

## ***5 or maybe more cases.....***

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Cole Eye Institute

## ***Financial Disclosure***

- Consultant/Advisory Board: Bausch and Lomb, Allergan, Alimera, Clearside, Regeneron, Eleven, Santen, Sanofi, Zeiss
- Research Grants: Bausch and Lomb, Allergan, Novartis, Clearside, Zeiss, Sanofi
- Licensing Royalty – Bioptigen, Synergetics
- I will be discussing the off-label use of immunosuppressive agents to treat chronic uveitis

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## ***Purpose of this talk***

- Show you a few cases that display a range of pathologies
- How to handle management of complex patients
- Highlight mistakes and how we can learn from them

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## ***Laboratory Testing For Uveitis***

- A. I order the same battery of tests on each patient
- B. I tailor my tests based on the patient and clinical situation
- C. I do not order tests, I just treat
- D. I order everything on the sheet
- E. I throw darts at my lab sheet and pick the ones I hit

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## Case Presentation

- 62-year-old white male referred for scleritis
- 5-month history of red painful left eye
- History of CK OU, no other ocular history
- ROS – positive for arthritis
- Seen by rheumatologist
- W/U positive for markedly positive ANA, positive ANCA

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## Case Presentation

- Treated with topical steroids – no relief
- Prednisone bad side effects
- MTX – up to 20 mg q week – no improvement
- Cyclophosphamide added – no improvement
- Subconj steroids (after hearing a lecture on it) – no improvement
- Both rheumatologist and ophthalmologist confused why patient with mixed connective tissue disease is not responding – and looks worse?

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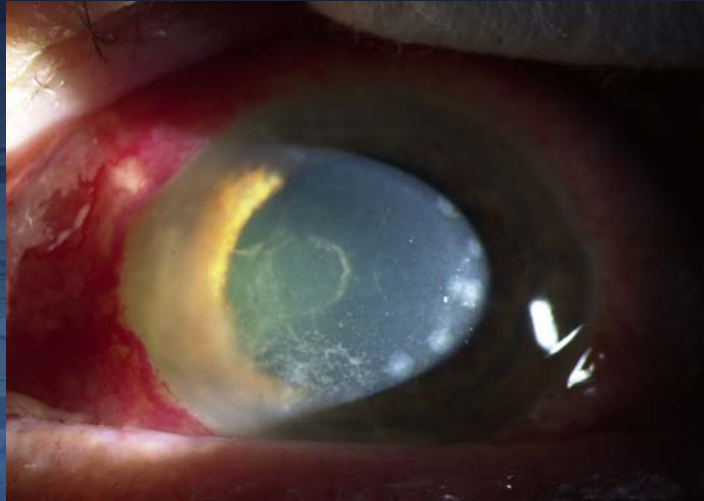


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### ***Next step?***

- A. Increase oral steroids for longer duration
- B. Switch steroid sparing agents
- C. Intravitreal steroid injection
- D. Order additional laboratory tests
- E. Diagnostic procedure

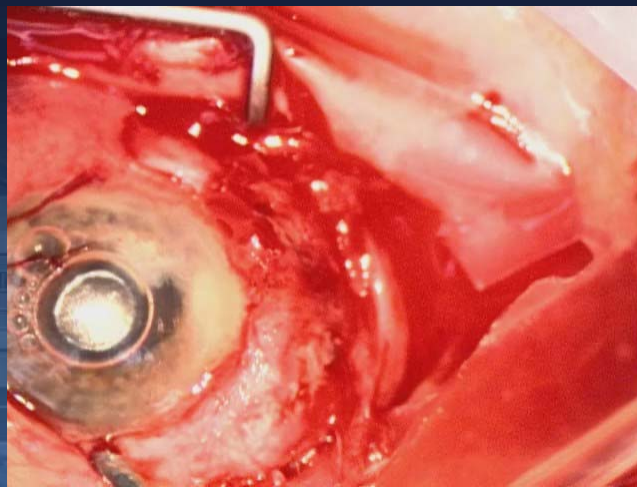
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## ***Case Presentation: Treatment Plan***

- Diagnostic AC tap
- Friday afternoon
- Leaving for Vegas at 6

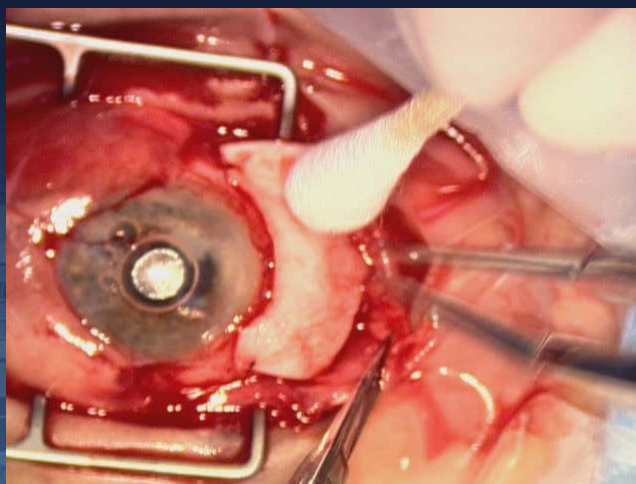
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## ***Intraoperative***



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## Intraoperative



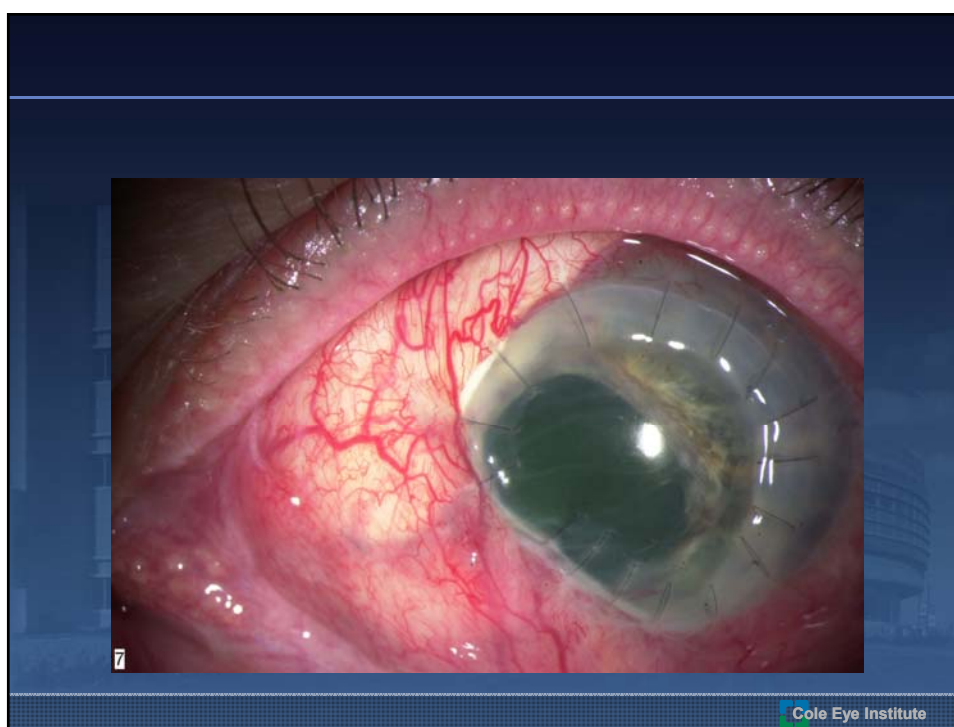
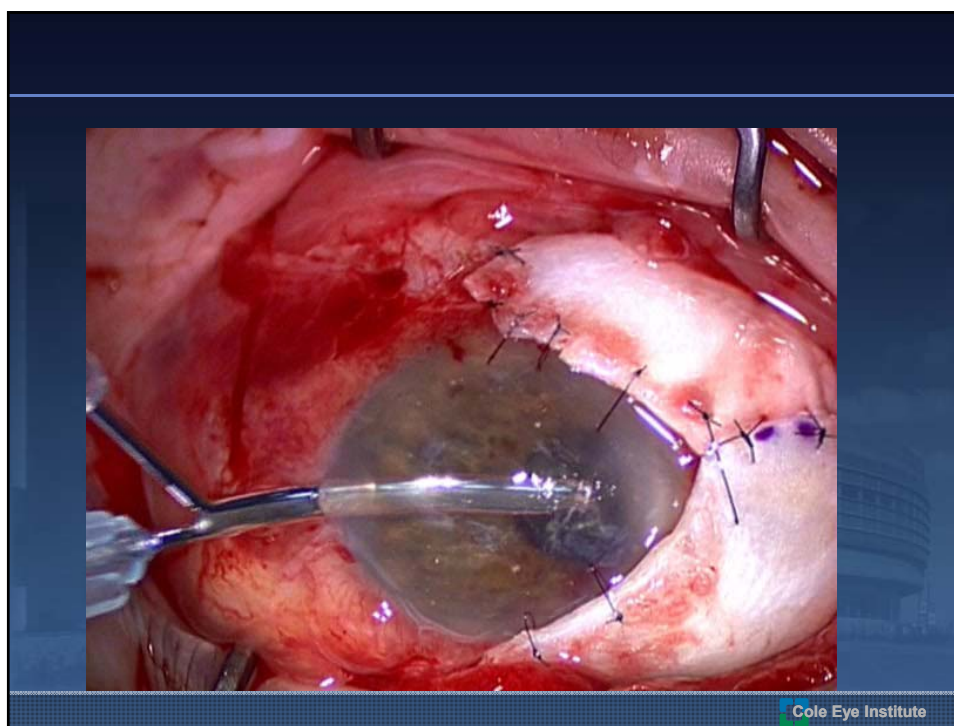
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## Postoperative Course

- CT scan of orbit – WNL
- Micro
  - Called 3 days later
  - 2 + mold species growing in every specimen
  - Paecilomyces
  - Begun on oral voriconazole
  - Cyclophosphamide stopped



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## *The Power of the Lab*

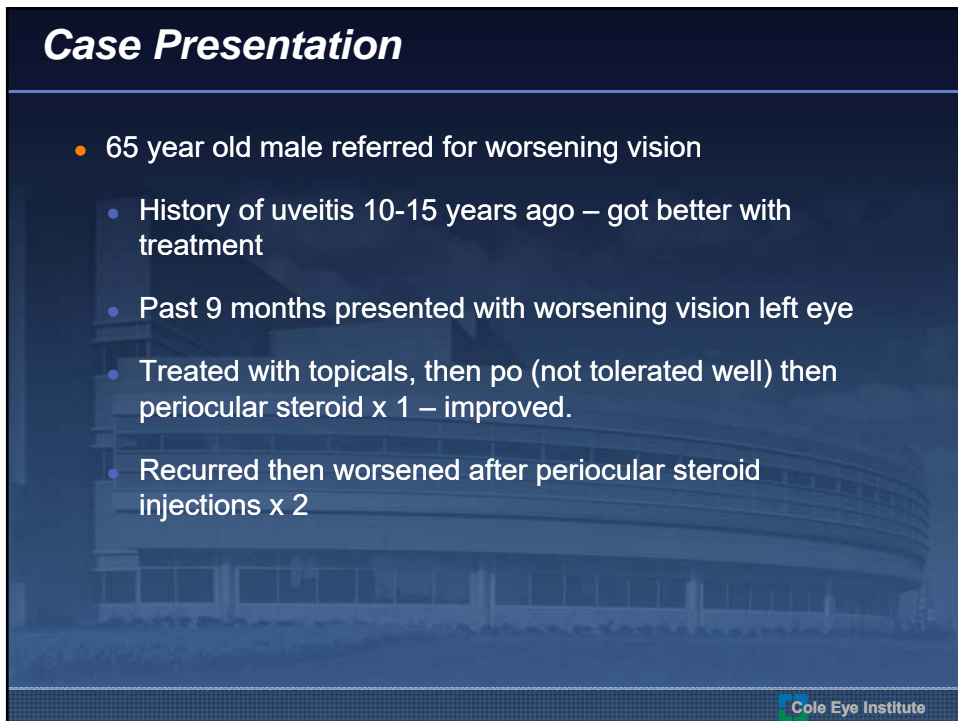
- Labs



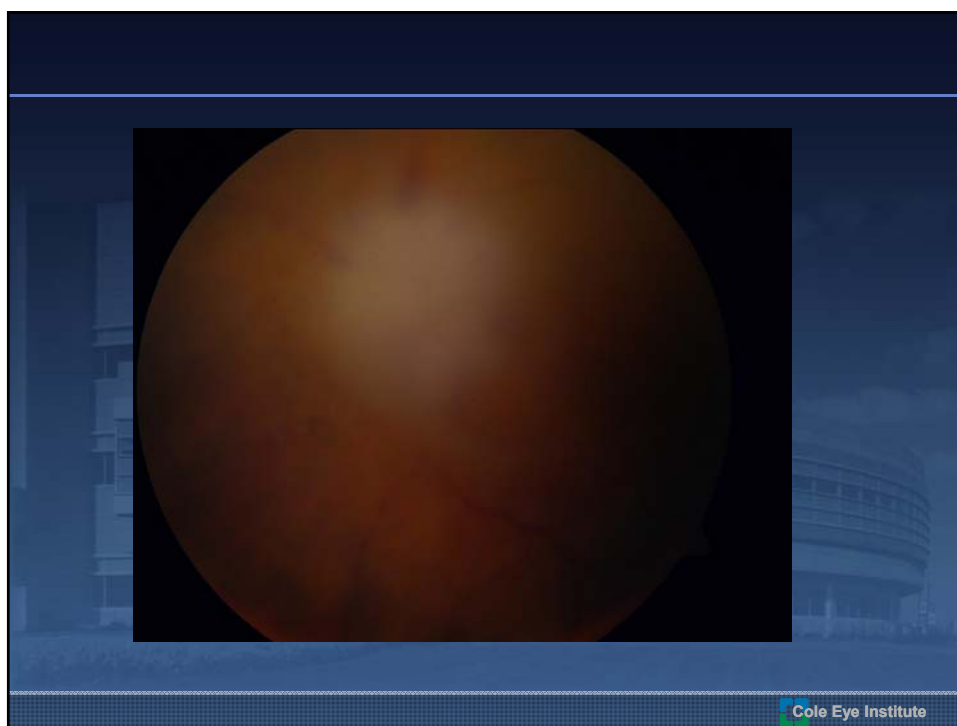
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## *Case Presentation*

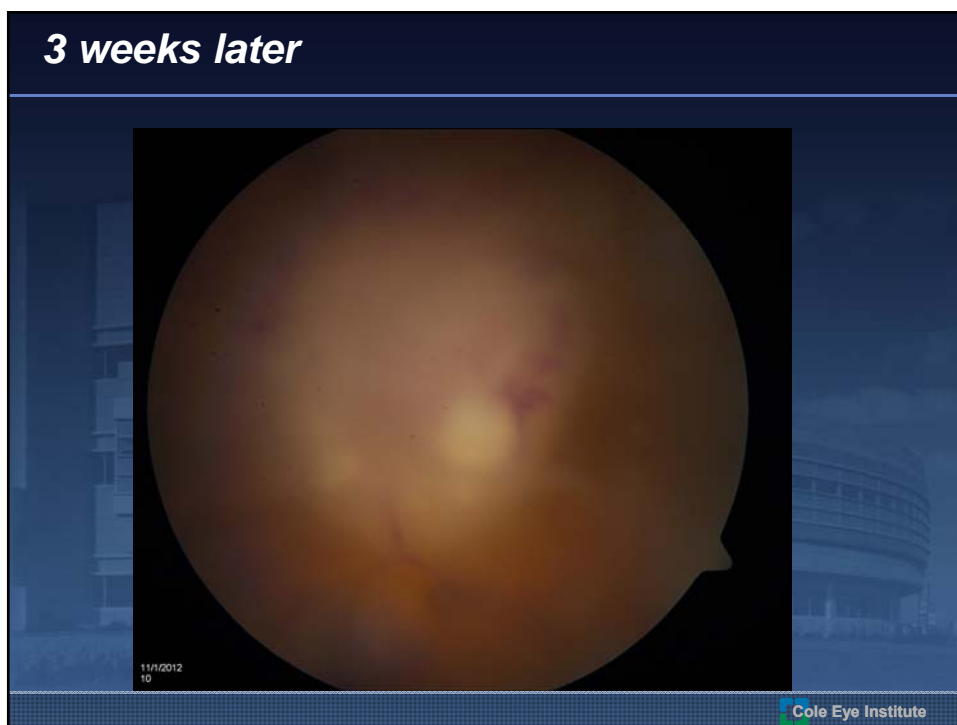
- 65 year old male referred for worsening vision
  - History of uveitis 10-15 years ago – got better with treatment
  - Past 9 months presented with worsening vision left eye
  - Treated with topicals, then po (not tolerated well) then periocular steroid x 1 – improved.
  - Recurred then worsened after periocular steroid injections x 2



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***3 weeks later***



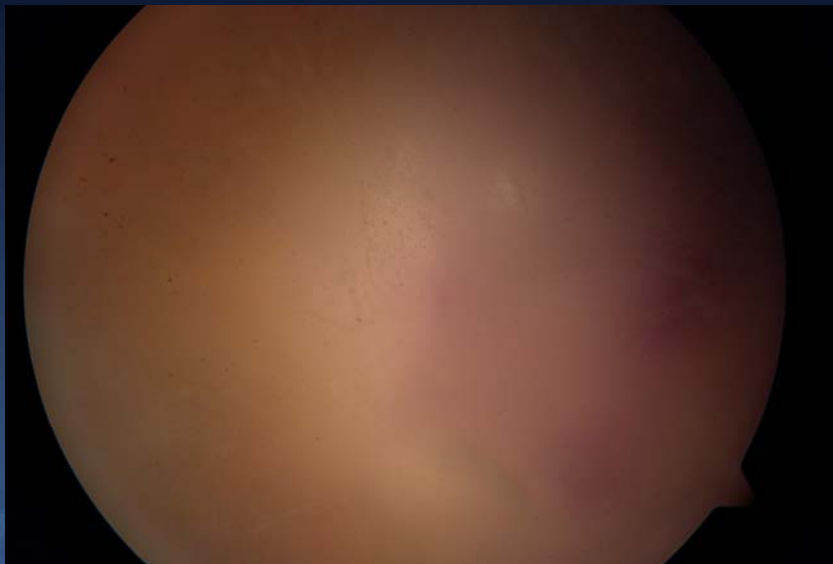


## *Review old records*

- Toxo titers IgG>200
- IgM negative
- Never treated for toxo
- Treat with Trimethoprim/Sulfa DS BID
- Intravitreal clindamycin delivered x 3

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## *1 month later*



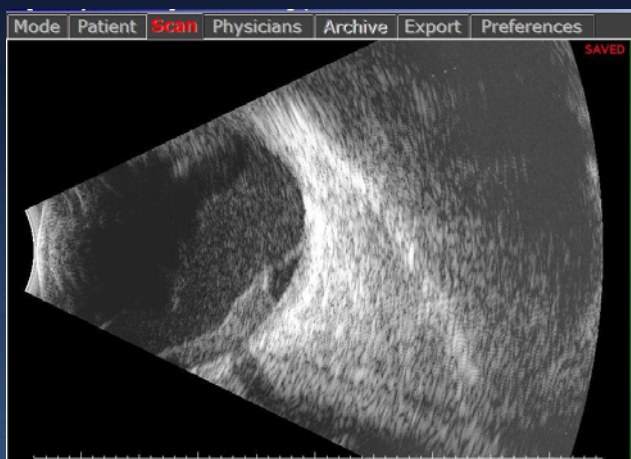
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## Options?

- Treated with additional clindamycin
  - AC tap negative for toxo PCR
  - RPR, Bartonella, ACE negative
- Unchanged
- Biopsy planned
- A few days prior – falls and develops subdural hematoma
- Surgery delayed

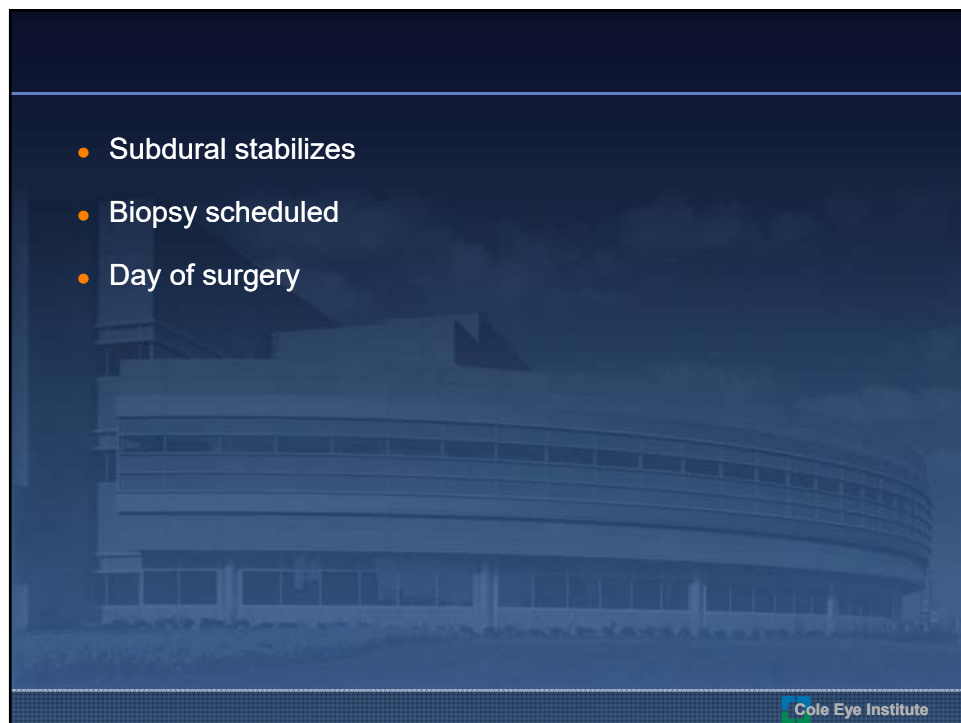
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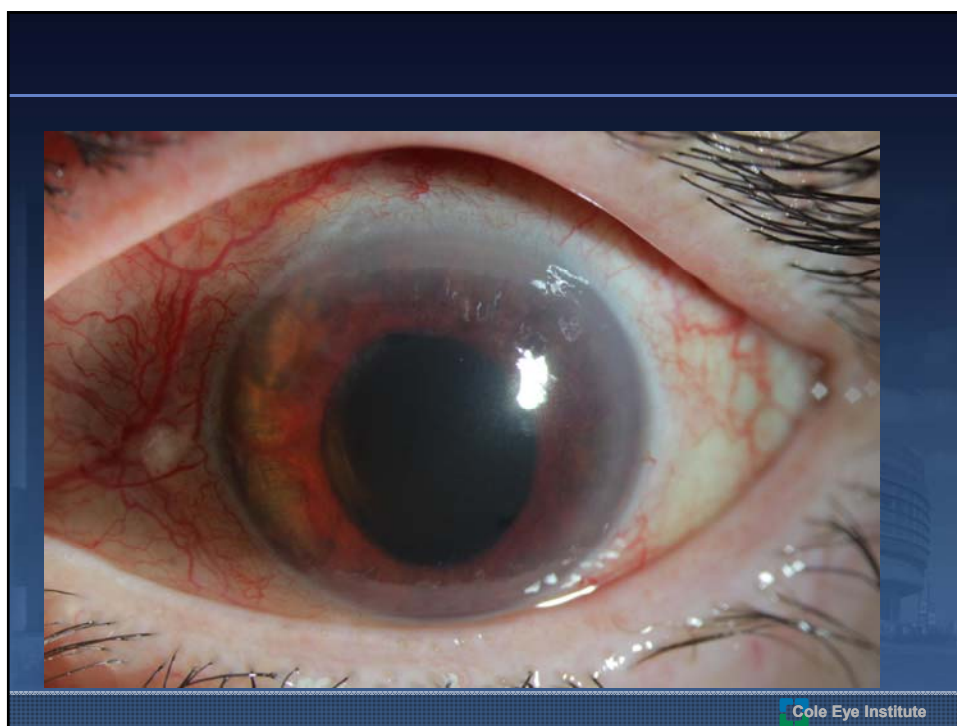


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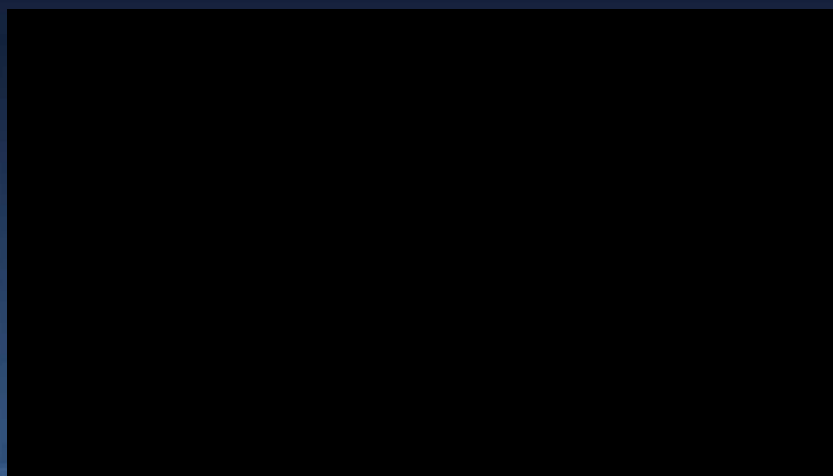


- Subdural stabilizes
- Biopsy scheduled
- Day of surgery





***“All I do is win?”***



## *No, I am not winning....*

- Vitreous hemorrhage
- Subretinal hemorrhage
- Exudative RD
- Ischemic appearing eye
- My fellow (Dilsher Dhoot) states:
- “Looks like endstage toxo to me, never seen lymphoma do this”

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- Biopsy results
  - Toxo PCR negative
  - Cytology reported negative
  - Flow Cytometry highly positive for lymphoma
  - Cytology reviewed again – looks like lymphoma

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- Subdural drained
- LP performed
- Dura biopsied
- All negative
- Enucleation performed

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## ***Enucleation Specimen***

- infiltration predominantly within and expanding the retina by diffuse sheets of atypical mononuclear cells with vesicular chromatin, scant to moderate amounts of eosinophilic cytoplasm and apoptotic bodies. The optic disc is involved and tumor is also seen within a central retinal vessel and focally in the choroid and vitreous.
- Overall, the findings are consistent with diffuse large B-cell lymphoma of germinal center phenotype.
- Correlation with the clinical findings is suggested.

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## *Lessons*

- Lab tests
- Clinical correlation easier with an enucleated specimen

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## *Case Presentation*

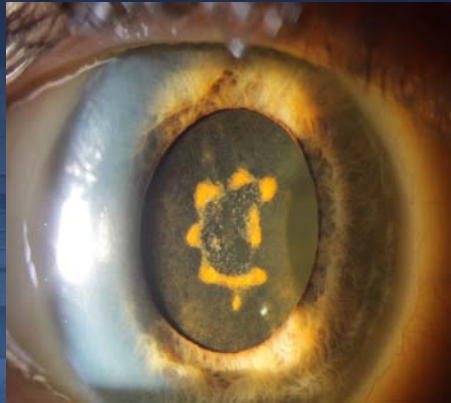
- 47 year old male being treated for recurrent anterior uveitis in one eye that is resistant to treatment
- Develops heterochromia
- Referred for second opinion



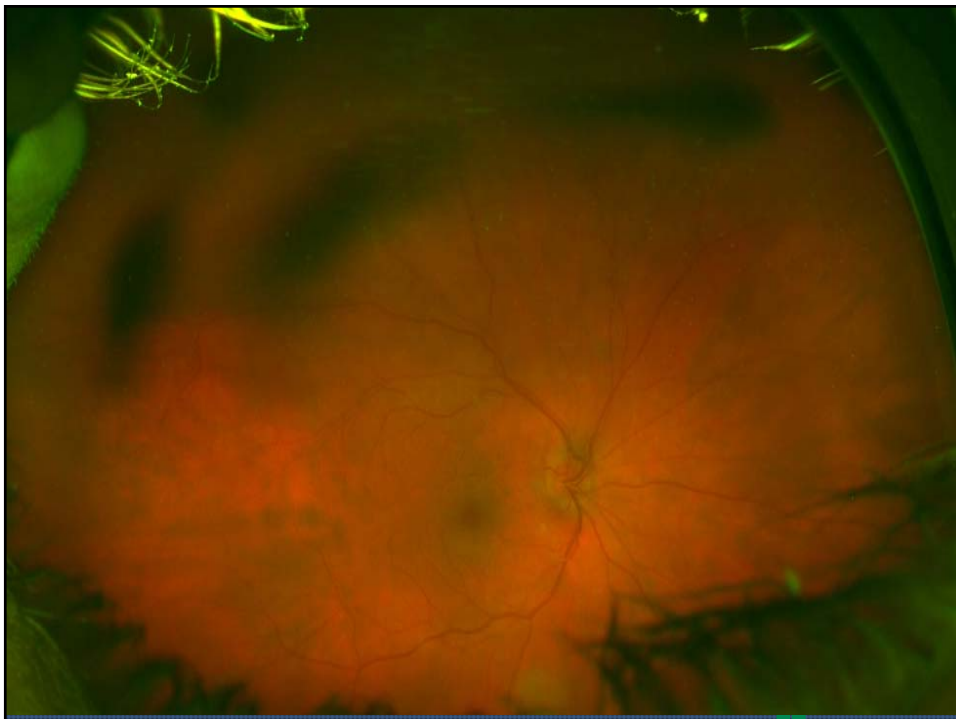
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## Case Presentation

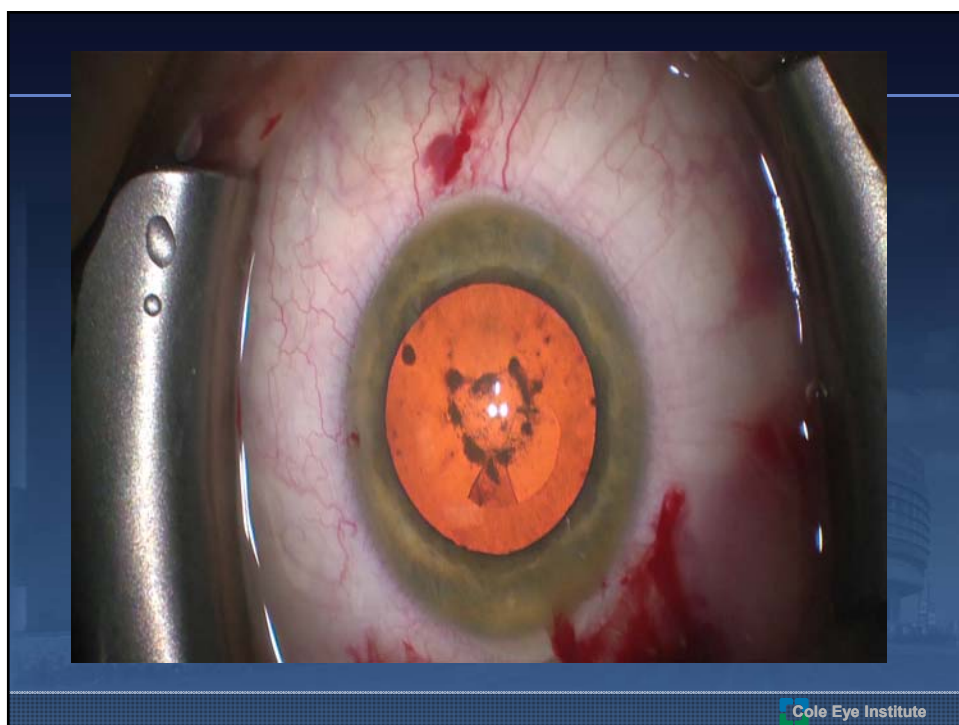
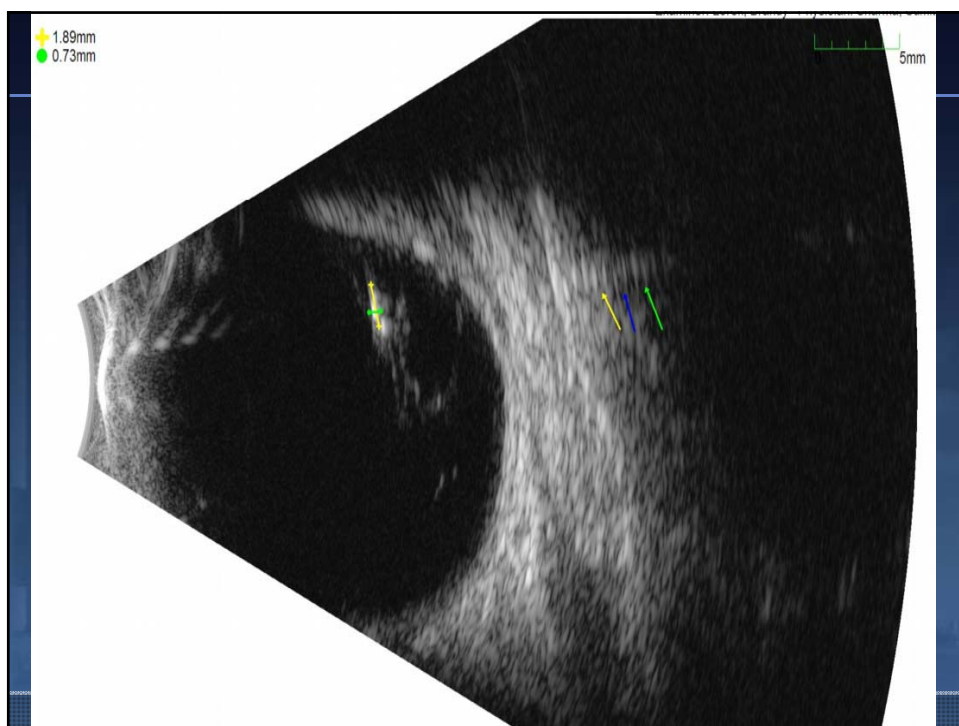
- On review of history tells us that he had a corneal foreign body removed
- Works as a mechanic



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## ***Lesson***

- History always important
- Foreign body with post inflammation warrants a scan
- I can still do a capsulorhexis



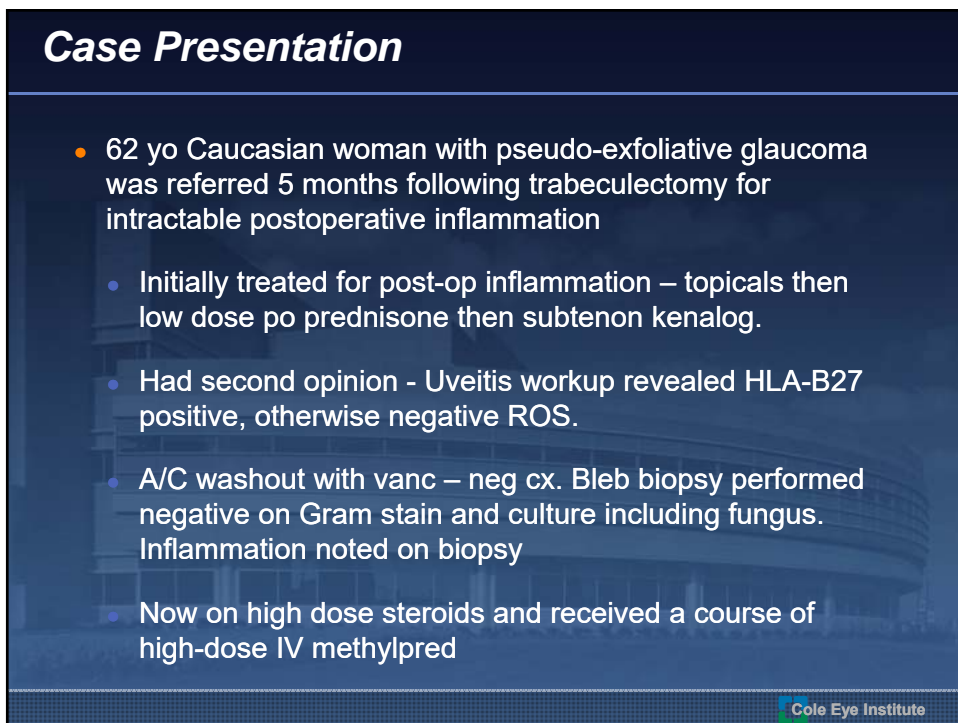
## Next Case

- Sometimes you can't win

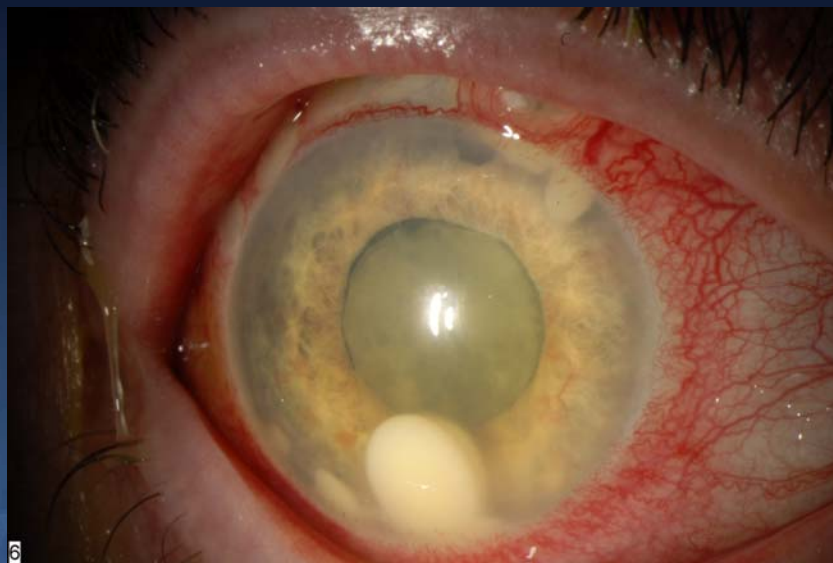


## Case Presentation

- 62 yo Caucasian woman with pseudo-exfoliative glaucoma was referred 5 months following trabeculectomy for intractable postoperative inflammation
  - Initially treated for post-op inflammation – topicals then low dose po prednisone then subtenon kenalog.
  - Had second opinion - Uveitis workup revealed HLA-B27 positive, otherwise negative ROS.
  - A/C washout with vanc – neg cx. Bleb biopsy performed negative on Gram stain and culture including fungus. Inflammation noted on biopsy
  - Now on high dose steroids and received a course of high-dose IV methylpred



***Our initial visit – POM #5***



6

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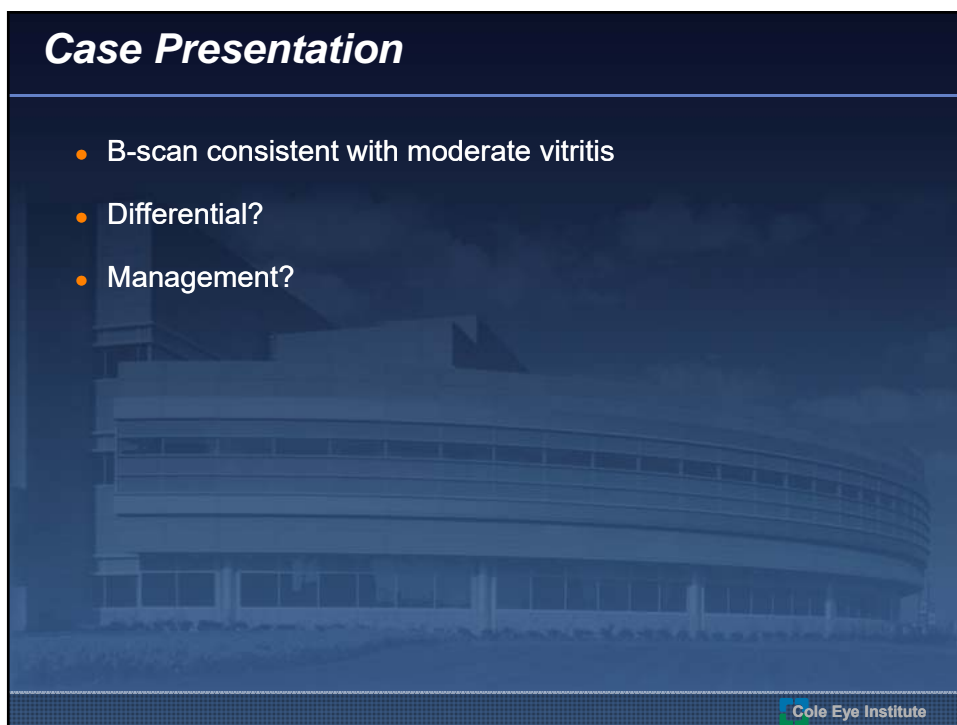
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## ***Case Presentation***

- B-scan consistent with moderate vitritis
- Differential?
- Management?





## ***Our initial visit – POM #5***

- Vitreous tap and inject
- Given intravitreal Vancomycin, Ceftazidime, Amphotericin
- A/C, vitreous tap negative on Gram stain and culture

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## ***Sometimes I am really helpful***



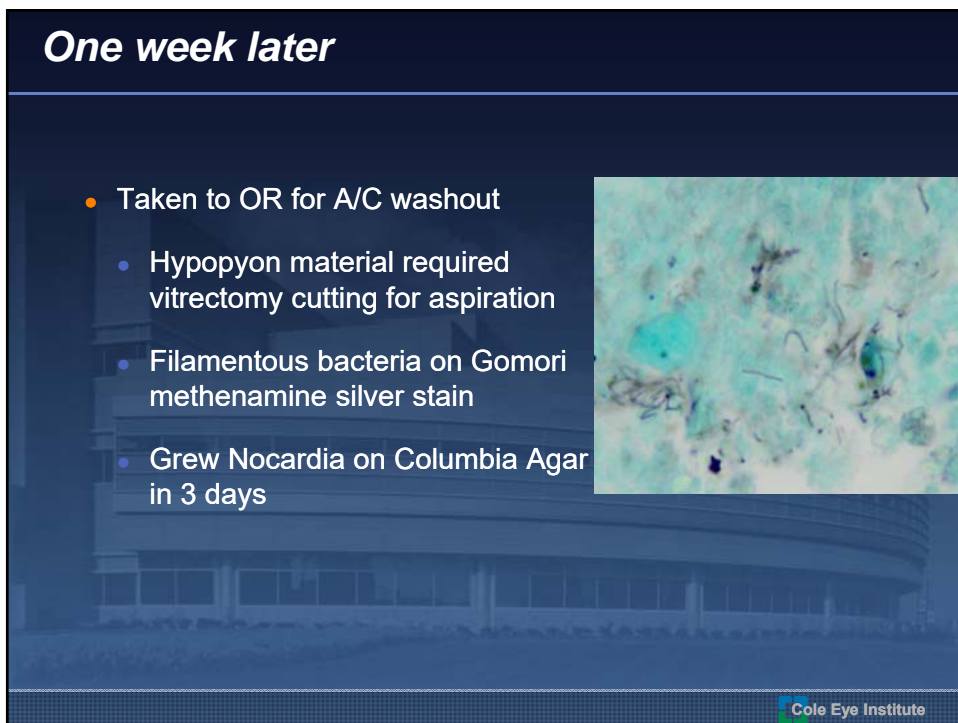
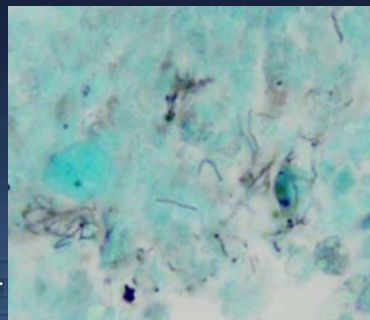
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## *Next step?*



## *One week later*

- Taken to OR for A/C washout
  - Hypopyon material required vitrectomy cutting for aspiration
  - Filamentous bacteria on Gomori methenamine silver stain
  - Grew Nocardia on Columbia Agar in 3 days





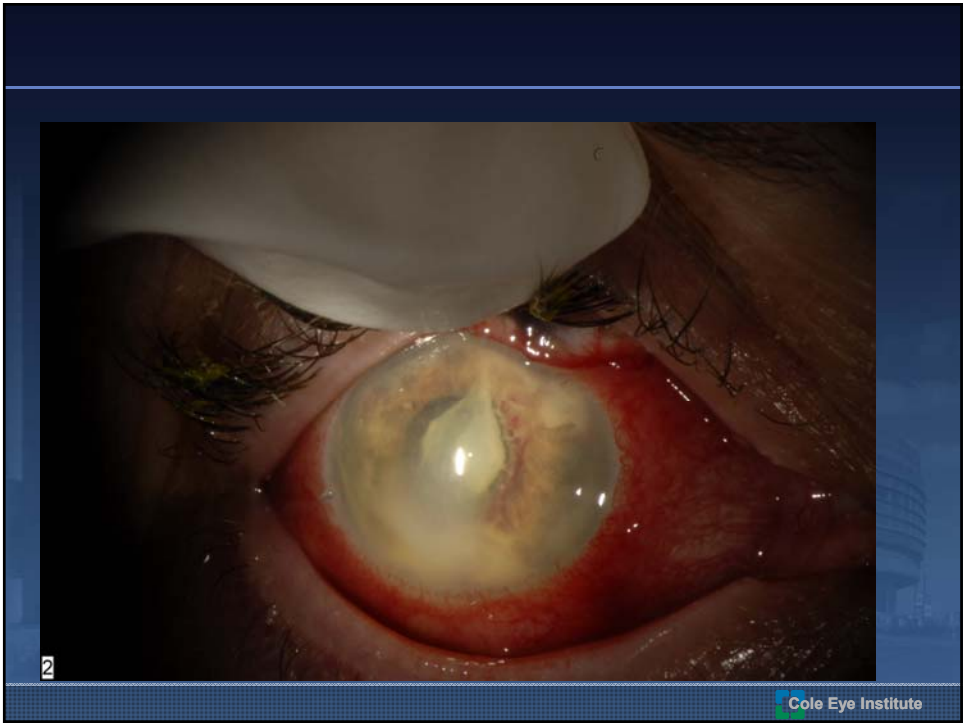
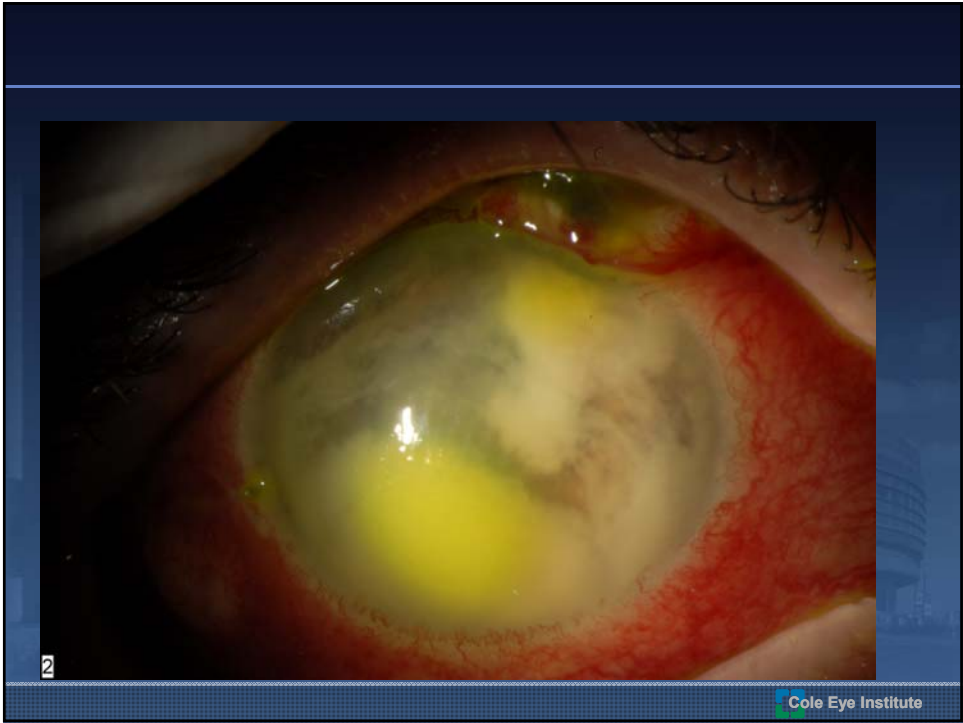
***The reason I am not on Best Doctors in America***

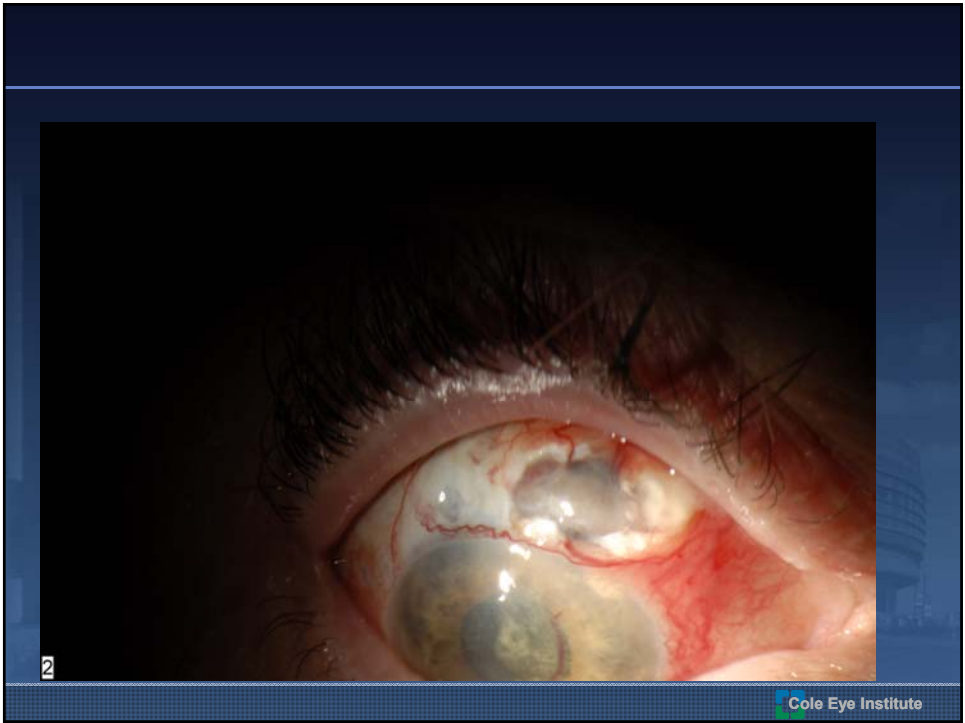
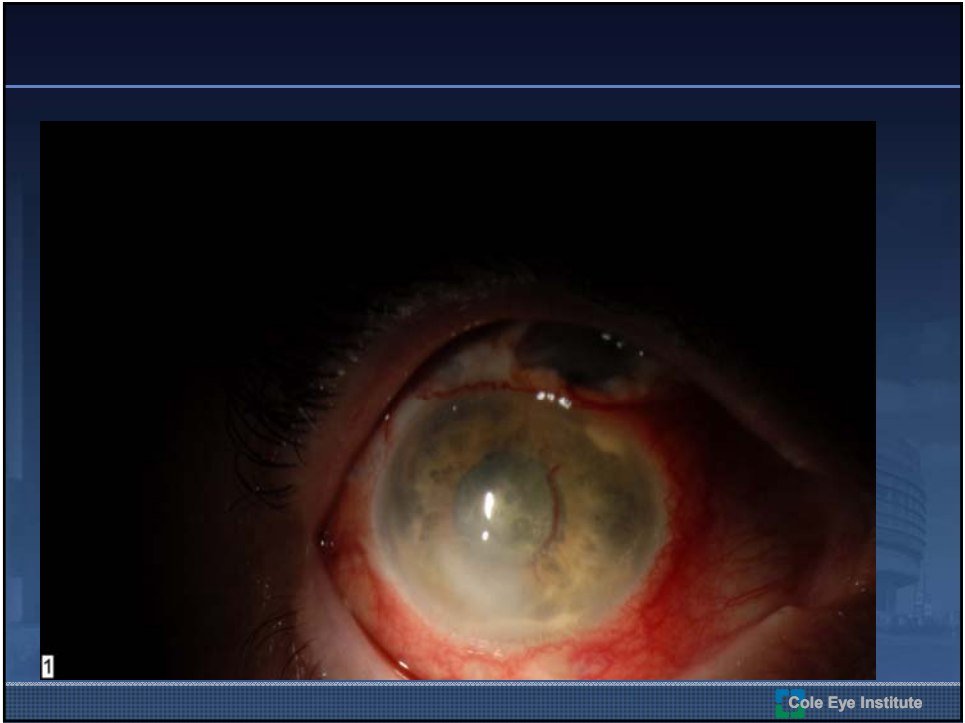


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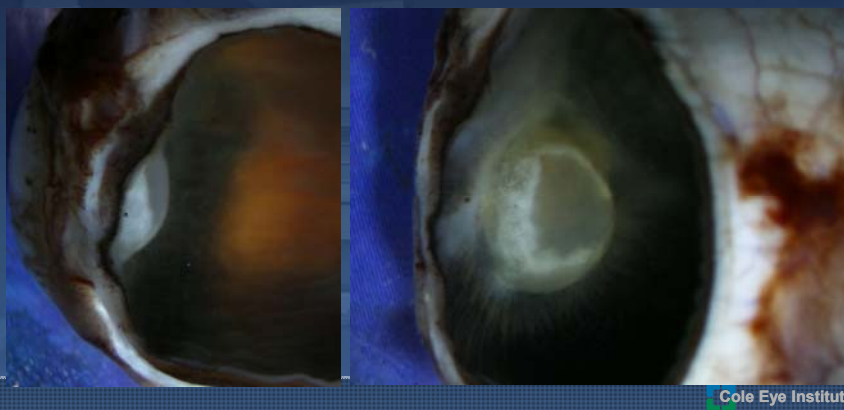






### *6 months later*

- Despite aggressive topical, PO and intravitreal antibiotics, she continued to decline



## ***Local steroid injections***

- Great tool for the treatment of uveitis patients
- Be careful when you use it
- Can't take it back
- Consider trying a course of po steroids to assess response prior to steroid injections
- You could unknowingly unmask an infectious agent

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## ***Next Case***

- Watch out for the cows....

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## ***Case Presentation***

- 58 year old female with vision loss after attacked by a cow
- Owns a farm, attacked by cow – hospitalized in ICU
- Develops blurry vision OS, but not seen
- 1 month later develops pain
- Told she has Purtscher's like retinopathy, has a laser for blood in the eye
- 2 months later develops panuveitis, has periocular steroid with worsening.

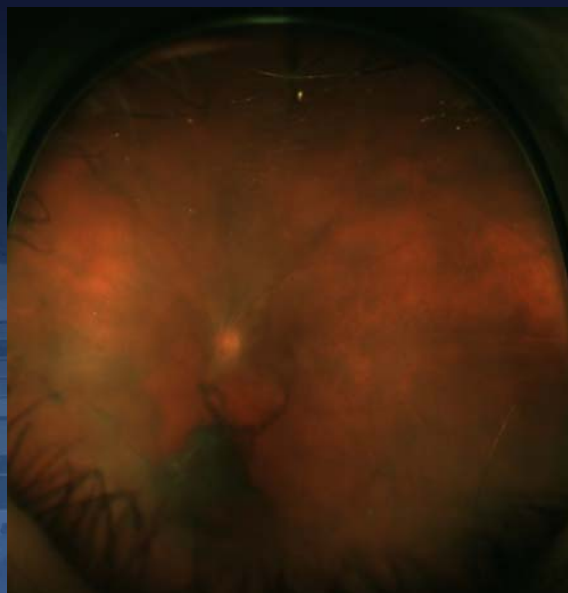
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## ***Exam***

- Vision: 20/40 OD, 20/200 OS
- 2-3+ NS OU
- 4+ AC cell OS, 3+ vit haze OS, 3+ vit cell OS

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## *Photo OS*



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## *Photo OS*



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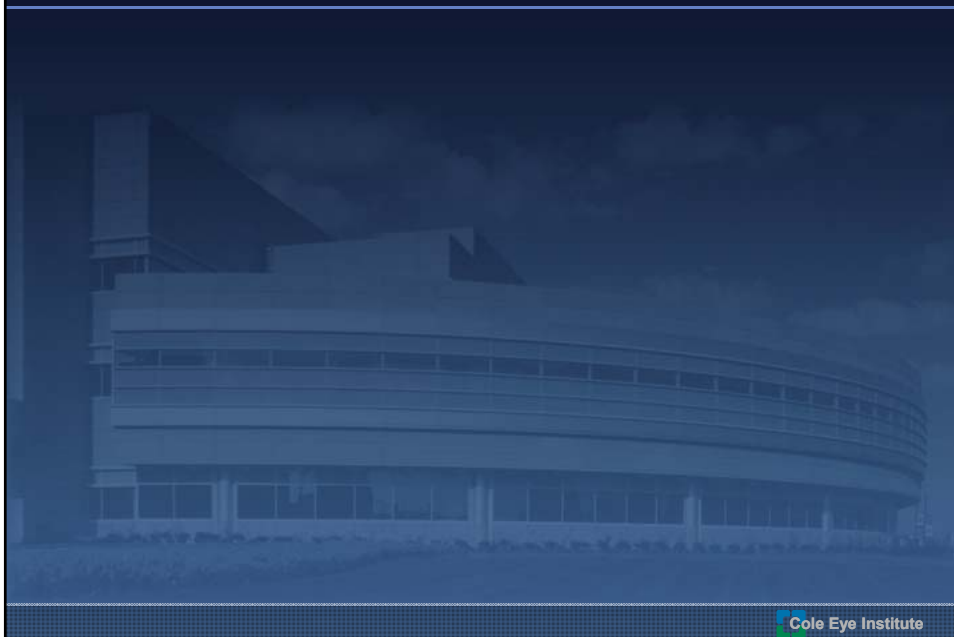


## ***B Scan***



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## ***Thoughts?***



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## ***Plan***

- Tap and inject with Vanc/Ceftaz/Ampho
- Started PF q 1 hour OS
- Started Cyclogyl BID OS
- Labs drawn

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## ***Labs***

- Lab work up
  - Toxo IgG positive (66), IgM negative
  - ACE: normal
  - Syphilis serology and Quantiferon negative
  - Cultures all negative
  - No history of infections in hospital, Imaging negative

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## ***Plan***

- Started Clindamycin 300mg QID because allergic to sulfa
- Started Prednisone 40mg
- Does not improve after a few days

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## ***Surgical video***



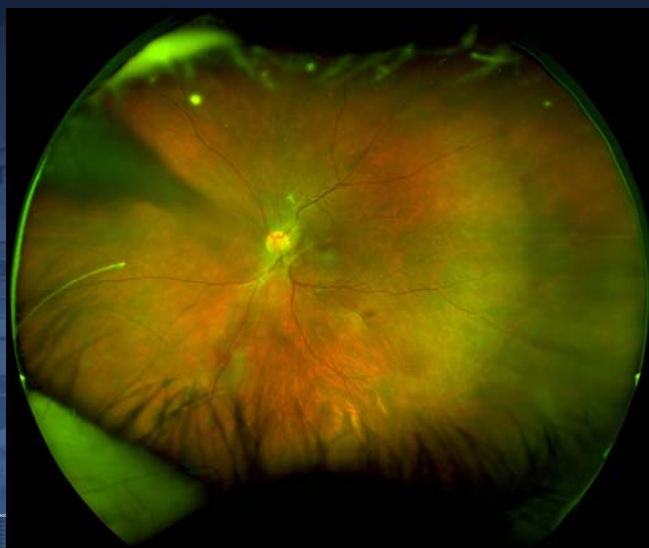
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## ***Next step?***

- Cultures negative
- Cytology negative
- Universal fungal PCR positive for *Candida albicans*

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## ***Photo Post Op***



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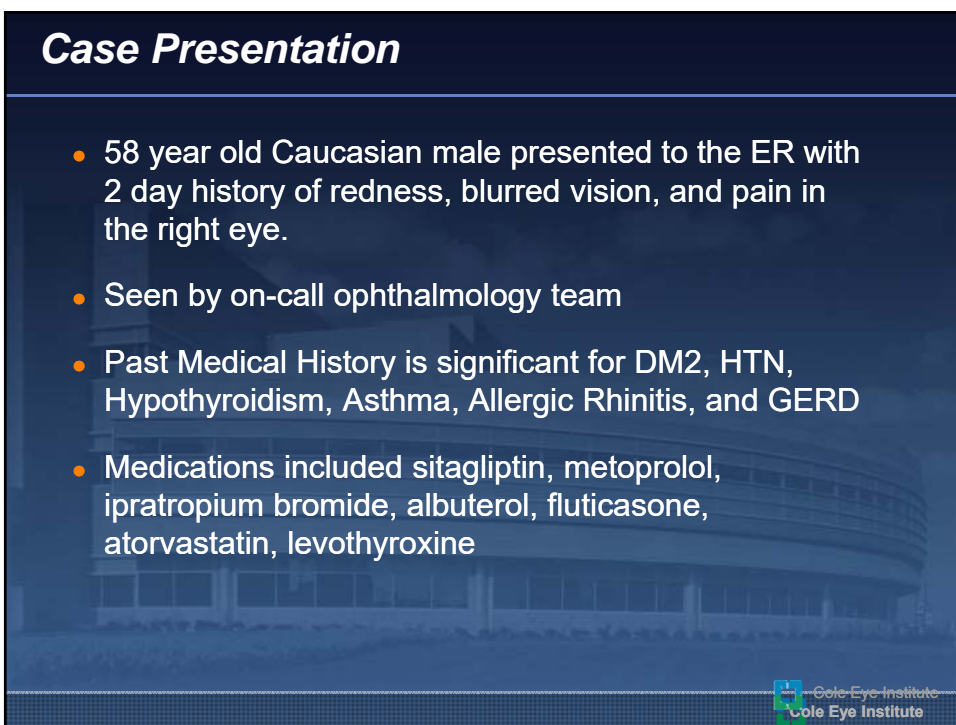
## Case Presentation

- Being a lounge singer can be hazardous to your health.



## Case Presentation

- 58 year old Caucasian male presented to the ER with 2 day history of redness, blurred vision, and pain in the right eye.
- Seen by on-call ophthalmology team
- Past Medical History is significant for DM2, HTN, Hypothyroidism, Asthma, Allergic Rhinitis, and GERD
- Medications included sitagliptin, metoprolol, ipratropium bromide, albuterol, fluticasone, atorvastatin, levothyroxine



## ***Exam and Treatment***

- Vision 20/ 400 OD, 20/20 OS
- IOP 51 OD 17 OS
- Unremarkable exam OS
- OD with 3+ injection, + corneal edema, difficult view into AC but likely cell, no hypopyon, no DFE or B scan performed
- No response to IOP treatment, AC tap performed, sample discarded → sent home on diamox, cosopt and brimonidine



## ***Follow-Up***

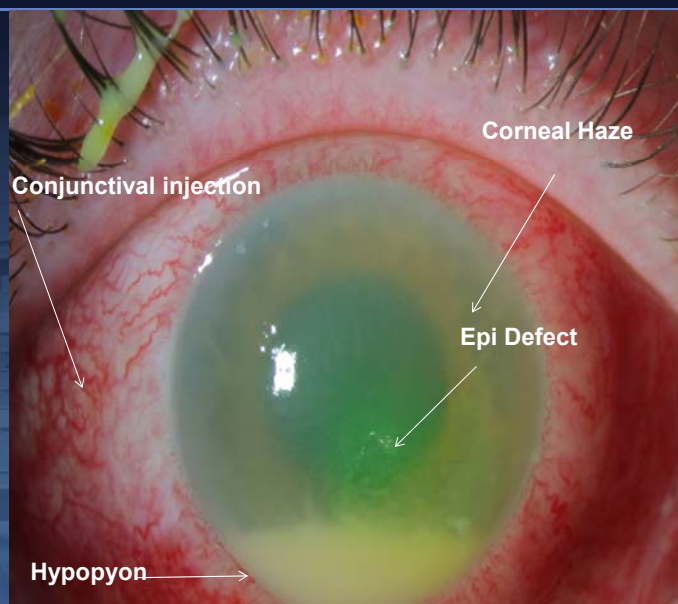
- Seen by glaucoma service
- Exam unchanged, but IOP improved to 43
- Continued on IOP meds and started on Valtrex
- Referred to Uveitis Service for follow-up the next day





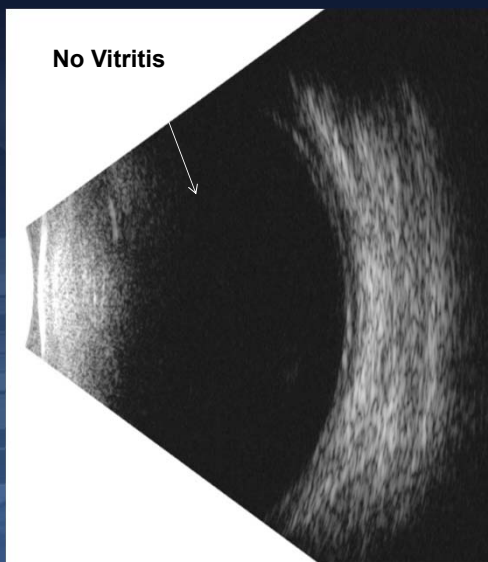
**Exam 7/30/14**

Vision OD: 20/300  
IOP OD: 49



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**No Vitritis**



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## *Hypopyon?*

- Why?
- Working dx – viral associated uveitis
- Rare to have large hypopyon
- Endophthalmitis from AC tap?
- Really rare – but fellow may have breathed on the needle
- Not really responding
- Concerned about infection

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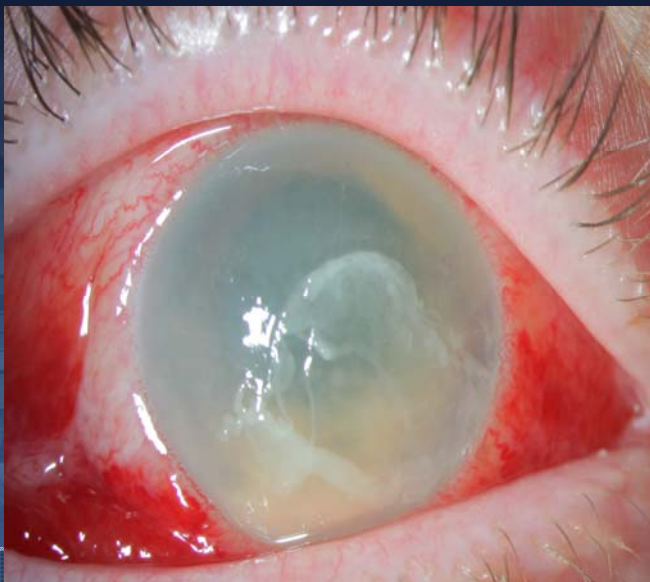
## *Plan*

- Underwent AC tap and inject of Vancomycin and Ceftazidime
- “Doubt we get anything”
- Drops:
  - Prednisolone Acetate 1% QID
  - Fortified vancomycin q 1 hour
  - Fortified ceftazidime q 1 hour
  - Continue acetazolamide, timolol-dorzolamide, brimonidine

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### *Next day*

- Vision HM
- IOP 12
- Clinically appeared worse
- Started PO Prednisone



### *Exam 2 days post tap and inject*

- Vision CF
- IOP 15
- Culture + for *Listeria Monocytogenes*
- Discussed with ID service, patient had PICC line placed and started IV ampicillin
- Underwent intravitreal amikacin



## ***Listeria??***

- Have you ever seen Listeria?
- Careen Lowder – “in 30 years never seen it”
- Dan Martin – “incredible, never seen it in 25 years”
- VR fellow – “wow, in my vast experience I have never seen this before, and you know I trained a really busy program before coming here and I am pretty sure I have seen everything, and if I haven’t seen it before, well it must be reportable”
- Me – audible eye roll

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## ***5 days post tap and inject – how am I doing?***



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## *2 weeks post-op*

- Vision 20/400 OD
- IOP 20
- Decision made for patient to undergo AC wash out
- Prednisone tapered



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## *1 month post presentation*

- Vision 20/25 OD
- IOP 13
- Current Meds:
  - Predforte QID
  - Cosopt BID
  - Bactrim DS BID
  - IV ampicillin



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## *Unremarkable DFE*



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## *2 months post presentation*

- Returns with increased discomfort OD.
- Vision 20/40 OD
- IOP 20 OD
- AC had 2+ cell with 1+ anterior vitreous cell
- What now?

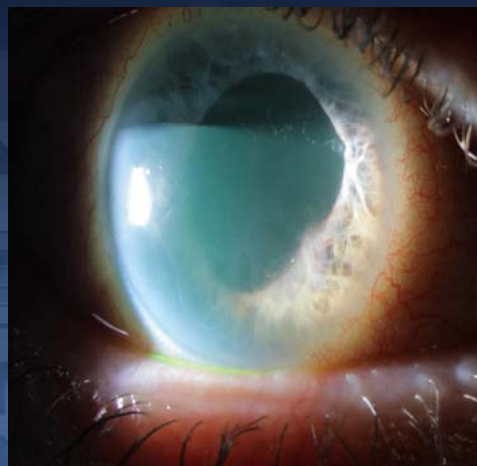


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## *Exam 1 week later*

- Returns with VA of 20/60 and IOP of 36 OD
- Placed on:
  - Increase PF to q 1 hour
  - Start Cosopt and brimonidine
  - Given intravitreal amikacin
  - Continue gentamicin gtts and PO bactrim



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## *Case Presentation*

- Topical steroids increased then tapered
- Became inactive
- Slowly tapered off topicals
- Finished po course
- 3 months later – 20/20 no recurrence

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## *Where did the Listeria come from?*

- Patient is a lounge singer
- ID believed patient ingested infected cheese
- Patient now does not eat during performances
- Only drinks beer
- Flew to Hollywood to film his first movie – plays a lounge singer

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## *Listeria Endophthalmitis*

- Elliot et al (1992)
  - 14 cases of listeria monocytogenes endophthalmitis
    - Patients
      - 5 immunocompromised, 9 immunocompetent
    - IOP: Average 45, range 30-68
    - All had fibrinous AC reaction
    - 11 of 14 had hypopyon, 4 of which were dark (pigmented)
    - + Pigment Dispersion
    - Final vision was 20/200 or worse for most patients
    - All cases assumed to be endogenous in etiology

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## *Listeria Endophthalmitis*

- Thought that the infection likely enters through the gastrointestinal tract.
- Stool cultures not useful
- Thought Listeria may be able to penetrate an intact intestinal tract
- Treatment
  - Ampicillin and Gentamicin
  - Ciprofloxacin and Bactrim have activity against listeria



## *Lesson*

- Diagnosis
  - Acute IOP rise
  - HSV keratouveitis
  - Infectious endophthalmitis from AC tap
  - Infectious endophthalmitis from endogenous source (from a rare bug)
- Sometimes as experienced as you are – you really have not seen everything
- Multi-team approach
- Watch for rebound inflammation



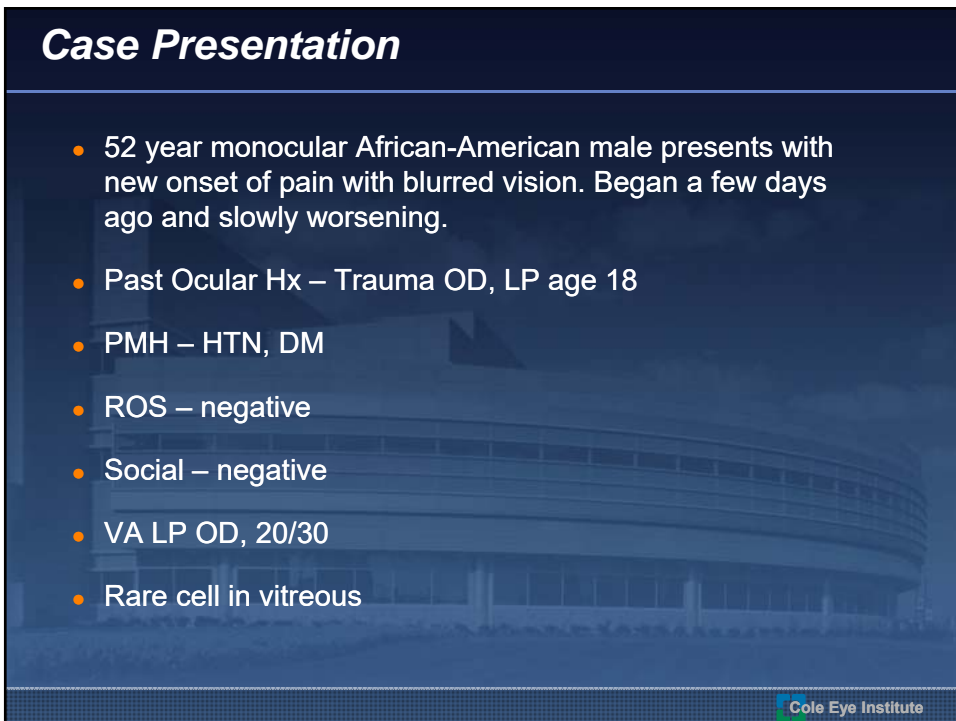
## ***Next Case***

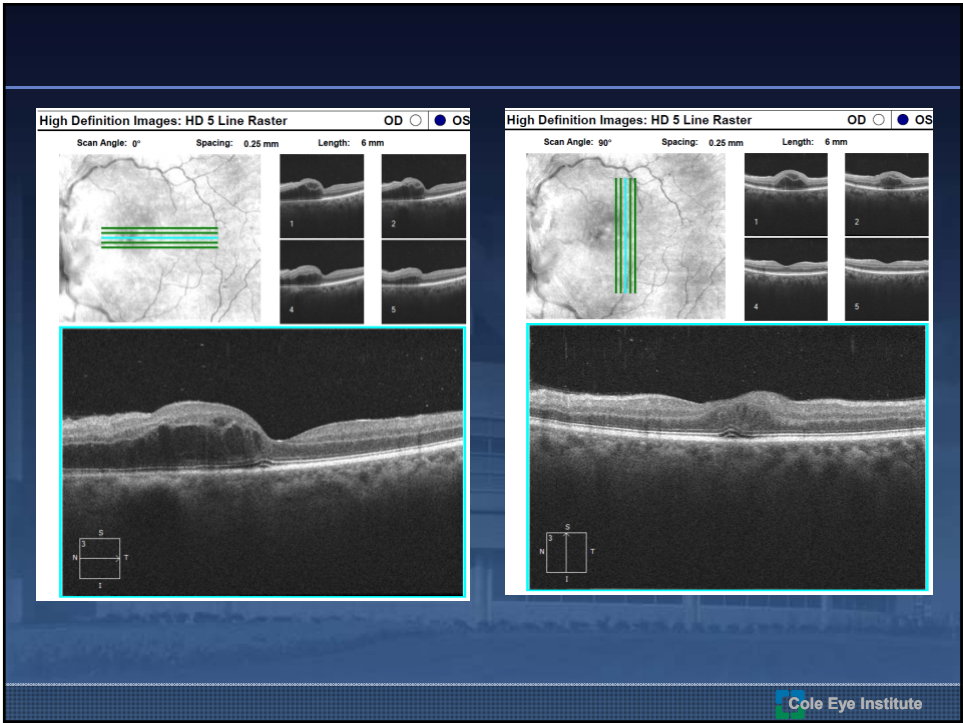
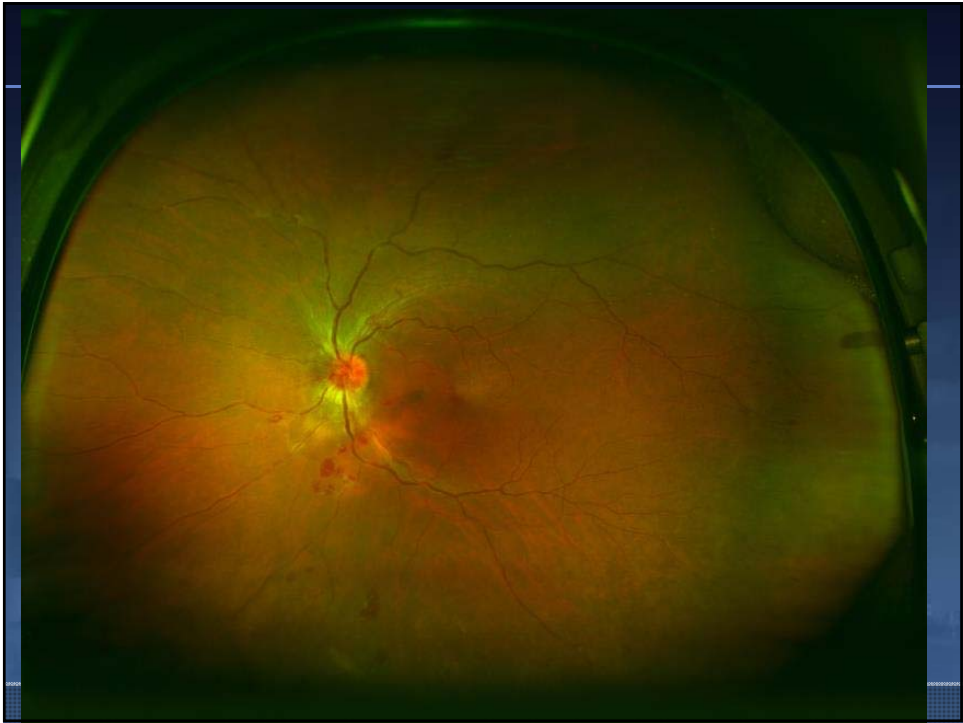
- Graduation caps can be dangerous.

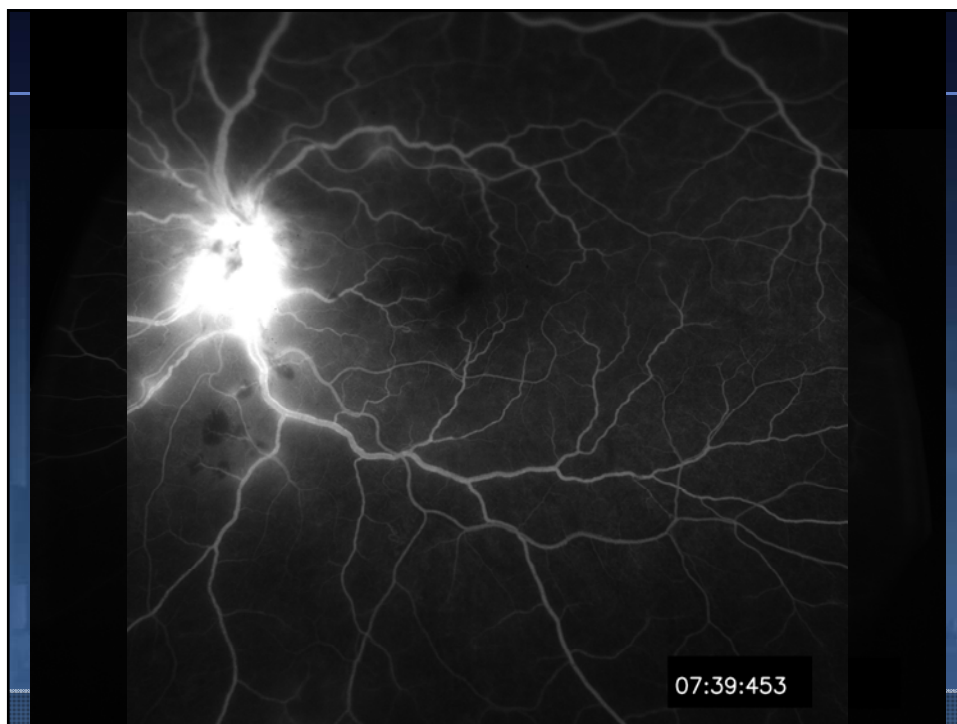


## ***Case Presentation***

- 52 year monocular African-American male presents with new onset of pain with blurred vision. Began a few days ago and slowly worsening.
- Past Ocular Hx – Trauma OD, LP age 18
- PMH – HTN, DM
- ROS – negative
- Social – negative
- VA LP OD, 20/30
- Rare cell in vitreous







## *Thoughts?*

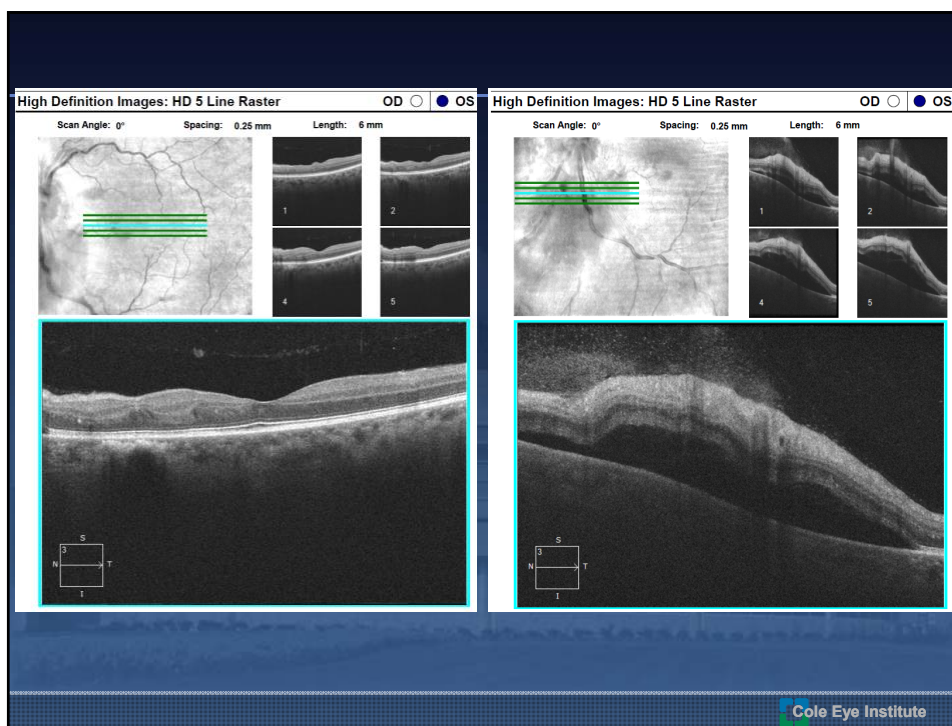
- Posterior Uveitis, Retinal vasculitis?
- Infectious – Herpes, toxo, syphilis, viral
- Inflammatory – Behcet's, Sarcoid, etc
- Plan: Treat for everything
  - Valtrex 2 grams daily
  - Bactrim, Prednisone



## *Returns 3 days later*

- Labs negative for syphilis, TB, toxo

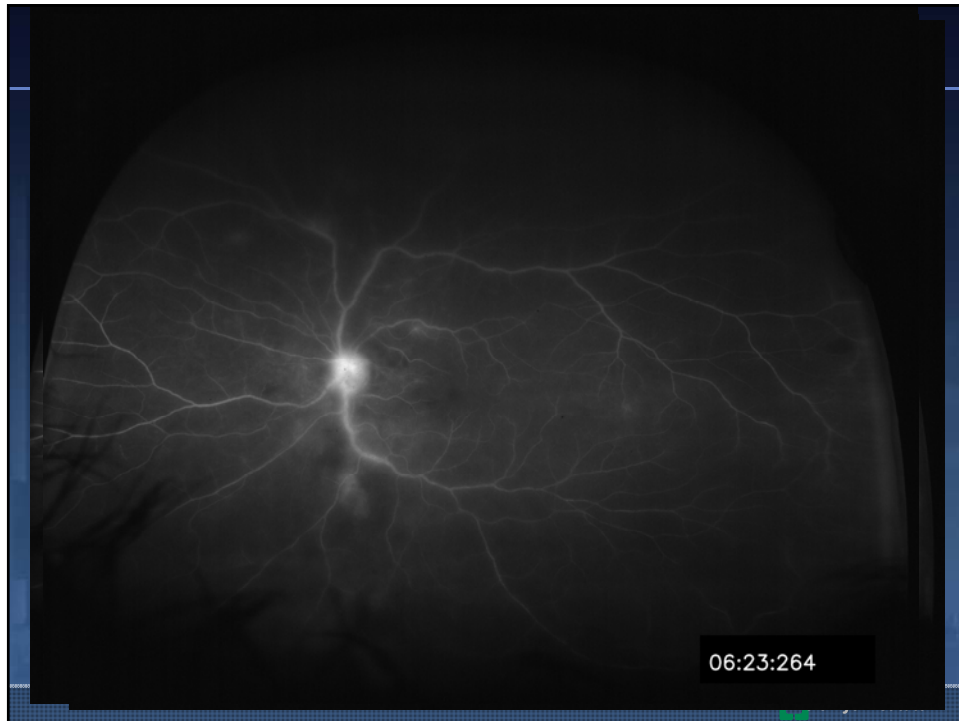




## Case Presentation

- Hmm....
- I get pulled into the room
- “Lets talks about that right eye”
- “How did you lose it?”
- “I was hit in the eye with my graduation cap.”
- “You lost vision from a graduation cap?”
- “Well, a few weeks later I developed an infection in the eye, I had shots in it, I then developed a retinal detachment. “
- “They thought it was a virus’





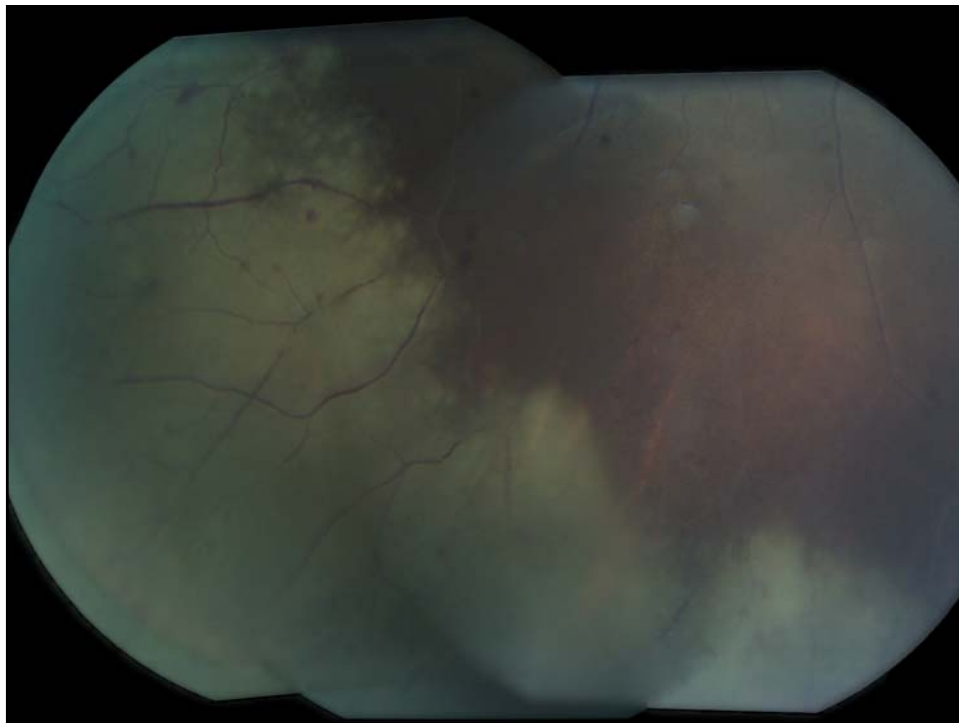
## ***Assessment/Plan***

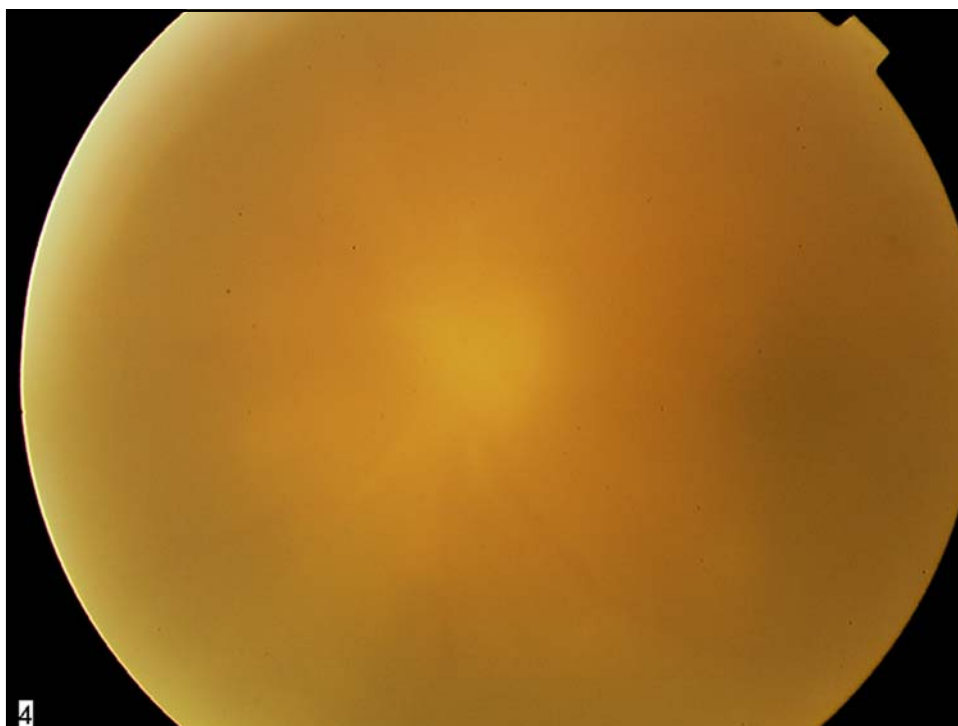
- Acute Retinal Necrosis
- AC tap PCR positive for HSV-2
- Receives multiple injections
- Detaches
- Repair – 20/25

## ***Acute Retinal Necrosis - Progressive Outer Retinal Necrosis***

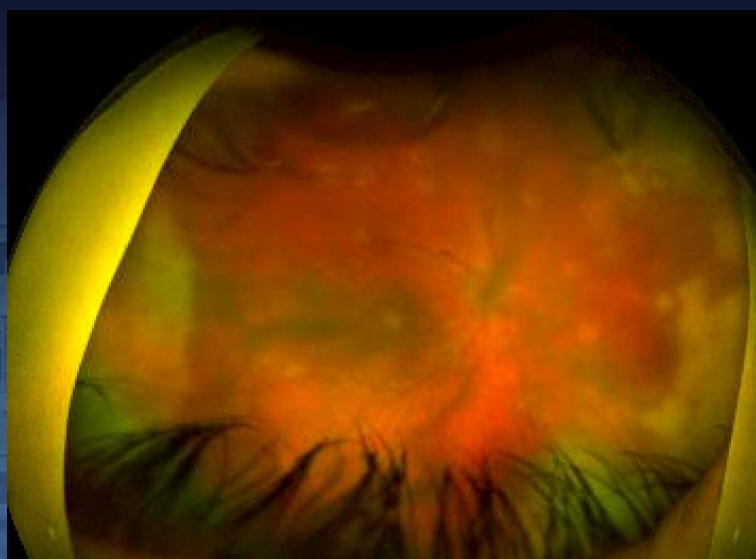
- What we know...
- Viral associated retinitis
  - Most often HSV or VZV infection
- Represent a continuum of disease
  - Acute retinal necrosis (ARN) in the immunocompetent
  - Progressive outer retinal necrosis (PORN) in the immunosuppressed
- Historically poor visual outcomes
- Limited long term follow-up

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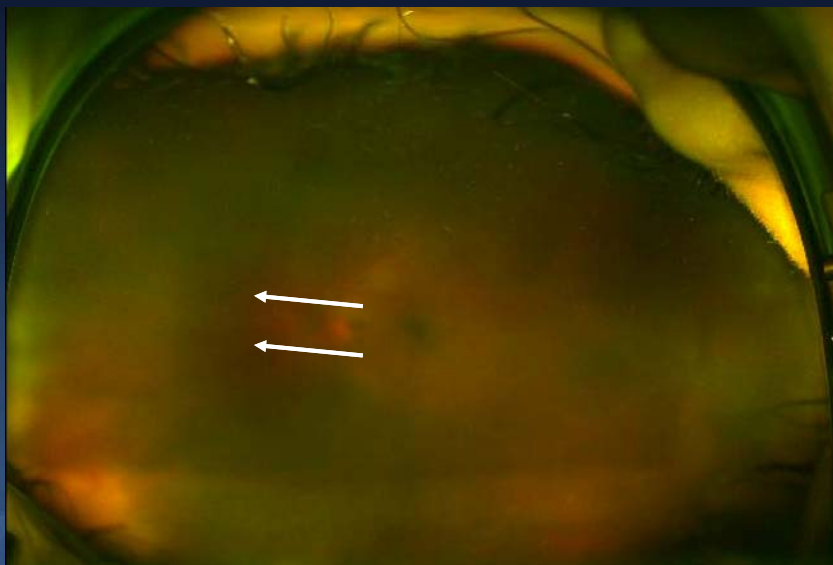


*Fundus photos in tough views*





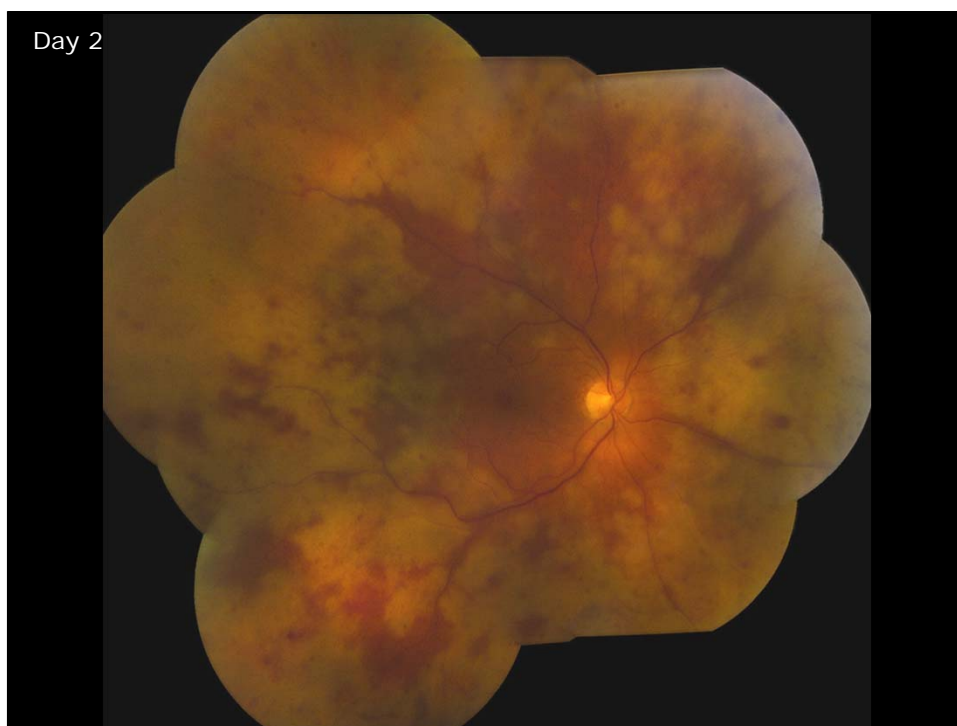
## *Fundus photos in tough views*



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Day 0





### ***What can be done to limit VA loss?***

- Poor presenting vision – poor final vision
  - 20/400 or worse – 70% with CF or worse
- Delayed diagnosis – very poor vision
  - 1/3 no light perception
  - 80% 20/400 or worse
  - Most treated with steroids without anti-virals
  - Misdiagnosed as disc edema, toxoplasmosis

## ***Recommendations***

- Prompt anti-viral therapy
- Low threshold for initiation of oral val-acyclovir therapy/intravitreal injection of anti-viral
- Accurate diagnosis
  - Aqueous/vitreous PCR
  - Diagnostic vitrectomy
- I don't laser

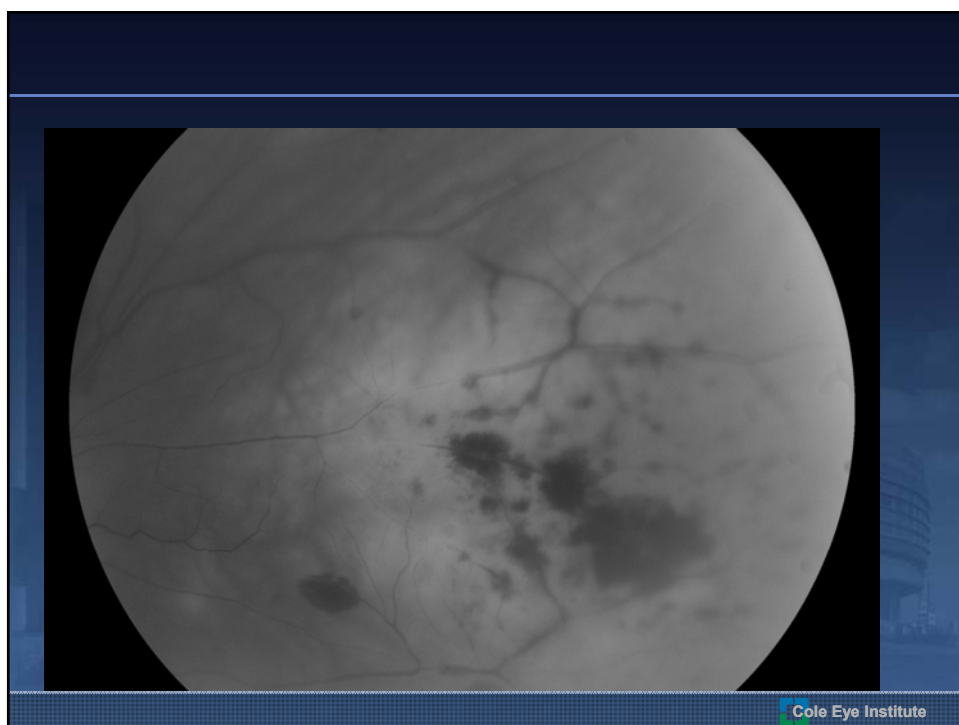
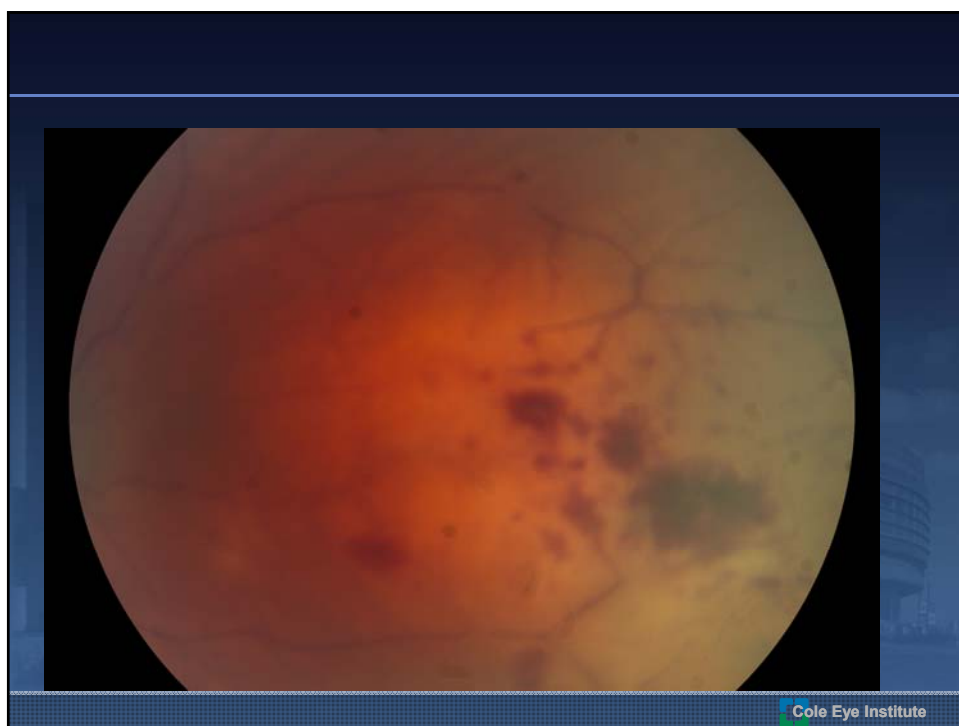
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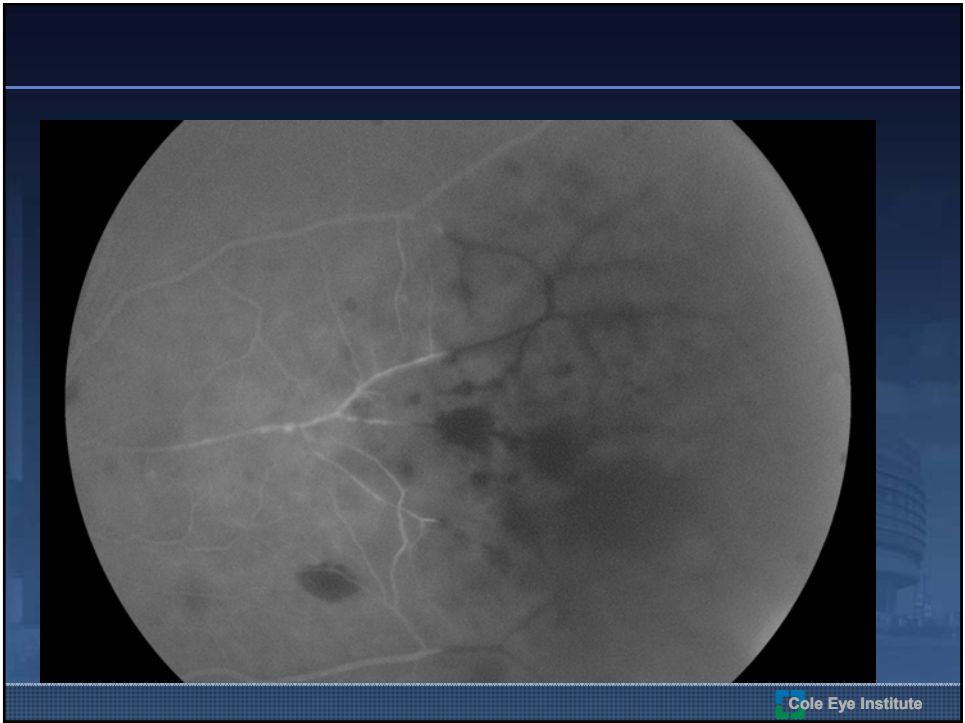
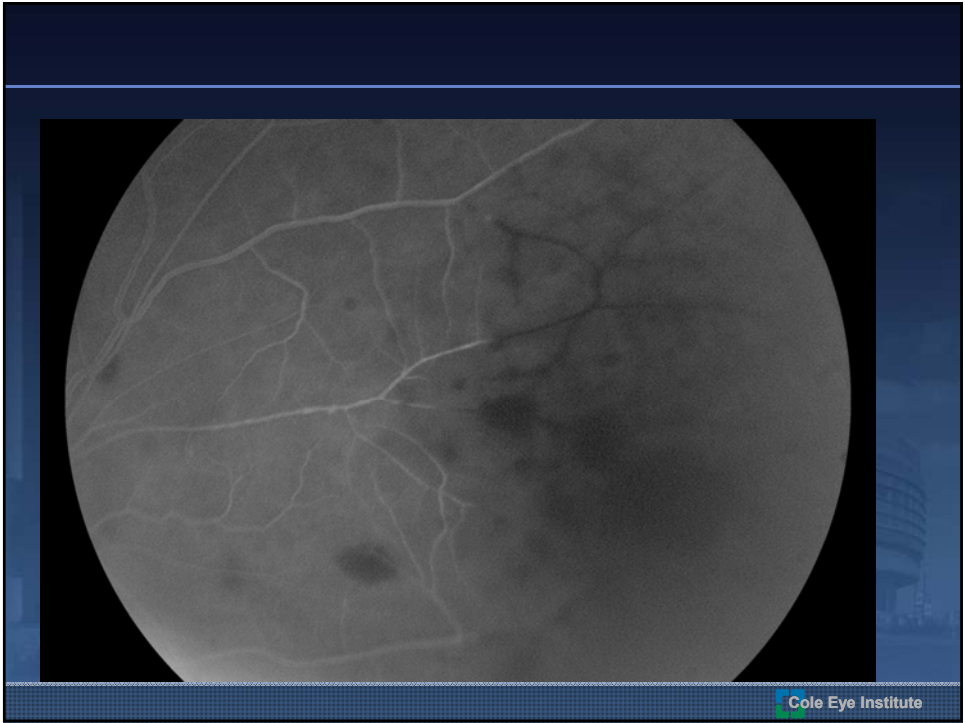
## ***Case Presentation***

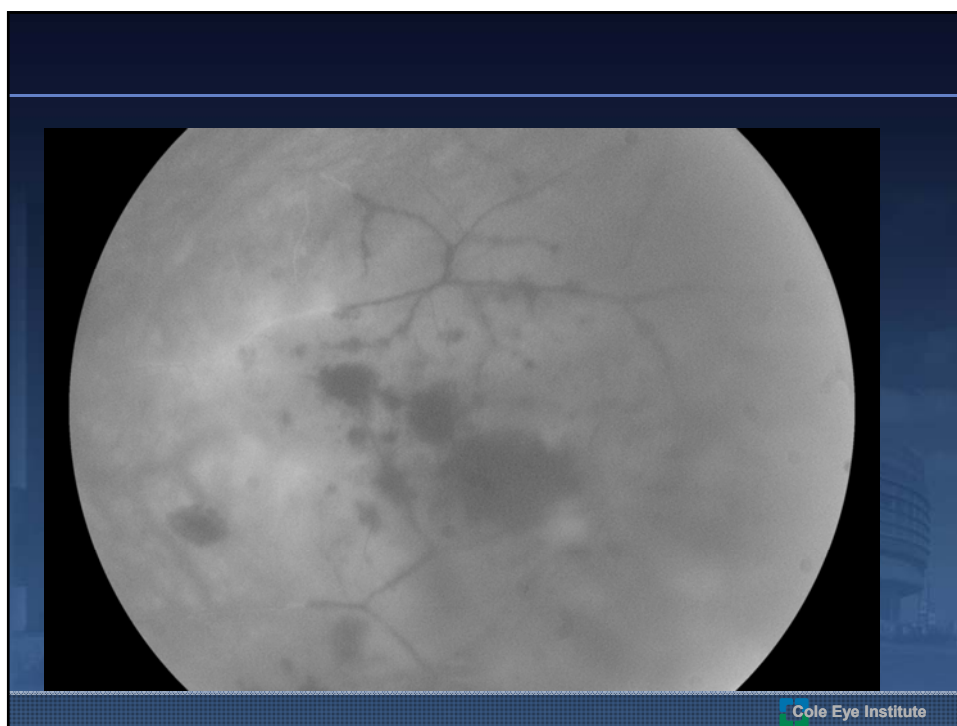
- 53 year old male with vision loss OS 3 months prior. Saw local optom – diagnosed with probable CRAO.
- Sent to internist – admitted. Cardiac w/u neg, temp artery bx – negative
- Started on po pred – tapered
- 2 months later sees retina
- OD – WNL, OS – extensive heme – infectious w/u neg. OS enucleated for pain. Path negative for infection
- Now with changes OD. 20/60 2 + cell

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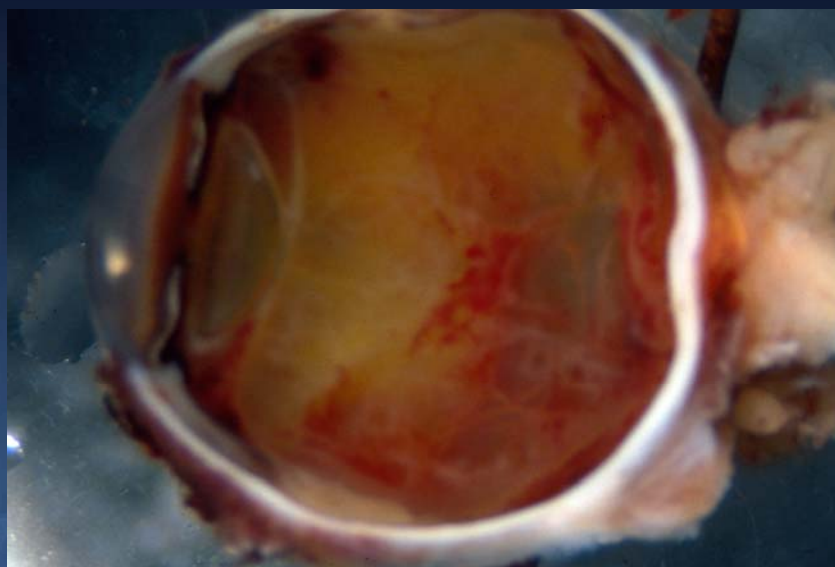




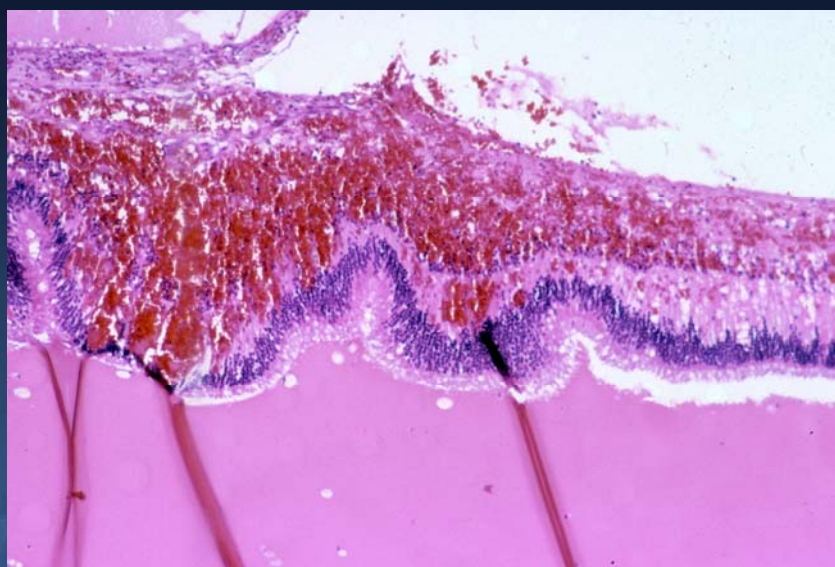
## ***Differential Diagnosis***

- Infectious
  - Viral Retinitis
  - Toxo
  - Syphilis
- Vasculitis
  - Behcet's

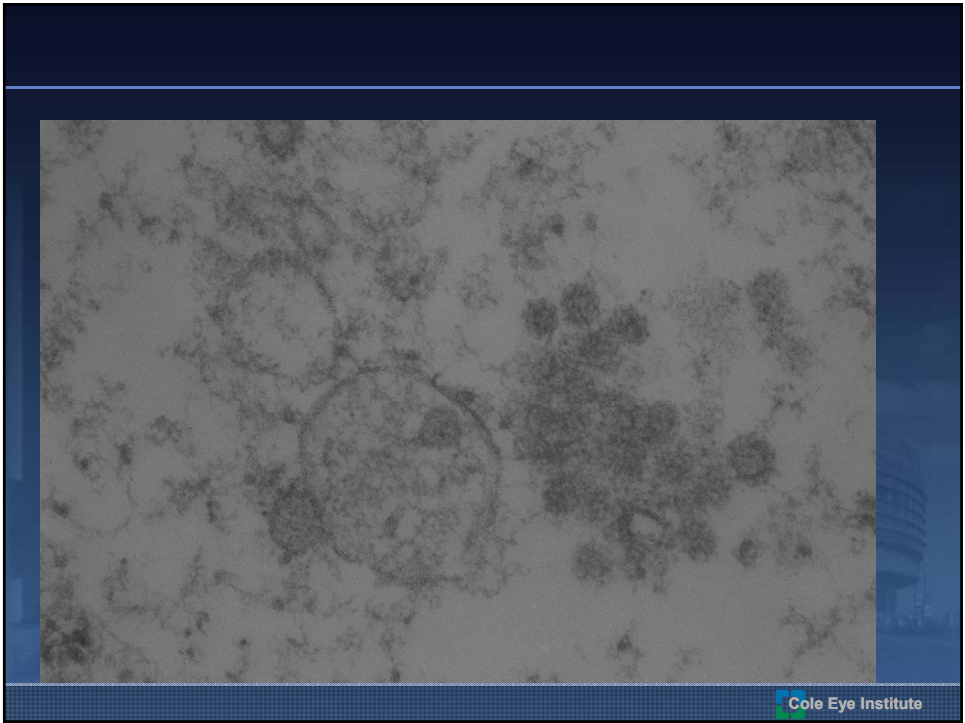
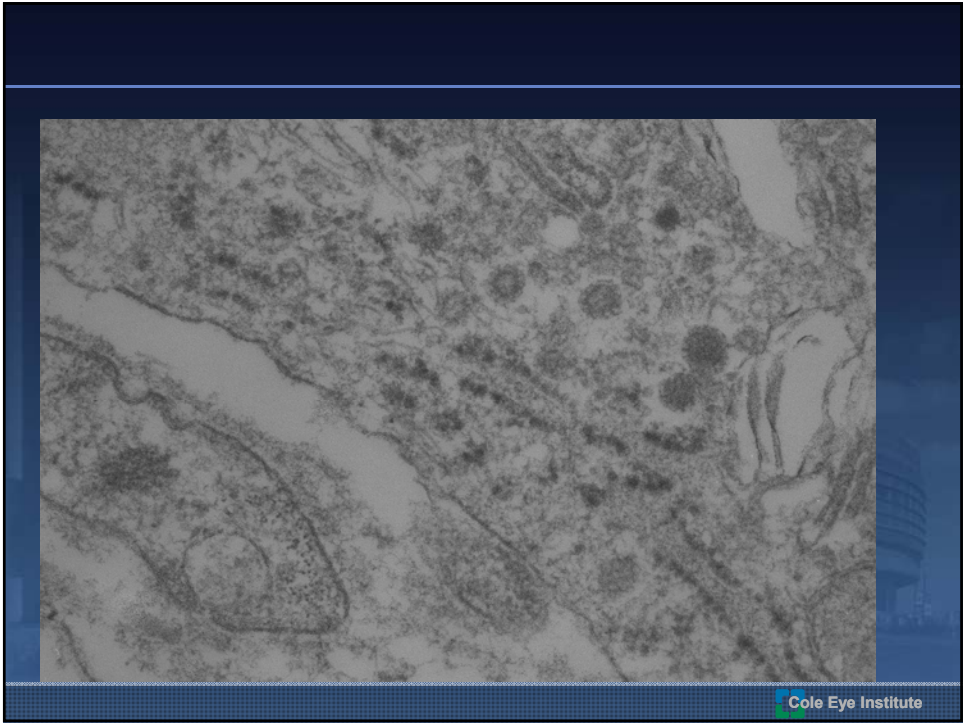


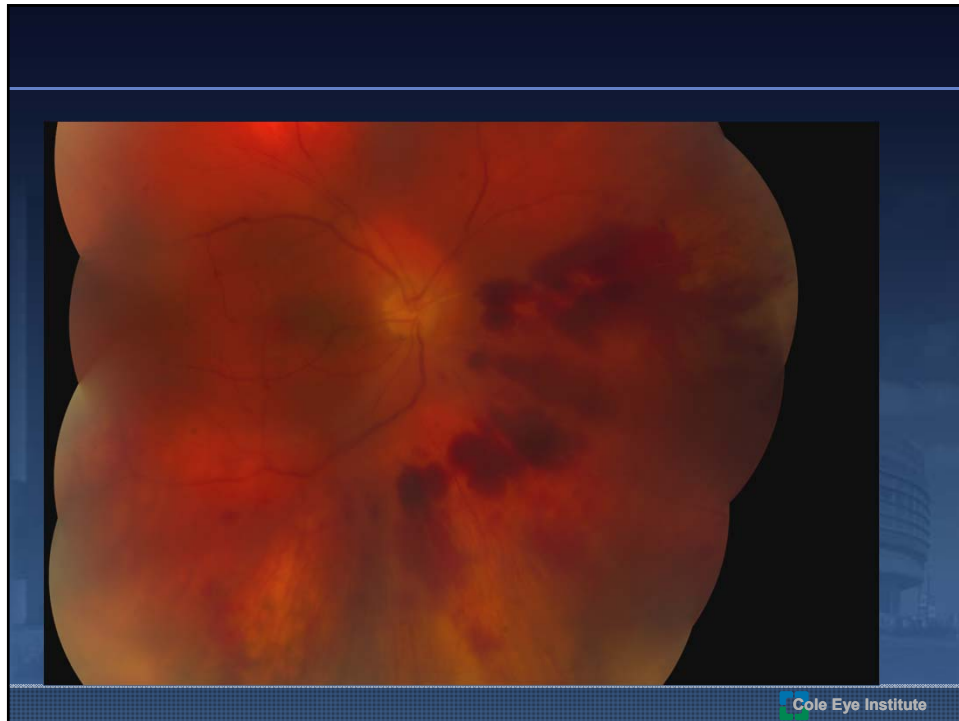


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## ***Recommendations***

- Oral val-acyclovir therapy for at least 3 months.
- Immunocompromised patient – maintain anti-viral therapy until recovery
- Long term anti-viral therapy
  - Significant number of patients with recurrence or delayed bilateral involvement
  - Potential for breeding resistance

## ***Next Case***

- It looks weird, but you know the answer...



## ***Case Presentation***

- 48 year old male who has not seen a doctor in over 10 years presented to ED
- CC: decreased vision in both eyes.
- Duration 1.5 weeks, stable.
- No improvement so decided to get it checked out.



- PMH: heart murmur when young
- PSH: none
- Meds: None
- Pets: two cats, two dogs and a turtle at home
- Social History:
  - not currently sexually active, women only
  - occasional marijuana use
  - works as a laundry attendant at a hotel

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## ***Systemic ROS:***

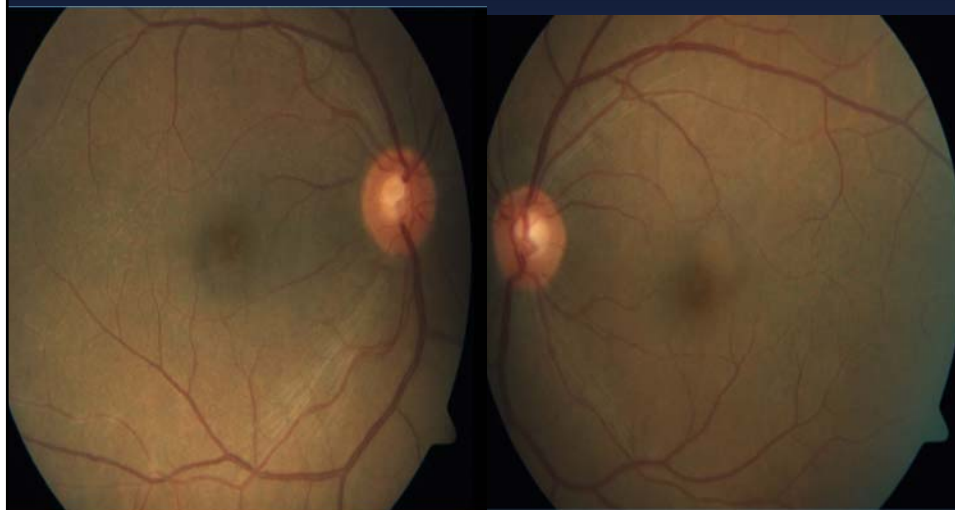
- **POSITIVE** - +night sweats
- **NEGATIVE** - denies any recent weight loss/gain, fevers/chills, fatigue, generalized weakness, easy bruising/bleeding, tremor or intolerance to heat or cold, sicca symptoms, nasal ulcers, oral ulcers, cold sores, genital ulcers, difficulty swallowing, chest pain, shortness of breath, wheezing, cough, blood in sputum, nausea, vomiting, abdominal pain, diarrhea, changes in bowel or bladder patterns, change in urine, weakness/numbness/tingling of limbs/digits, muscle pain, joint aches/pains, rash, hives, sun sensitivity, hair loss, skin discoloration, headache, dizziness, seizure, tinnitus, hearing loss, depression, anxiety, enlarged lymph nodes. Denies h/o STDs, recent foreign travel

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**Base Exam**

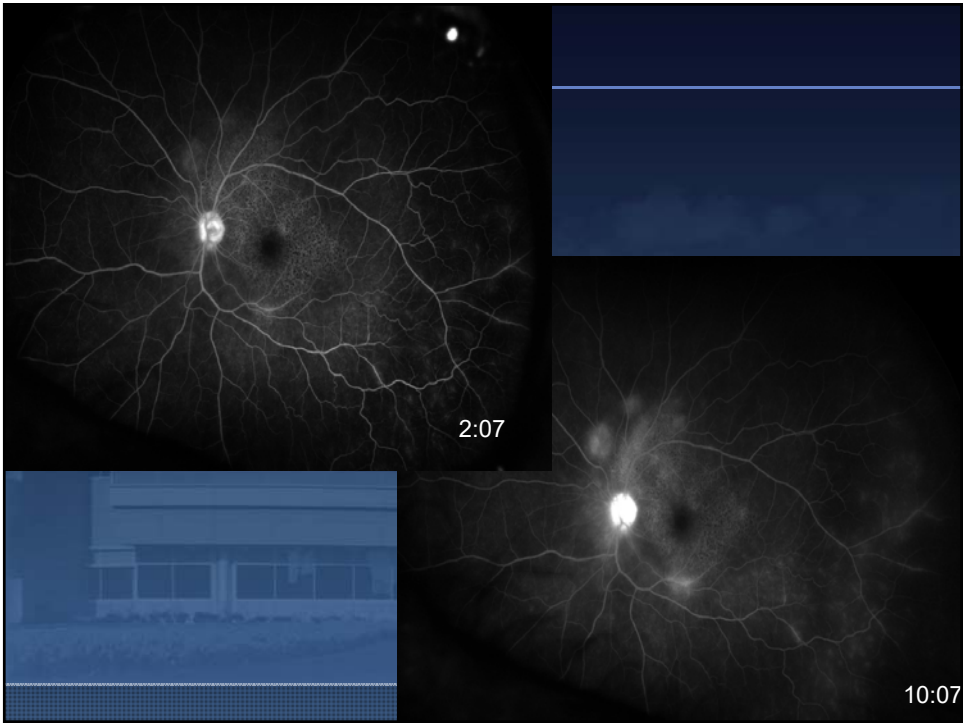
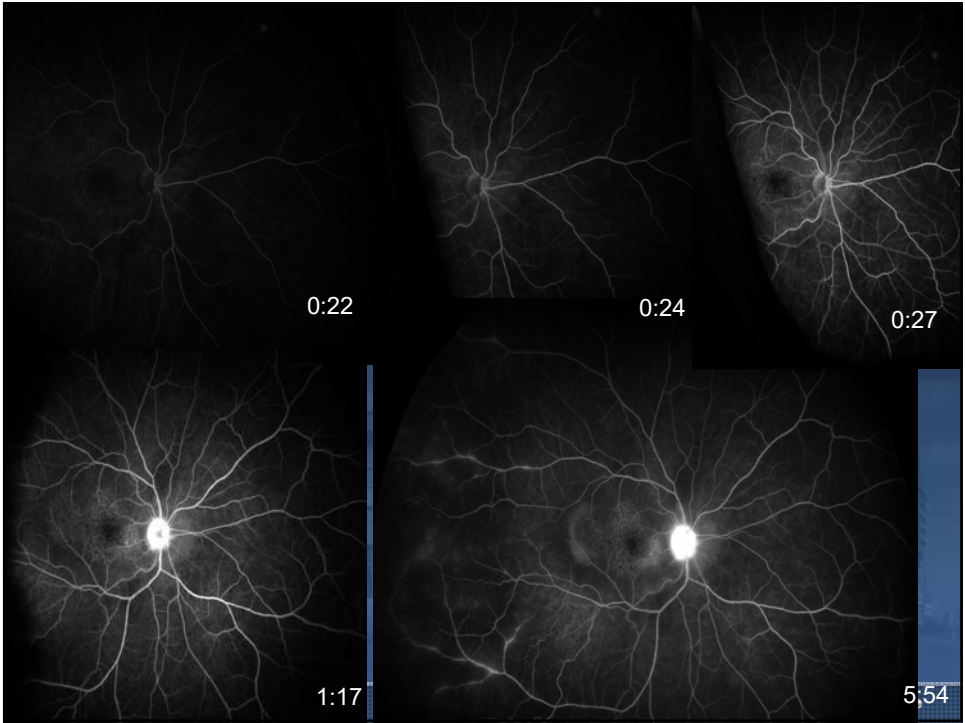
	<b>OD</b>	<b>OS</b>
BCVA	20/250	20/80
Pinhole	NI	NI
IOP	13	25
Pupils	4 → 2 no APD	4 → 2 no APD
EOM	Full	Full
CVF	Full	full

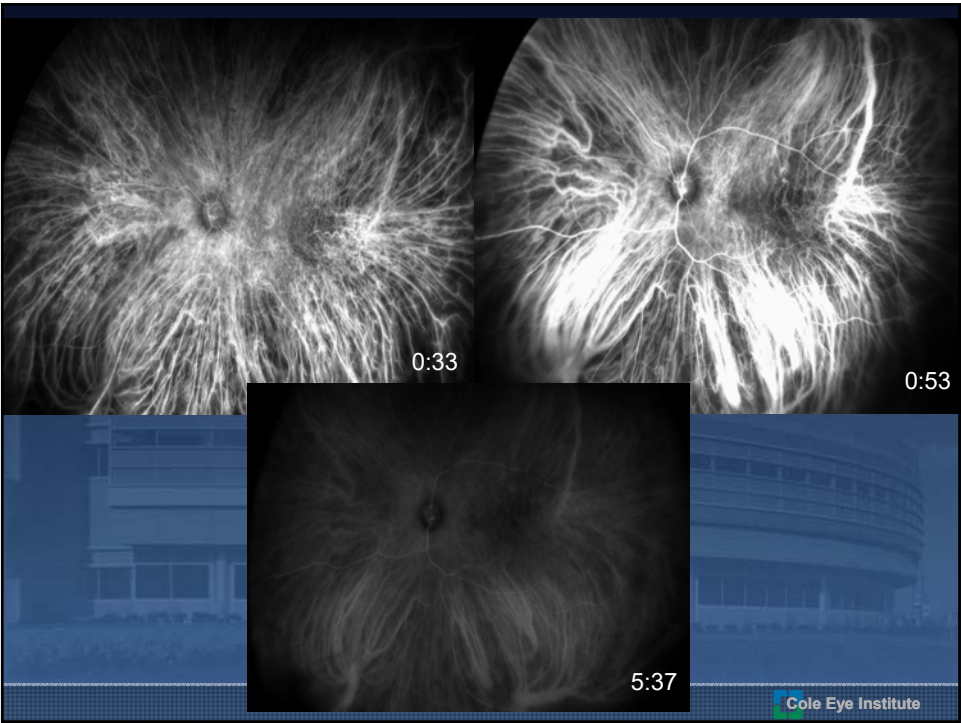
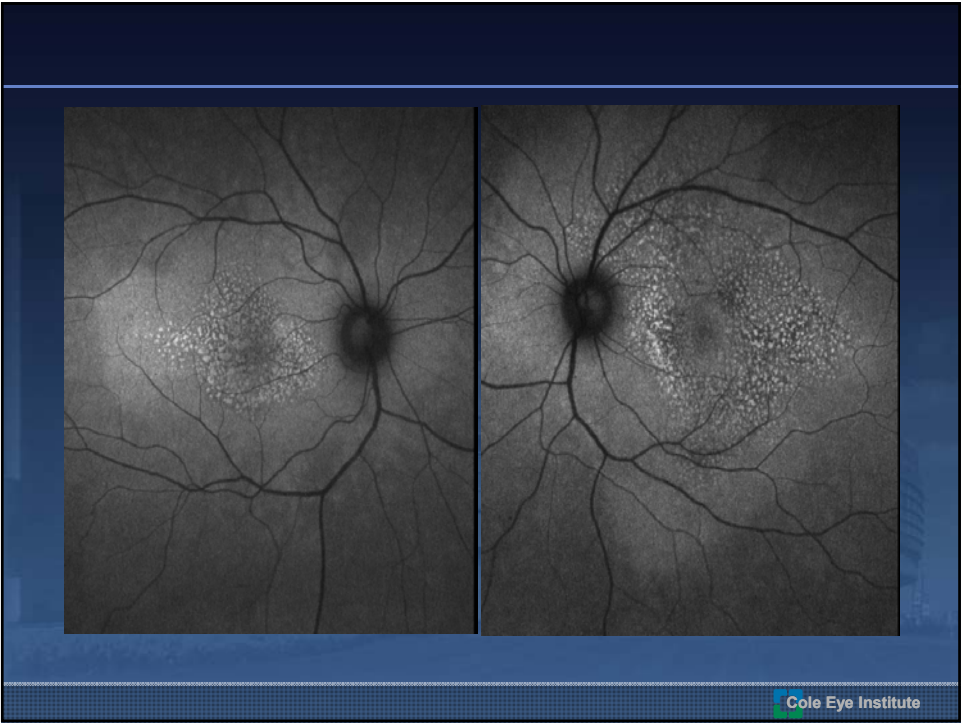
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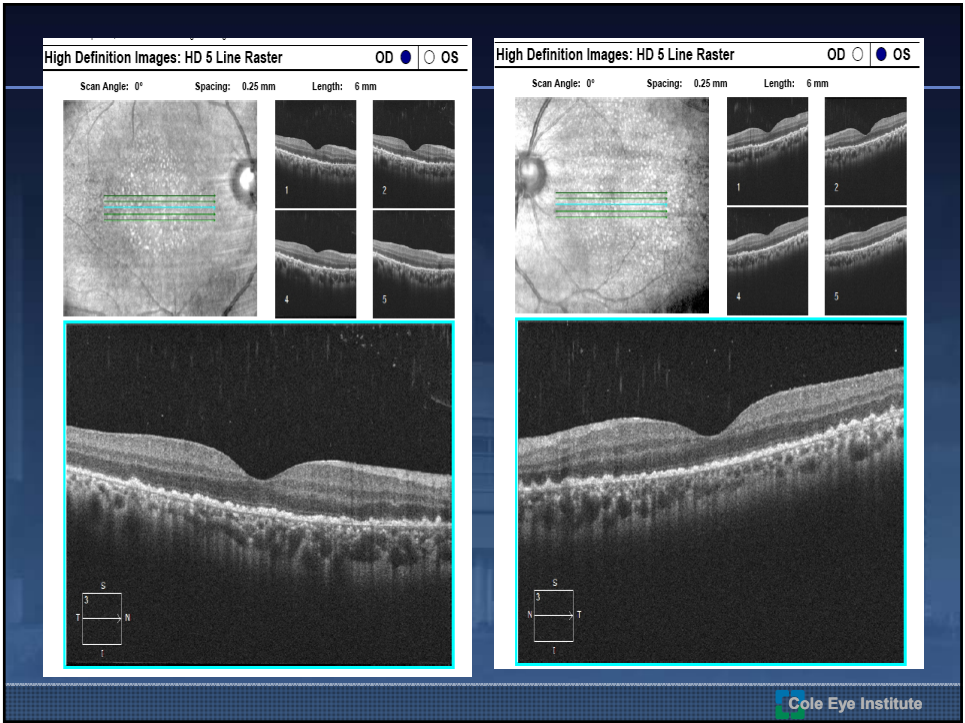
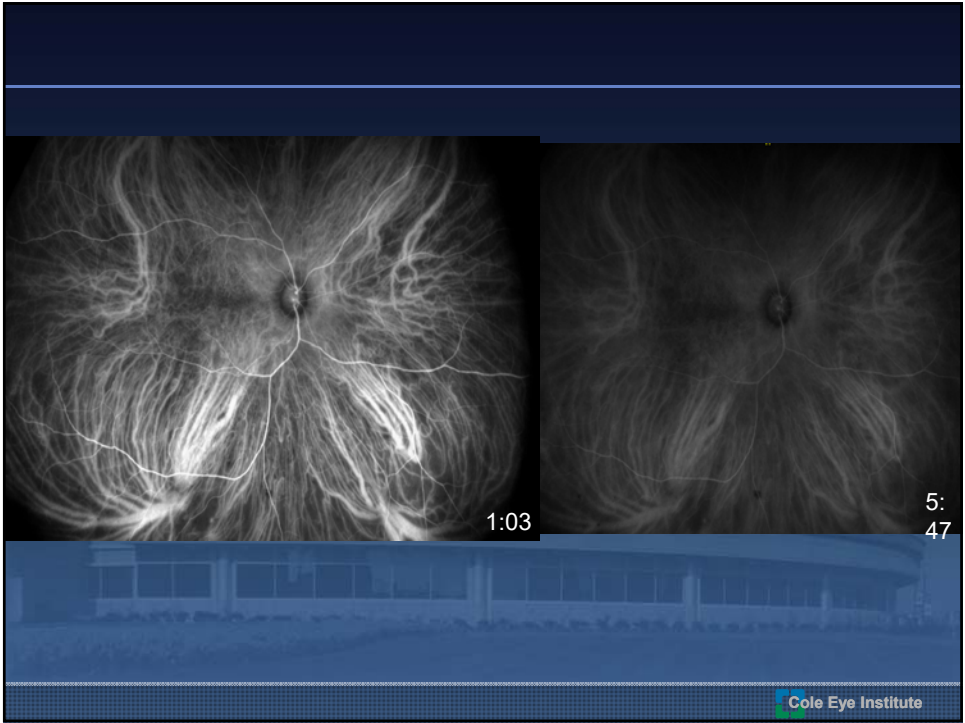


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## *Differential for panuveitis? Workup?*

- Lymphoma
- Syphilis
- Sarcoid
- TB
- Wegner's
- VKH
- Lupus
- Autoimmune retinopathy

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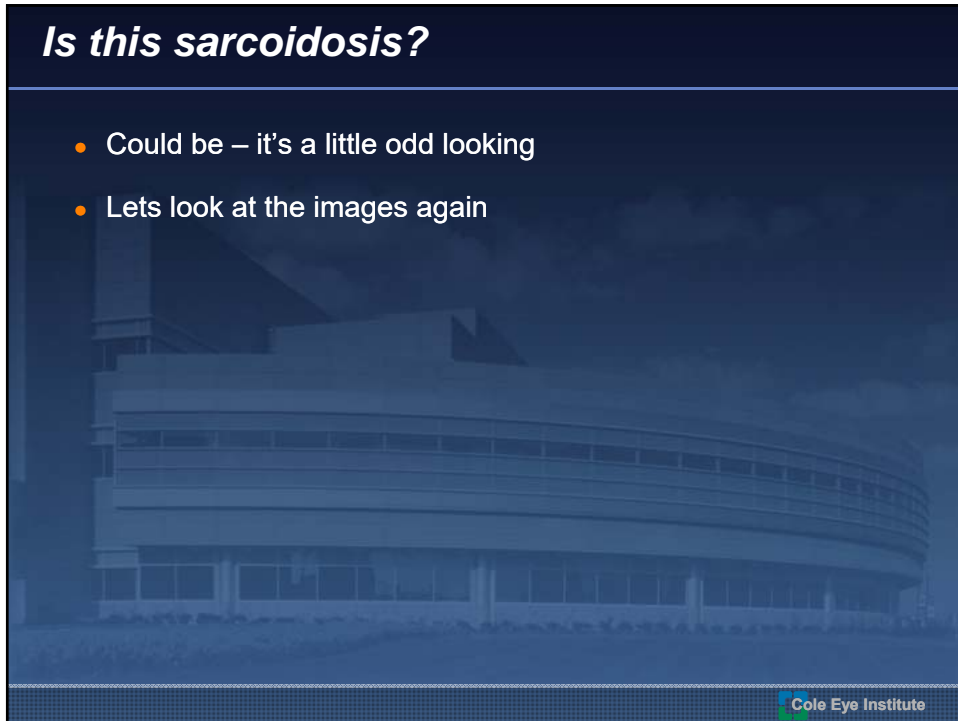
## *Testing*

- |          |          |
|----------|----------|
| • TB     | negative |
| • ACE    | 94 (H)   |
| • C-ANCA | negative |
| • P-ANCA | negative |
| • HIV    | (+)      |

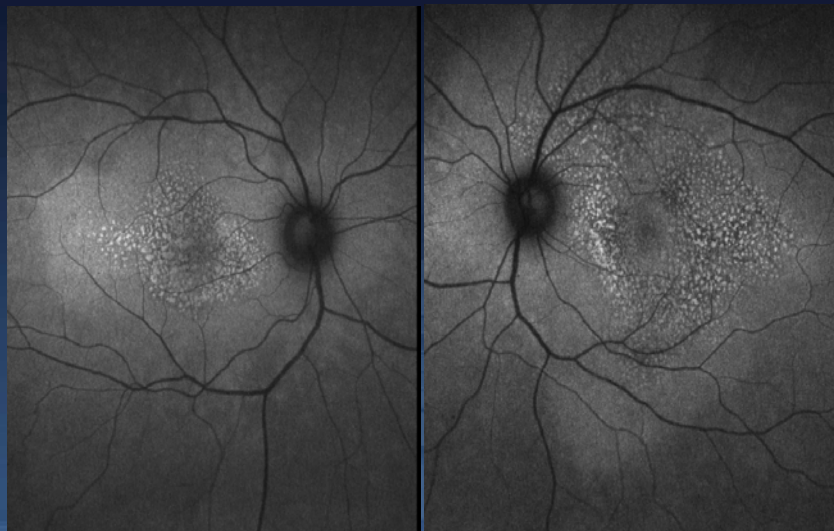
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## *Is this sarcoidosis?*

- Could be – it's a little odd looking
- Lets look at the images again

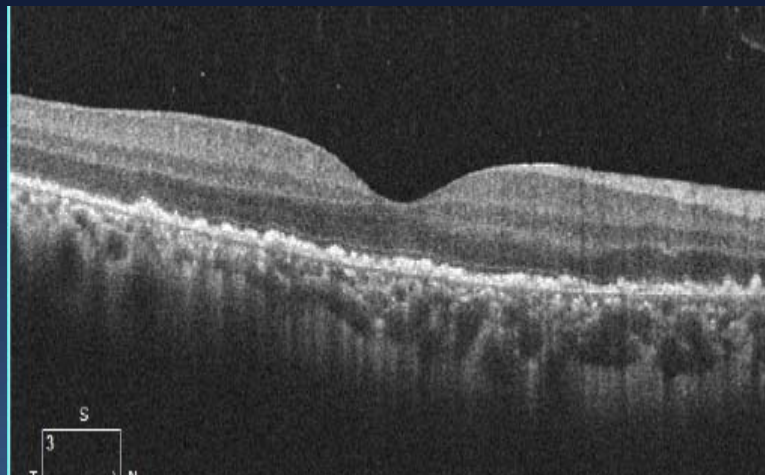


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## ***Case Presentation***

- Syphilis IgG positive
- HIV +
- Admitted for IV penicillin for ocular syphilis and workup
- Topical pred forte QID

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## Neurosyphilis Work up

- CSF RPR reactive 1:256
- CSF VDRL negative
- CSF FTA-ABS negative
- CSF with no pleocytosis

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## Lymphoma work up

- MRI Brain – normal
- CSF Cytology – no malignant cells
- CT abd/pelvis – no lymph nodes enlarged enough for biopsy

## Sarcoidosis work up

- CXR - negative
- CT chest - inconclusive

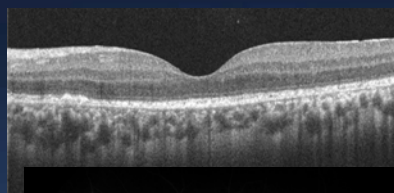
### IMPRESSION:

1. No mediastinal lymphadenopathy noted, with bilateral hilar lymph nodes measuring about 9 mm or less. Peribronchovascular opacities are noted, with 1-2 subcentimeter nodular lesions. All of these findings may relate to presence of sarcoidosis (fine micronodules or alveolar sarcoid pattern?). However typical perilymphatic nodular pattern is not appreciated. Infection/inflammation may contribute.
2. Mild axillary lymphadenopathy noted, left worse than right. Lymphoproliferative process in the differential.

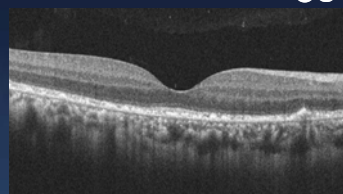
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## 2 weeks later

- OD 20/20 and



OS



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## Case Presentation

- Last patient of the day, Dinner plans at 6 pm
- Was away at AAO for 7 days, this is my first date night in a few months
- 31 y/o female presents with sudden loss of vision OU.
- Flu like symptoms starting six days ago.
- Four days ago noted pain over entire body.
- Seen in ER on the following day and diagnosed with viral infection.

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## Case Presentation

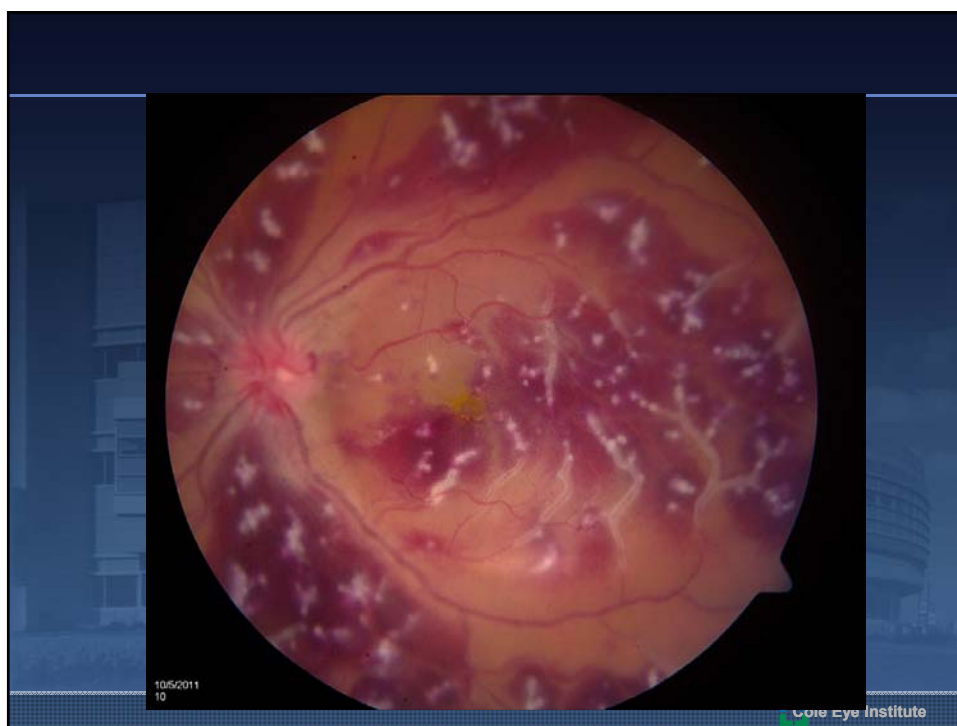
- VA
  - OD: HM
  - OS: 20/200
- Anterior Segment
  - OD: 4+ cell in A/C
  - OS: 2-3+ cell in A/C

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10/5/2011  
2

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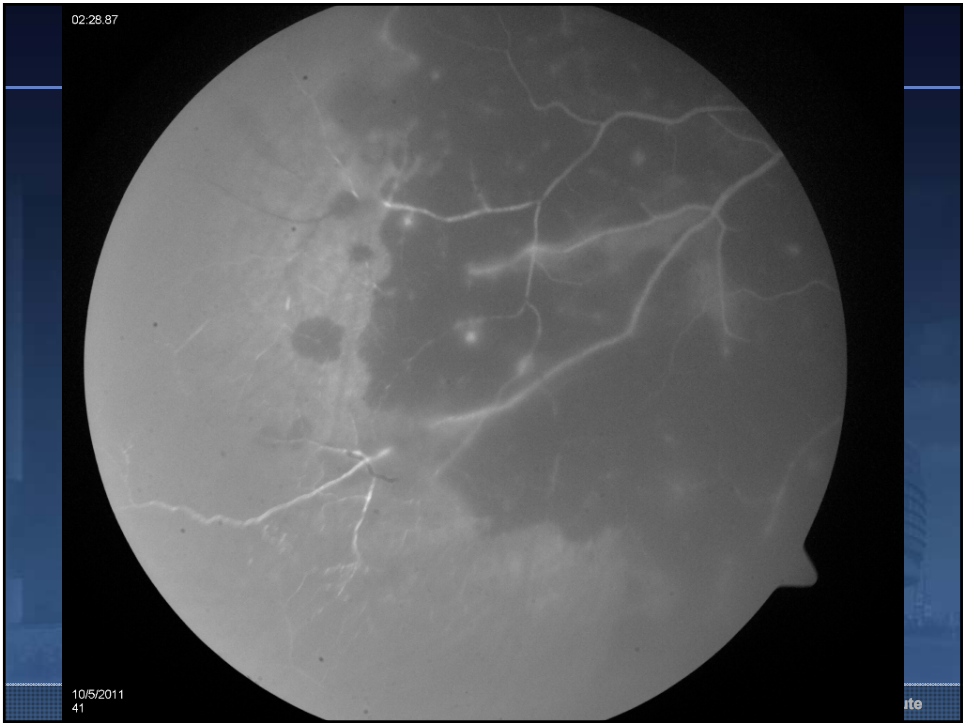


## ***Case Presentation***

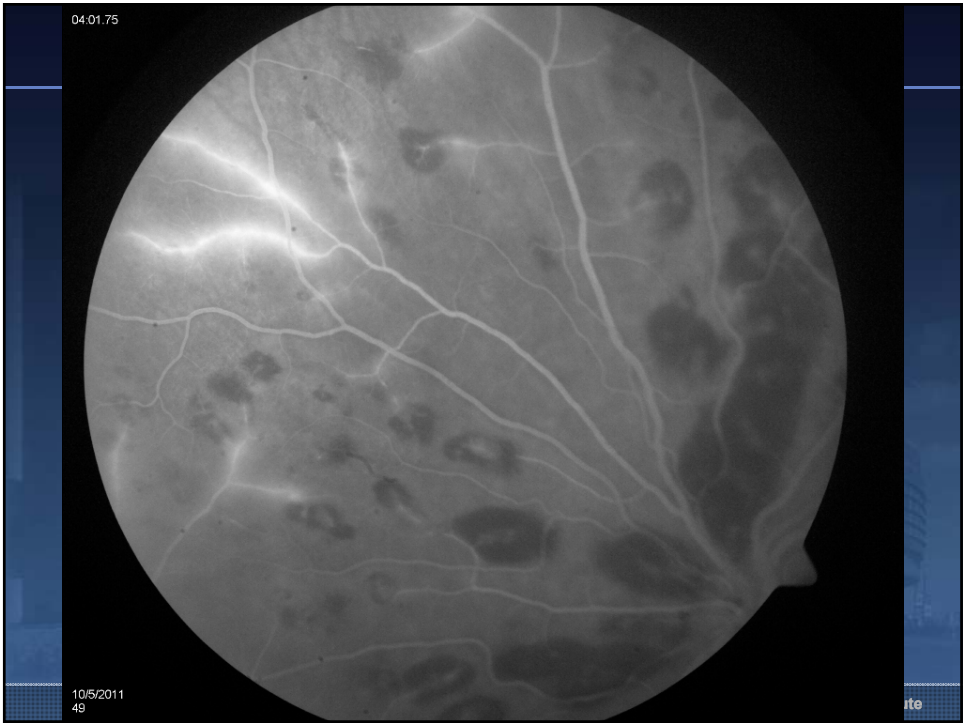
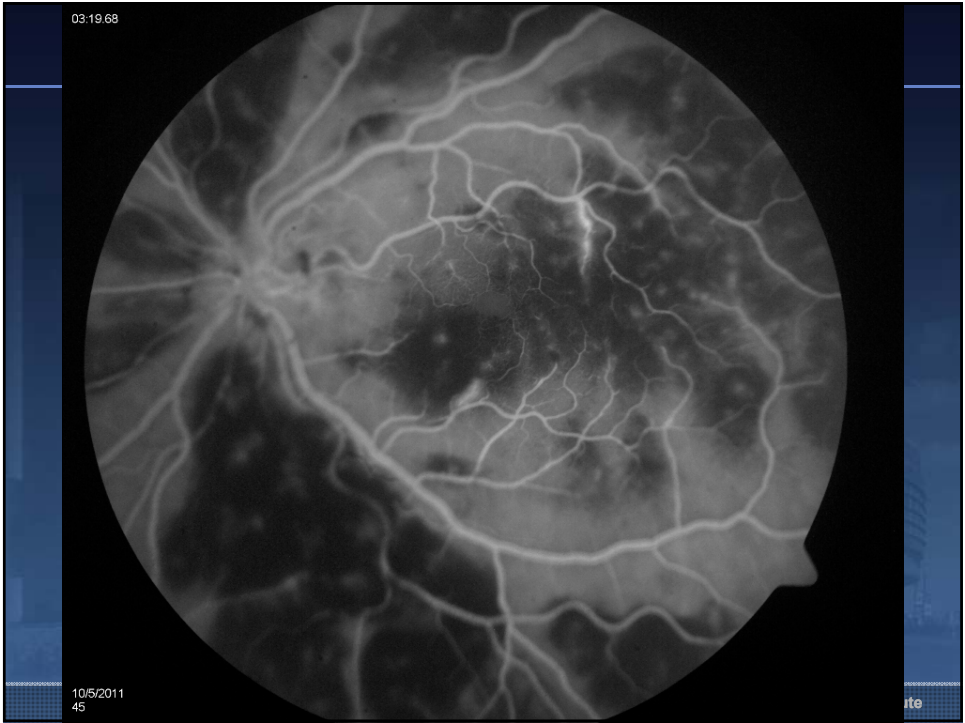
- At this point should I cancel my dinner plans?

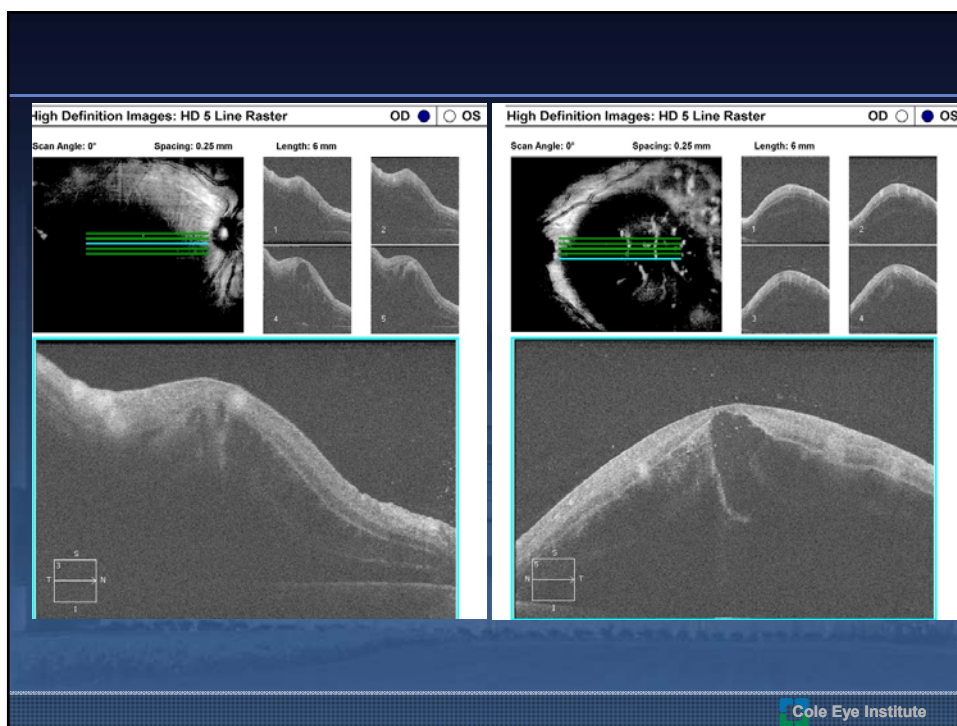












## Case Presentation

- Thoughts?
- What would you do next?





## Case Presentation

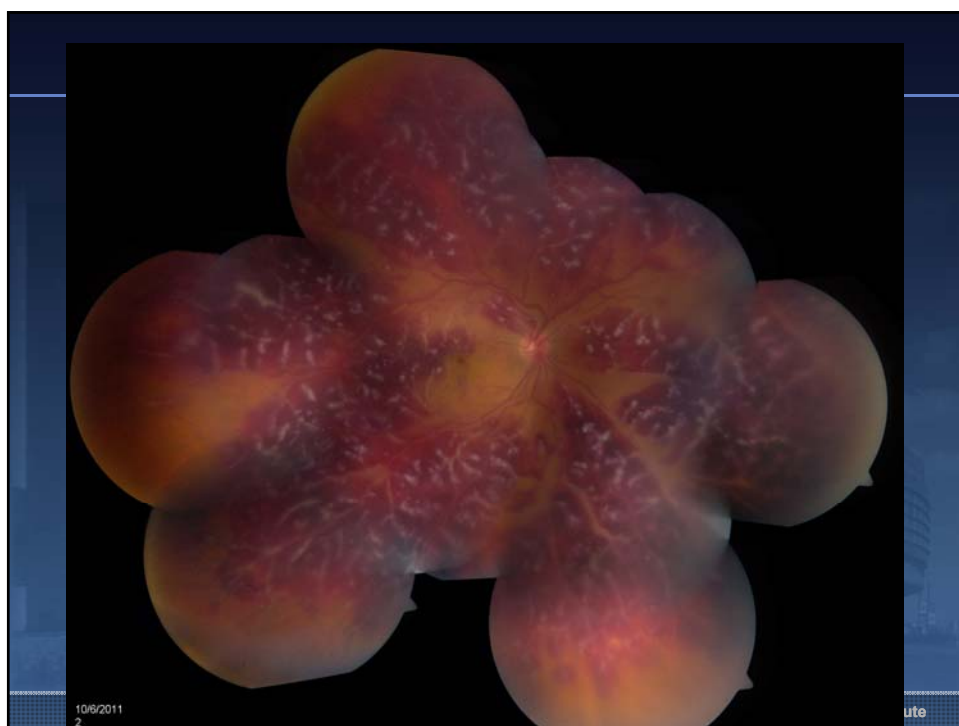
- Heliotrope
  - Purplish discoloration around the eyes
- Gottron's sign
  - Erythematous rash over the extensor surface of the metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints

The logo for the Cole Eye Institute, featuring a stylized 'C' and 'E' in blue and green, followed by the text 'Cole Eye Institute'.

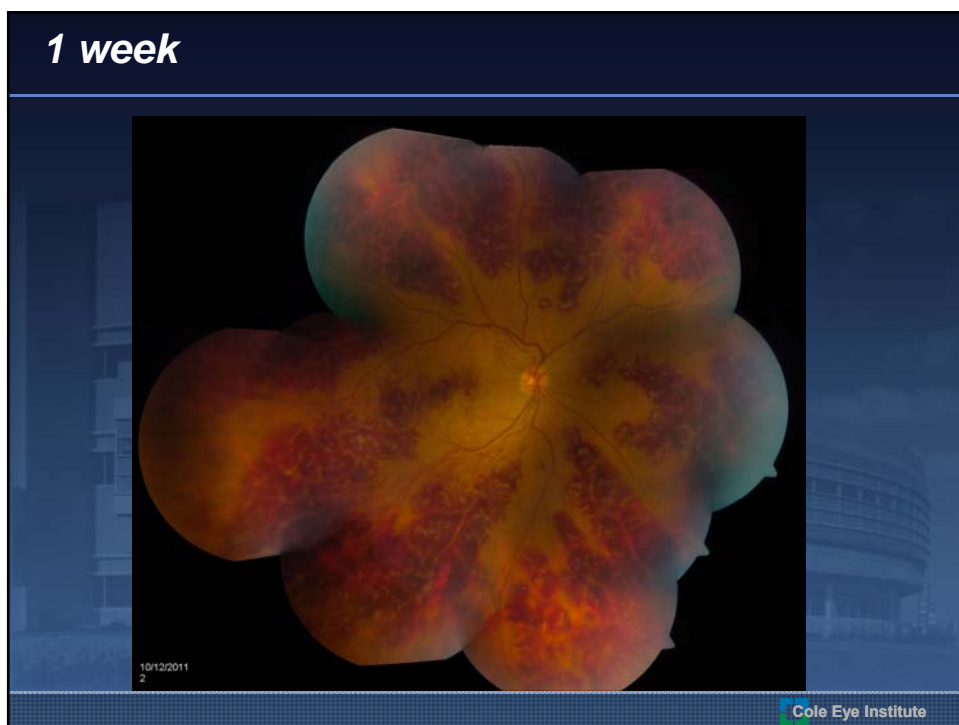
## Diagnosis

- Dermatomyositis
- Recent pregnancy and currently post partum
- On prednisone only 20 mg
- Was on Imuran, but taken off for pregnancy
- Admit
- IV Solumedrol
- Covered with antivirals as well

The logo for the Cole Eye Institute, featuring a stylized 'C' and 'E' in blue and green, followed by the text 'Cole Eye Institute'.

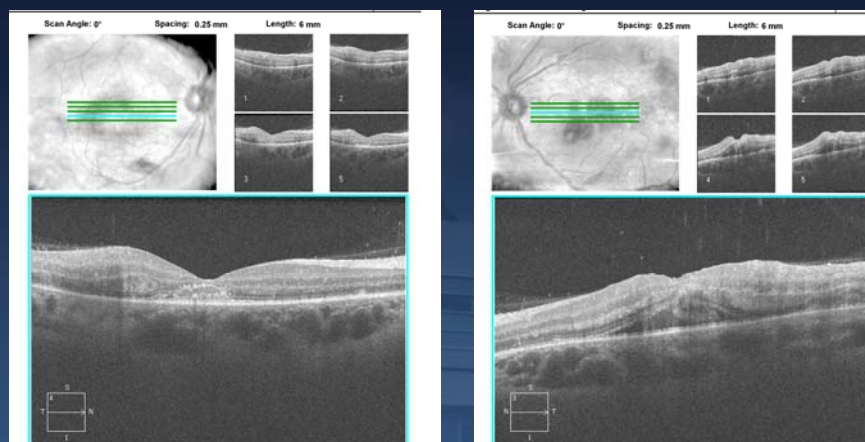


**1 week**



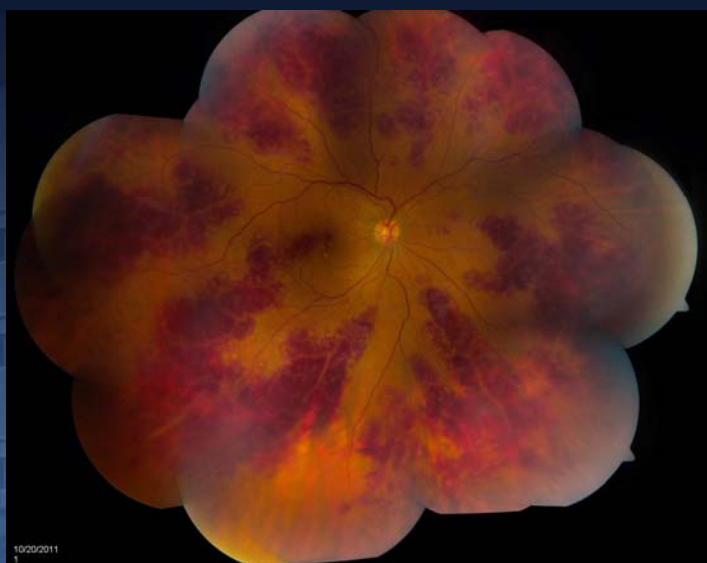


## 1 week



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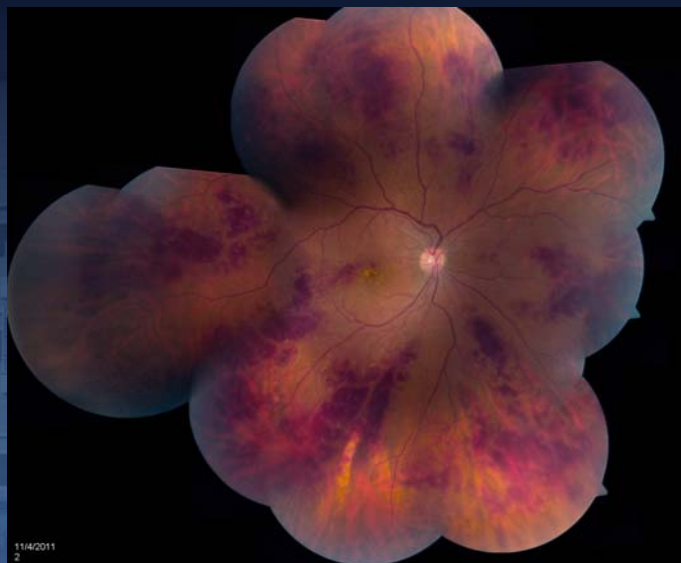
## 2 weeks



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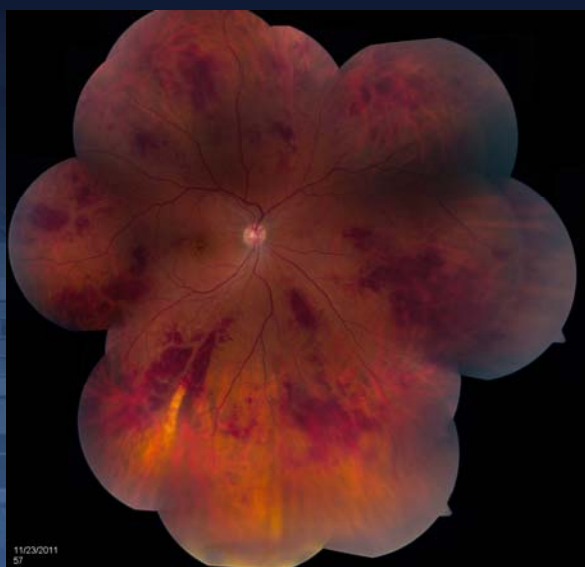
**1 month**



11/4/2011  
2

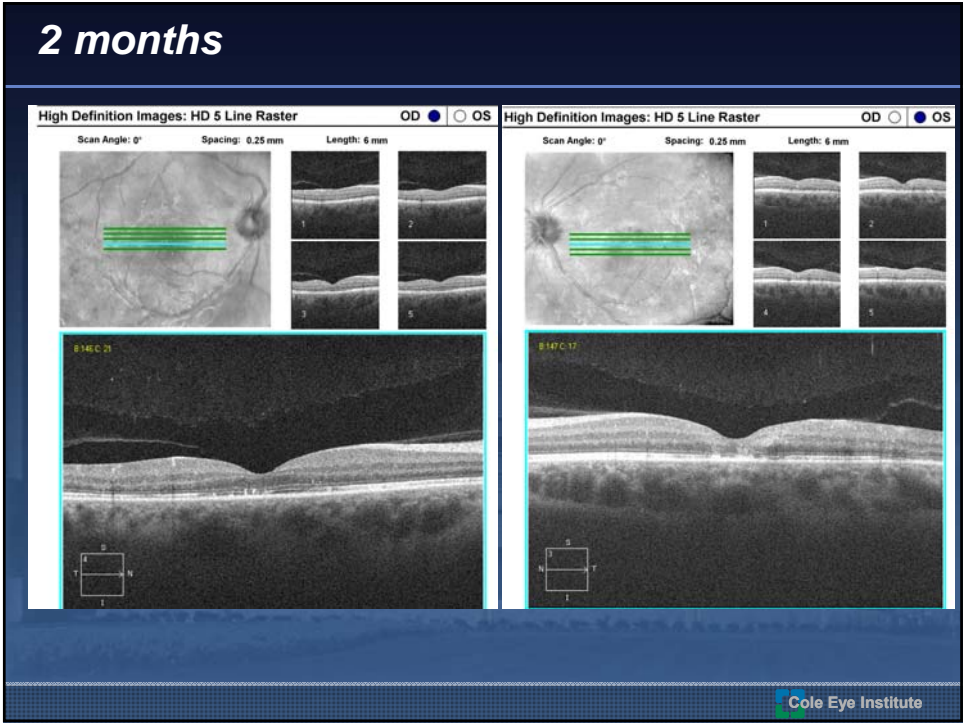
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**2 months**



11/23/2011  
57

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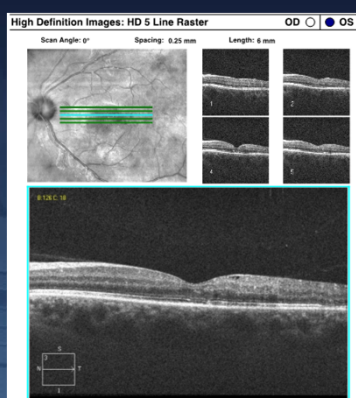
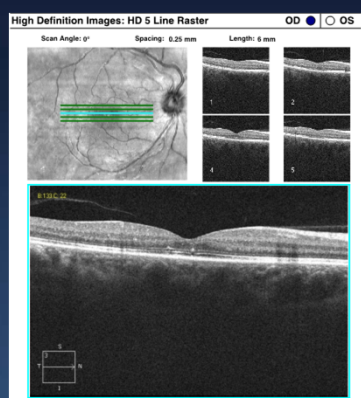
## 6 Months



55F9F4B5F13E4c56B859CA45E4DCB357  
2/23/2012  
14

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## 6 Months



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## Case Presentation

- At 1 year – 20/40 OD, 20/30 OS

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## Summary

- Don't let the lab test dictate treatment
- Care with local steroids
- Persistence in obtaining biopsy – watch for pre-surgery prednisone
- Common presentation with a rare bug
- Aggressive treatment in those with aggressive vasculitis
- Multi-team approach for complex patients
- Never forget syphilis
- Just in case: [shivass2@ccf.org](mailto:shivass2@ccf.org)

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