

# Fundus Autofluorescence: Applications for Clinical Practice

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## Disclosures

- No financial disclosures
- [brsutton@indiana.edu](mailto:brsutton@indiana.edu)

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## History of fundus imaging

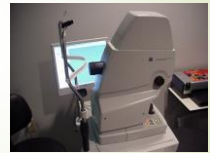
- Direct Ophthalmoscope
- Helmholtz in 1850
- BIO
- Ruethe in 1852



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## Fundus photography

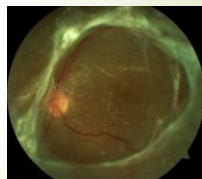
- Jackson and Weber in 1886
- Camera was fixed to the patients head
- Exposure time of 2.5 MINUTES!



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## Fundus Photography

- 1959: electronic flash tube, black and white film
- 1980's: digital retinal imaging
- Color segmentation / multispectral imaging
- 25% R, 25% B, 50% G
- Blue: superficial NFL
- Green: retina / vessels
- Red: Choroid / RPE



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## IVFA

- 1961 by Novotny and Alvis
- Indocyanine green angiography in the 1990's
- Statistically very safe, but invasive with extremely small chance of significant complications
- Common "nuisance" complications



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## OCT

- 1991 James Fujimoto at MIT
- Original research instrument 400 A-scans / second
- Current SD-OCT 27,000 A-scans / sec
- Current Swept Source-OCT 249,000 A-scans / sec



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## OCT

- First commercial OCT company in 1992: Advanced Ophthalmic Devices
- Sold on August 27<sup>th</sup> of 1993 to Humphrey-Now Carl Zeiss Meditec
- First commercial OCT from them in 1996, 10,000 units sold by 2008
- Now 8 companies with OCT's



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## OCT Angiography

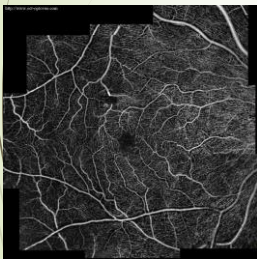
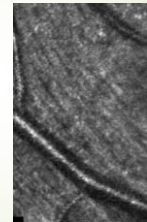
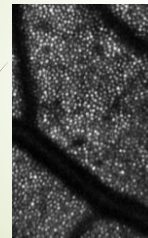


Image: oct.optovue.com

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## Adaptive Optics (Images courtesy of Dr. Steve Burns)



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## Fundus Autofluorescence: FAF

- Heidelberg, Zeiss, Optos, Others
- Gaining traction over about the last 15 years or so
- Recently becoming more integrated into clinical practice, with applications in multiple disease states
- Can be performed with a confocal Scanning Laser Ophthalmoscope (CSLO): example.....Heidelberg Spectralis
- Or with an FAF Camera: example Zeiss, others
- CSLO: uses a low energy laser and averages up to 30 scans
- FAF camera: uses a single, VERY bright flash (300 watt-seconds) yielding a single image

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## FAF

- Images are entirely based upon the presence of lipofuscin in the RPE
- In the eye, a byproduct of photoreceptor outer segment phagocytosis
- Accumulates in the RPE with age and certain diseases
- Also accumulates in other tissues and organs with age or disease (brain, liver, heart)
- Lipofuscin autofluoresces in the 300nm-600nm wavelength range, which is very close to visible light (400nm-700nm), so visible light can excite an emission
- Valuable diagnostic and monitoring tool in an ever increasing list of ocular conditions
- Can show damage well before it is visible to examination or in regular photos

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## FAF interpretation

- Sick or stressed RPE hyper fluoresces
- Dead, absent, or hypertrophic RPE hypo fluoresces
- The optic nerve head, blood vessels, and fovea are always hypo fluorescent (dark)
- Normal fundi are diffusely, mildly hyper fluorescent and grainy



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## Conditions in which FAF is useful

- AMD
- ICSC (central serous retinopathy)
- Plaquenil toxicity
- Nevi / melanomas, choroidal lesions
- Glaucoma
- ONH Drusen
- Macular / retinal dystrophies



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## FAF: AMD

- Useful in detecting reticular pseudo drusen, and extent of geographic RPE loss
- Very common for FAF to reveal RPE loss / stress that is not as visible or even not visible at all to examination or color photography.
- Study performed to compare the phenotypic FAF AMD appearance in various patients to the color photographs
- Fundus Auto fluorescence in Age-Related Macular Degeneration Study (FAM Study)

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## FAF AMD

- Eight different FAF phenotypes identified based upon appearance at the junctional zone
- Most had little to no correlation with the color photo appearance
- Authors concluded that FAF revealed damage not yet visible to observation
- Normal
- Minimal change
- Focal increase
- Patchy
- Linear pattern
- Lacelike pattern
- Reticular pattern
- Speckled pattern

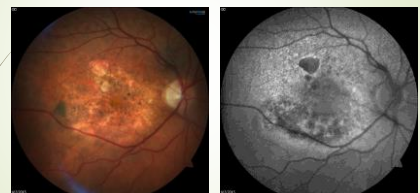
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## AMD FAF

- Very interesting finding that the rate of progression of geographic atrophy is most dependent upon the FAF pattern at the junctional zone.
- Hyperfluorescence at the junctional zone is a bad sign
- Hypo fluorescence / normal fluorescence portends slow progression
- Hyper fluorescence that is.....
- Focal = slow progression
- Banded = rapid progression
- Diffuse = rapid progression
- More predictive of progression than any other factor studied

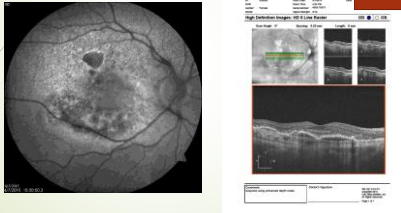
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## AMD FAF



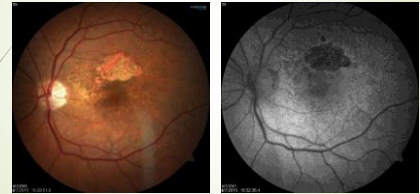
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# AMD FAF



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# AMD FAF



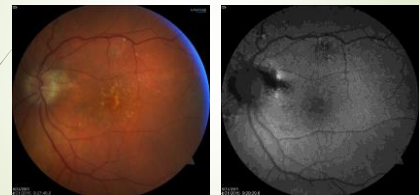
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# AMD FAF



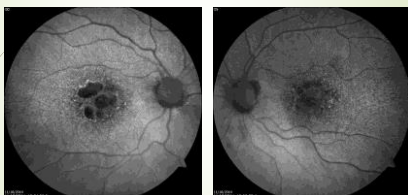
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# AMD FAF



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# AMD FAF



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# AMD FAF: 2012 TO 2015



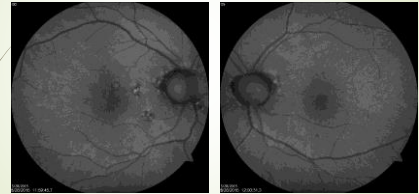
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## AMD FAF: 2012 TO 2015



25

## AMD FAF: 2012 TO 2015



26

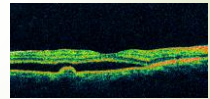
## ICSC FAF

- ICSC: related to steroids / cortisol, either by taking steroids or endogenously elevating steroids through stress
- Type A personalities
- Also linked to sleep apnea and testosterone injections / supplementation
- Focal RPE damage / PED with secondary neurosensory retinal detachment
- Metamorphopsia, decreased vision
- Recurrent and often multifocal
- Observation typically
- Topical NSAIDs, laser PDT, spirinolactone, possibly Diamox

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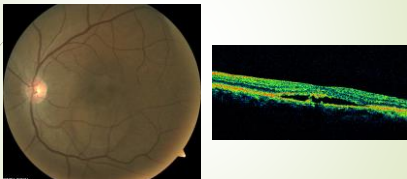
## ICSC

- FAF paints a completely different picture than funduscopy / color photography
- RPE damage and death, "troughing"
- Much greater multifocality
- ICSC has abnormally thick choroid on SD OCT EDI: Normal is 250 microns.



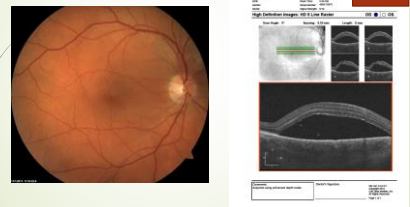
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## ICSC OCT



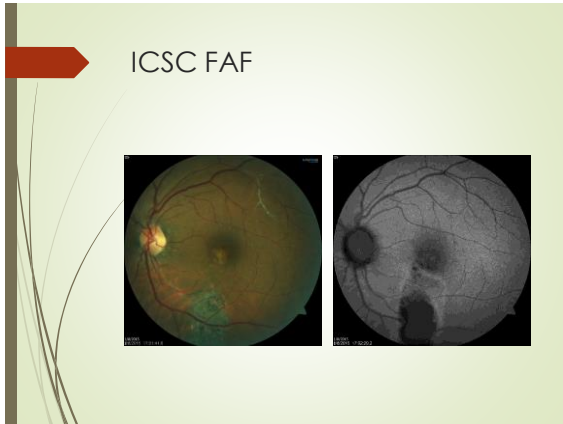
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## ICSC OCT

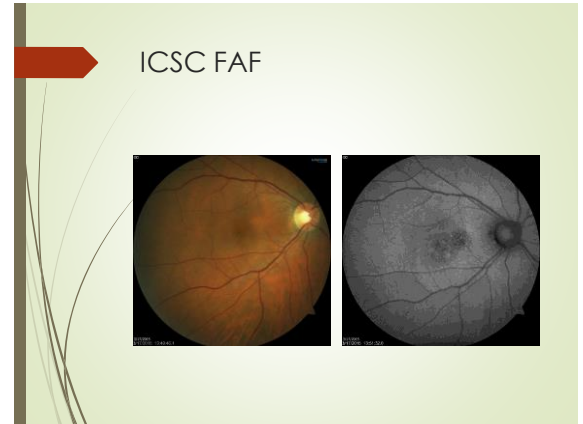


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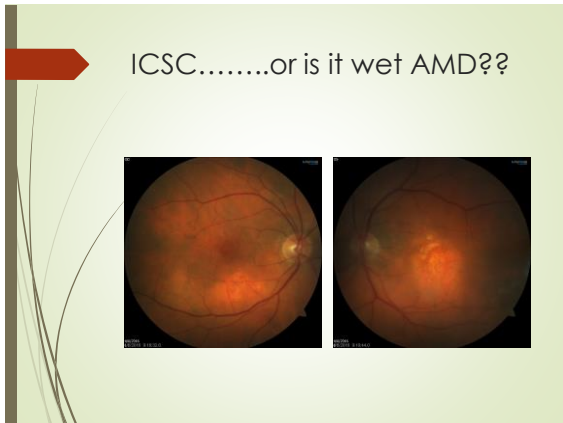




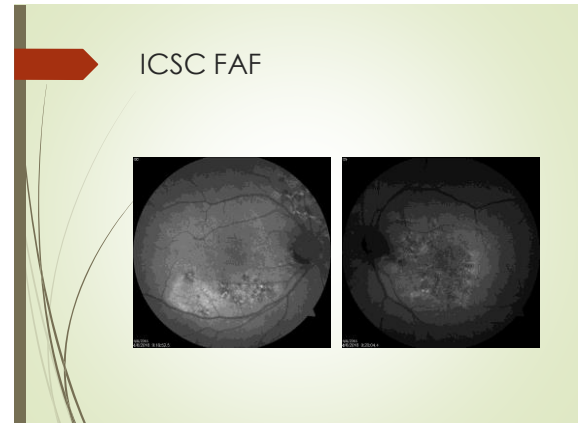
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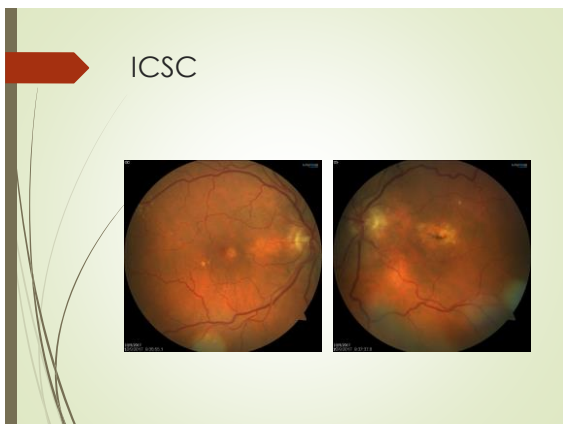
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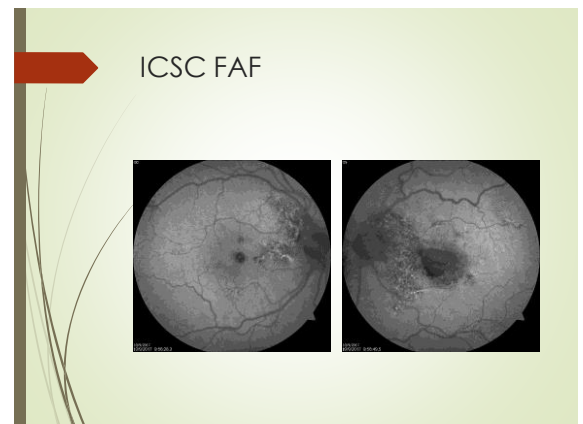
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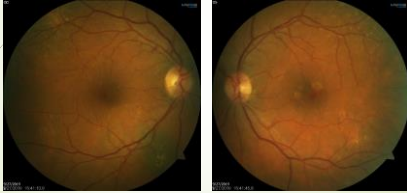


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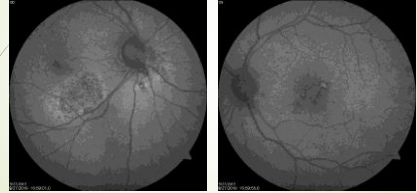
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### ICSC



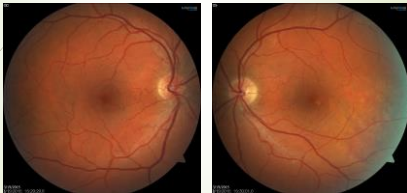
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### ICSC FAF



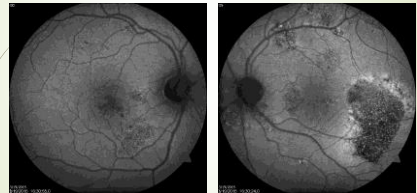
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### ICSC



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### ICSC FAF



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### ICSC FAF- Widefield



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### Plaquenil toxicity FAF

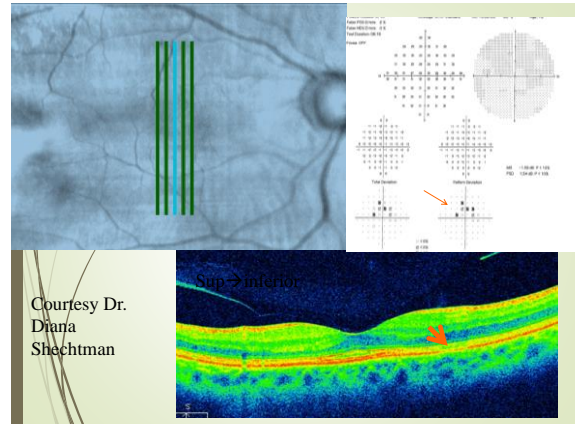
- Plaquenil toxicity first occurs in a ring shaped area surrounding the center of the fovea
- can be imaged before easily visible to funduscopy by several means
- Multifocal ERG
- SD-OCT
- IVFA
- FAF

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## Plaquenil



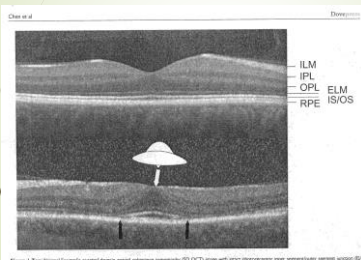
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Courtesy Dr.  
Diana  
Shechtman

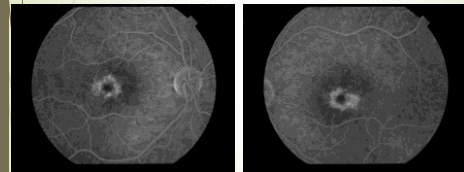
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## Chen et al. Clinical Ophthalmology 2010;4 p. 1151



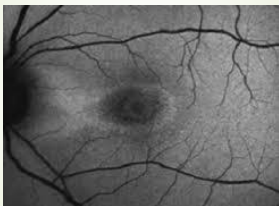
45

## Bull's Eye IVFA



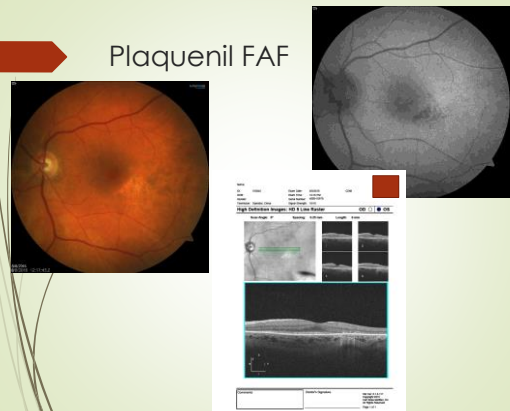
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## Plaquenil FAF



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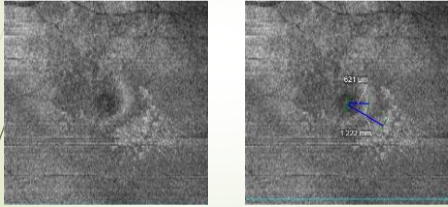
## Plaquenil FAF



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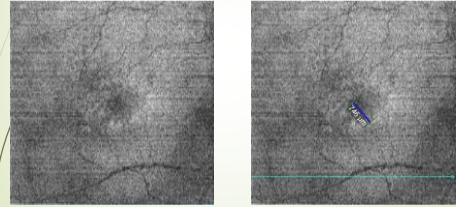


### Plaquenil toxicity En Face OS



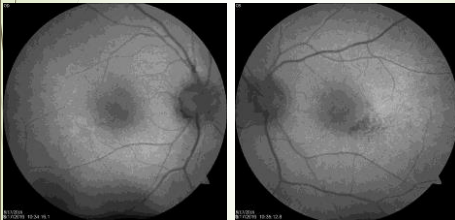
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### Plaquenil toxicity En Face OD



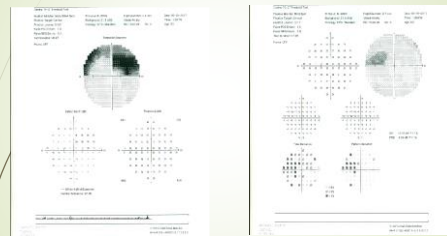
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### Plaquenil Toxicity FAF



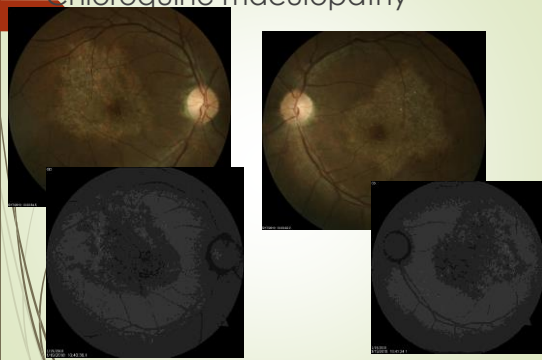
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### Plaquenil VF OU



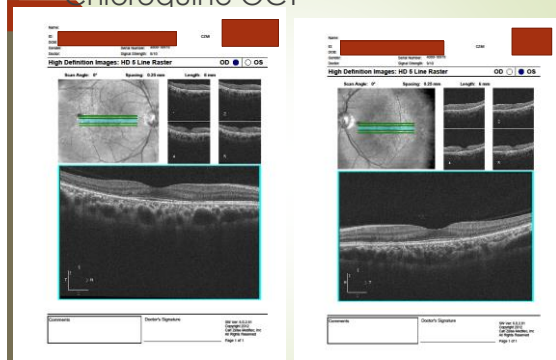
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### Chloroquine maculopathy



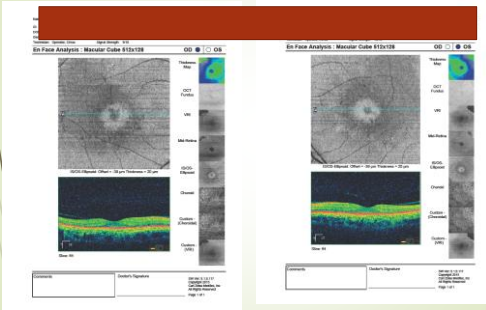
53

### Chloroquine OCT



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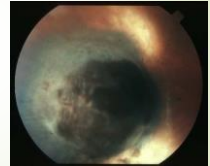
## Chloroquine OCT En-face



55

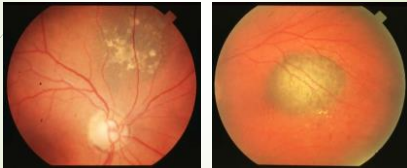
## Choroidal lesions FAF

- Can FAF help to distinguish choroidal nevi from choroidal melanomas? Maybe.
- Typically we look for things like diameter, thickness / height, symptoms, subretinal fluid, proximity to the ONH, and lipofuscin



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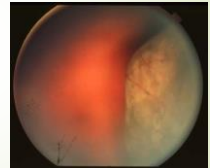
## Choroidal lesions FAF: Nevus or Melanoma?



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## Choroidal lesions FAF

- On FAF.....
- Nevi tend to show patchy but distinct areas of hyperfluorescence or no hyperfluorescence.
- Melanomas tend to show diffuse reticular branching hyperfluorescence plaques with less distinct borders, typically covering at least 50% of the lesion



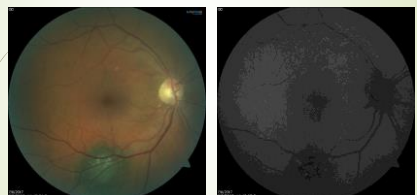
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## Small choroidal nevus with FAF



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## Choroidal nevus FAF



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## 57 year old WF Nevi

2010

2013



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## 57 year old WF melanoma

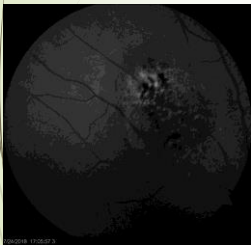
2016

2018 : symptoms of blur



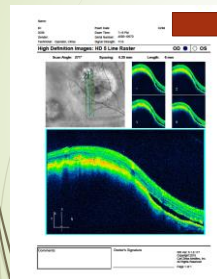
62

## 57 year old WF FAF



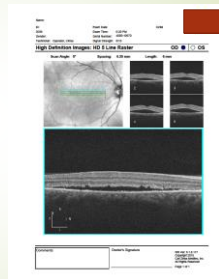
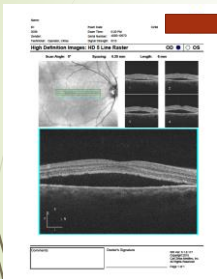
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## 57 year old WF OCT



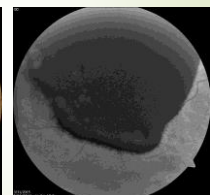
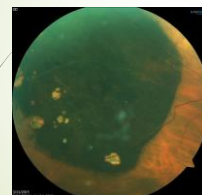
64

## 57 year old white female



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## FAF choroidal lesions: CHRPE



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## FAF glaucoma

- Glaucoma patients and even patients with ocular hypertension exhibit increased hyperfluorescence of the peripapillary RPE adjoining PPA
- May be correlated with the severity of the disease
- Due to increased lipofuscin accumulation in this area



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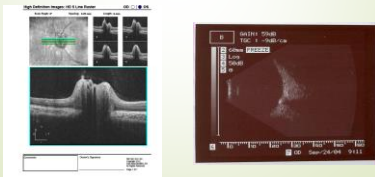
## FAF glaucoma



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## FAF ONH Drusen

- FAF can image ONH drusen
- SLO FAF does this well, camera based FAF not as well
- Very good with visible drusen (when you don't need it!), marginal with buried drusen (when confirmation is useful)



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## FAF ONH Drusen



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## FAF ONH Drusen



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## FAF ONH Drusen



72



### FAF ONH Drusen



73

### FAF ONH Drusen



74

### FAF ONH Drusen



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### White dot syndromes FAF

- APMPE:
  - Early/ acute: hypo
  - Late: hyper
- MEWDS
  - Early/ acute: hyper
  - Late: returns to normal
- Multifocal choroiditis
  - Early/ acute: hypo of spots > 125 microns
  - Late : Hypo of all spots

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### White dot syndromes FAF

- Serpiginous Choroiditis
  - Early / acute: hyper
  - Late: Hypo
- Birdshot
  - Early/ acute : hypo
  - Late: Returns to normal?

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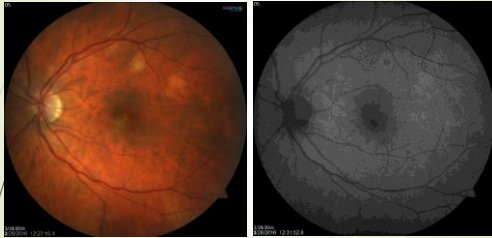
### AMPIGENOUS OD



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### AMPIGENOUS OS



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### AMPIGENOUS 3 week FU on oral steroids OD



80

### AMPIGENOUS 3 week FU on oral steroids OS



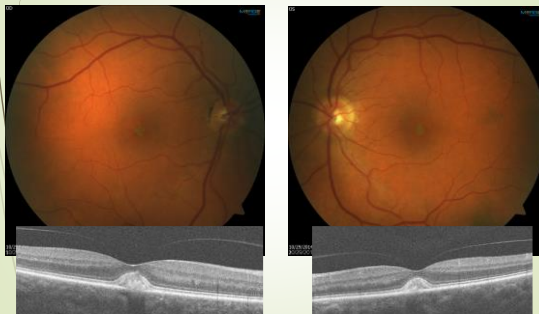
81

### Retinal Dystrophies

- Causes lipofuscin build up in the RPE
- Utility of FAF:
  - Aid in proper diagnosis
  - Earlier diagnosis
  - Examine family members at risk to diagnosis before clinically visible changes
  - Track progression over time

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### Adult Vitelliform Dystrophy (Pattern Dystrophy)



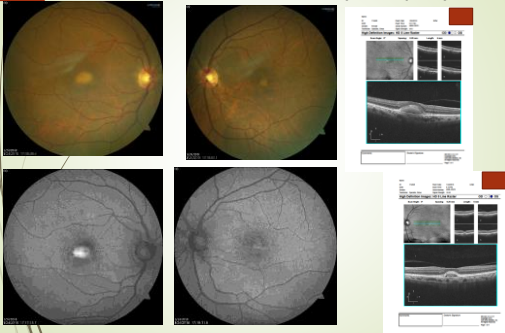
83

### Adult Vitelliform Dystrophy - FAF



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### Adult Vitelliform Dystrophy



85

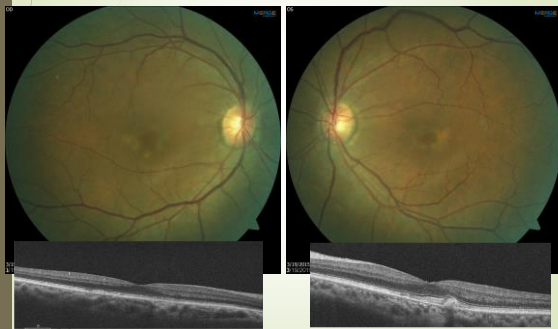
### Best's Vitelliform Dystrophy

Atrophic Stage



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### Butterfly Dystrophy (Pattern Dystrophy)



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### Butterfly Dystrophy - FAF



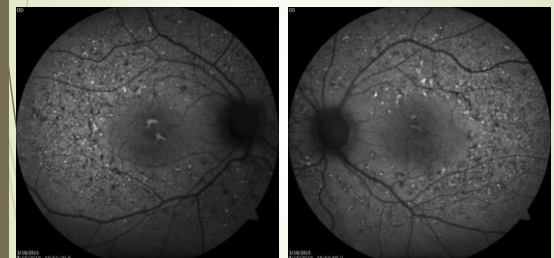
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### Fundus Flavimaculatus



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### Fundus Flavimaculatus - FAF



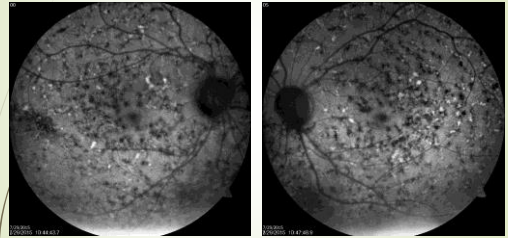
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## Fundus Flavimaculatus



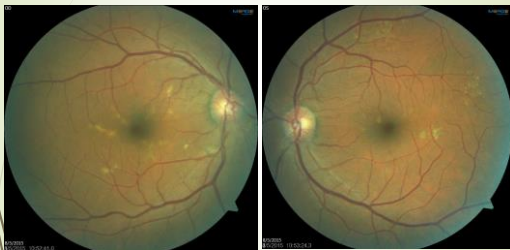
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## Fundus Flavimaculatus FAF



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## Fundus Flavimaculatus



56 year old AA male - daughter in early 30s recently dx'ed with Stargardt's

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## Fundus Flavimaculatus FAF



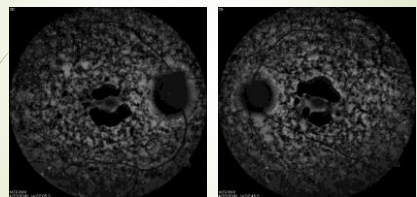
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## Stargardt's



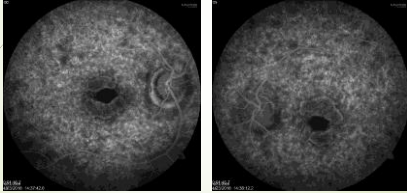
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## Stargardt's FAF



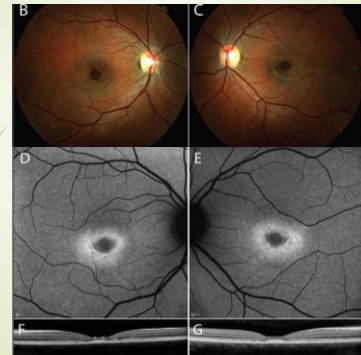
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### Stargardt's IVFA



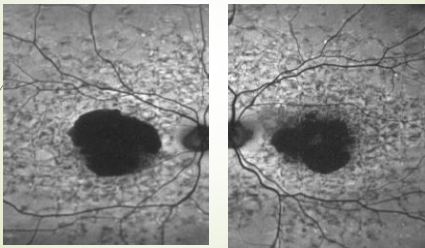
97

### Stargardt's disease

Pang  
et al

98

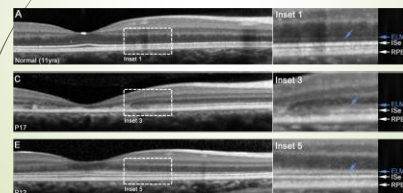
### Widefield FAF Stargardts & Fundus Flav: Courtesy Dr. Jerome Sherman



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### OCT in Stargardt's Disease

- Thickening and increased hyper reflectivity of the ELM early in disease
- Occurs prior to photoreceptor atrophy
- Could use SD OCT and FAF for early diagnosis



Lee et al

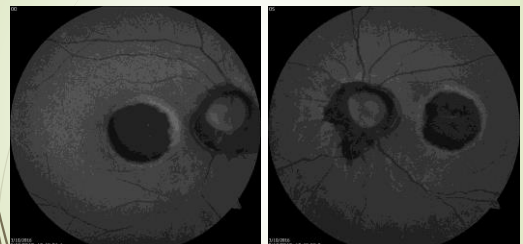
100

### Cone-rod dystrophy



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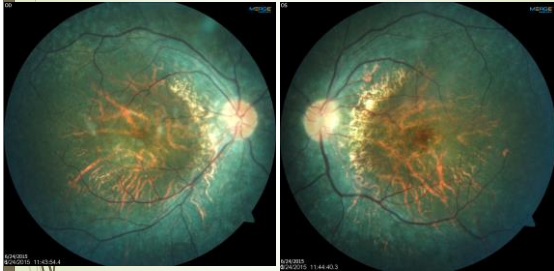
### Cone-rod dystrophy FAF



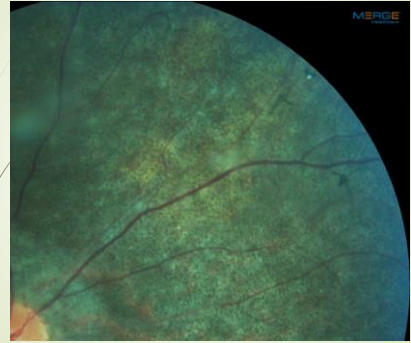
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## Retinitis Pigmentosa

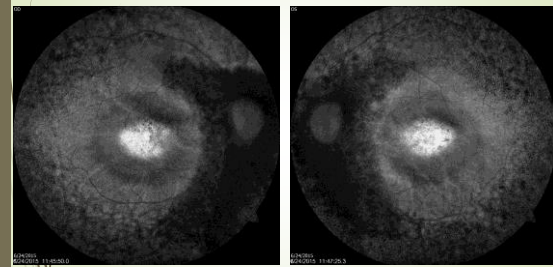


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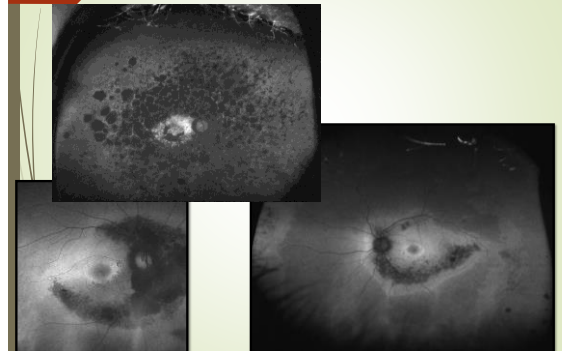
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## RP - FAF



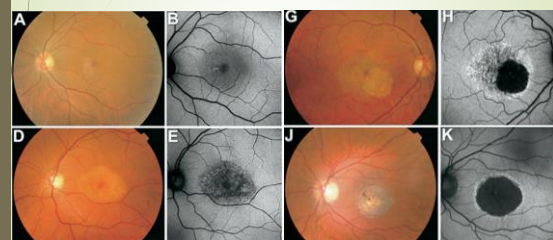
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## RP wide field FAF: Courtesy Dr. Jerome Sherman



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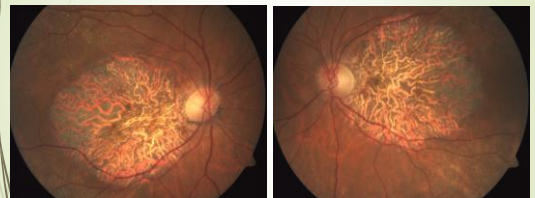
## Central Areolar Choroidal Dystrophy



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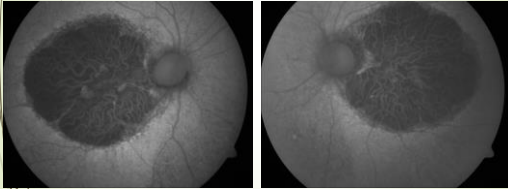
## CACD – images courtesy Dr. Mohammad Rafieetary



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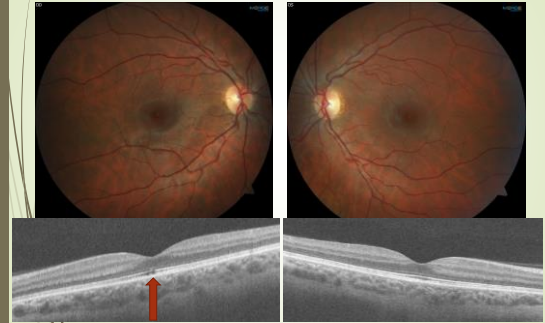


### CACD FAF



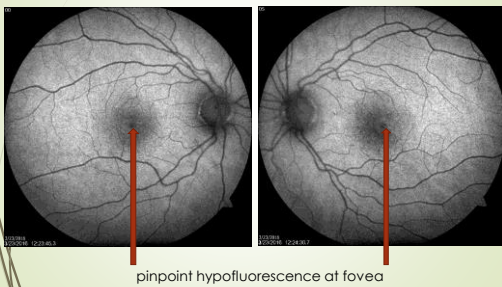
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### Solar Retinopathy



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### Solar Maculopathy



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### Questions?



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