPPE (Acute posterior multifocal pigment placoid epitheliopathy)
- Vitiliginous choroiditis (Birdshot)
- MEWDS (Multiple Evanescent White Dot Syndrome)
- DUSN (Diffuse Unilateral Subacute Neuroretinitis)
- Punctate Inner Choroidopathy (PIC)
- Sarcoid Choroidopathy
- Intraocular lymphoma (Retinal/Vitreal or Uveal)

White Dot Syndromes

Non-infectious Choroidopathies

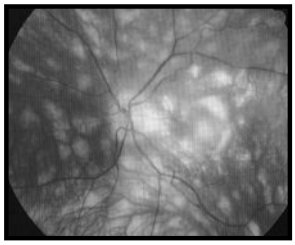
APMPPE

Pathology:
- Immune response from a virus ?
- Infarction of the choroid secondary to a vasculitis
- Described with Mumps, Strep infections, TB, Hep B vaccine, Lyme, Sarcoidosis, Thyroiditis

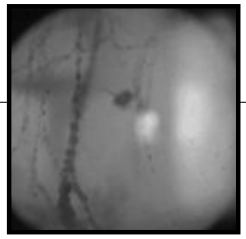
Treatment:
- No systemic or ocular treatment needed
- VA 20/40 or better within 8 weeks in 80% of untreated patients
- Systemic steroids if central nervous system or foveal involvement

Systemic Evaluation:
- No systemic evaluation needed unless CNS involvement
  - Headaches or neuro signs – get MRI
- Associations with adenovirus type 5, cerebral vasculitis – must undergo a systemic and neurologic evaluation

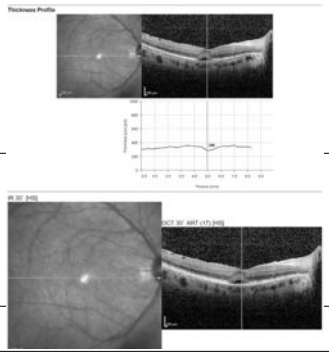
Birdshot Retinochoroidopathy



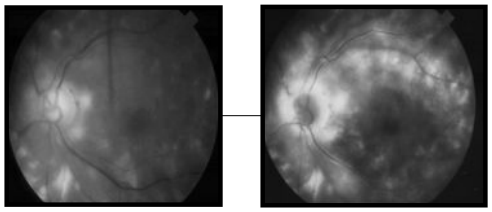
Cellular debris in vitreous



RPED, ERM in Birdshot



Birdshot in another patient: FA



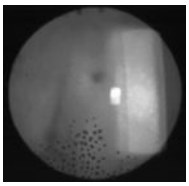
- Venous stage hyperfluorescence
- Extensive late intraretinal and disc leakage

Birdshot Retinochoroidopathy

- Treatment:
  - Immunosuppressive therapy reduces the risk of vision loss from CME. (Cyclosporine)
  - Chronic low dose oral corticosteroids (10mg or less), does not seem to prevent the occurrence of CME.
  - Immunosuppressive therapy may reduce the risk of progressive diffuse retinal dysfunction.

JE Thorne, DA Jabs, et al. AJO 2005;140:45-51.

Importance of Dilated Post Seg Exam in All Uveitis Cases



- Vitreous Exam
  - Technique
    - Anterior vitreous
    - Posterior vitreous
  - Inflammatory cells and protein
  - Comes from the choroid, retina and ciliary body
  - "Vitritis"??

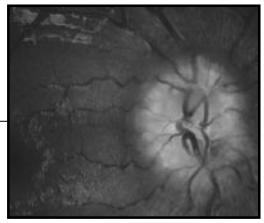
Immune Privilege

- The eye enjoys a special relationship with the immune system.
  - Ability to quench unwanted immune-mediated inflammation.
  - This ability is known as immune privilege.
  - Immune privilege enables ocular tissues to remain clear.

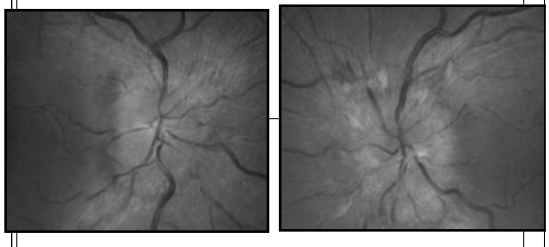
We do encounter situations in clinical practice when the eye's immune privilege is overcome. Uveitis is an example.

The Optic Nerve in Posterior Uveitis

- Disc hyperemia
- Papillitis

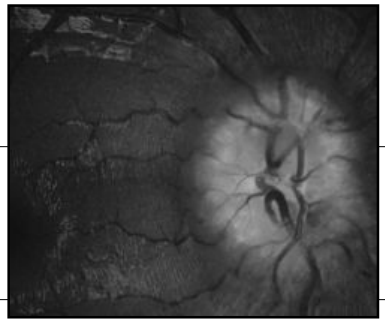


- Disc edema may occur with toxoplasmosis, viral retinitis, lymphoma, or sarcoidosis.

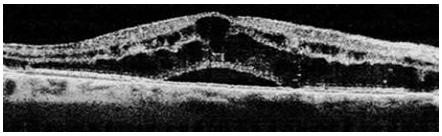


Sarcoid

Sarcoid



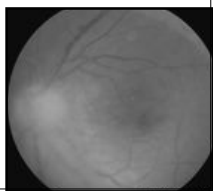
OCT



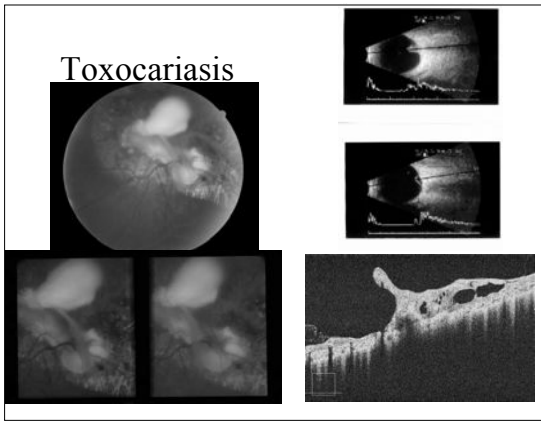
- Cystoid Macular Edema in a Sarcoid patient with chronic uveitis.

Common Etiologies of Posterior Uveitis

- Toxoplasmosis (photo below)
- HSV, HZV
- Granulomatous disease (e.g. tuberculosis, sarcoidosis, Lyme disease, syphilis)
- Histoplasmosis
- Birdshot or Serpiginous
- Inflammatory choroidopathies

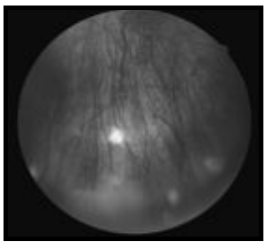


Toxocariasis



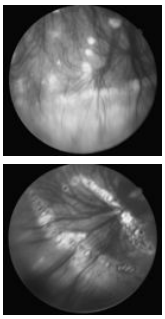
Common Etiologies of Panuveitis

- Infections, such as
  - Infantile toxocariasis
  - Post-op bacterial endophthalmitis
  - Toxoplasmosis
- Granulomatous Dx.
- Multifocal Choroiditis and Panuveitis (right)
  - MCP in a 27 y/o Asian Female



Multifocal Choroiditis and Panuveitis

- Bilateral, chronic uveitis
  - Punched-out chorioretinal lesions similar to POHS.
- CNV is the most worrisome potential complication.
- Conservative monitoring and timely steroid treatment essential to care.
- Immunosuppressive drug therapy appears to limit the number of recurrences.



Beyond Anterior Uveitis

Table. Common Causes of Uveitis

Intermediate Uveitis	Panuveitis	Posterior Uveitis
Sarcoidosis	Syphilis	Taxoplasmosis
Inflammatory bowel syndrome	Sarcoidosis	Herpetic virus
Multiple sclerosis	Vogt-Koyanagi-Harada syndrome (VKH)	Sarcoidosis
Lyme disease	Infectious endophthalmitis	Taxocariasis
Pars planitis*	Behçet's disease	Histoplasmosis

* Intermediate uveitis with no known etiology, this subtype tends to have a worse prognosis.

Thank you!

Joe

pizzimen@uiwtx.edu