The Use of Fundus Autoflourescence in Hereditary and Acquired Retinal Disease

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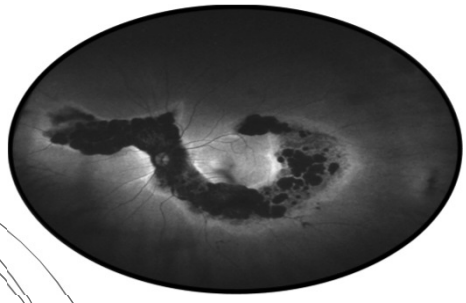
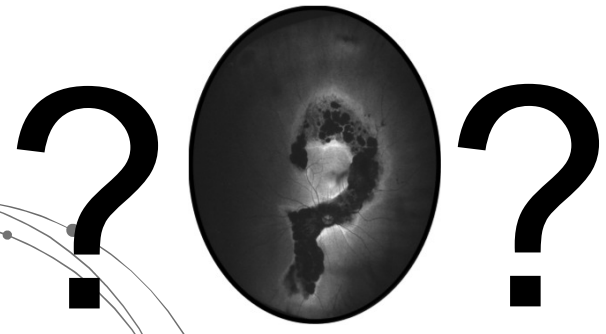
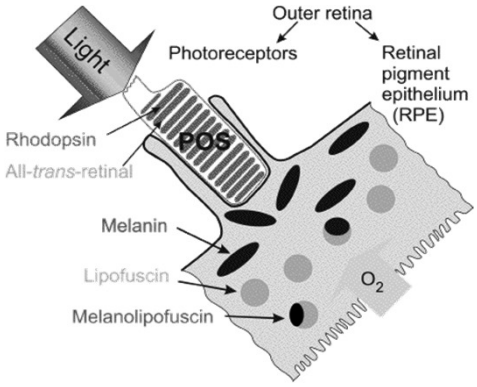
Fundus Autofluorescence Imaging



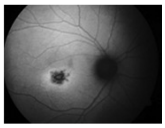
What novel information does AF give us?



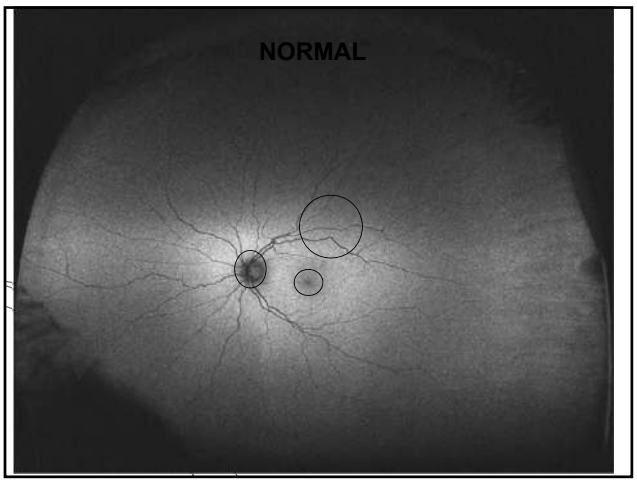


Autofluorescence Imaging

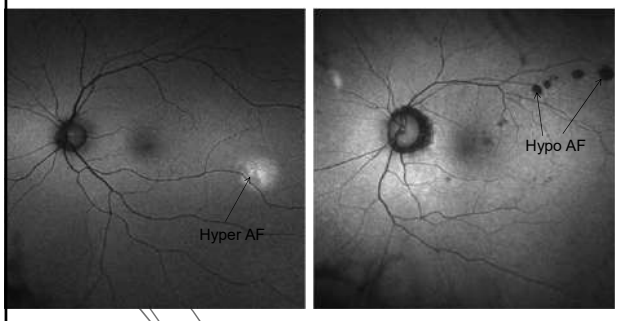
- Autofluorescence
  - An imaging method to topographically mark ***lipofuscin*** in the outer retina
    - Incomplete phagocytization of photoreceptor outer segments by the RPE
    - Hallmark of aging RPE cells
- Hyperautofluorescence "bright areas"
  - Lipofusccin
  - Metabolically stressed RPE and photoreceptors



- Hypoautofluorescence "dark areas"
  - Degenerated RPE and photoreceptors
  - Lipofuscin is gone, cells are degenerated



Exemplary cases of hyper and hypo AF

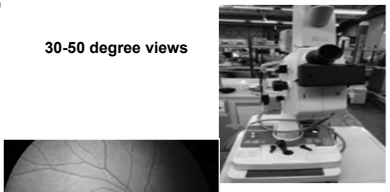


Indirect Ophthalmoscopy

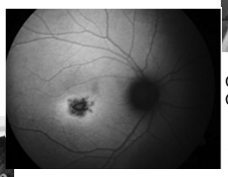
No form of ophthalmoscopy for fundus AF exists!

Heidelberg Spectralis Blue Peak (Heidelbergengineering, Inc.)

30-50 degree views



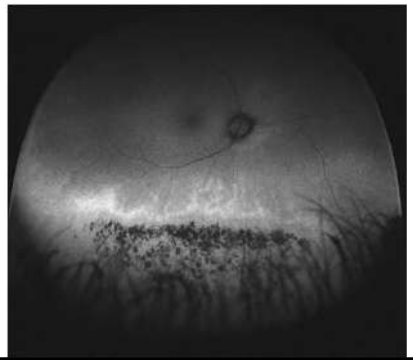
Topcon TRC-501X



Zeiss FF 450

CR2Plus Non-Mydriatic Camera (Canon, Inc.)

Ultrawide-field FAF Daytona (Optos, Inc.)



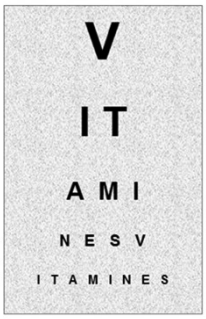
Clinical Applications of FAF

- Detection of disease
  - Ophthalmoscopy and color photography may look normal
- Progression of disease
  - Ophthalmoscopy and color photography may look stable
- Diagnosis of disease
  - Specific patterns of FAF abnormalities help to define the disease

Retinal Diseases Studied Using FAF Imaging

- Hereditary
  - Retinitis pigmentosa
  - Stargardt disease
  - Cone Dystrophy
  - Cone/Rod Dystrophy
  - Best Disease
  - Ocular Albinism
  - Central Aereolar Choroidal Dystrophy (CACD)
- Acquired
  - Age-Related Macular Degeneration
  - Choroidal Masses
  - Toxic Retinopathy
  - Angioid Streaks
  - Central Serous
  - AZOOR
  - Drusen
    - Disc Drusen
    - Retinal Drusen

AF abnormalities have myriad etiologies



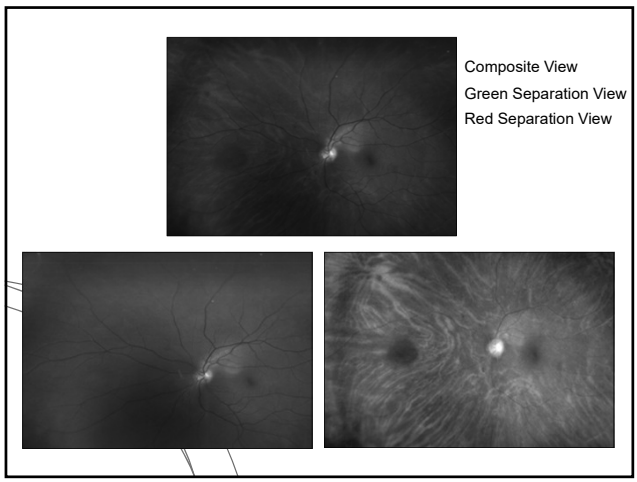
V – vascular, vitamin deficiency
I – infectious, inflammatory
T – trauma, toxic
A – autoimmune, allergic
M – metabolic, mass lesions
I – inherited, idiopathic
N – neurodegenerative
E – endocrine, environmental
S – senile, stress

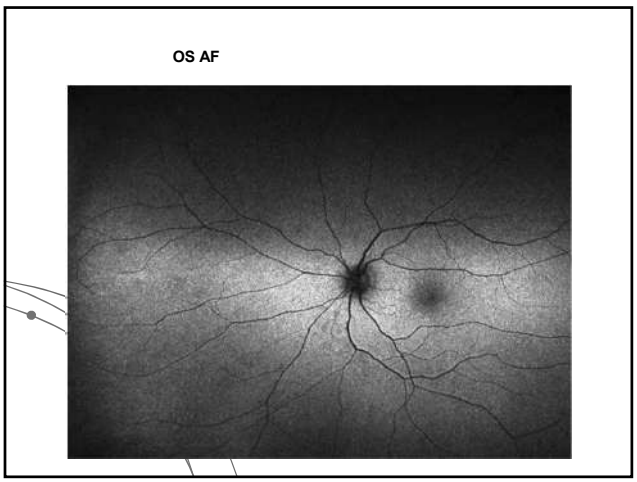
Figure : VITAMINESx2
This mnemonic is helpful to remember possible etiologies of AF abnormalities.

Choroidal Nevus

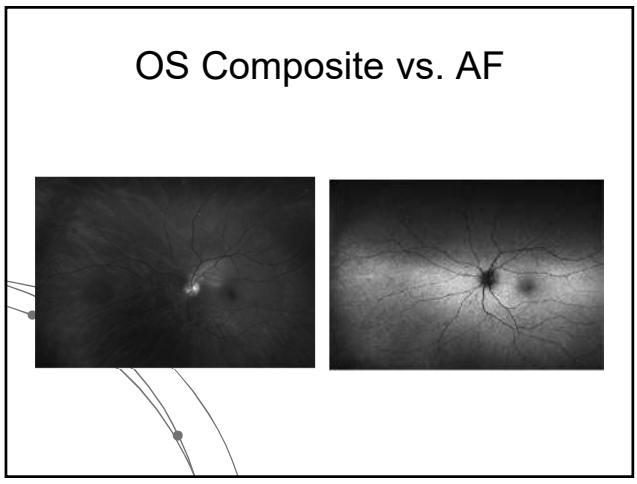
In addition to hyper and hypo AF, there is also iso AF

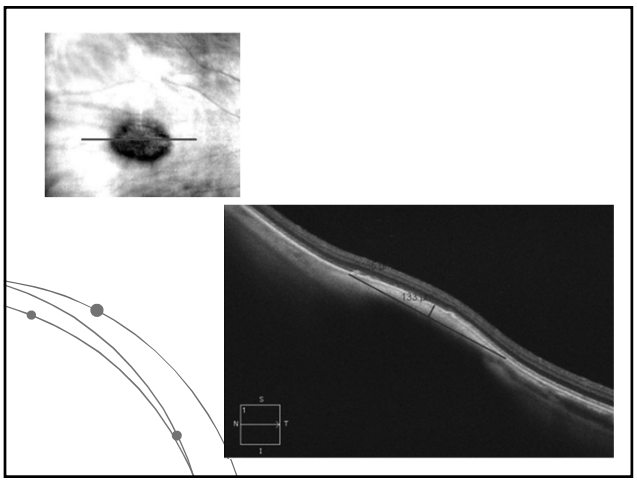
OS Composite



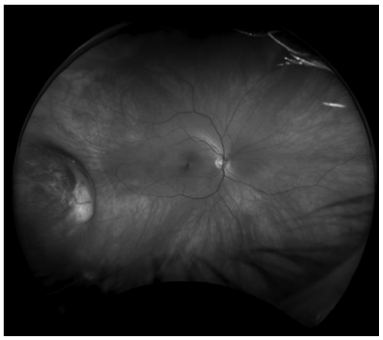


OS Composite vs. AF

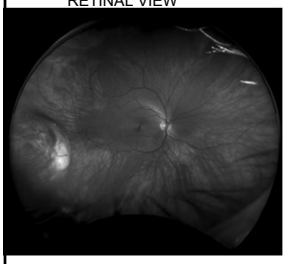




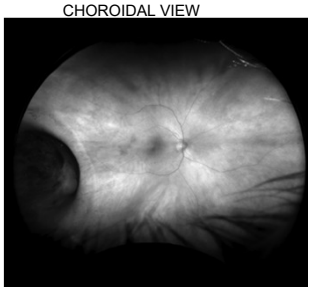
BUT…



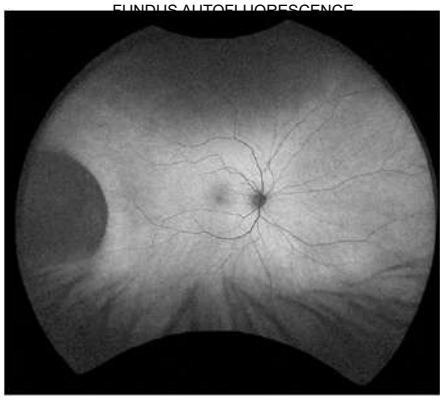
GREEN SEPARATION
RETINAL VIEW



RED SEPARATION
CHOROIDAL VIEW

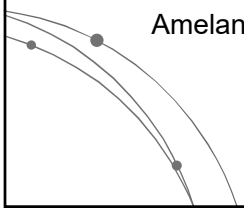


FUNDUS AUTOFLUORESCENCE

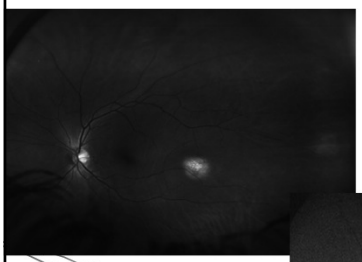


Next Case

Amelanotic choroidal mass

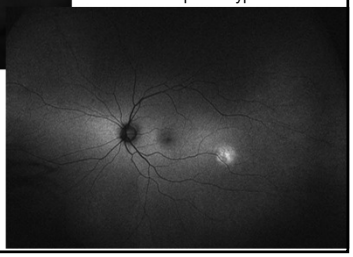


OS Composite vs. AF



- This lesion is a amelanotic choroidal mass that could represent inflammatory granuloma (sarcoid, syphilis, tb), metastasis, nevus, or melanoma.[1]

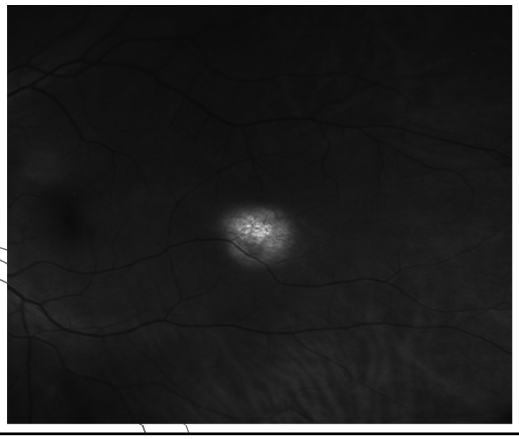
Example of hyper-AF



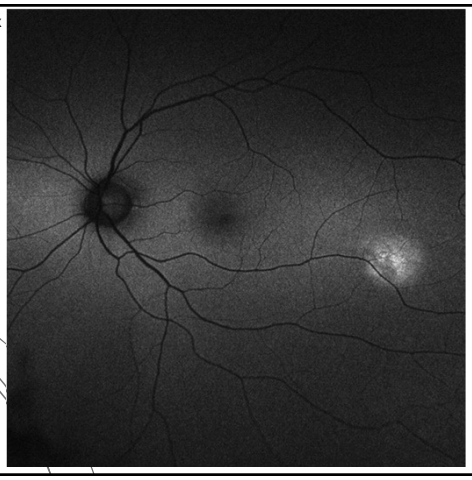
- It is sometimes impossible to differentiate a stable granuloma from amelanotic nevus. Some would include this lesion under the umbrella of solitary idiopathic choroiditis.[1]

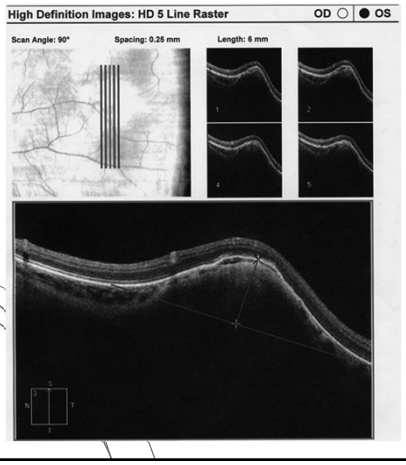
[1] Person of communication is Carol Shields

OS Res Max



OS AF Res Max



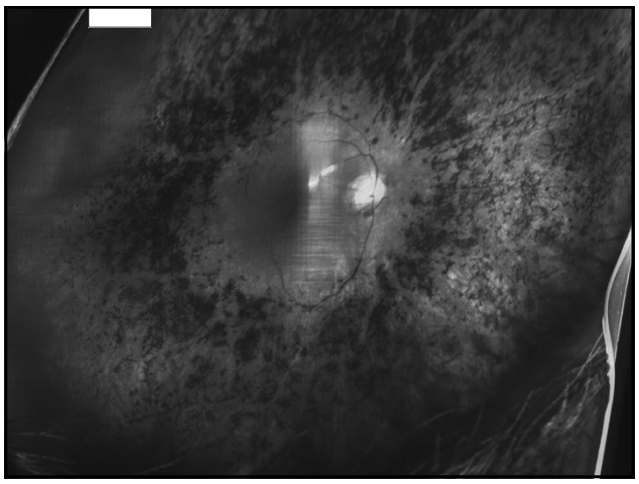


Retinitis Pigmentosa

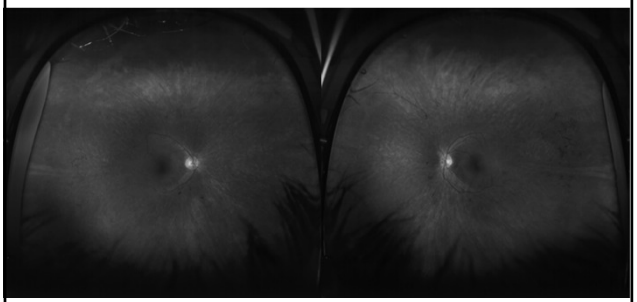
- 1: 3500 people worldwide
- 100,000 in the US

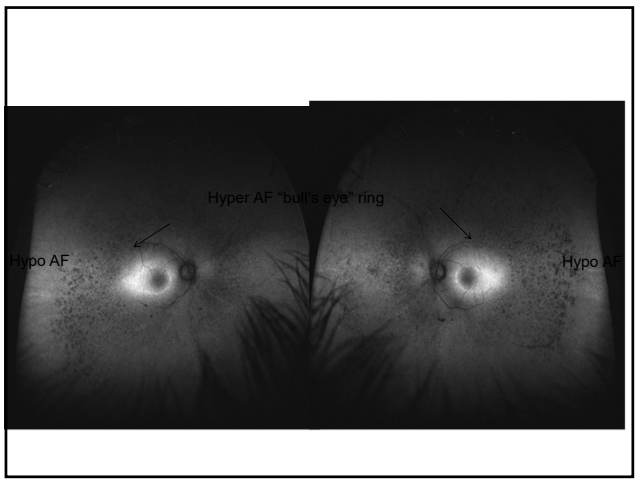
Retinitis Pigmentosa

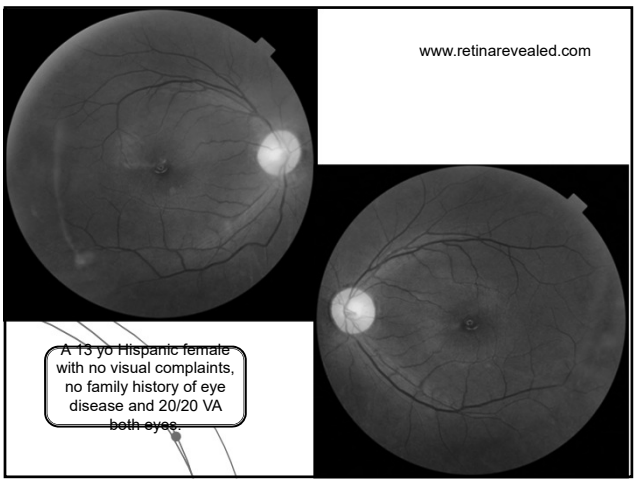
- A complex group of diseases resulting in photoreceptor degeneration
- Symptoms
  - Nyctalopia
  - Peripheral field loss
  - No symptoms
- Signs
  - ***Arteriolar attenuation***
  - Bone spicule pigmentation
  - Pale waxy disc
  - Disc drusen
  - CME
  - PSC cataract



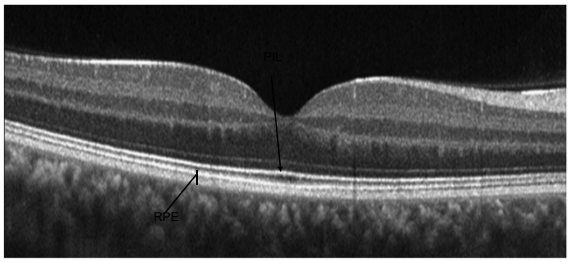
24 year-old male with night vision complaints



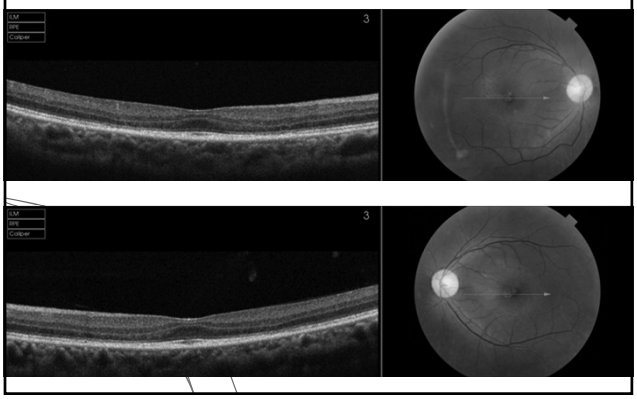




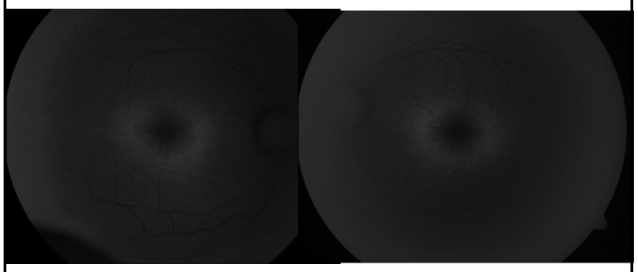
A NORMAL OCT



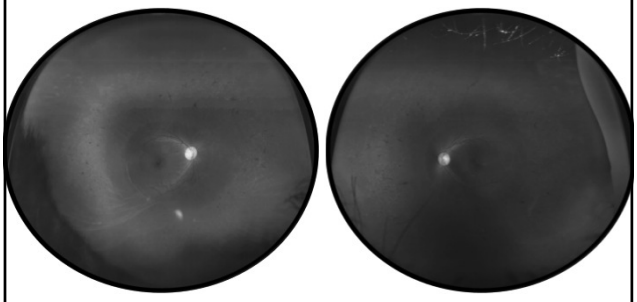
Patient's OCTs



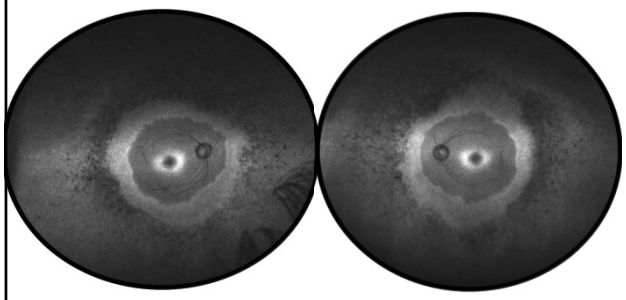
FAF 50 Degree –Zeiss Camera

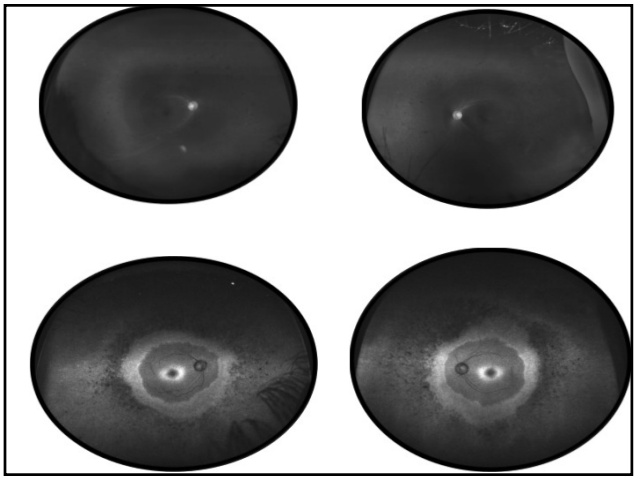


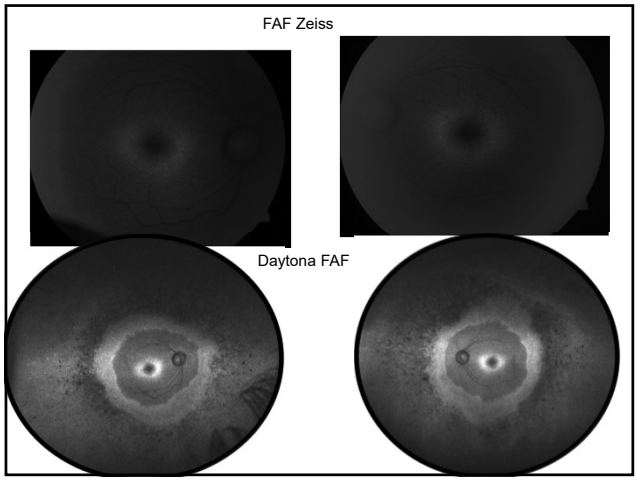
OPTOS 200 DEGREE ULTRAWIDE VIEW

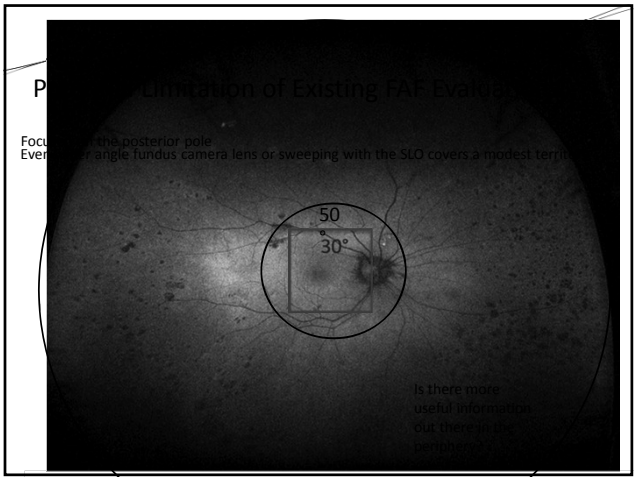


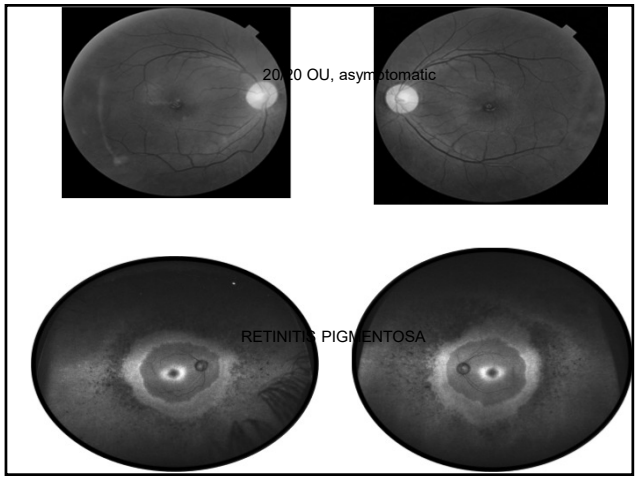
ULTRA-WIDEFIELD
AUTOFLUORESCENCE
DART BOARD PATTERN REVEALED

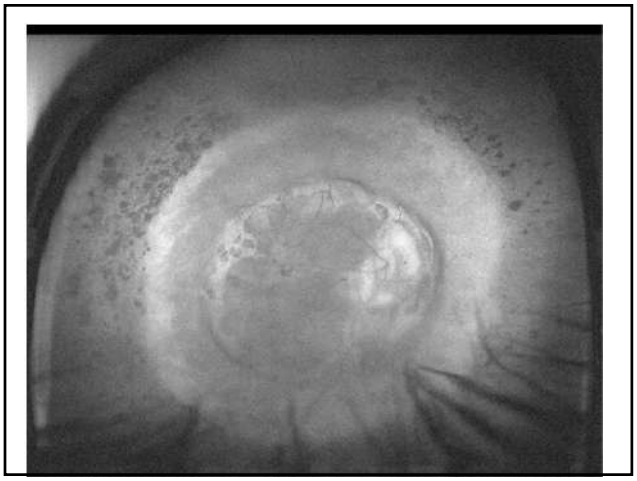


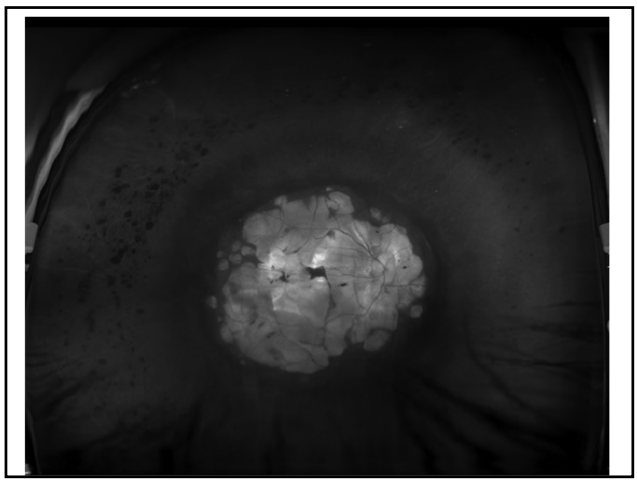


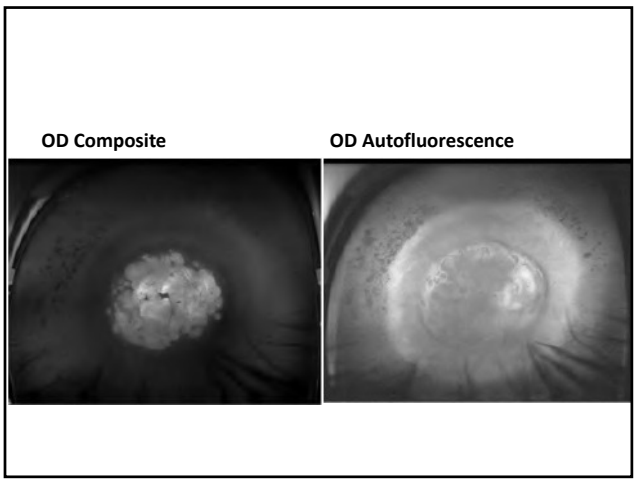

FAF Zeiss
Daytona FAF

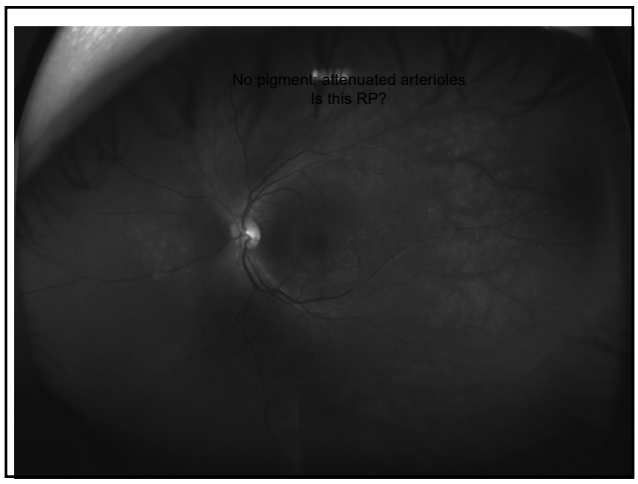

50°
30°

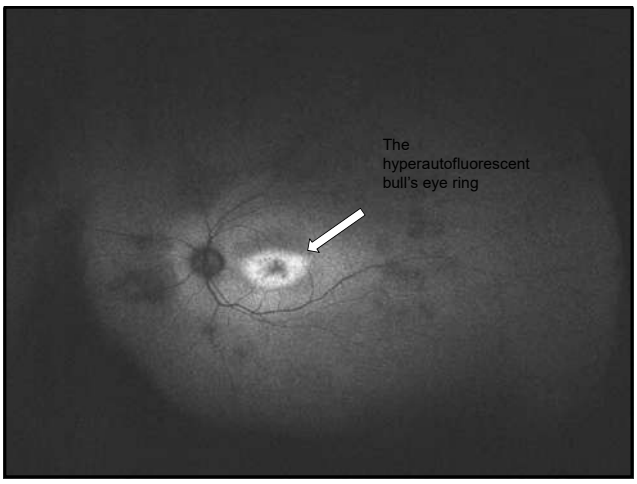

20/20 OU, asymptomatic
RETINITIS PIGMENTOSA



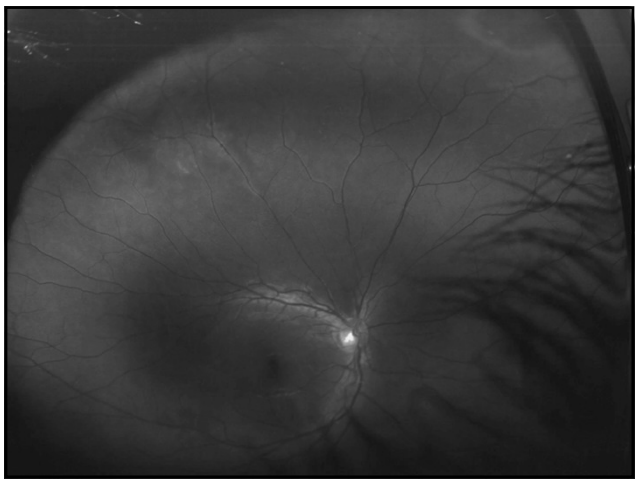


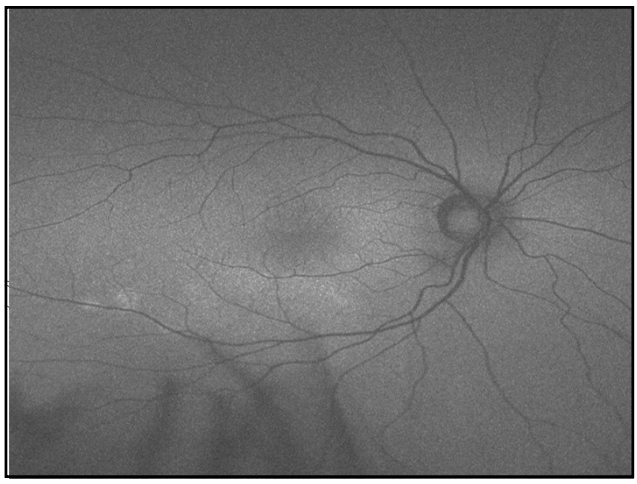

OD Composite
OD Autofluorescence


No pigment, attenuated arterioles
Is this RP?

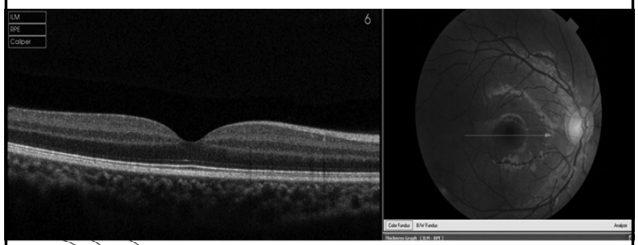

The
hyperautofluorescent
bull's eye ring

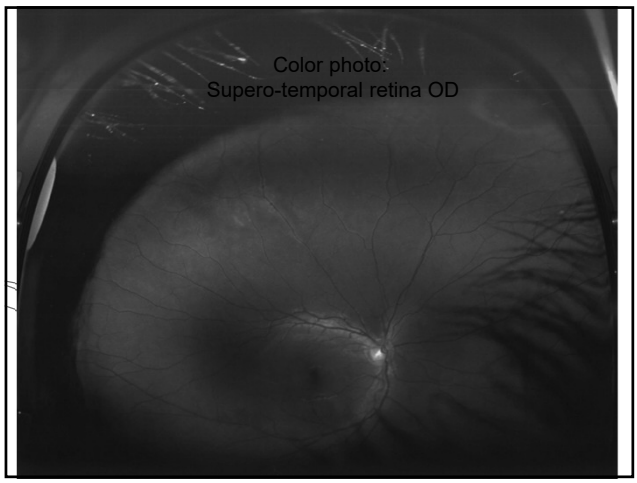
Asymmetric RP: OS>>OD

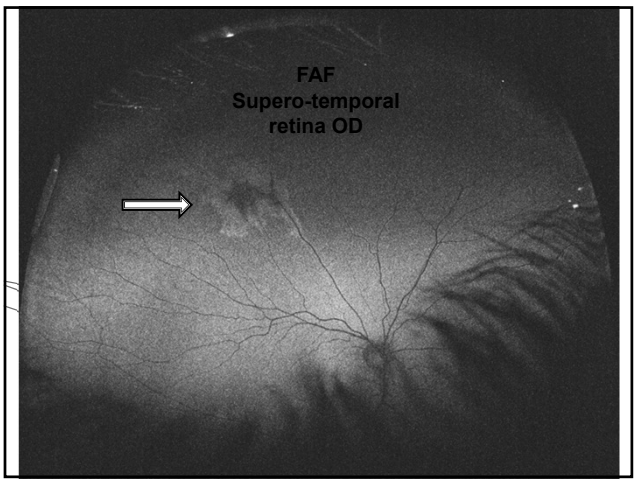




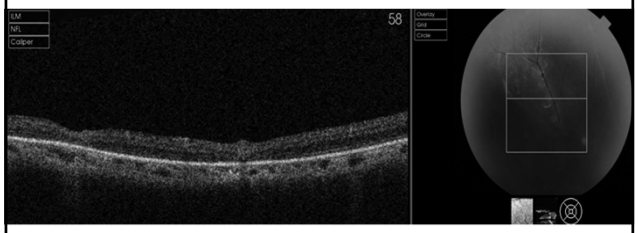
OCT OD: Normal

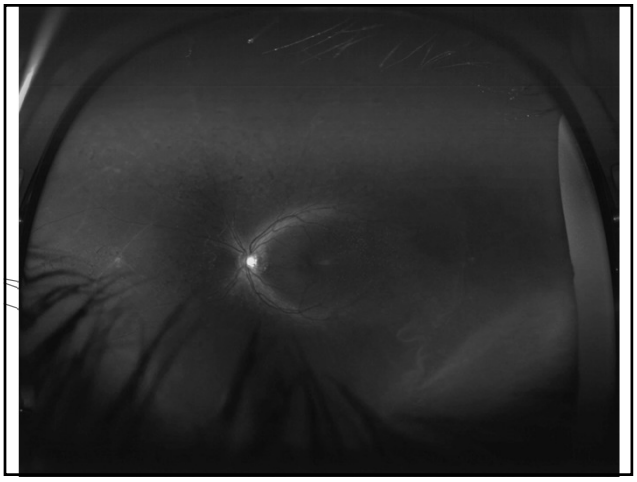


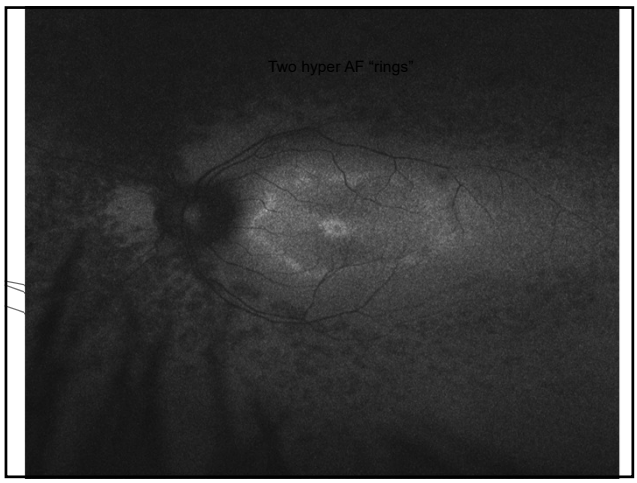


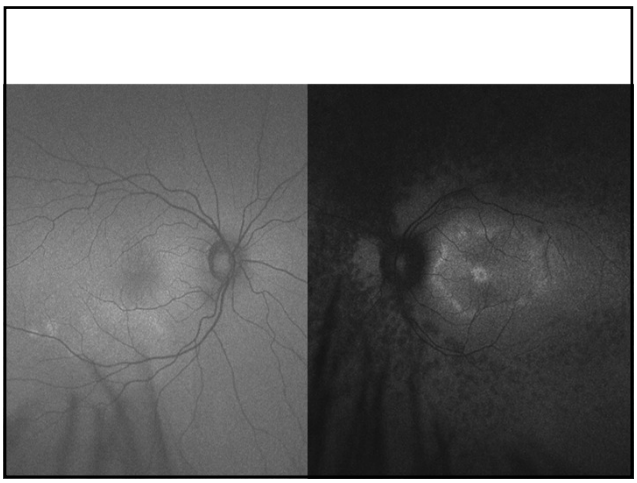


OCT OD through abnormal area:
PIL attenuated

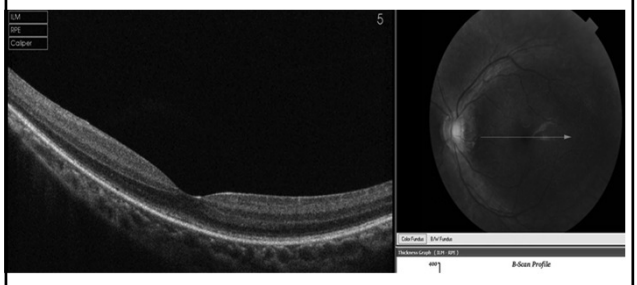




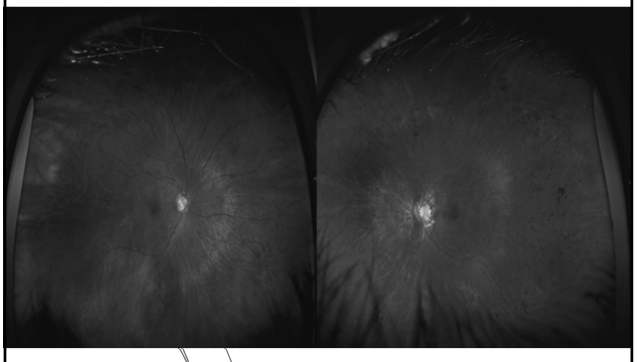




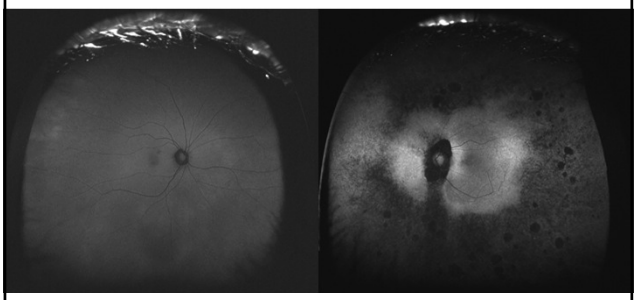
OCT OS: PIL attenuated



Is This Unilateral RP?



OD OS



Fundus Autofluorescence Images

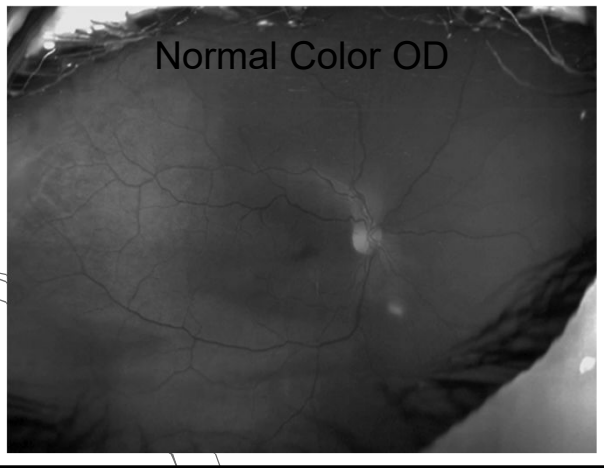
Ophthalmic Artery Occlusion

- Patient admits to surgery with face mask anesthesia followed by reduced vision, OS

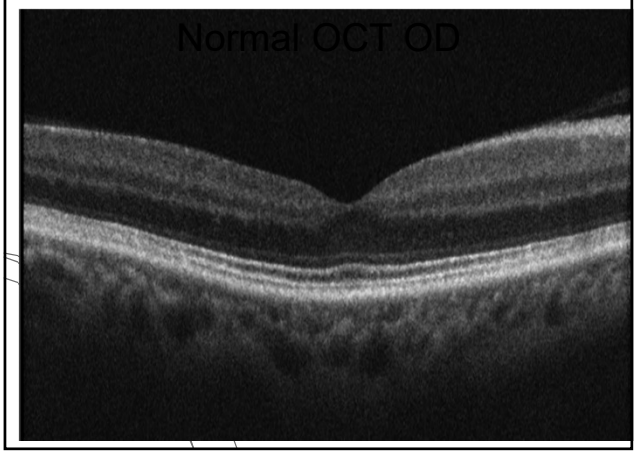
Next Case:FC Vision OS: Why?

- 61 y-o asymptomatic Asian male
- No known eye history
- No prior eye examinations until 8 years ago
  - OD 20/25 OS: FC vision
  - Dense cortical cataracts OU
  - Unaware of poor vision OS until that examination
- Normal ERG OD; Flat ERG OS

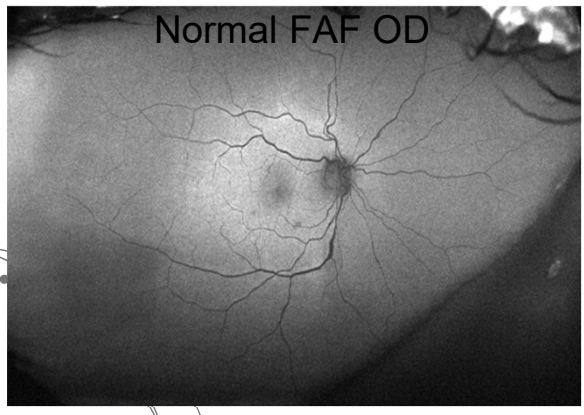
Normal Color OD



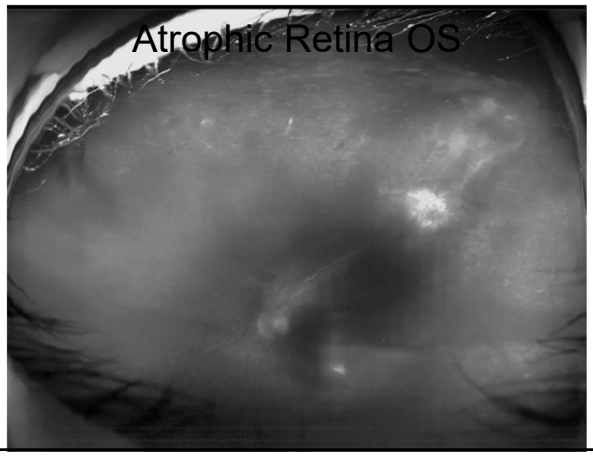
Normal OCT OD



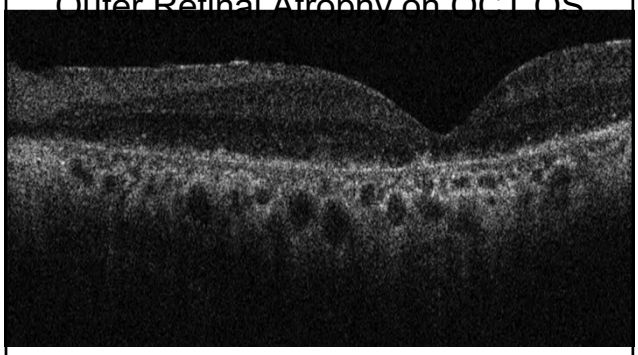
Normal FAF OD

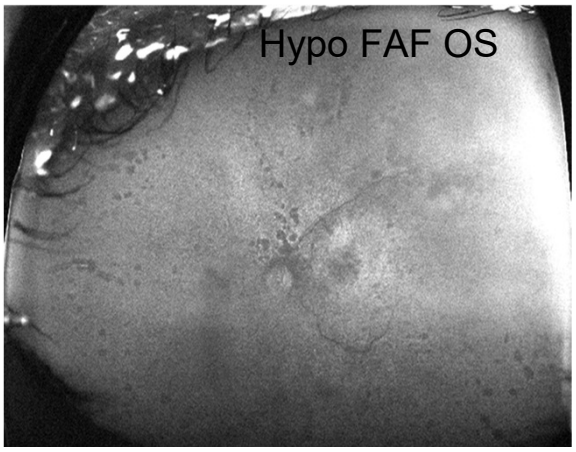


Atrophic Retina OS



Outer Retinal Atrophy on OCT OS

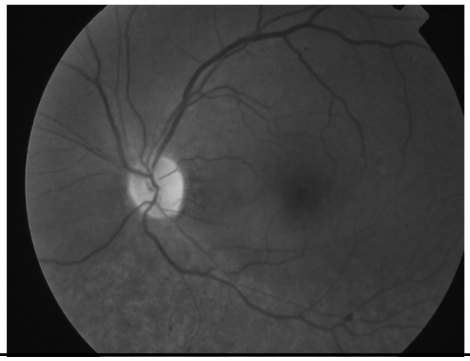


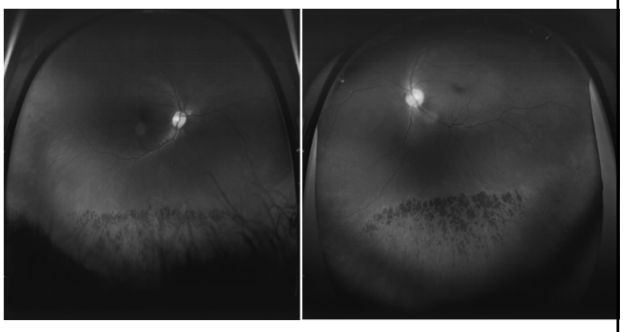


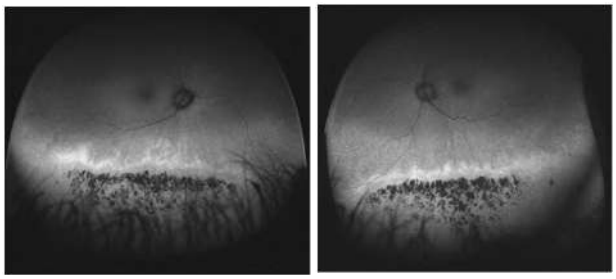
Diffuse Unilateral Subacute Neuroretinitis (DUSN) ?

- Parasitic infection caused by a nematode infection
  - h/o ingestion of dirt or fecal material with infested larvae
- Usually affects only one eye
- Results in diffuse outer retinal atrophy

Sector RP

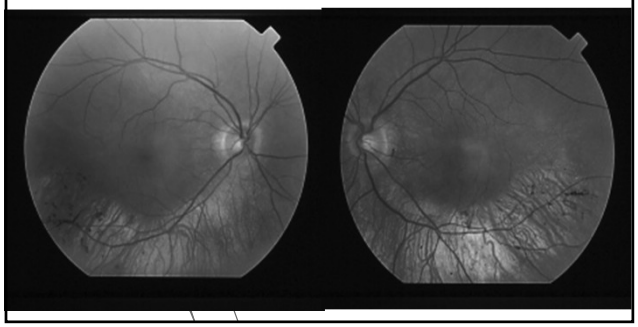




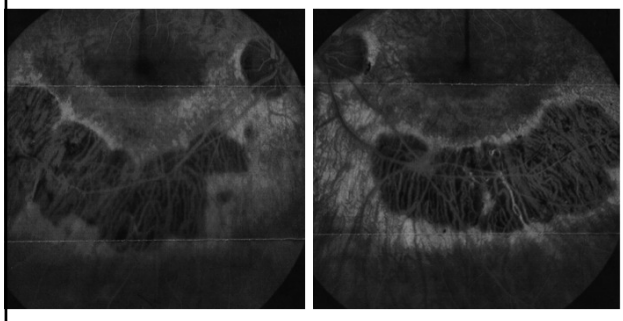


REGIONALIZED RP ?

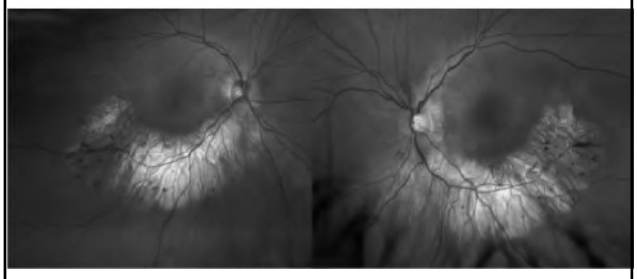
58 Y-O ASYMPTOMATIC MALE BCVA=20/20 OD AND OS



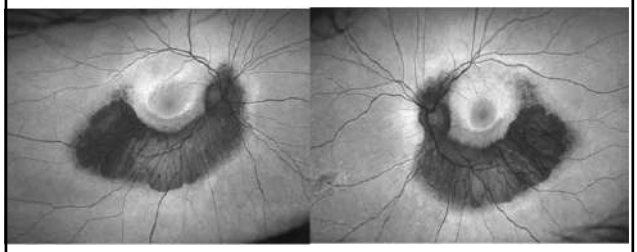
Fluorescein Angiography (FA)

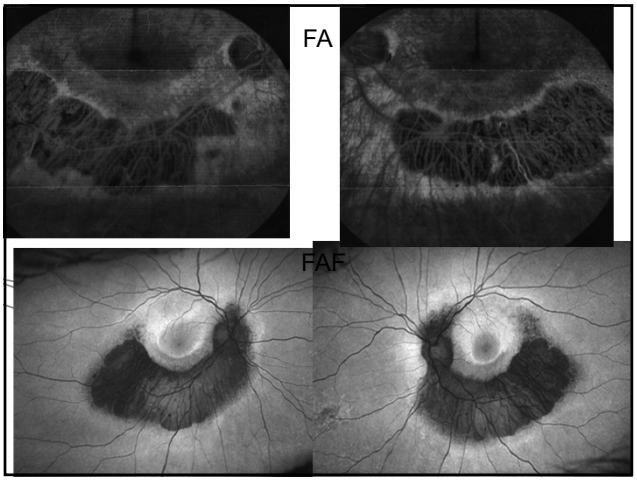


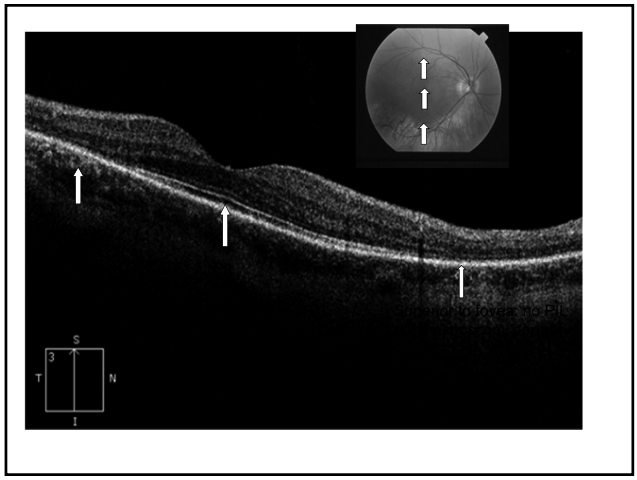
OPTOS IMAGES

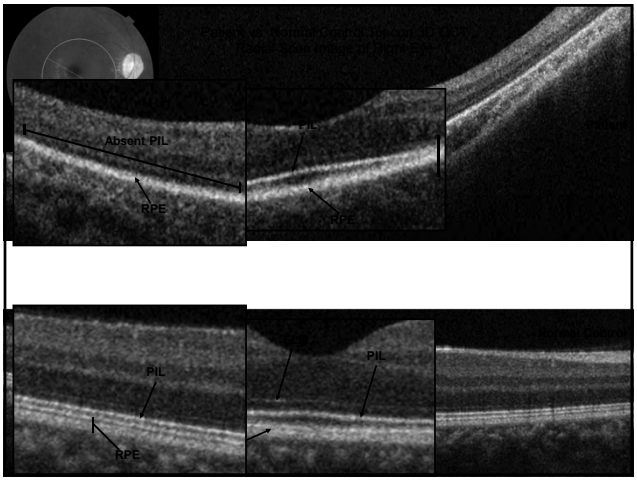


Fundus Autofluorescence (FAF)

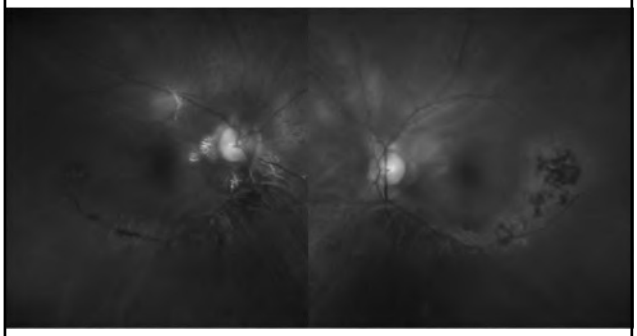


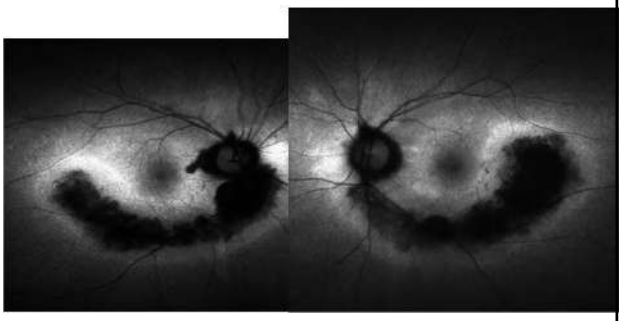




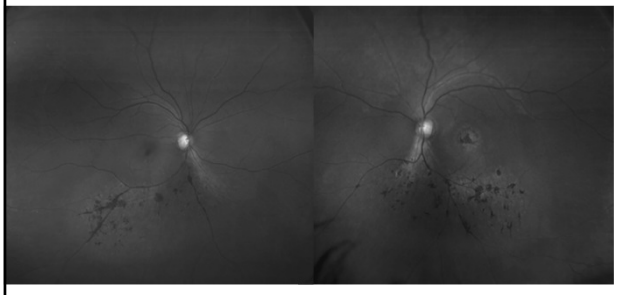


PERIPAPILLARY PERICENTRAL REGIONALIZED RP?

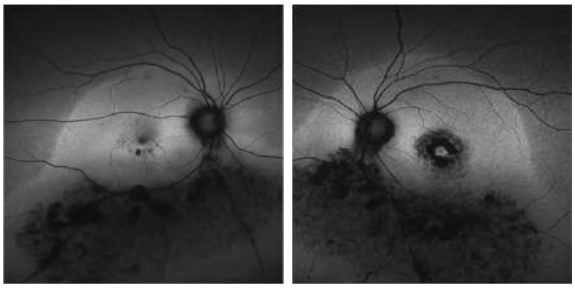




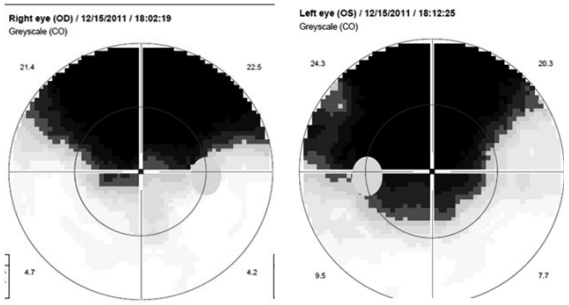
Pericentral RP? in a Diabetic with CSME treated by Laser



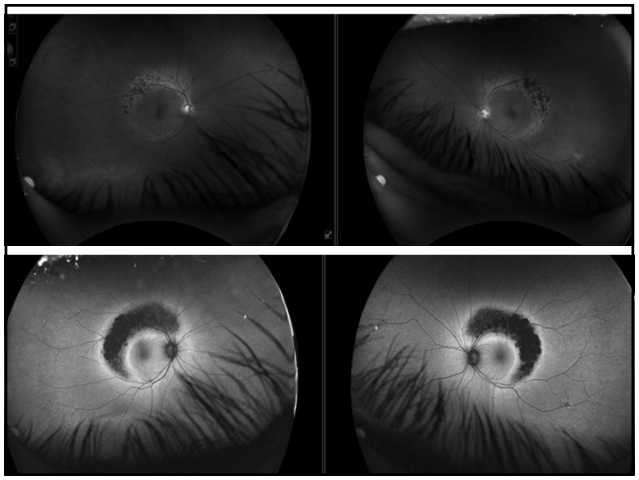
Optos FAF



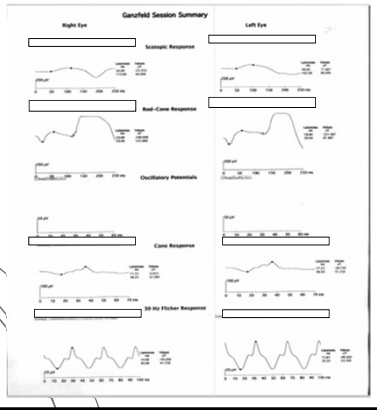
OD vs. OS Visual Field



Next Case:
Patient complains of worsening inferior field loss

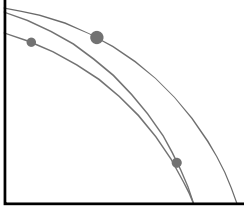


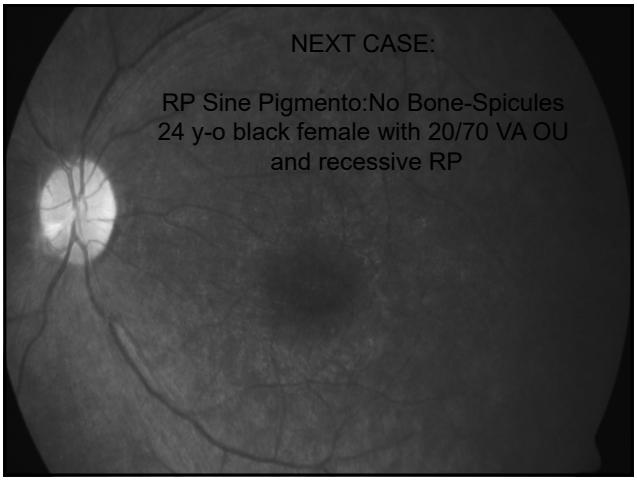
ERGs



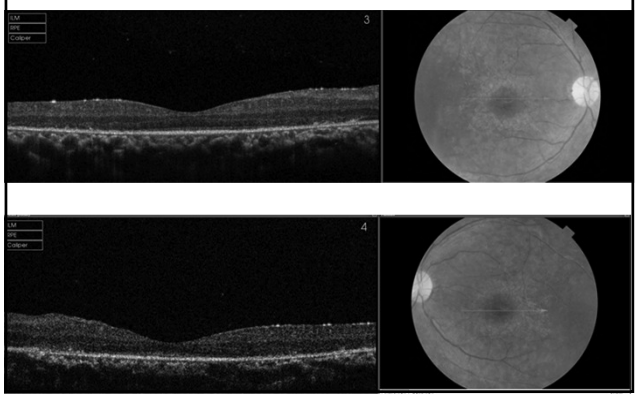
Superior pericentral RP

Rare

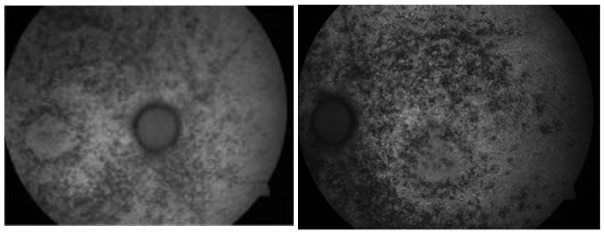




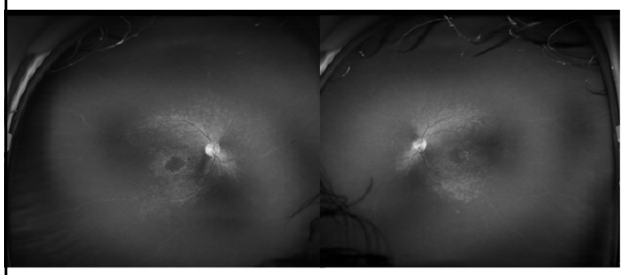
OCTs



FAF with Standard Fundus Camera

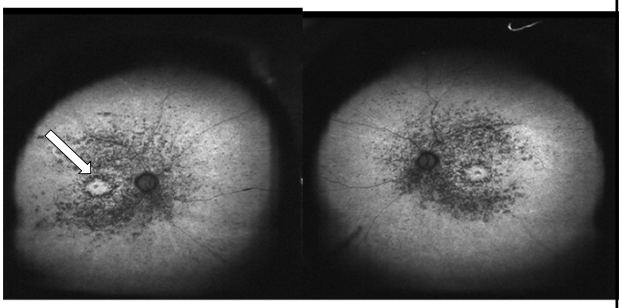


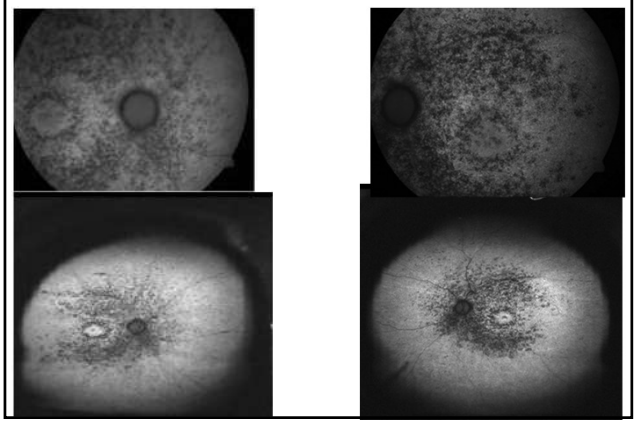
Optos Images: Color

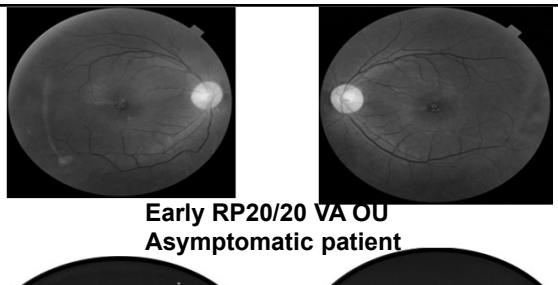


Optos Images: FAF

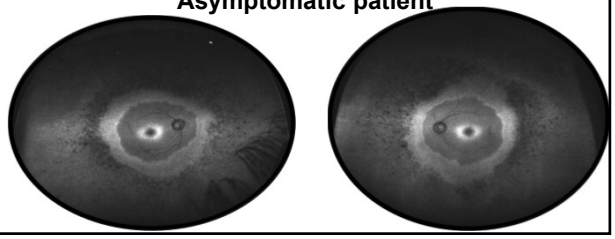
20/70 VA OU

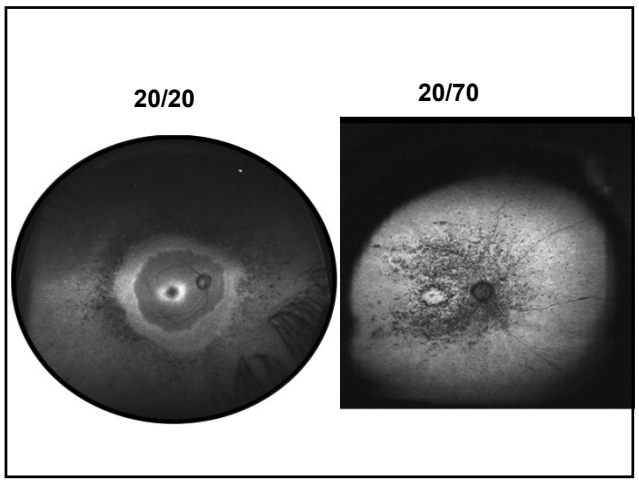






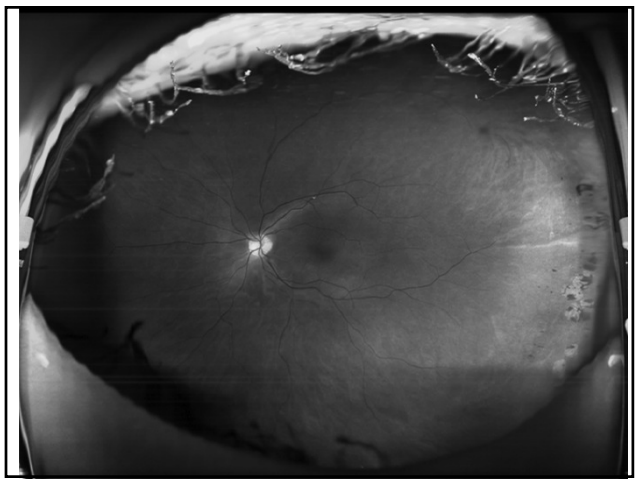
Early RP20/20 VA OU
Asymptomatic patient

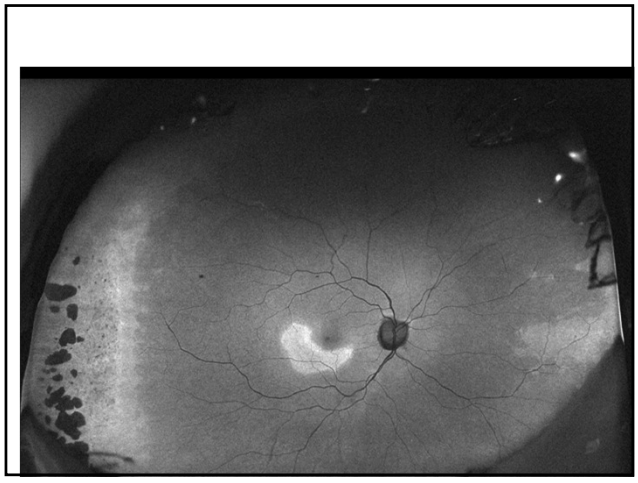


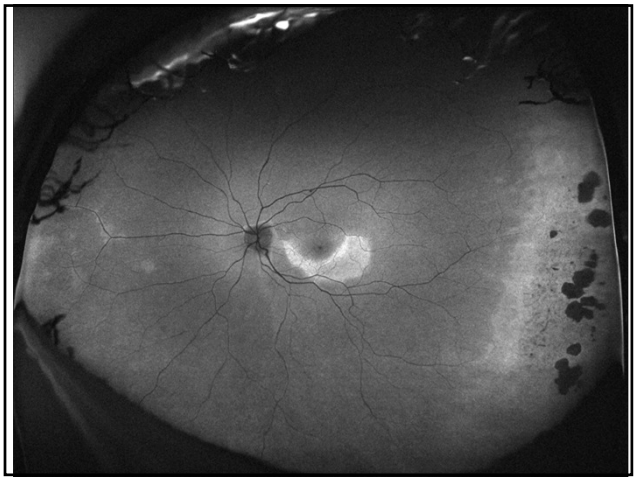


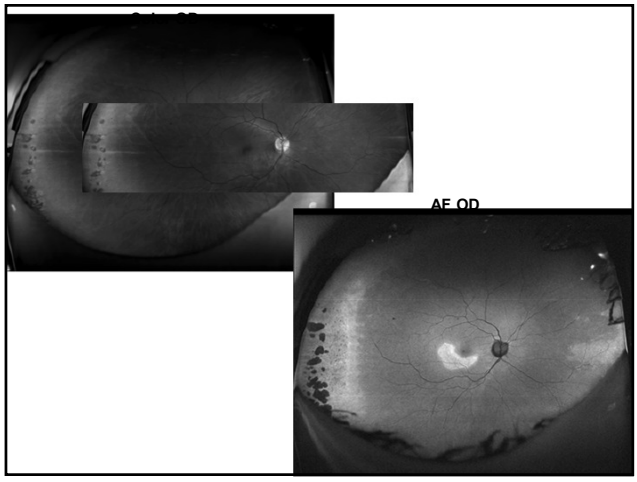
Invisible to Ophthalmoscopy

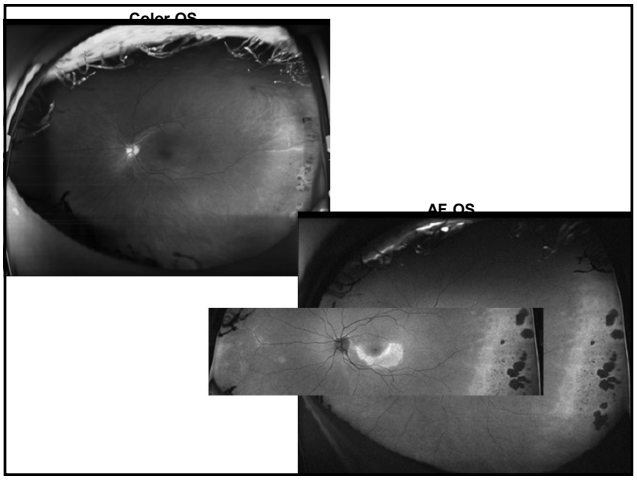
45 yo myopic female – night vision problem
VA 20/15 20/15

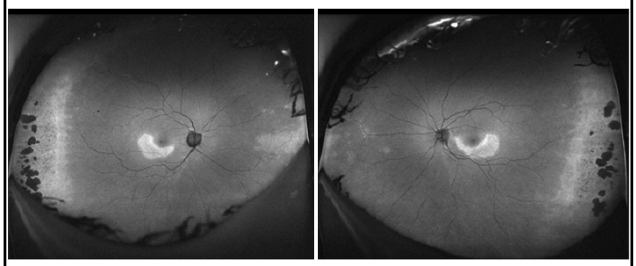







AF OD

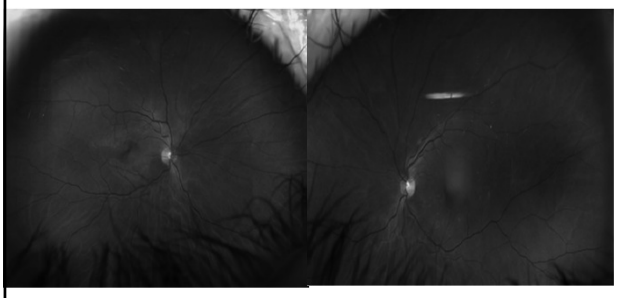

Color OS
AF OS

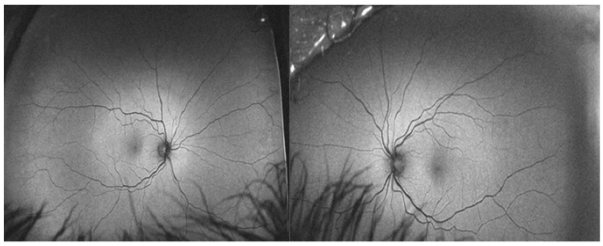


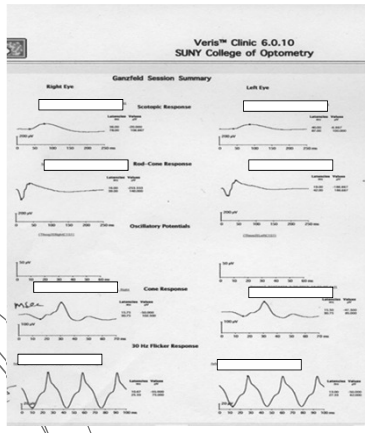
A Family Affair

- 41 year-old father with no RP
  - Mother has RP
- One 10 year-old son with advanced RP first diagnosed at age 4
- One 8 year-old son who is asymptomatic for any eye disease

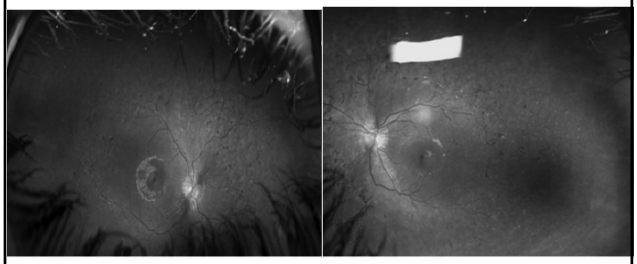
41 y-o father- No RP



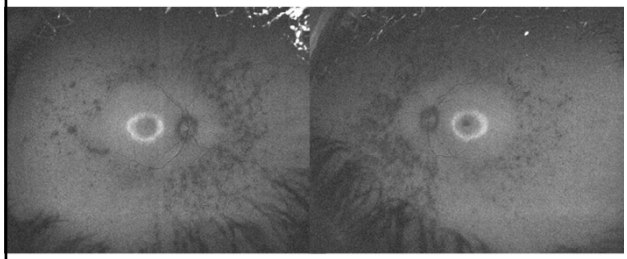




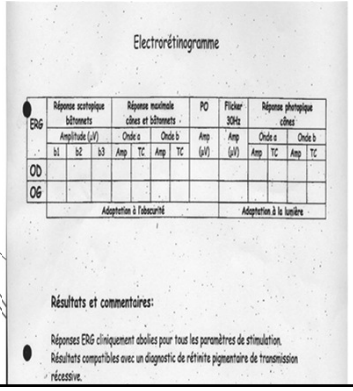
10 y-o son; advanced RP



FAF



Translation: ERG responses are abolished for all parameters of stimulation. Results are compatible with a diagnosis of RP of recessive transmission



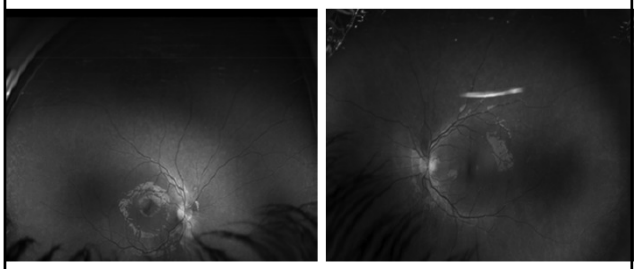
Electrorétinogramme

ERG	Réponse scotopique bâtonnets			Réponse maximale cônes et bâtonnets			PO	Flicker 30Hz	Réponse photopique cônes			
	Amplitude (µV)			Onde a		Onde b			Onde a		Onde b	
	b1	b2	b3	Amp	TC	Amp	TC	Amp (µV)	Amp (µV)	Amp	TC	Amp	TC
OD												
OG												
	Adaptation à l'obscurité								Adaptation à la lumière			

Résultats et commentaires:

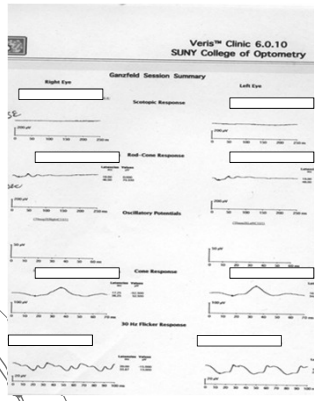
Réponses ERG cliniquement abolies pour tous les paramètres de stimulation.
Résultats compatibles avec un diagnostic de rétinite pigmentaire de transmission récessive.

8 y-o asymptomatic son

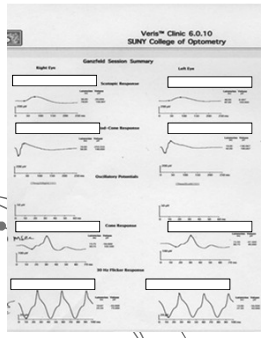


FAF

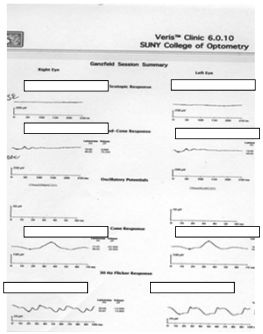
ERGs are reduced under all conditions

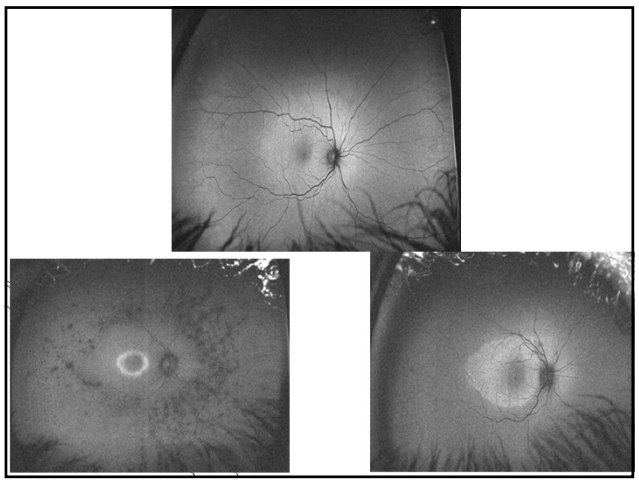


Father: Normal



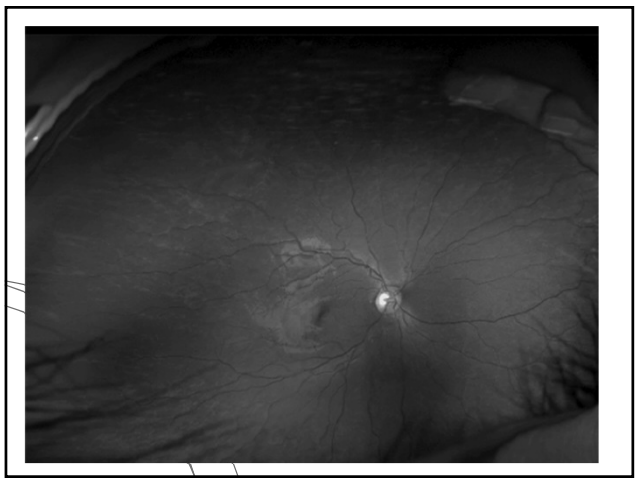
Asymptomatic son

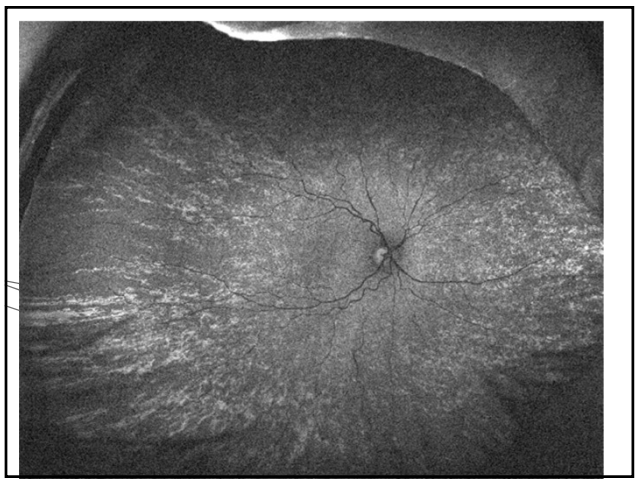


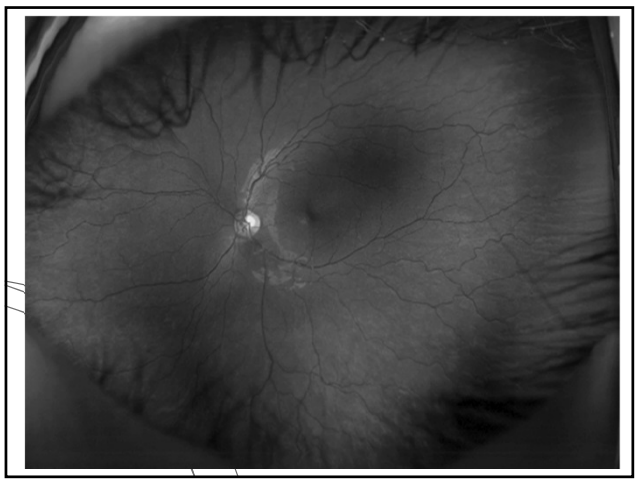


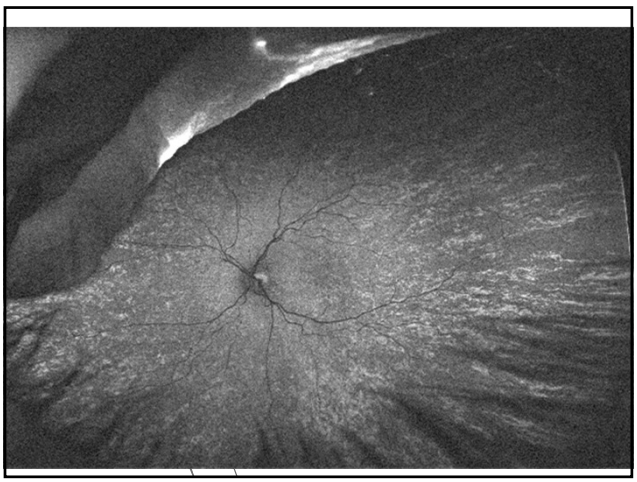
Radial Flecks?

- 21 y-o female
- 20/20 VA OD and OS
- No complaints
- Referred for evaluation of “radial flecks”

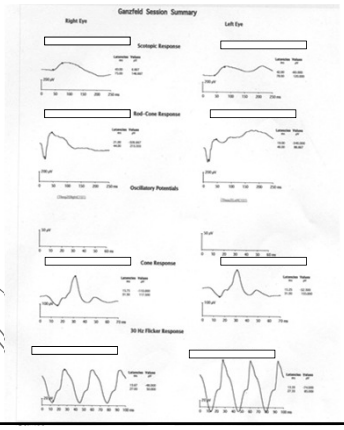


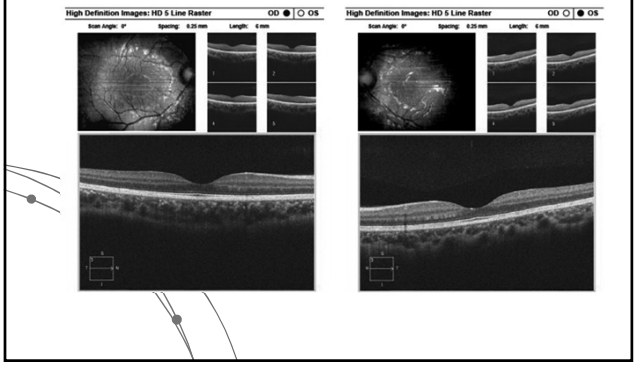






NORMAL ERGs


Ganzfeld Session Summary
Right Eye
Left Eye
Scotopic Response
Rod-Cone Response
Oscillatory Potentials
Cone Response
30 Hz Flicker Response

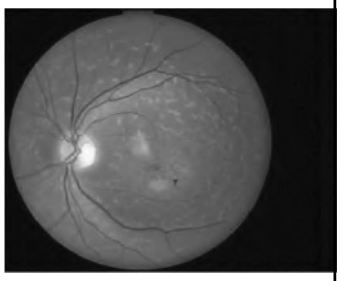

High Definition Images: HD 5 Line Raster
OD ● ○ OS
Scan Angle: 0°
Spacing: 0.25 mm
Length: 6 mm
High Definition Images: HD 5 Line Raster
OD ○ ● OS
Scan Angle: 0°
Spacing: 0.25 mm
Length: 6 mm

Ocular albinism carrier

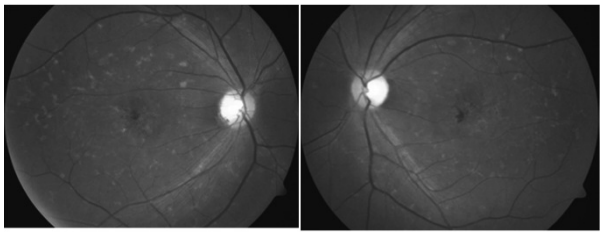
- Mud splattered appearance on FAF
- Father has ocular albinism
- Normal vision
- Normal ERG
- Normal OCT

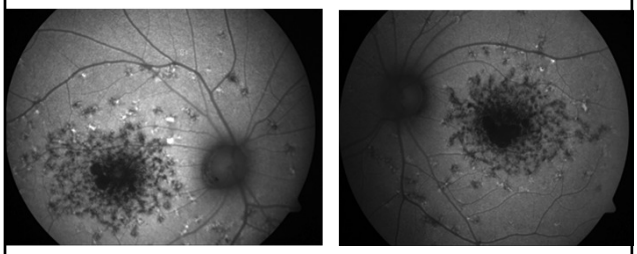
Stargardt Disease
(Stargardt/Fundus Flavimaculatus)

- Autosomal recessive
- 1:10,000 births in US
  - 30,000 cases
- May have macular Involvement
- May have scattered fish-tailed “flecks”
  - lipofuscin
- VA reduction in teen yrs.
- Usually symmetric



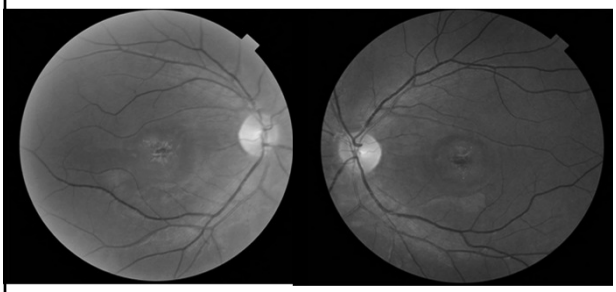
Typical Stargardt Disease

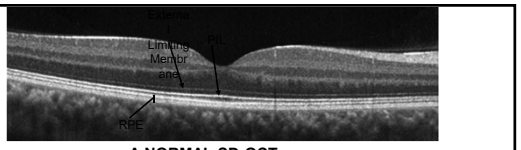




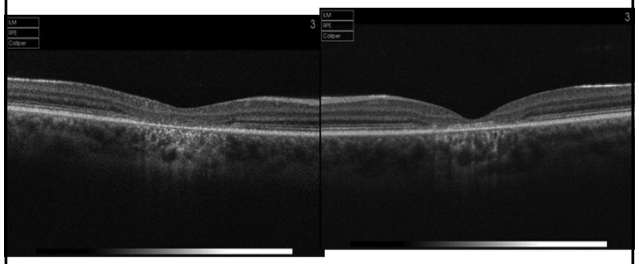
Law Student Can't Read!

- 22 year-old female law student
- CC: Having difficulty reading
- BCVA OD:20/70 OS: 20/70
- Went to "several" eye doctors
- Diagnoses:
  - Don't know
  - "Eye strain"; VT recommended

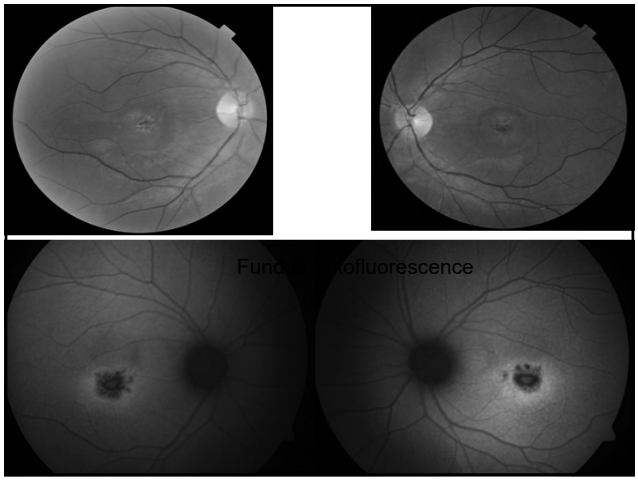


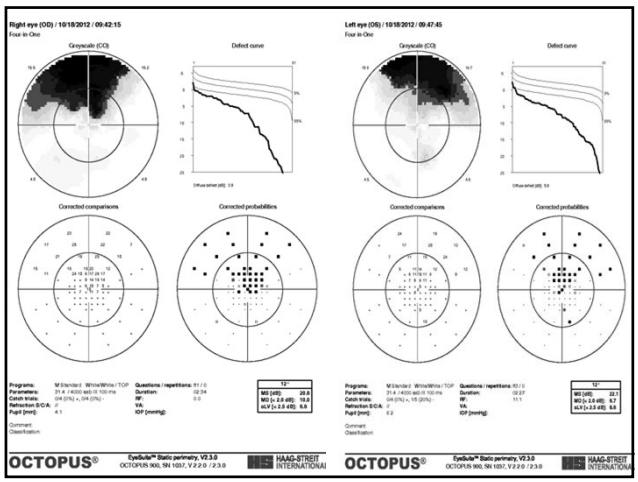


A NORMAL SD-OCT

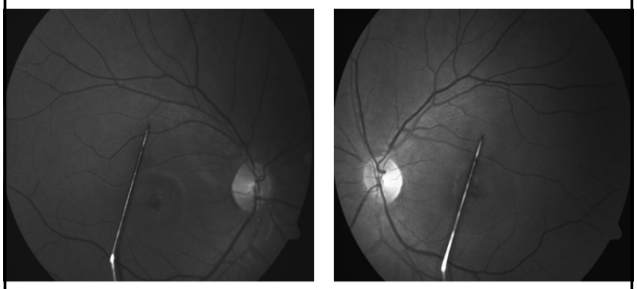


OD OS

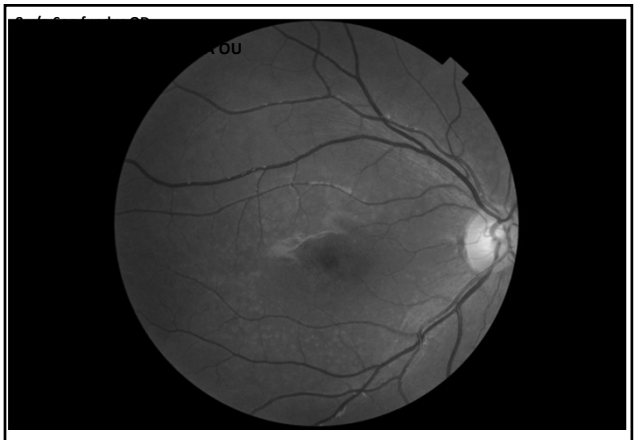




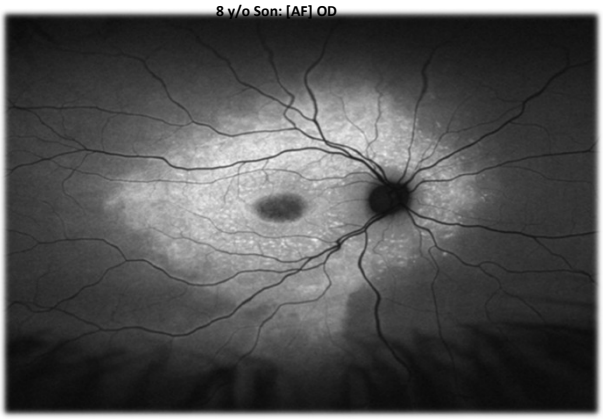
Why The Superior Paracentral Field Defect?

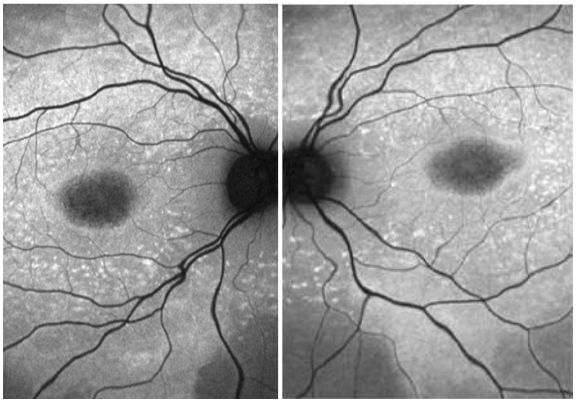


Early Stargardt Disease

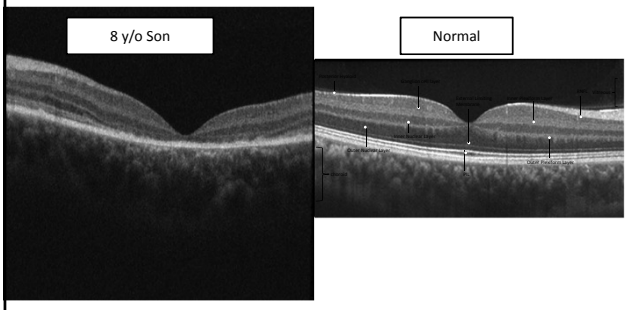


8 y/o Son: [AF] OD

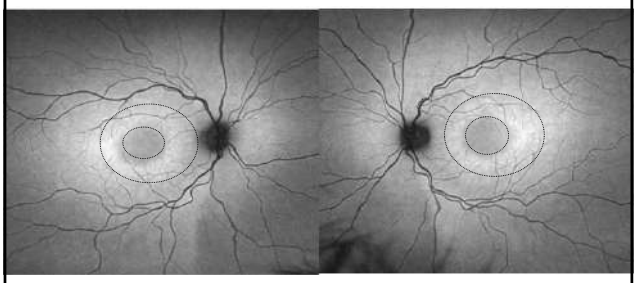




I

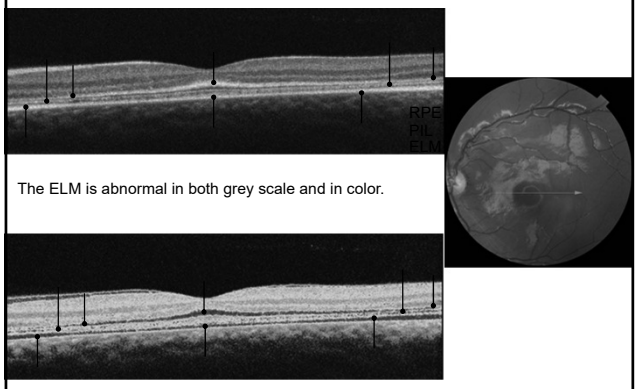


Case 2(5 yo daughter): Optomap® FAF Image OD and OS



The AF images reveal a subtle macula bulls eye in each eye. Note the hyper-AF ring around the macula in each eye. This pattern is abnormal.

Case 2(5 yo daughter): Topcon 3D OCT OS

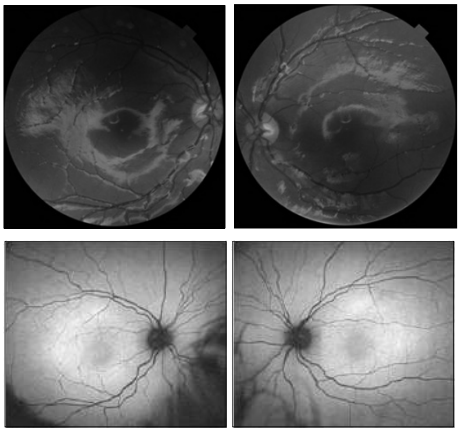


The ELM is abnormal in both grey scale and in color.

Case 3(4 yo daughter): Fundus Photography

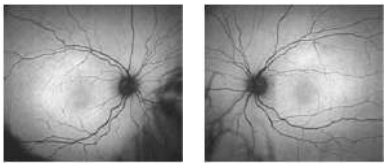
KEY:
Standard Photo
Auto Fluorescence

No marked abnormality is obvious in the color fundus photos or in the AF images in the 4 yo daughter.



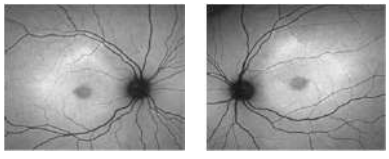
Stargardt Disease: 4yo female

initial presentation



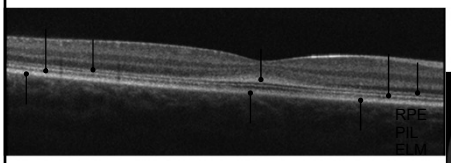
VA 20/25

39 mo follow up

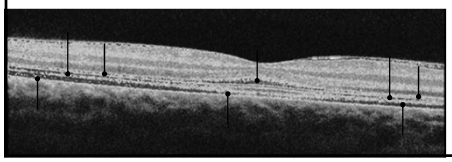


VA 20/20

Case 3(4 yo daughter): Topcon 3D OCT OD



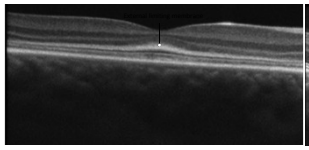
With parental consent, chocolate was used to bribe the 4 yo. Cooperation improved for the OCT images. As revealed in her 5 yo sister, the PIL is somewhat thin and the ELM is thickened, irregular and hyper-reflective here in the right eye.



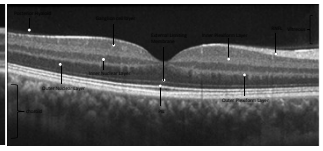
5 y/o daughter OD vs Normal

Does photoreceptor degeneration result in debris accumulating on ELM?

5 y/o daughter



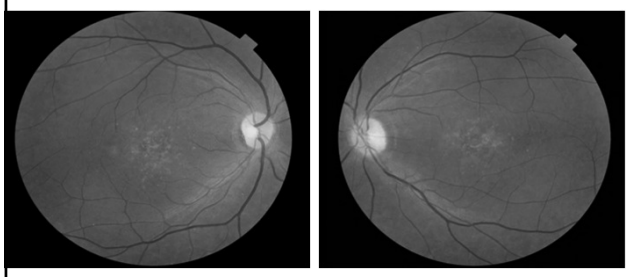
Normal



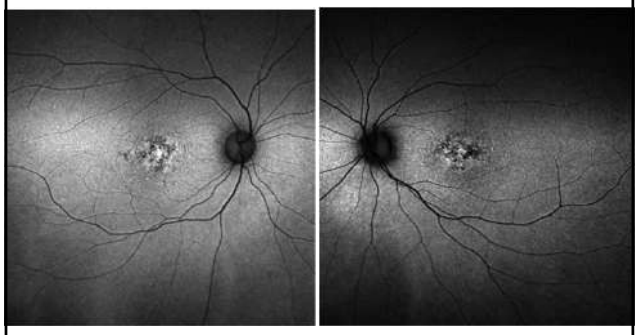
A Novel Finding which may be a biomarker for very early degen in SD

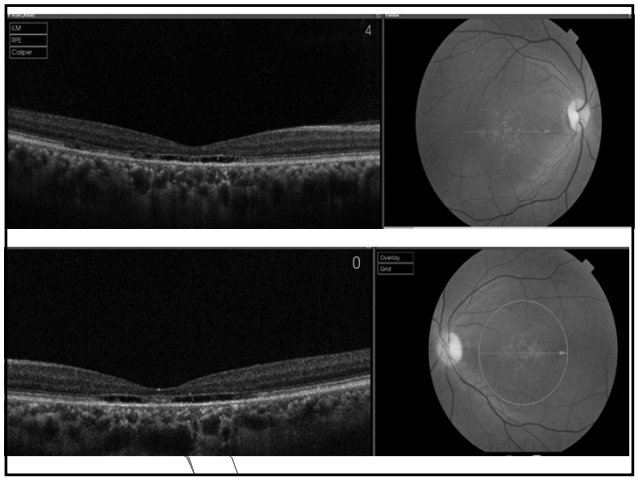
Decreasing Vision

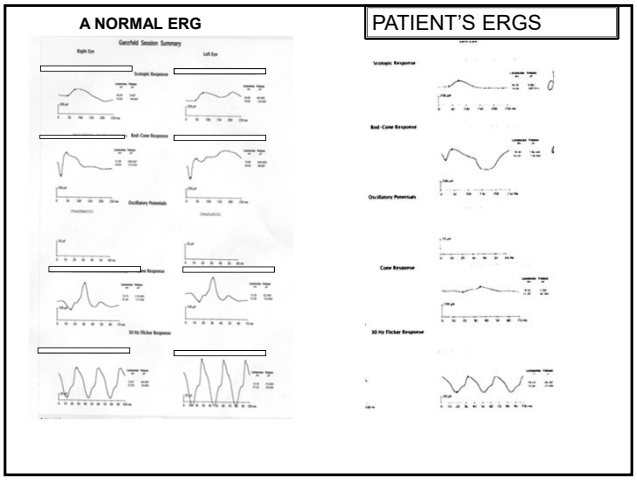
- 46 y-o black female
- h/o 20/20 to 20/25 OD and OS
  - Decreasing BCVA last few years
    - 20/30 OD and 20/40 OS in 2011
    - 20/40 OD and 20/60 OS in 2012
  - Poor color vision her whole life
    - Severe color defect on Ishihara plates
  - No family history of progressive vision loss



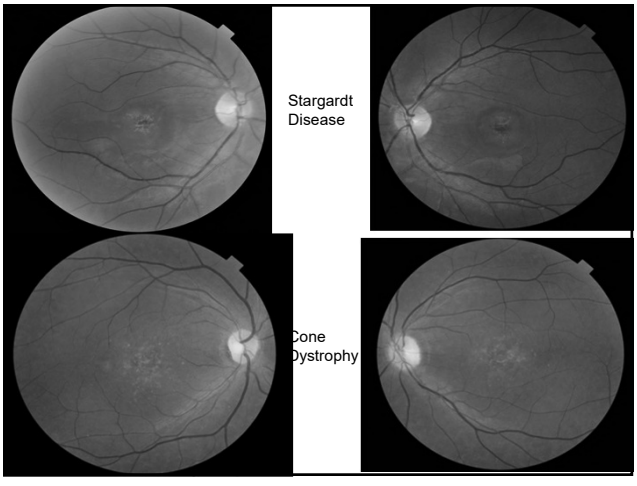
FUNDUS AUTOFLUORESCENCE PHOTOS



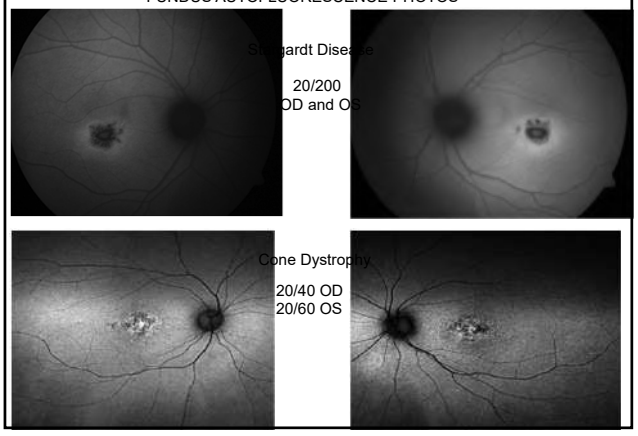




Cone Dystrophy



FUNDUS AUTOFLUORESCENCE PHOTOS



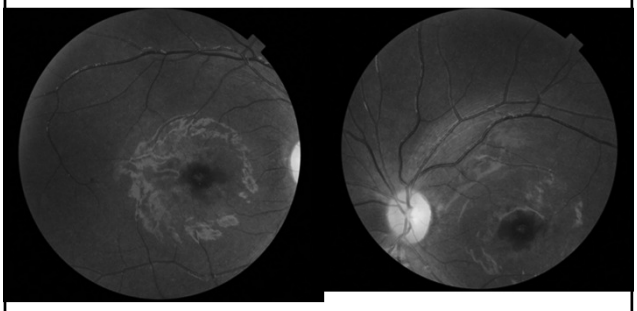
Stargardt Disease

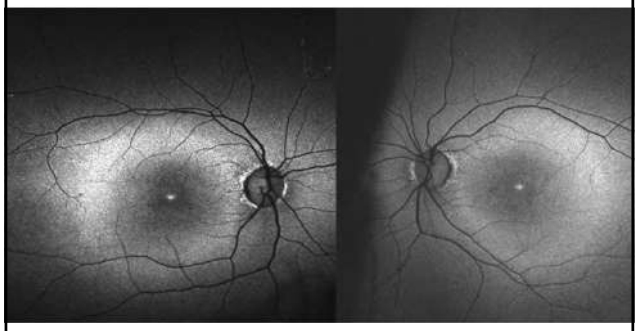
20/200
OD and OS

Cone Dystrophy

20/40 OD
20/60 OS

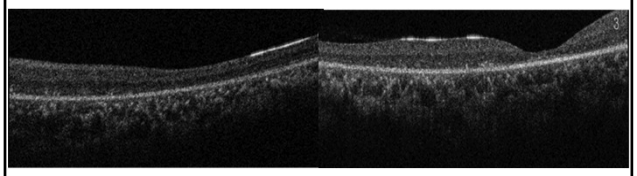
VA 20/60 OD and 20/70 OS; Fails color plates





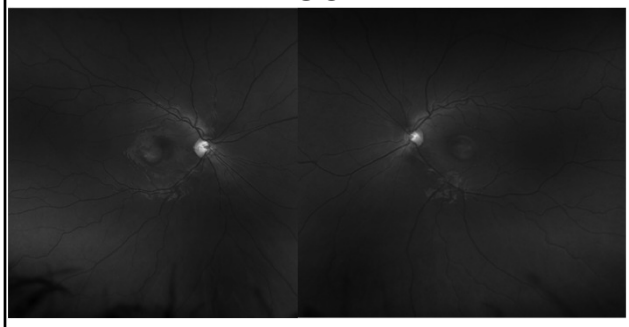
OCT

OD OS



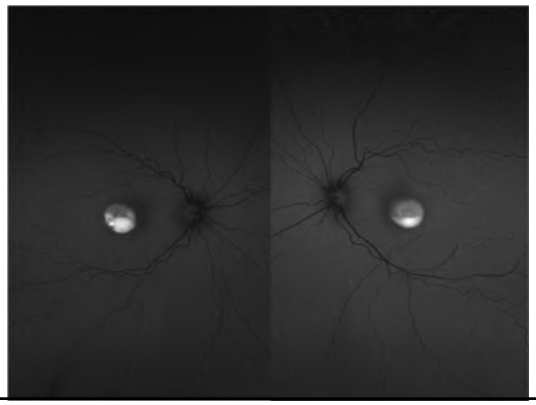
Cone Rod Dystrophy

OU



“Best” Best

OU



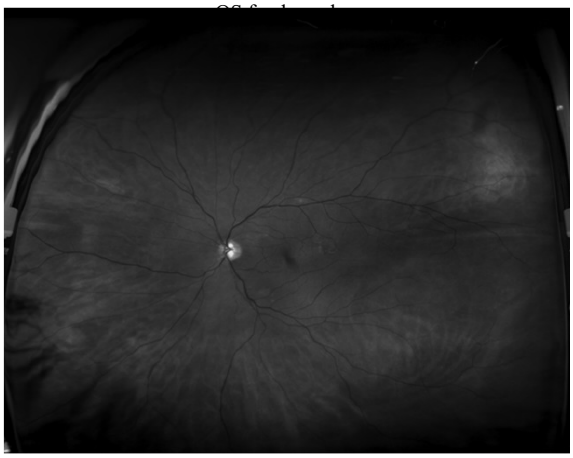
FAF in Acquired Retinal Disease

60 y/o HM

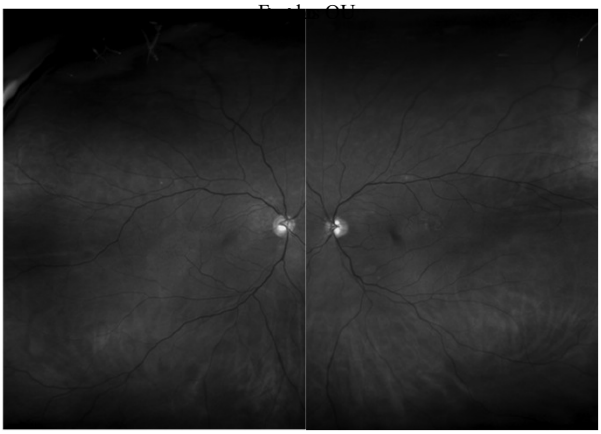
BCVA OD: 20/70
OS: 20/25

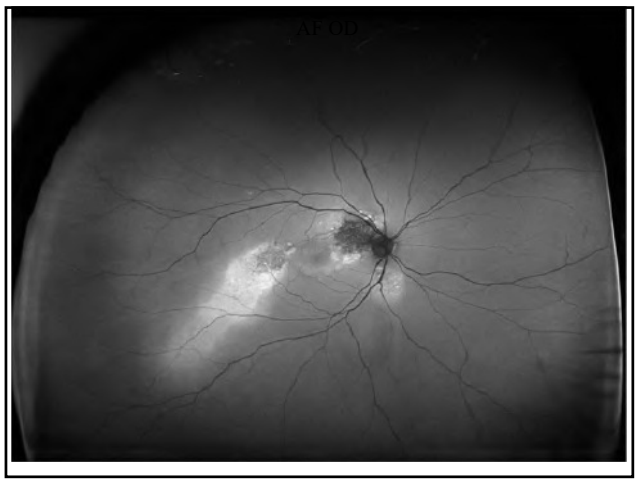
OD fundus color

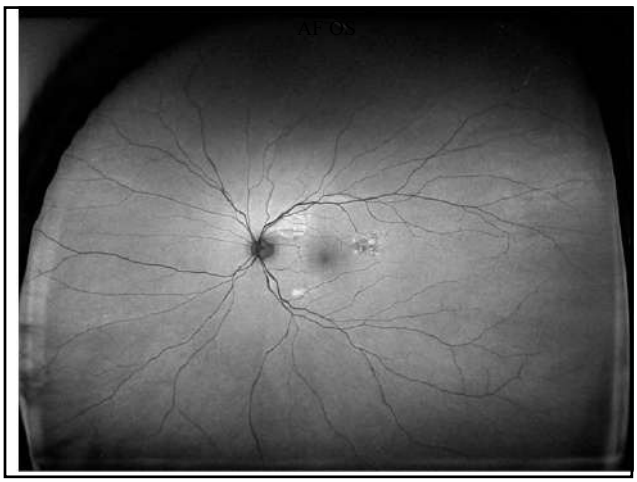
OS fundus color

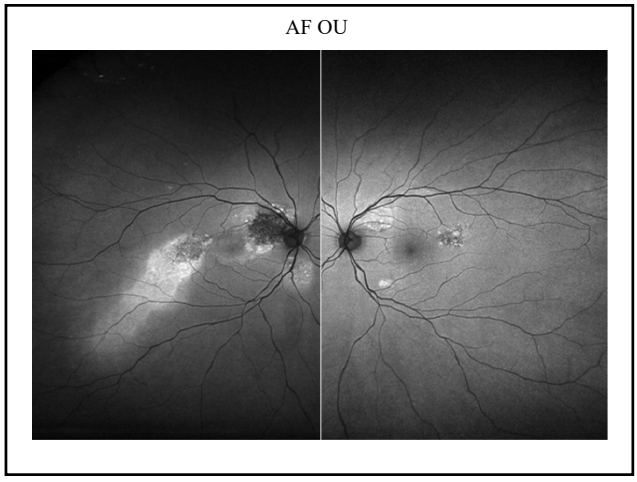


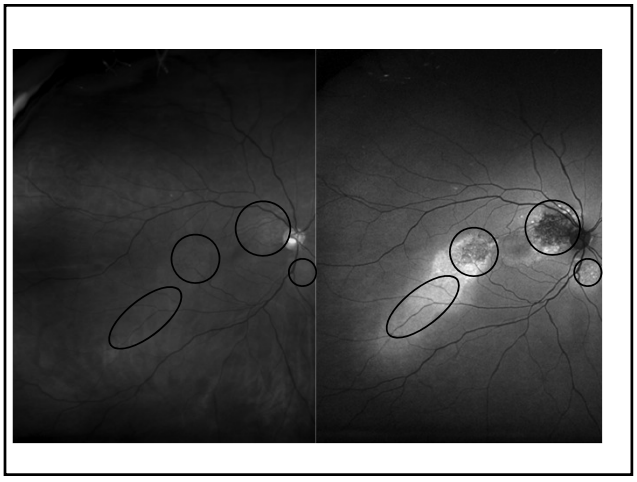
Fundus OU

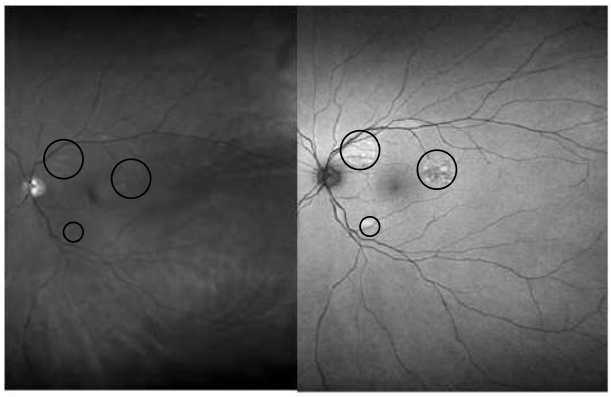



AF OD

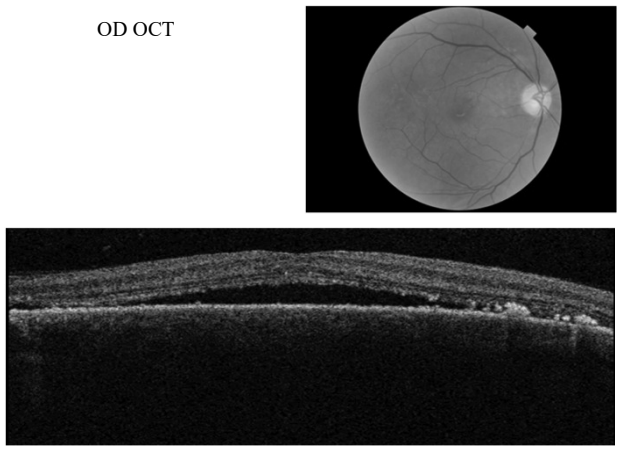

AF OS


AF OU



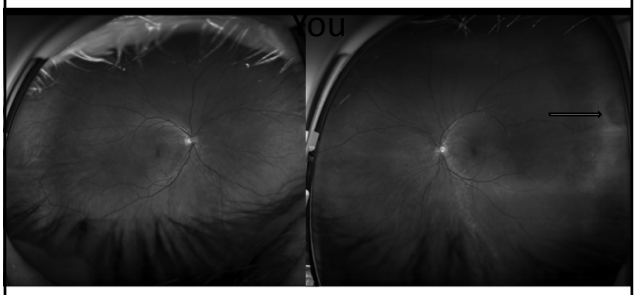


OD OCT

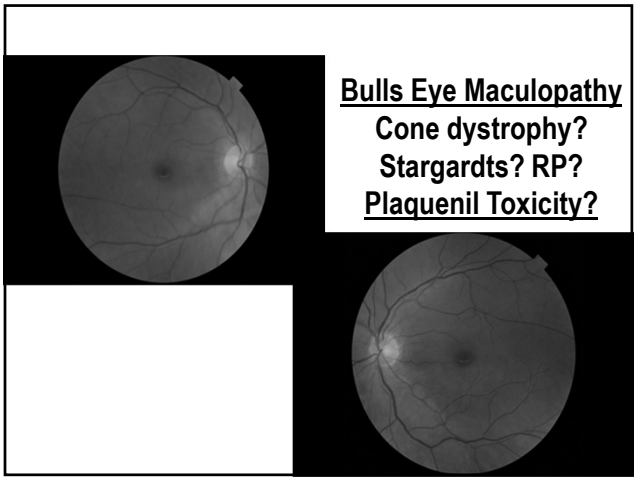


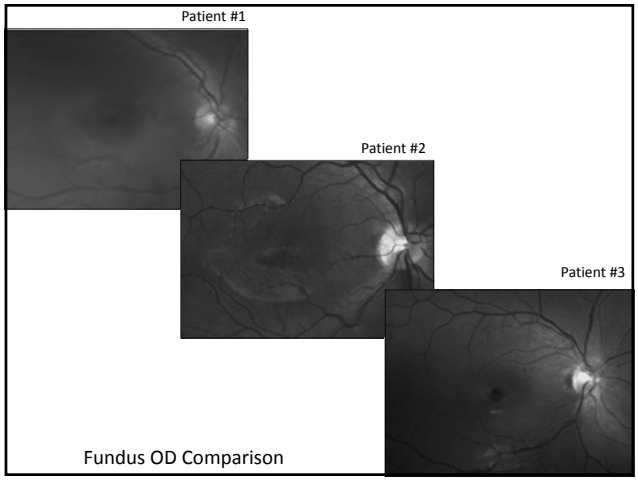
Chronic Central Serous Choroidopathy

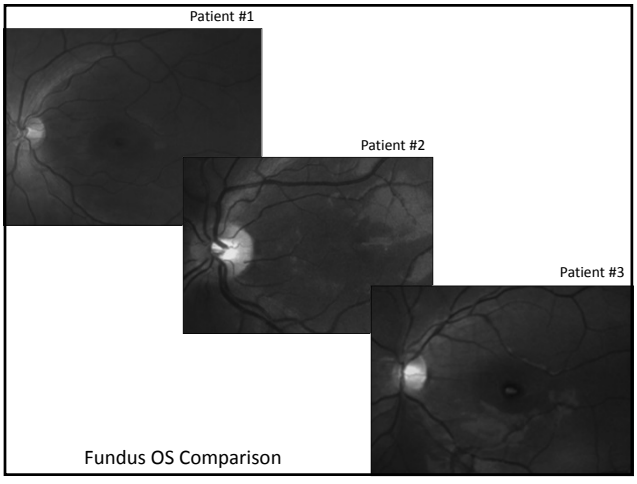
Next Case:
Referral for a possible hole OS?
You

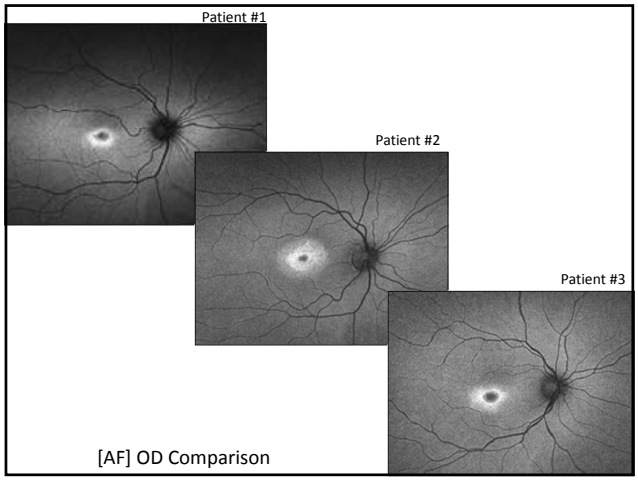


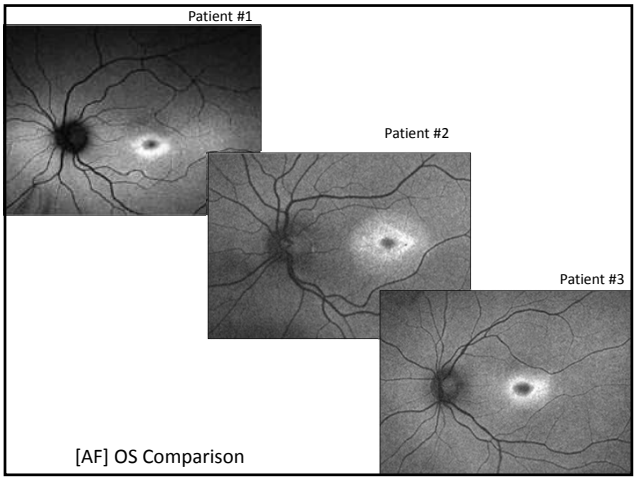

Descending Tracts

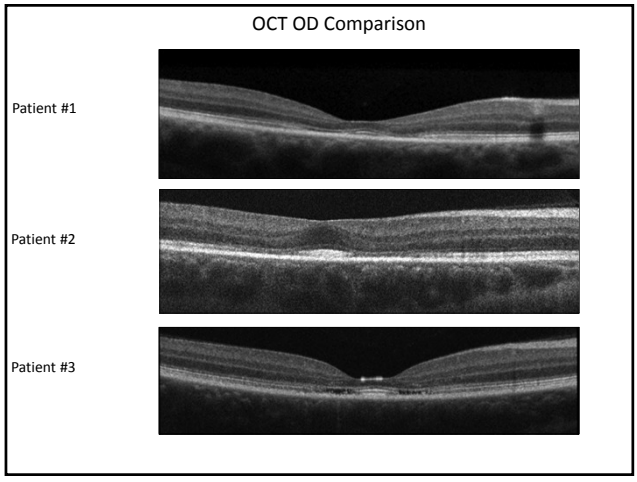

Bulls Eye Maculopathy
Cone dystrophy?
Stargardts? RP?
Plaquenil Toxicity?

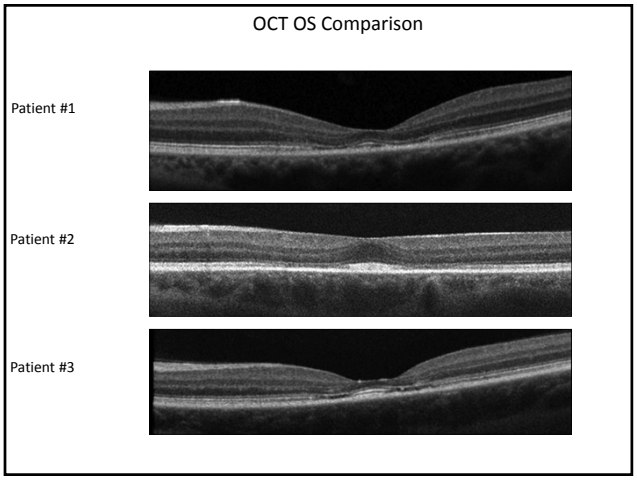

Patient #1
Patient #2
Patient #3
Fundus OD Comparison


Patient #1
Patient #2
Patient #3
Fundus OS Comparison


Patient #1
Patient #2
Patient #3
[AF] OD Comparison


Patient #1
Patient #2
Patient #3
[AF] OS Comparison


OCT OD Comparison
Patient #1
Patient #2
Patient #3


OCT OS Comparison
Patient #1
Patient #2
Patient #3

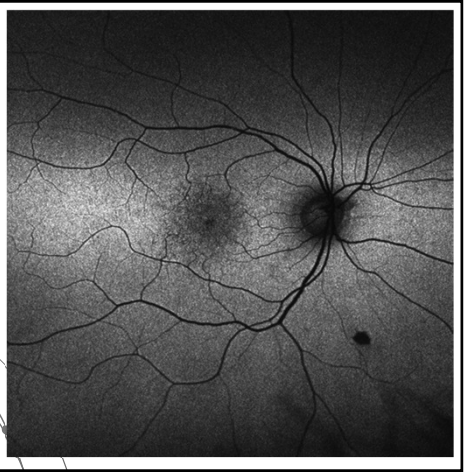
Drusen

Next Case

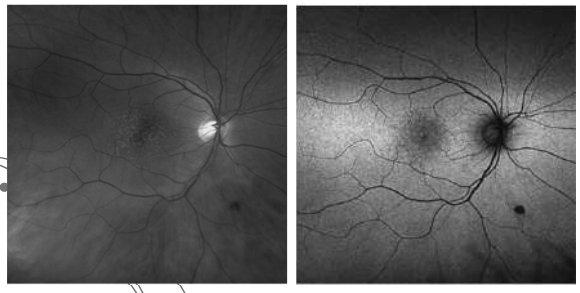
Central (Macula) Drusen

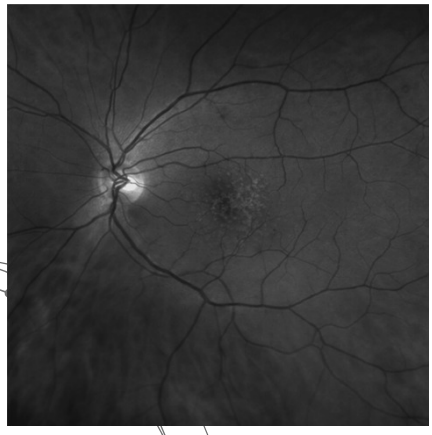
OD Res Max Composite

OD Res Max AF

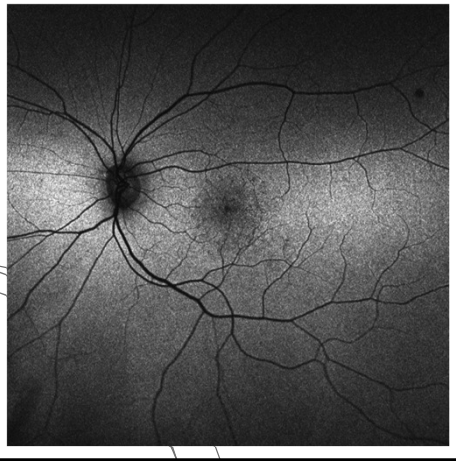


OD Res Max Composite vs. AF



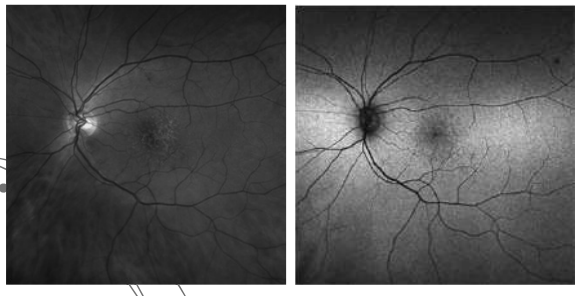


OS Res Max Composite



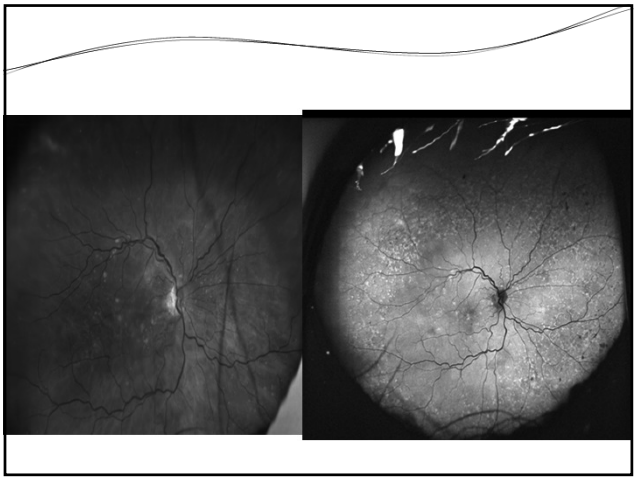
OS Res Max AF

OS Res Max Composite vs. AF

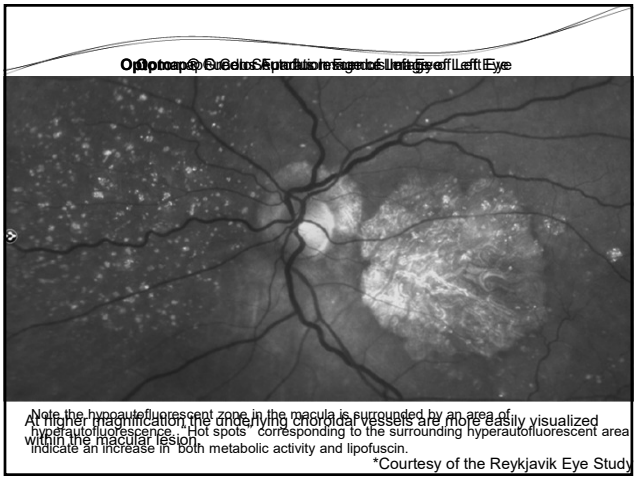


Next Case

Drusen and RPE changes

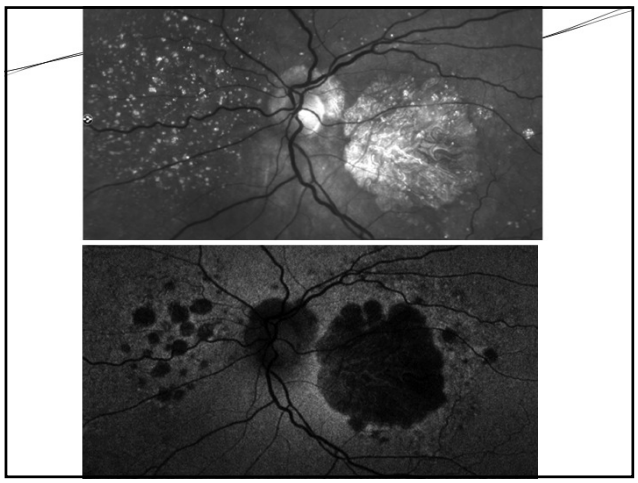


Geographic Atrophy of the RPE



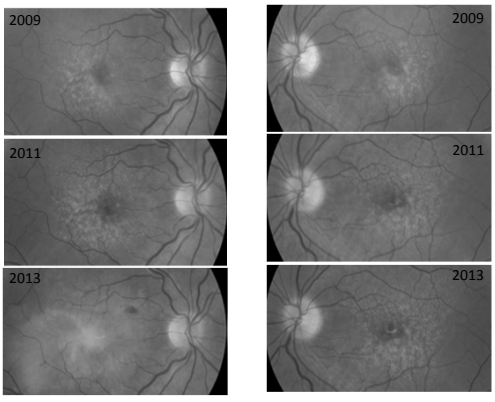
Note the hypoautofluorescent zone in the macula is surrounded by an area of hyperautofluorescence. "Hot spots" corresponding to the surrounding hyperautofluorescent area indicate an increase in both metabolic activity and lipofuscin.

*Courtesy of the Reykjavik Eye Study



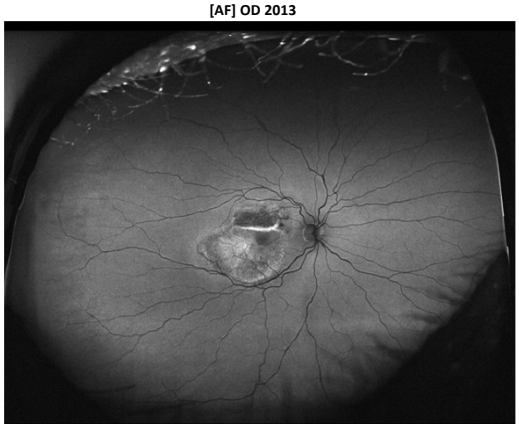
Wet AMD

2013

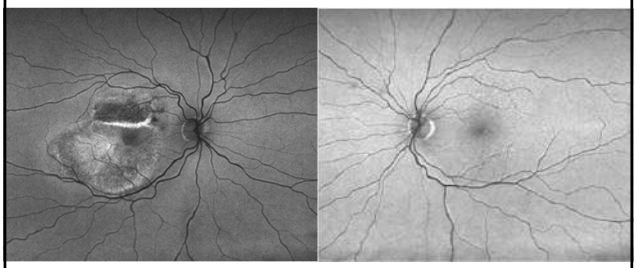


Optomap Color Fundus OD 2013

[AF] OD 2013

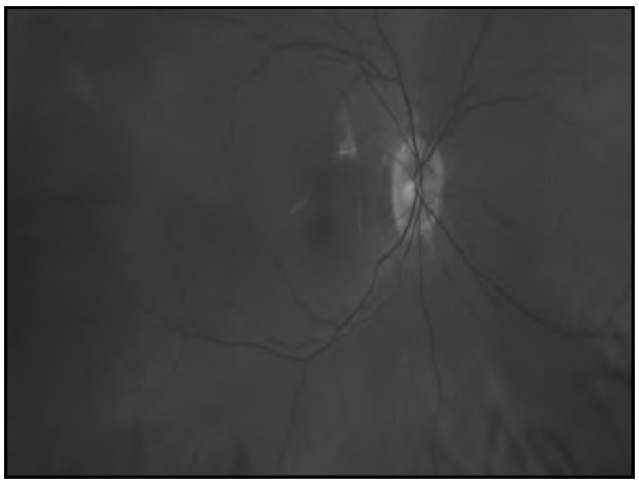


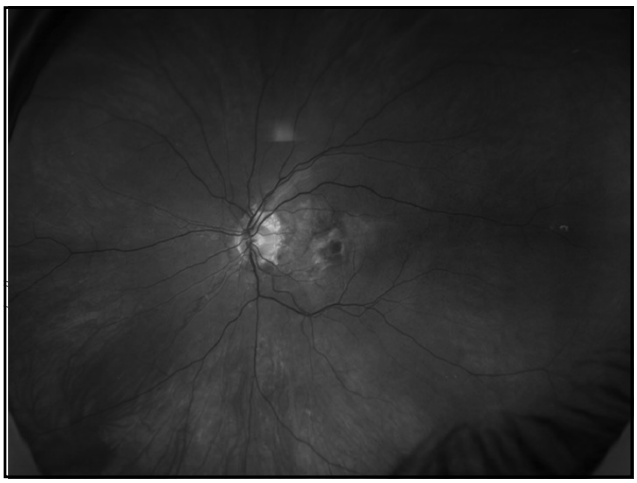
[AF] OD & OS 2013

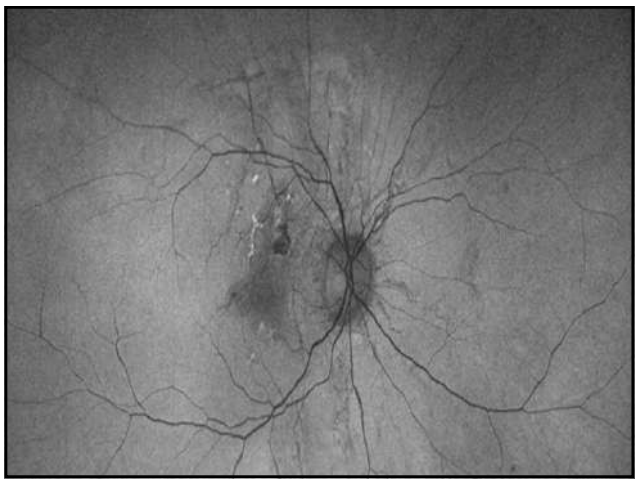


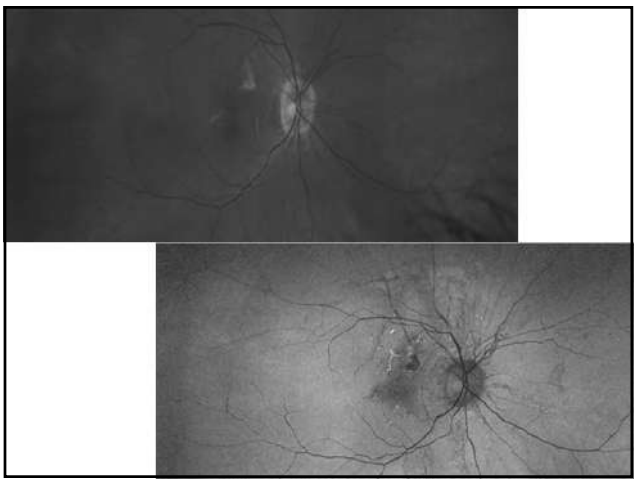
Next Case

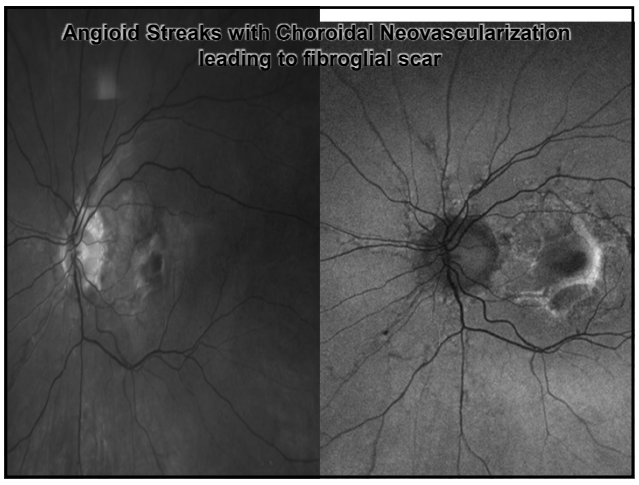
Referral: Why Wet AMD at age 40?



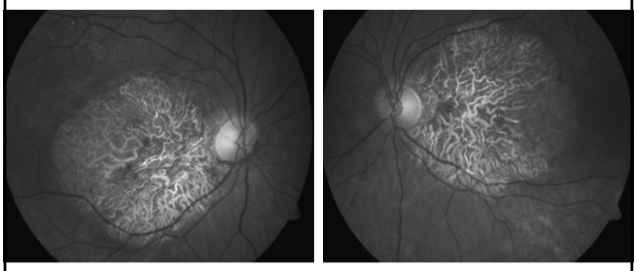




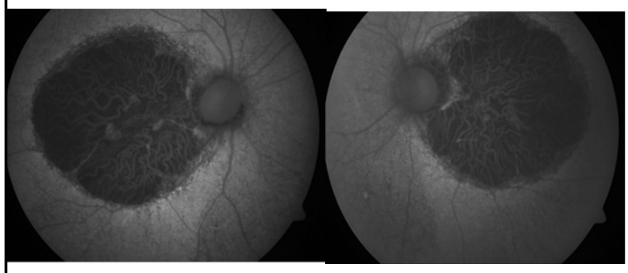


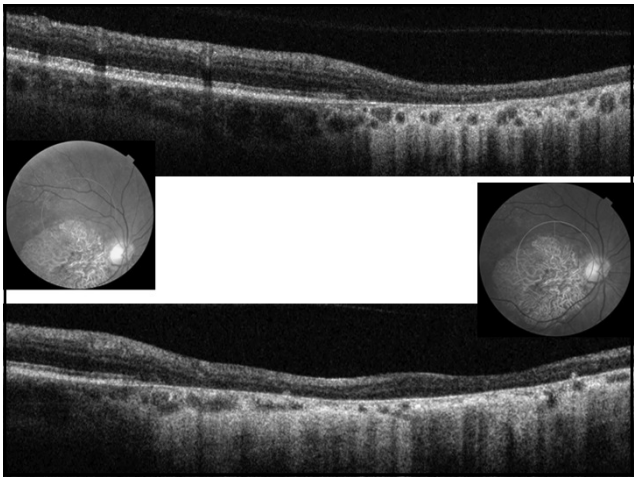


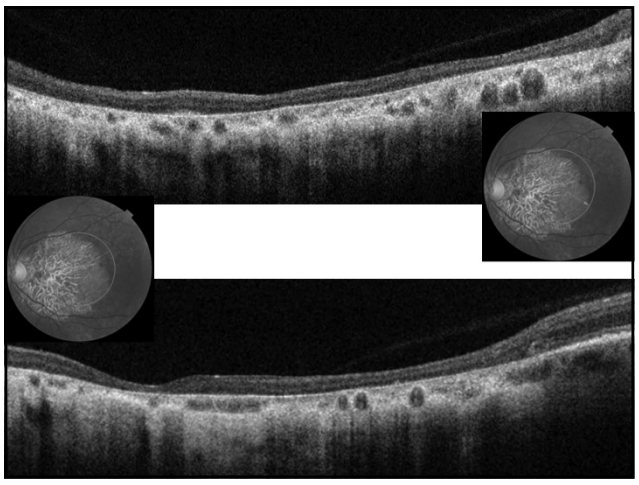
Diagnosis?



Dx: Geographic Atrophy of the RPE vs Central Areolar Choroidal Dystrophy (CACD)



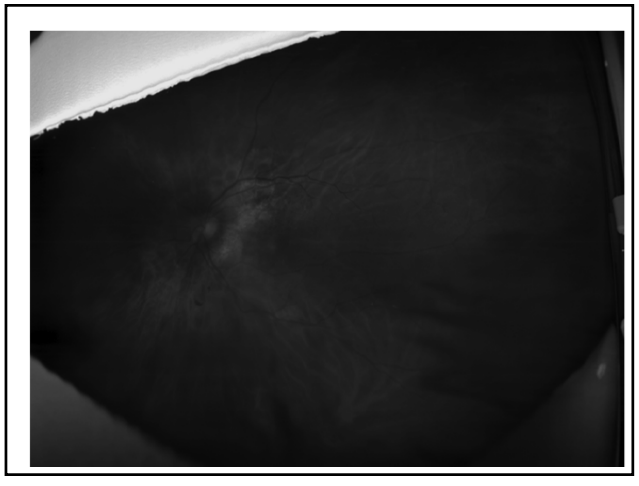


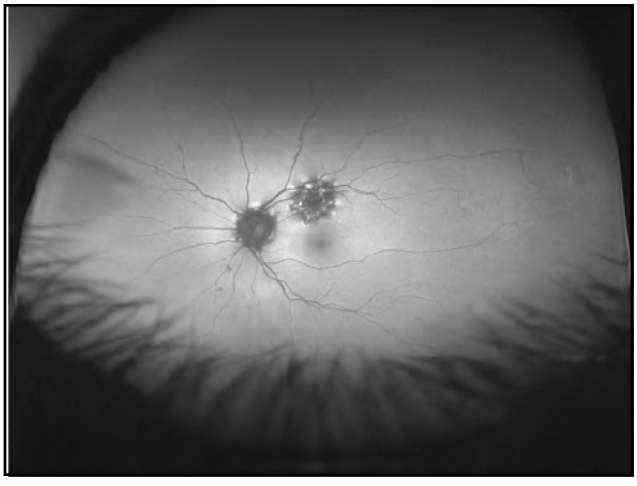


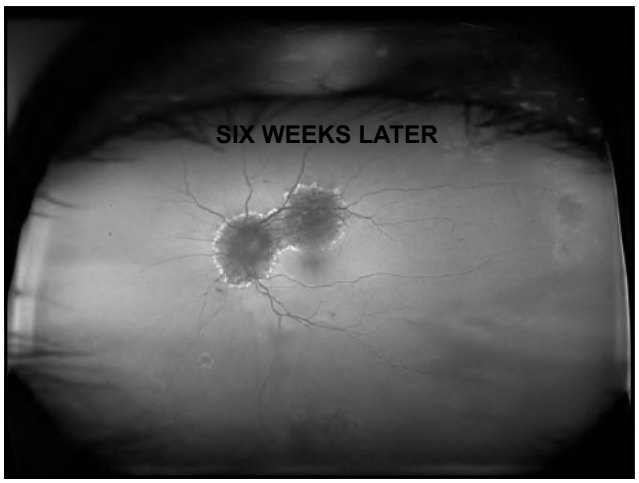
Mysterious Lights?

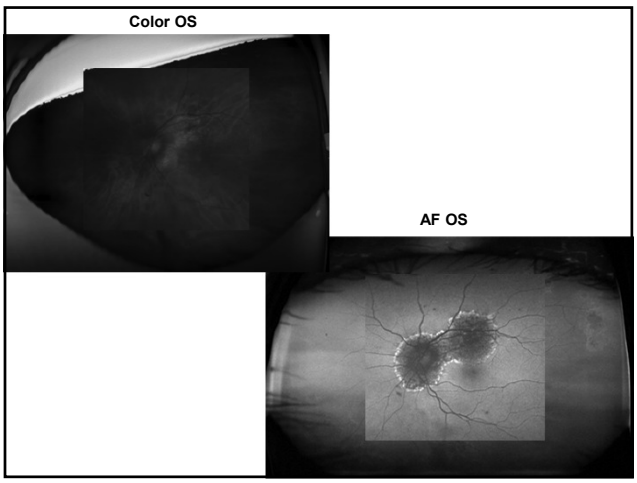
69 yo white female

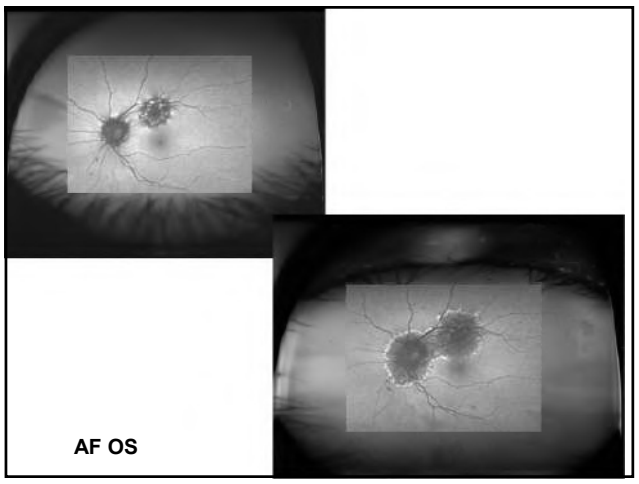
30 yr history of strange photopsias
OD but recent OS

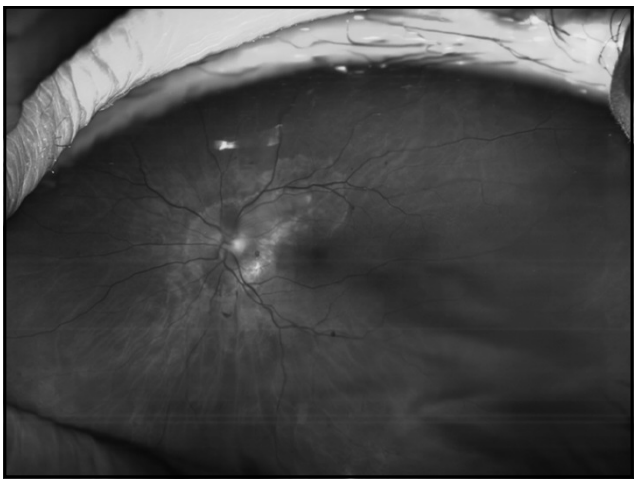


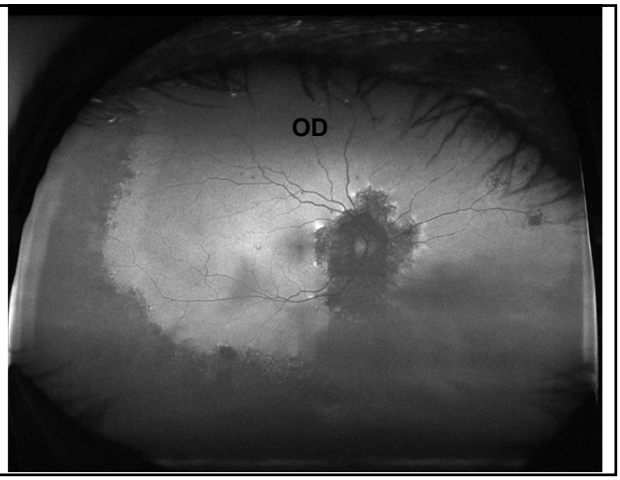


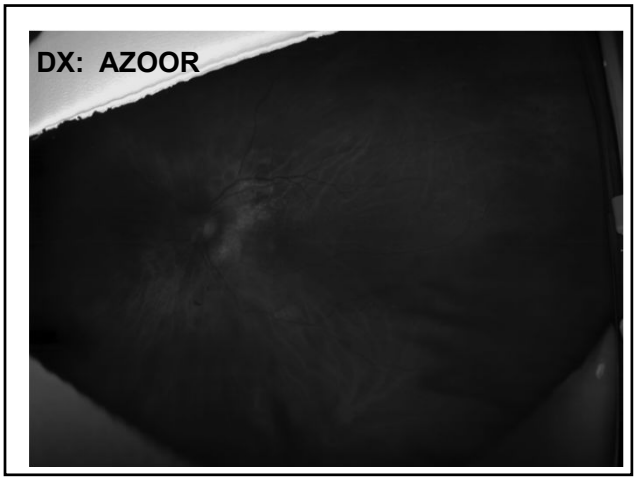

SIX WEEKS LATER


Color OS
AF OS


AF OS







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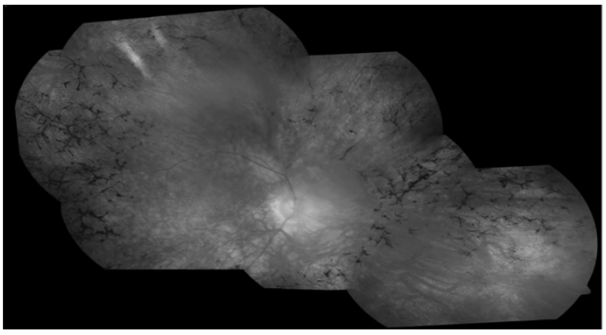
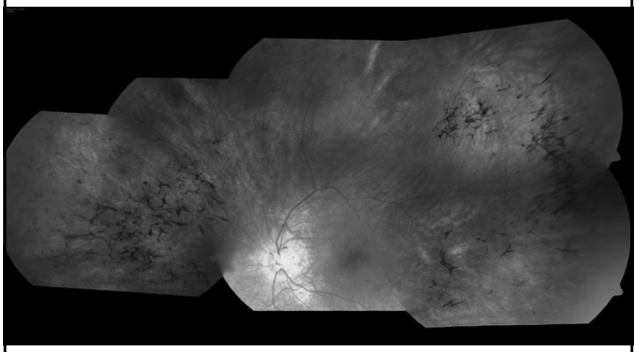
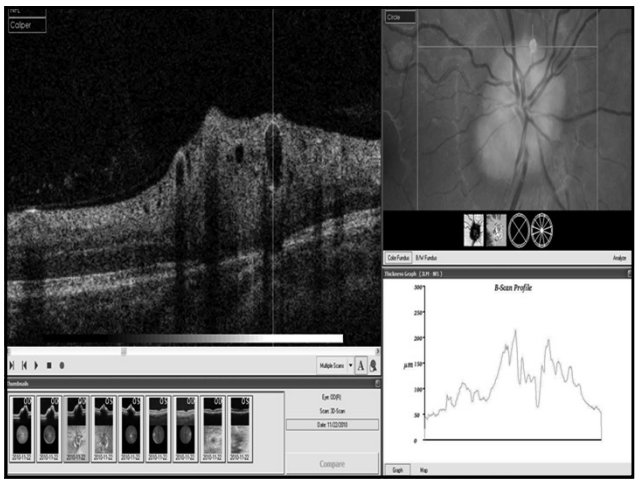
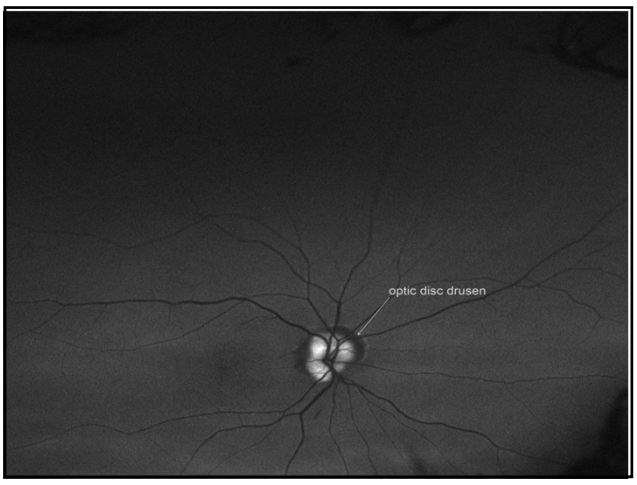
case 19



GASS AZOOR 1993

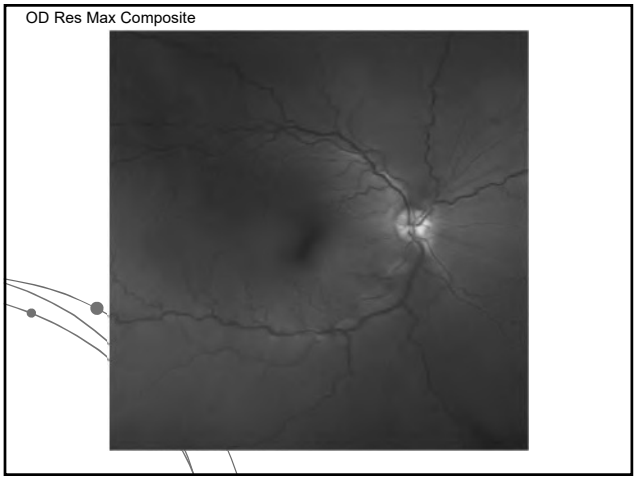




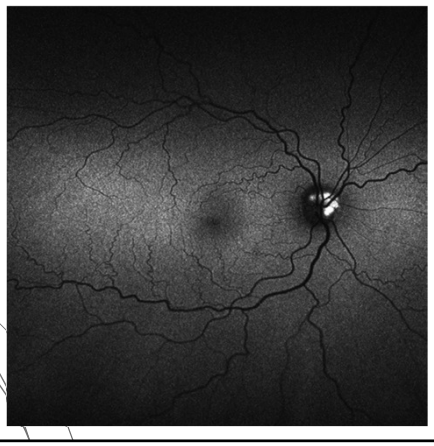


Next Case

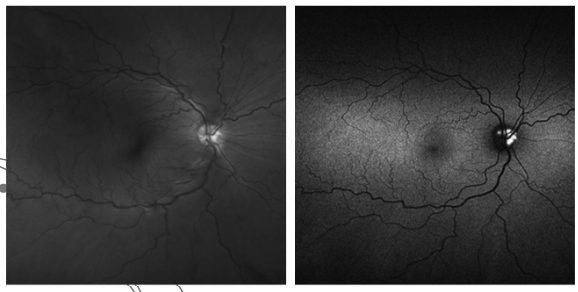
Buried Disc Drusen
revealed with AF
(with congenital tortuosity)



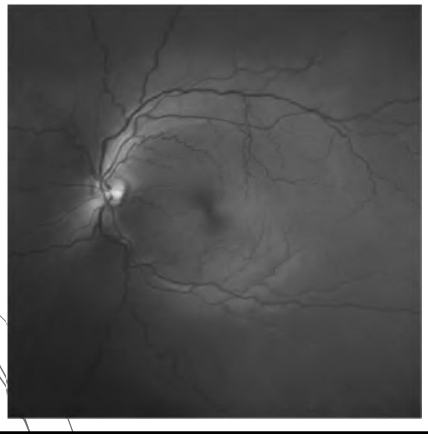
OD Res Max AF



OD Res Max Composite vs. AF

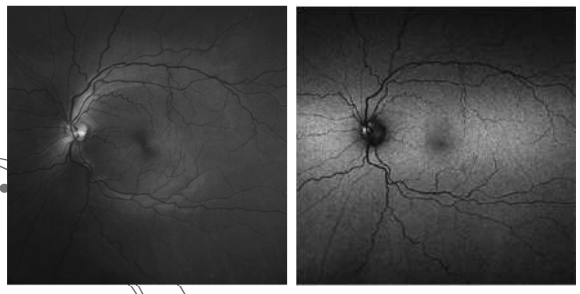


OS Res Max Composite



OS Res Max AF

OS Res Max Composite vs. AF

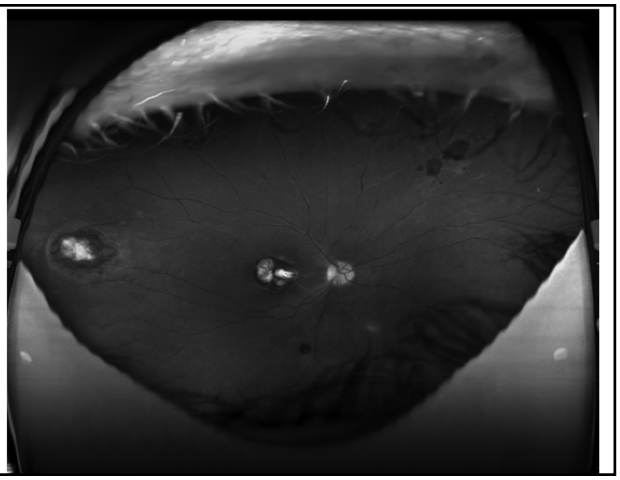


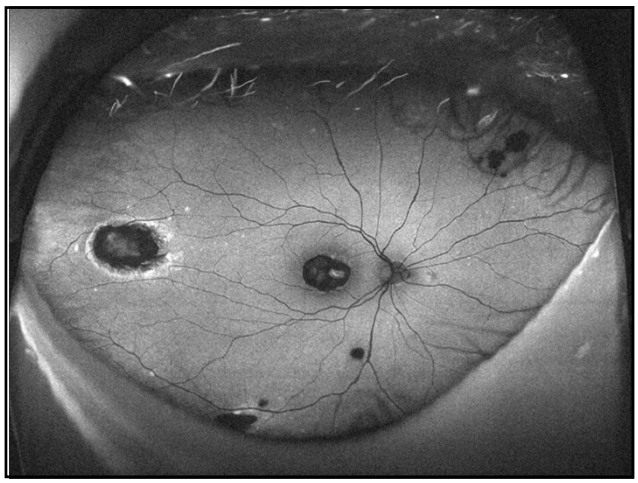
Next Case

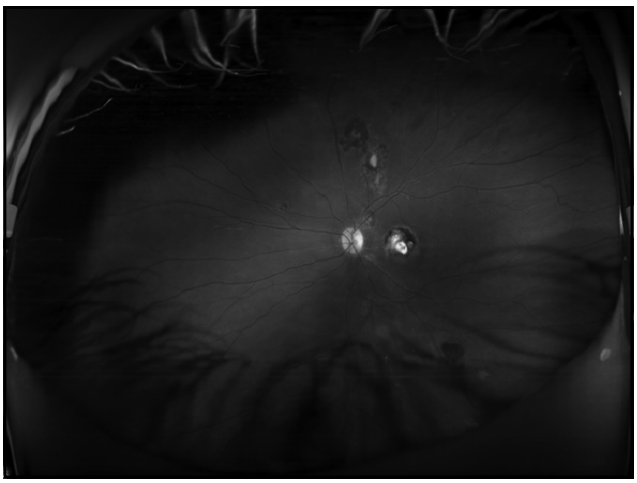
Congenital Toxoplasmosis
?reactivation

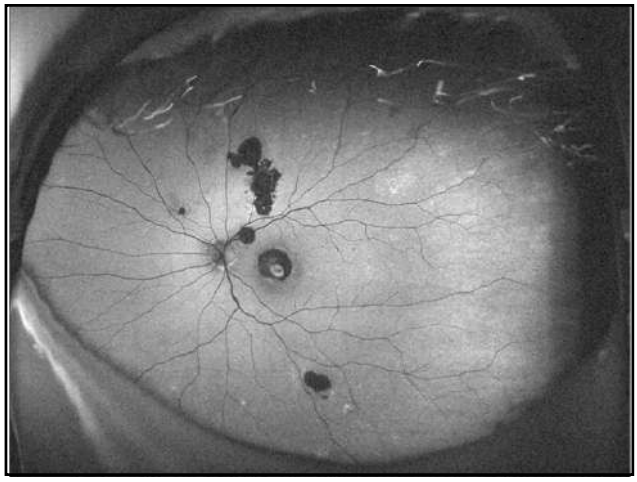
H/O congenital toxo

Explanation for hyper AF ring ?



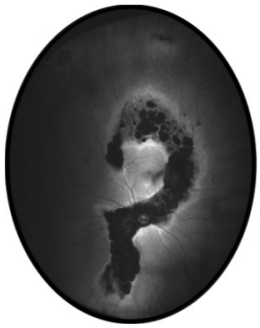




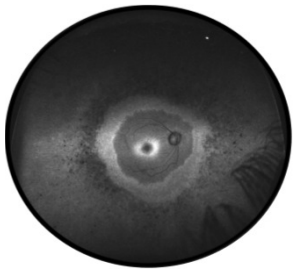


What novel information does it give us?

- Fundus Autofluorescence (FAF or AF) is a novel, non-invasive imaging procedure that often yields abnormalities that are invisible to ophthalmoscopy and standard color fundus photography.
- FAF is likely due to lipofuscin, the "wear and tear" pigment found in retinal cells, especially RPE cells.
- The normal retinal pigment epithelium (RPE) yields a slightly granular AF glow in contrast to the optic disc and retinal blood vessels which appear black.
- Hyper-AF: The accumulation of lipofuscin, often due to lysosomal dysfunction, results in increased AF and suggests RPE dysfunction or stress.[1]
- Hypo-AF: Decreased FAF suggests loss of RPE cells (as well as possibly photoreceptors) and correlates to reduced levels of lipofuscin



Thank You!



sbass@sunyopt.edu