

Retina Grand Rounds

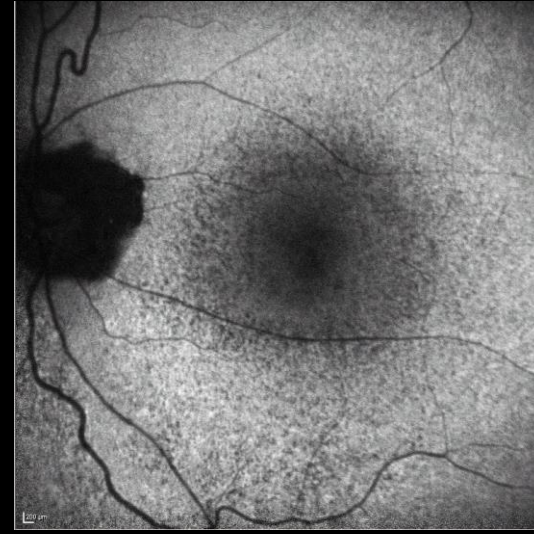
Stephen Huddleston MD

Charles Retina Institute

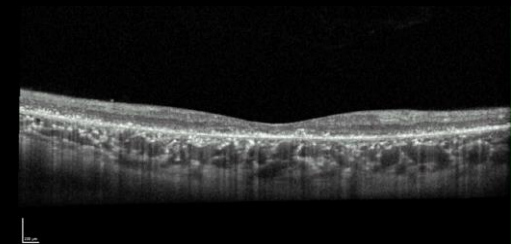
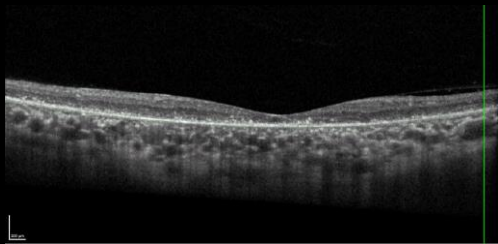
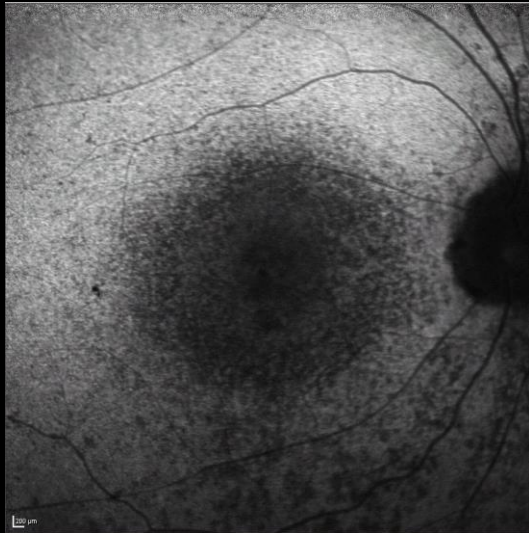
University of Tennessee Hamilton Eye Institute

Fundus Autofluorescence

2013

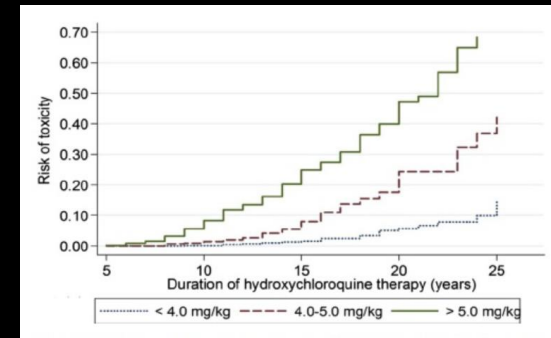


2016



Plaquenil Toxicity

- Excellent treatment for a variety of Auto immune conditions
 - Lupus, sarcoidosis, graft vs host, rheumatoid arthritis
- Efficacy marred by toxicity issues causing blindness
- Cumulative effect based on lifetime dose
- **Cases of toxicity have decreased with lower average dosing and better screening modalities**



Major Factors

The most important risk factors are listed in Table 1.

Table 1. Major Risk Factors for Toxic Retinopathy

Daily dosage	
HCQ	>5.0 mg/kg real weight
CQ	>2.3 mg/kg real weight
Duration of use	>5 Yrs, assuming no other risk factors
Renal disease	Subnormal glomerular filtration rate
Concomitant drugs	Tamoxifen use
Macular disease	May affect screening and susceptibility to HCQ/CQ

CQ = chloroquine; HCQ = hydroxychloroquine.



Plaquenil Toxicity

Table 2. Screening Frequency

Baseline Screening
Fundus examination within first year of use
Add visual fields and SD OCT if maculopathy is present
Annual Screening
Begin after 5 yrs of use
Sooner in the presence of major risk factors

SD OCT = spectral-domain optical coherence tomography.

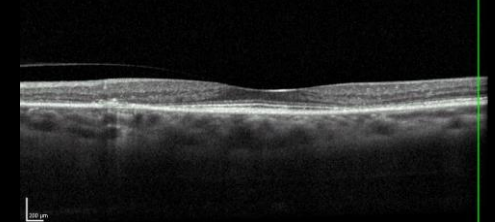
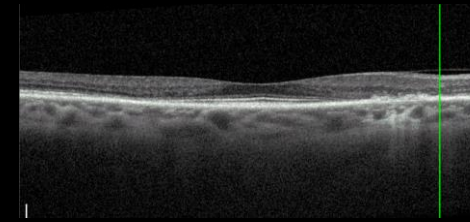


Table 3. Clinical Examination Techniques

Recommended Screening Tests

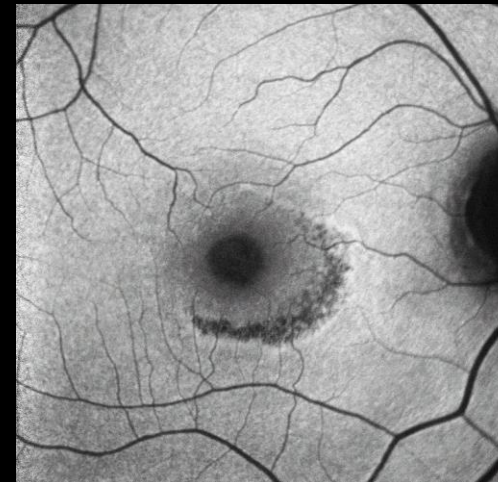
Primary tests: ideally do both
Automated visual fields (appropriate to race)
SD OCT
Other objective tests (as needed or available):
mfERG
FAF

Newer tests of possible value in future
Microperimetry
Adaptive optics retinal imaging

Not Recommended for Screening

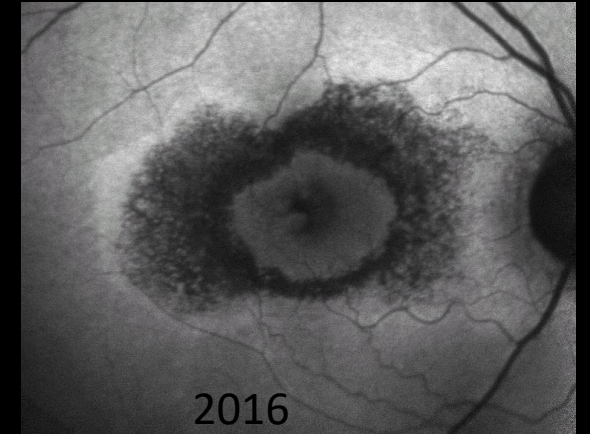
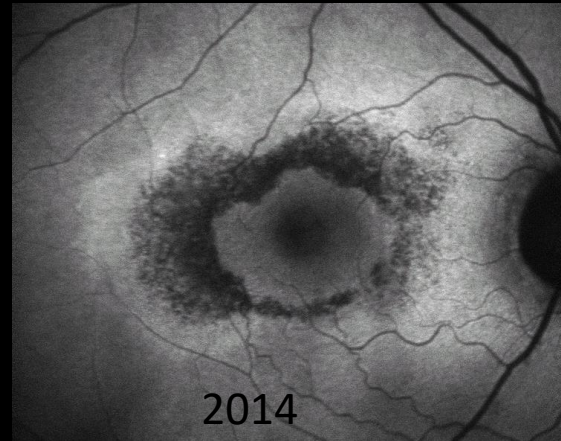
Fundus examination
Time-domain OCT
Fluorescein angiography
Full-field ERG
Amsler grid
Color testing
EOG

EOG = electro-oculogram; ERG = electroretinogram; FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; SD OCT = spectral-domain optical coherence tomography.



Plaquenil Toxicity

*Key Point: Caucasian/African Americans → parafoveal damage;
Asian americans → often extramacular*



Damage worsens after stopping treatment...

Early detection crucial

Q: Traumatic dialysis with RD?

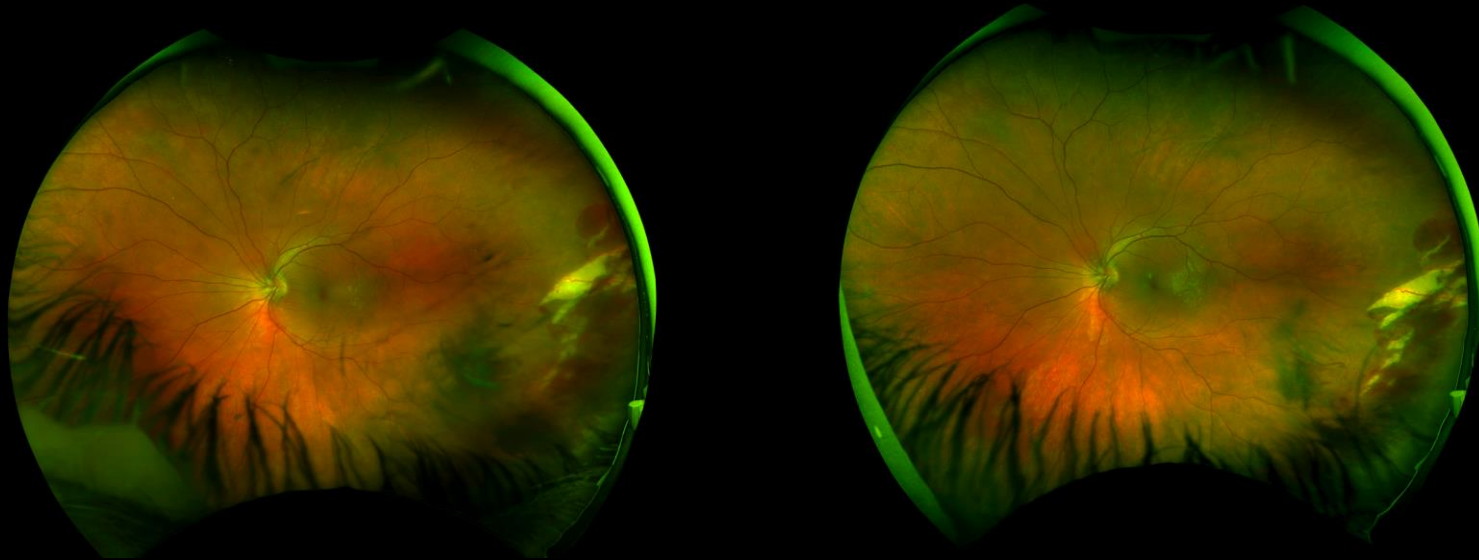
19 y/o athlete struck in eye with Baseball. Vitreous hemorrhage obscuring area of damage.

Emergent surgery with buckle?



A: Choroidal Rupture

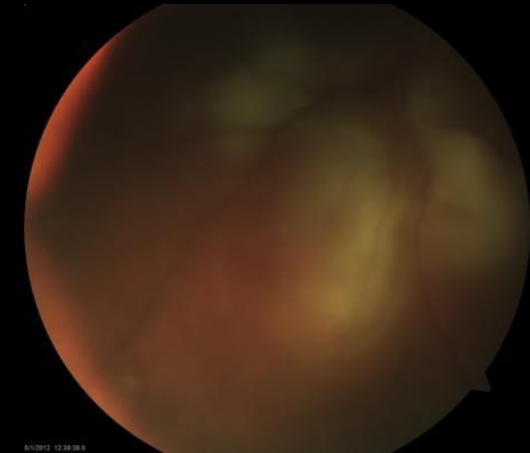
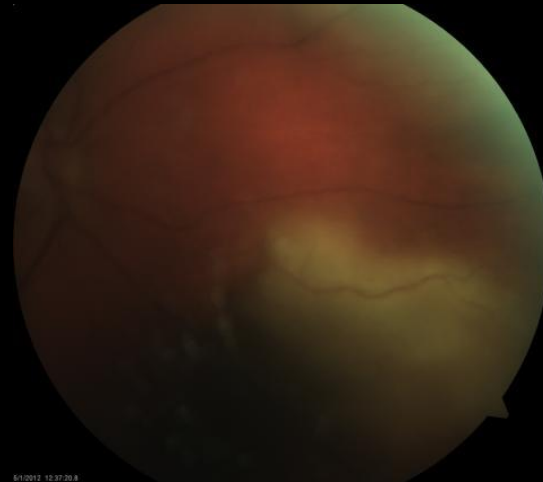
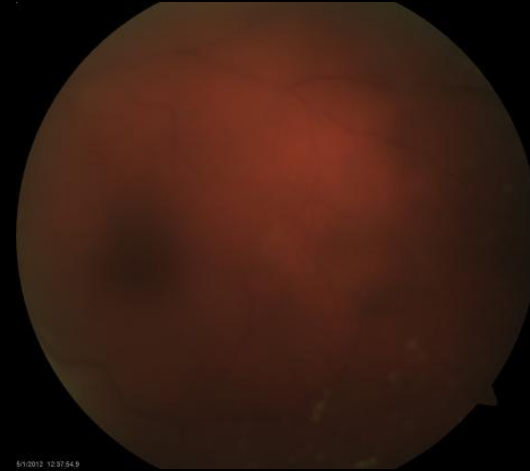
Observe: VH clears revealing choroidal rupture
without retinal tears



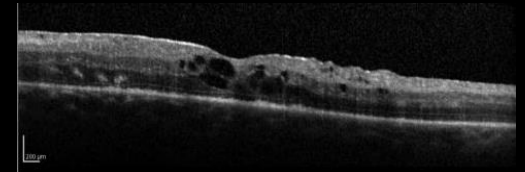
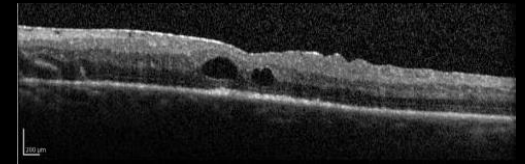
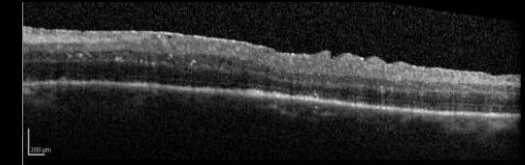
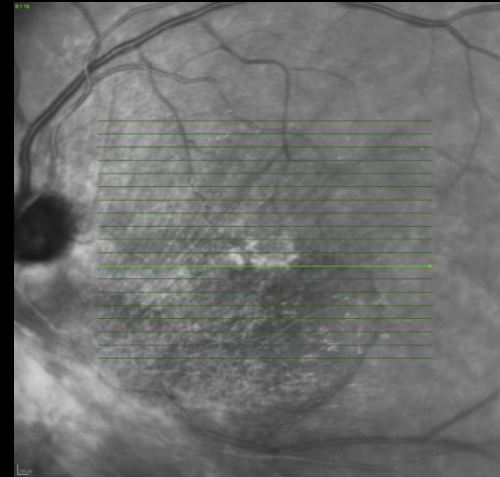
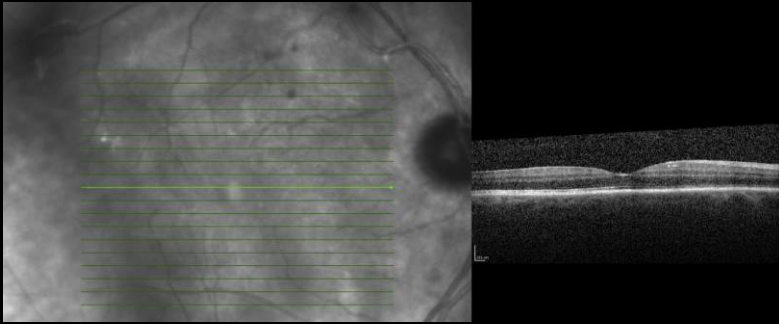
One week apart...

Acute Retinal Necrosis?

62 y/o immunocompetent
Man with blurriness.

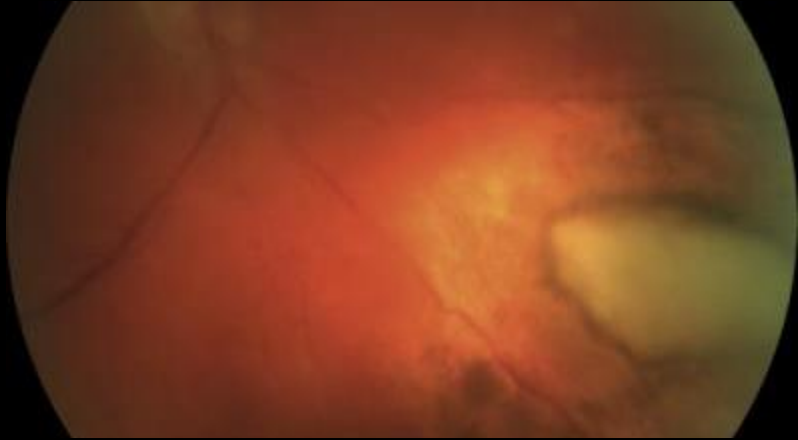


Acute Retinal Necrosis?



Suspicion for ARN, CNS lymphoma, TB, Etc.
MRI normal. Labs normal. Diagnostic PPV
And treated with Ganciclovir injection. Sample
obtained strongly positive for...

Toxoplasmosis



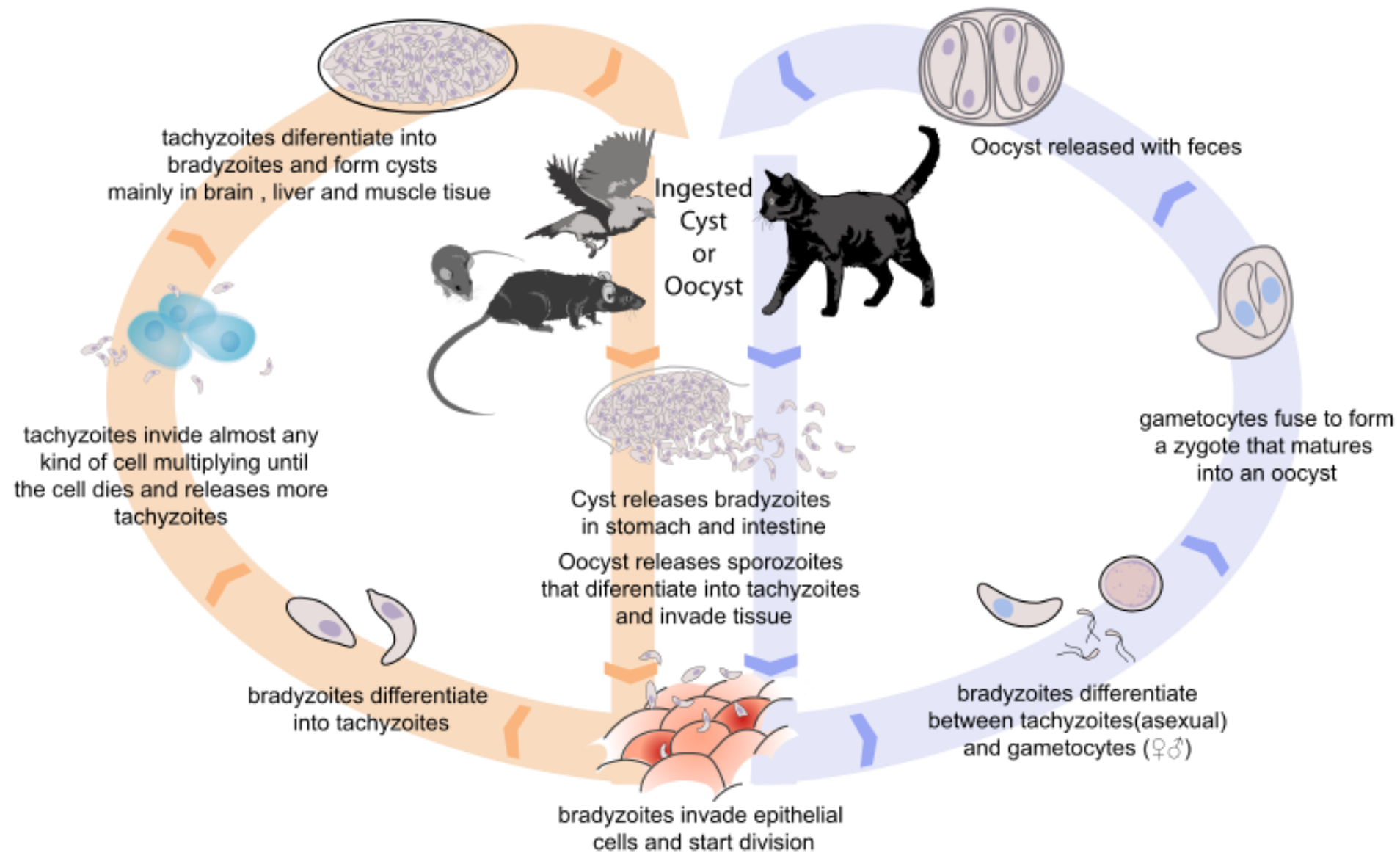
Successfully treated
with PO ABX and
intravitreal
clindamycin twice

6/19/2012 12:23:36.4

6/19/2012 12:22:17.7

Toxoplasmosis

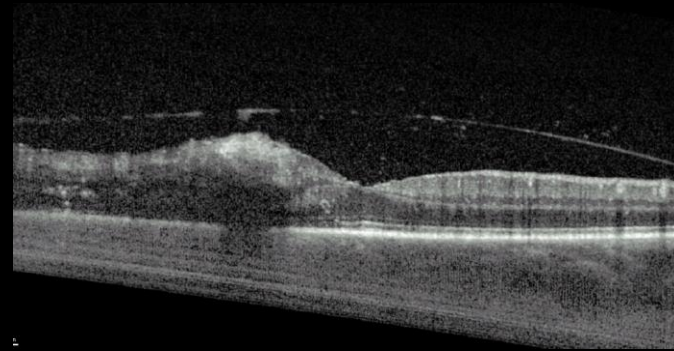
- Caused by the protozoan *toxoplasma gondii*
- Single-cell obligate intracellular parasite
 - 22.5% of US population infected
 - 2% of US pop with signs of ocular involvement
- 3 major forms:
 - Oocyst (soil form, hardy)
 - Tachyzoite (infectious form, fast growing, vulnerable)
 - Tissue cyst (contains infectious bradyzoites)
- Most common cause of infectious retinochoriditis in adults and children



Toxoplasmosis

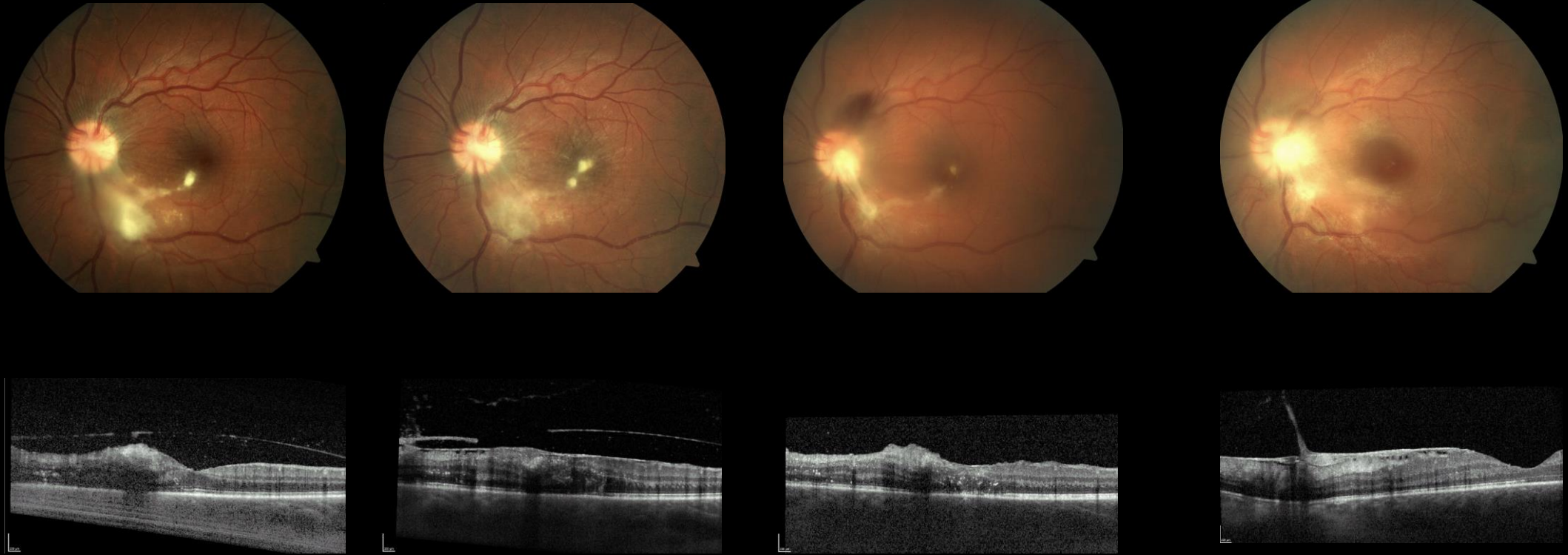
- Typical: Unilateral focal retinitis with overlying vitritis at edge of old chorioretinal scar
- Atypical: large areas of retinal necrosis or retinochoroiditis without pre-existing scar. Can be multifocal and/or bilateral with or without vasculitis
 - Elderly and immunocompromised
 - Rapid tachyzoite production and poor immune response
- Up to 20% with increased intraocular pressure
- Other secondary causes of vision loss: cataract, CME, serous retinal detachments, and CNV

TB or fungal retinitis?



22 y/o complaining of blurry vision and denying drug use

Atypical Toxoplasmosis



PPV, EMM peel, clinda

Starts to come back and he leaves the country...

Toxoplasmosis

- Diagnosis → primarily based on clinical signs
- Aqueous PCR with lower sensitivity than vitreous PCR
 - Vitreous has closer contact to necrotic lesions with theorized higher *T. Gondii* DNA concentration.
- IgG antibodies present within the first two weeks
 - Detectable for life, placental transfer in newborns
- IgM present acutely
 - Detectable for less than one year
- IgA present acutely as well
 - Disappears within 7 months

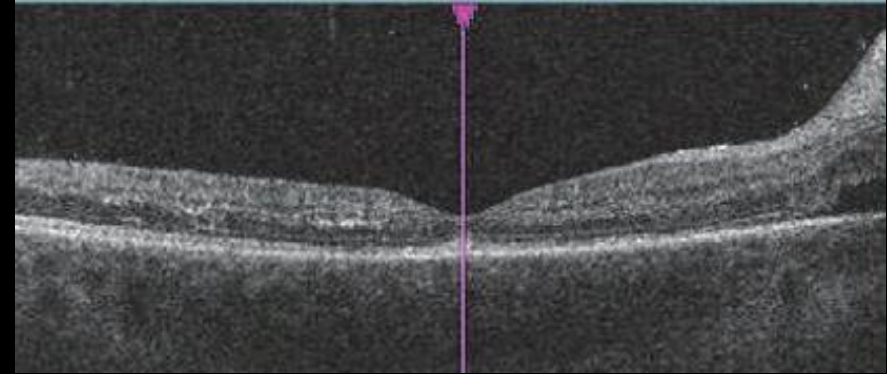
Toxoplasmosis

- Antibiotics highly effective against toxoplasma tachyzoites
 - Transition from tachyzoite to bradyzoite takes only days
 - Cysts form within weeks
- Triple therapy (gold standard, now irrelevant)
 - Pyrimethamine 50-100mg Qday (cost impossibly high 2/2 Martin Shkreli)
 - Needs folinic acid supplementation (5mg qday)
 - Sulfadiazine 25-50 mg Qday
 - Sulfa allergy? Consider clindamycin 300mg QID
 - Prednisone 0.5-1.0 mg/kg/day
- Treatment generally lasts 4-6 weeks

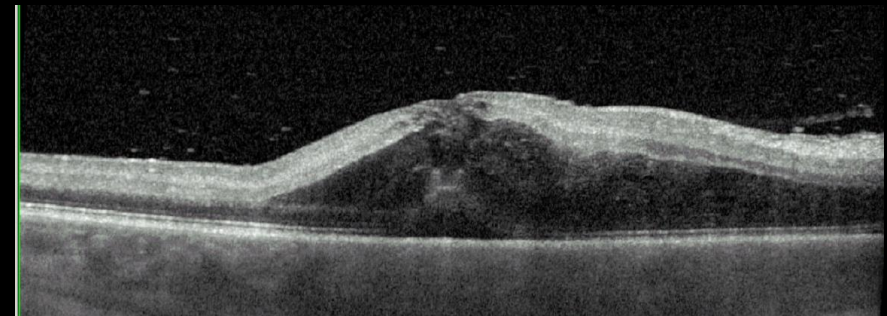
Toxoplasmosis

- TMP/SMX 160/80 mg BID
- Azithromycin 250mg Qday (combined with pyrimethamine)
- Pregnancy: spiramycin 400mg TID (poor availability)
 - Alternatives: azithromycin, clindamycin, atovaquone
 - Sulfas can be used in the first two trimesters
 - **Intravitreal clindamycin a better option**
- HIV: high risk of CNS and ocular recurrence. Consider long-term prophylaxis such as 1 tab TMP/SMX every third day after quiescence achieved
- Intravitreals: Intravitreal clinda/dex as effective as standard oral treatment with fewer side effects. No difference in recurrence rate. **Give Clindamycin alone if diagnosis not confirmed.**

Toxoplasmosis causing rapidly worsening optic nerve lesion...



Day 1



Day 2

22 y/o with 20/70 vision, followed with optic nerve whitening for several weeks prior to referral

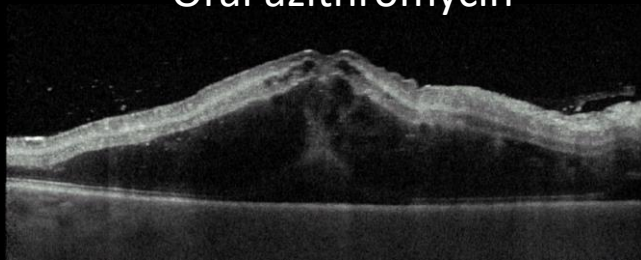
Final vision HM. What happened?

Week one



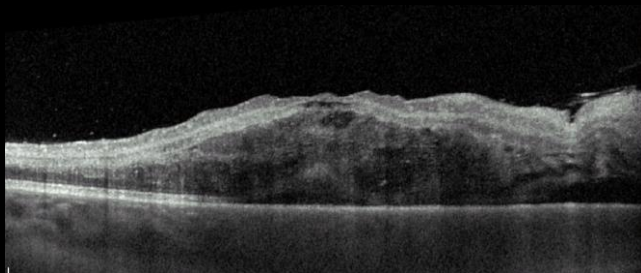
Tues

Oral azithromycin



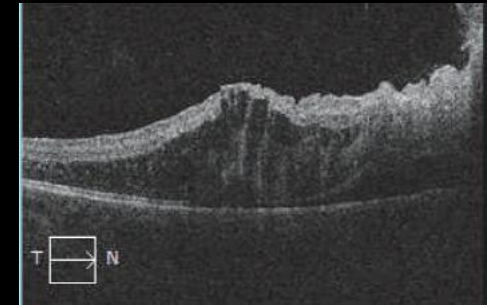
Wed

PPV clinda/dex



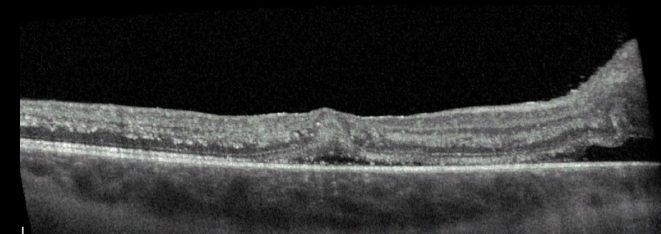
Fri

Week two



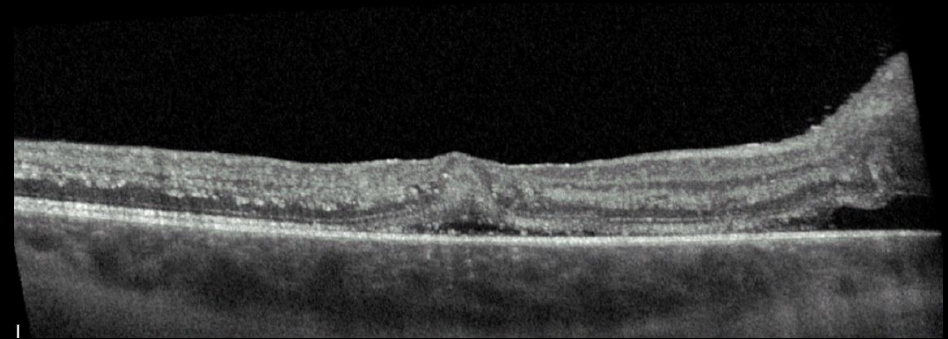
Mon

Clinda/Dex



Wed

BRAO/BRVO

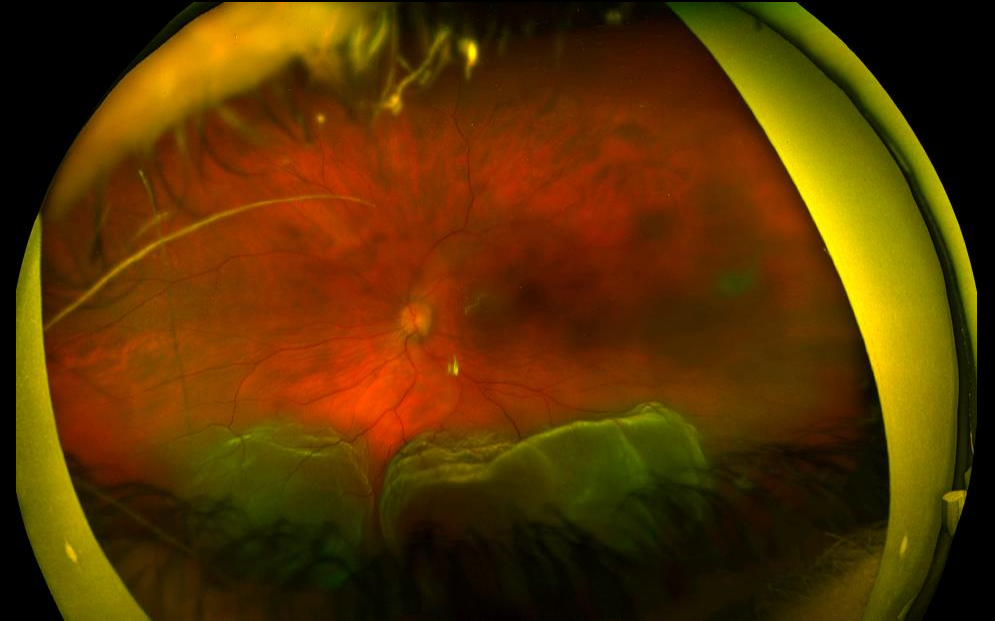


Current VA: 20/400...

Bilateral Retinal Detachment



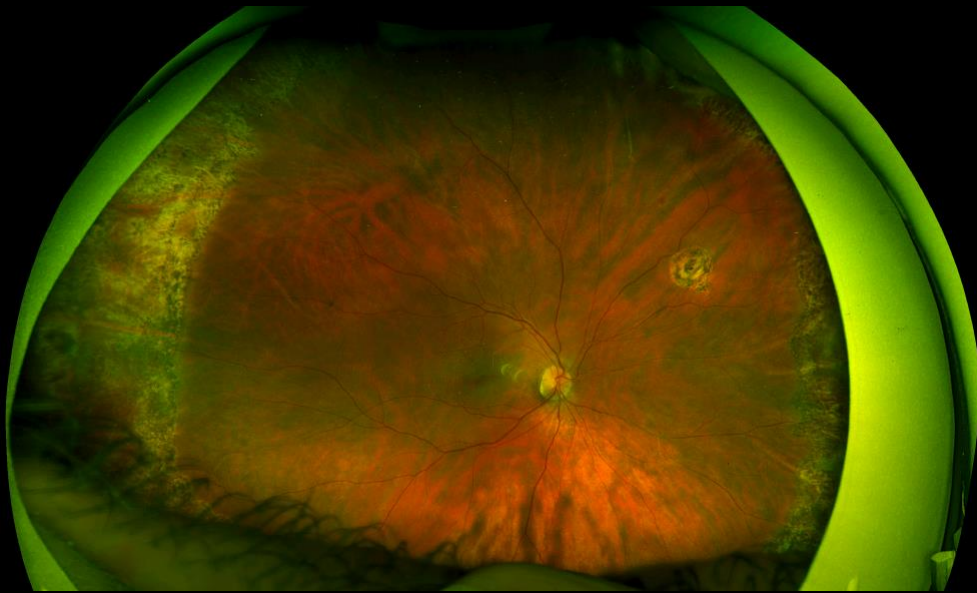
Mac on with 3 separate detachments



Mac off with macular hole

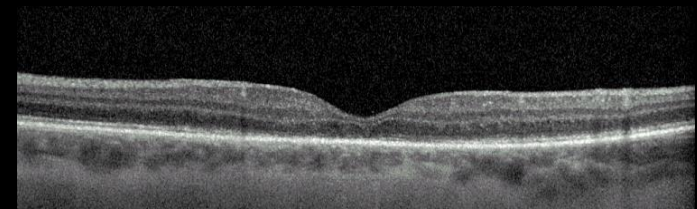


Bilateral Retinal Detachment



Same day bilateral PPV EPC FGX with ILM peel OS...

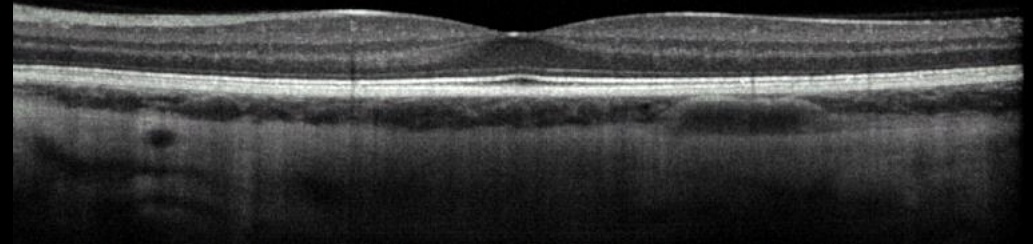
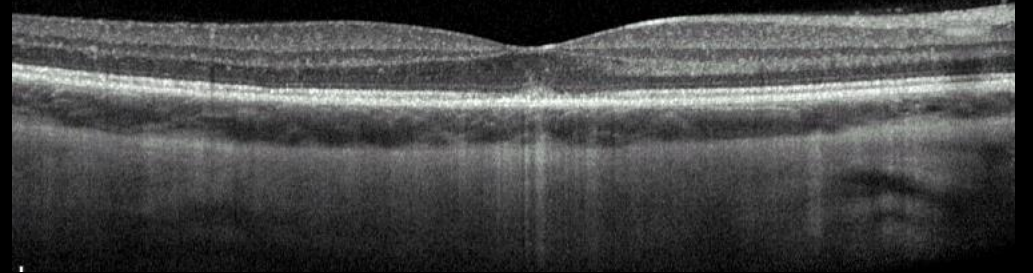
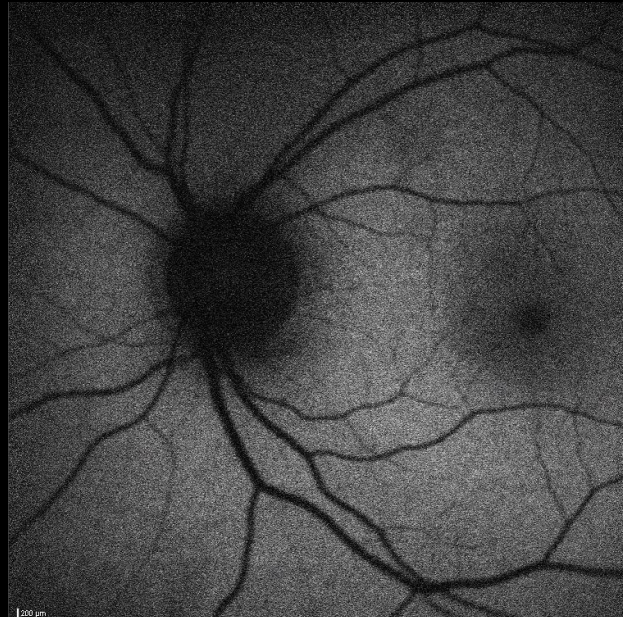
Tears everywhere → 360 laser



20/40 vision, should keep improving

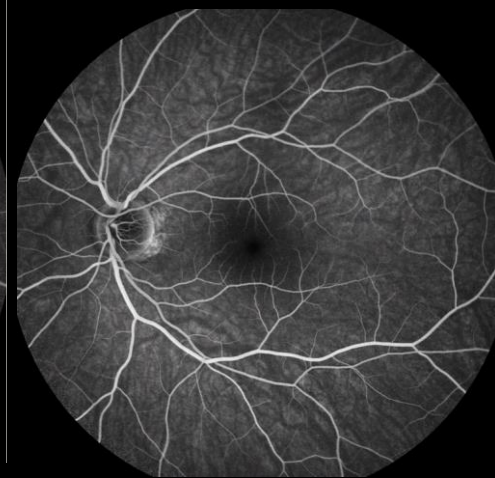
Last Case...

18 y/o Caucasian college student with 1 week of gray spot in vision OD and 20/70 vision





ICG early



IVFA

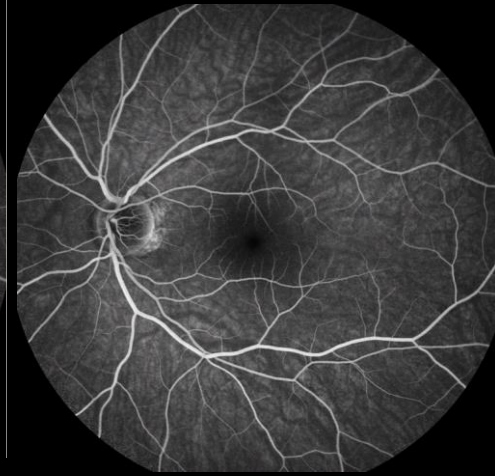
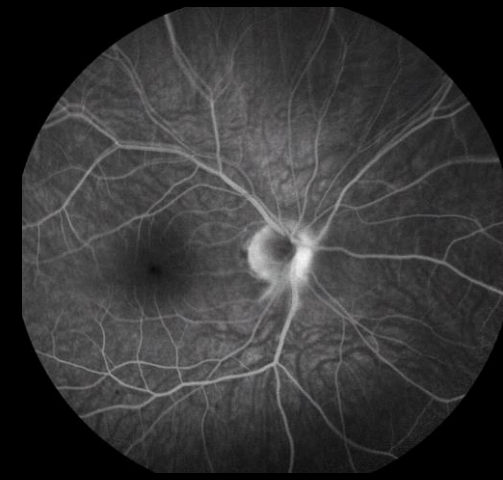
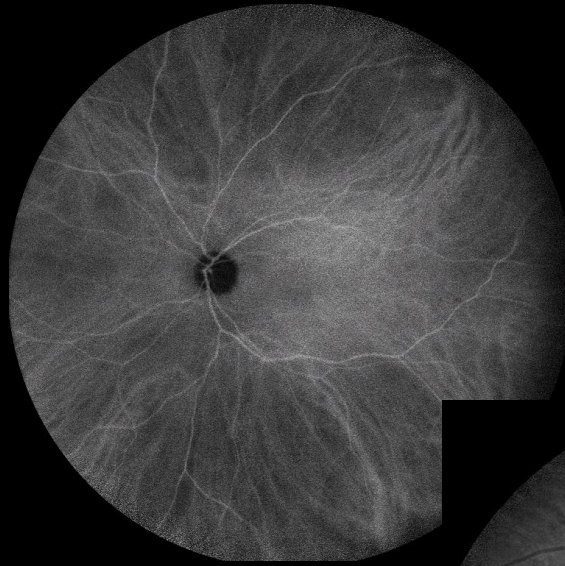


ICG late

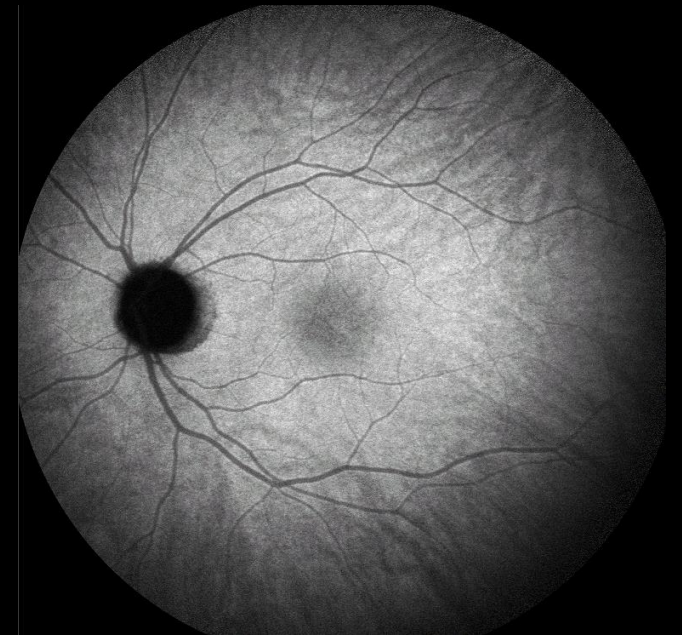
MEWDS: Multiple Evanescent White Dot Syndrome



ICG early



IVFA



ICG late

MEWDS: Multiple Evanescent White Dot Syndrome

- Primarily Healthy young women (80% female)
- Usually with preceding mild viral illness
- Acute painless unilateral vision loss (rarely bilateral)
- Perhaps the mildest of the white dot syndromes:
 - Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPEE)
 - Multifocal choroiditis and Panuveitis (MCP)
 - Punctate Inner Choroiditis (PIC)
 - Birdshot Choroidopathy
- Lesions at the level of the outer retina and RPE
- Self limiting with excellent prognosis

Questions?

Further Reading

- Marmor MF, Kellner U, Lai TY, et al. Revised recommendations on screening for chloroquine and hydroxychloroquine retinopathy. *Ophthalmology* 2011;118:415–22.
- Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. *JAMA Ophthalmol* 2014;132:1453–60.
- Marmor MF, Hu J. Effect of disease stage on progression of hydroxychloroquine retinopathy. *JAMA Ophthalmol* 2014;132:1105–12.
- American Academy of Ophthalmology. Retina/Vitreous: Multiple evanescent white dot syndrome Practicing Ophthalmologists Learning System, 2017 - 2019 San Francisco: American Academy of Ophthalmology, 2017.
- Joseph A, Rahimy E, Freund KB, et al. Fundus autofluorescence and photoreceptor bleaching in multiple evanescent white dot syndrome. *Ophthalmic Surg Lasers Imaging Retina*. 2013 Nov 1;44(6):588-92.
- American Academy of Ophthalmology. Retina/Vitreous: Toxoplasmosis Practicing Ophthalmologists Learning System, 2017 - 2019 San Francisco: American Academy of Ophthalmology, 2017.