Occult Retinal Diseases

A Clinical Approach to White-Dot Syndromes

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Disclosure statement:

Nothing to disclose.

Course objectives:

1. Familiarize with clinical signs and symptoms of various white dot retinal conditions
2. Review applicable tests and results for specific white dot retinal conditions
3. Recognize potential treatments for specific white dot retinal conditions

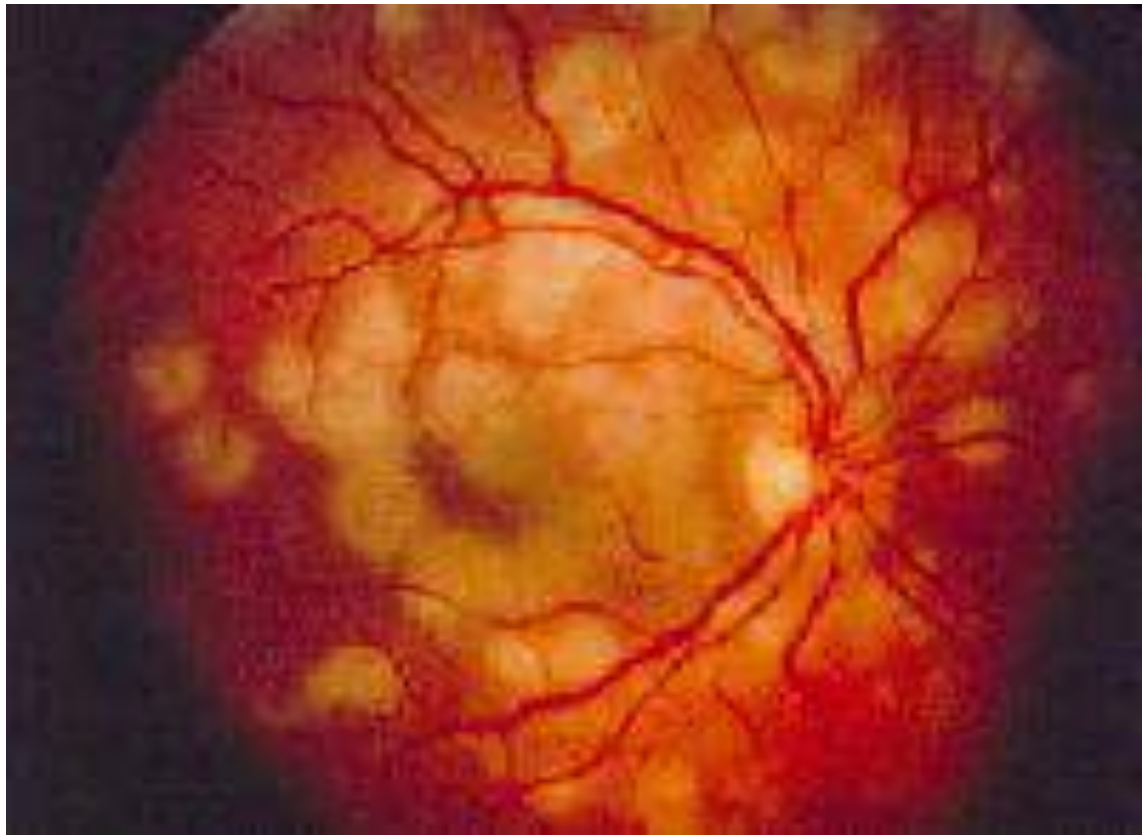
Occult Retinal Diseases

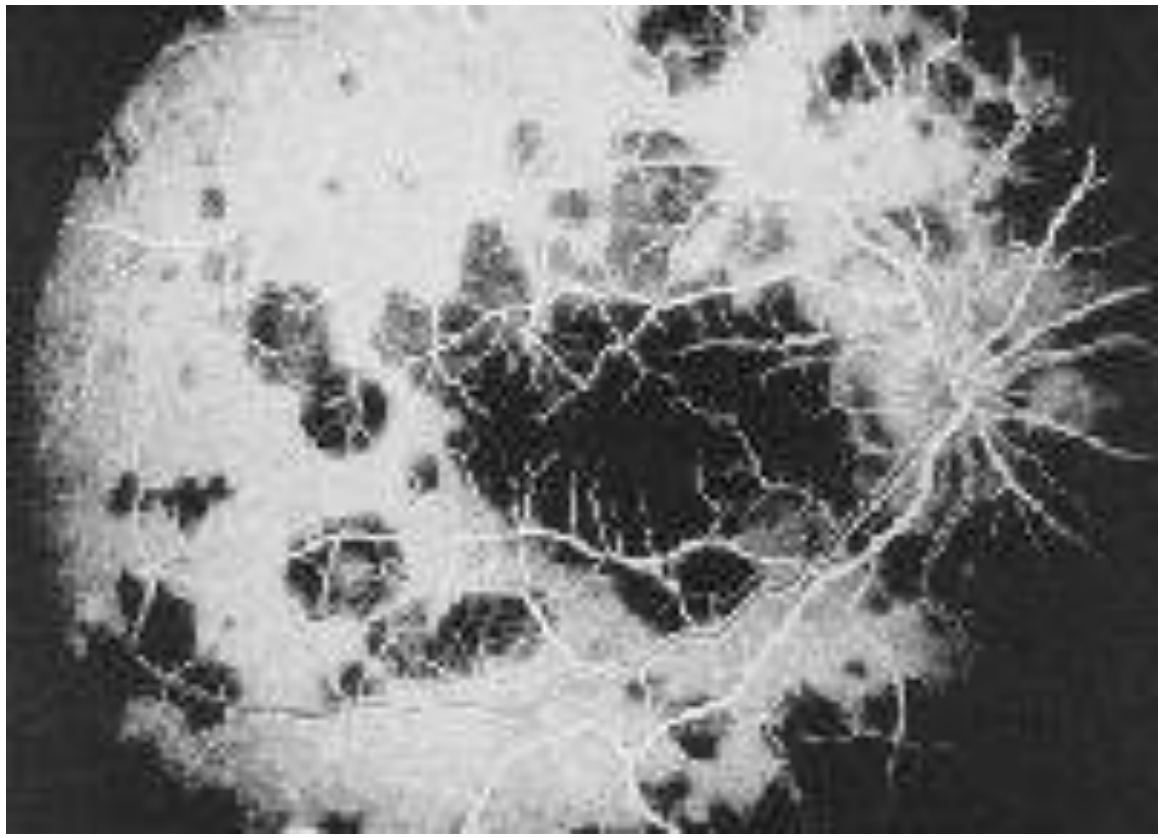
AKA:

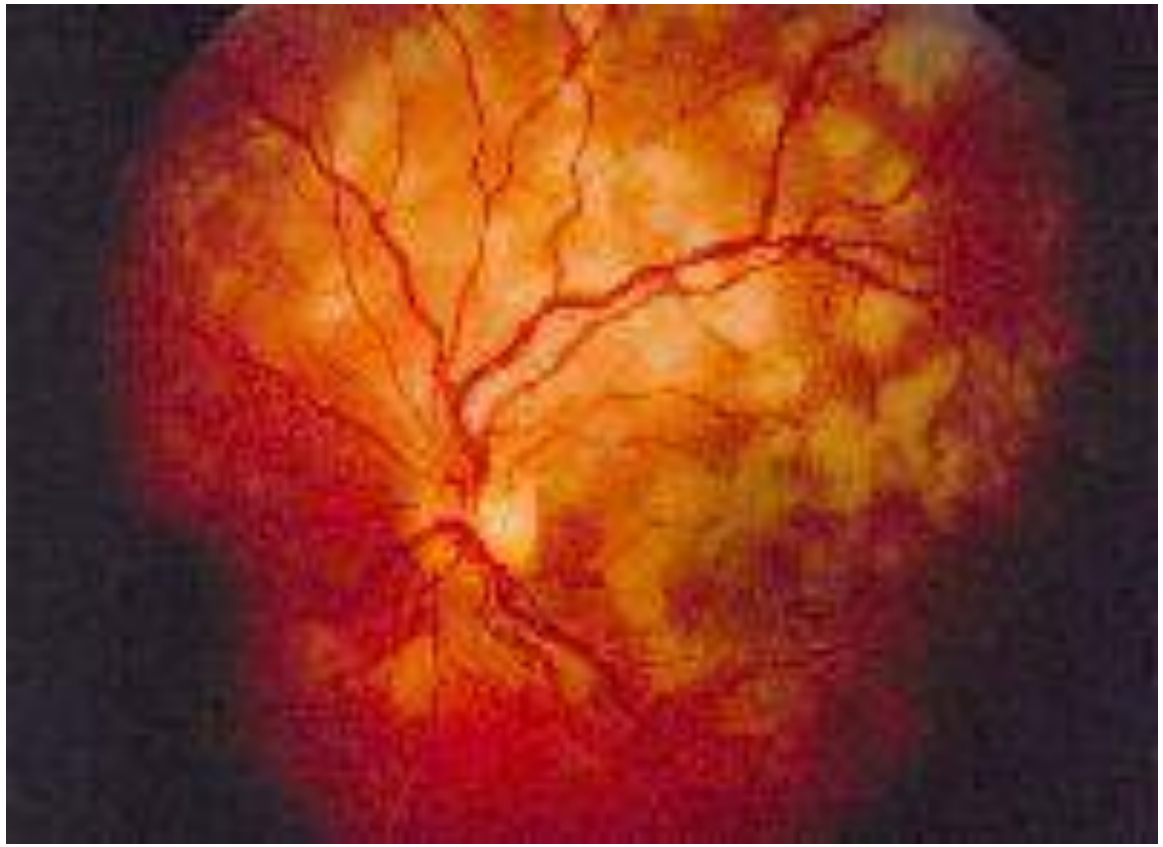
- Idiopathic Multifocal White Dot Syndromes
- Multifocal Choroidopathy Syndromes

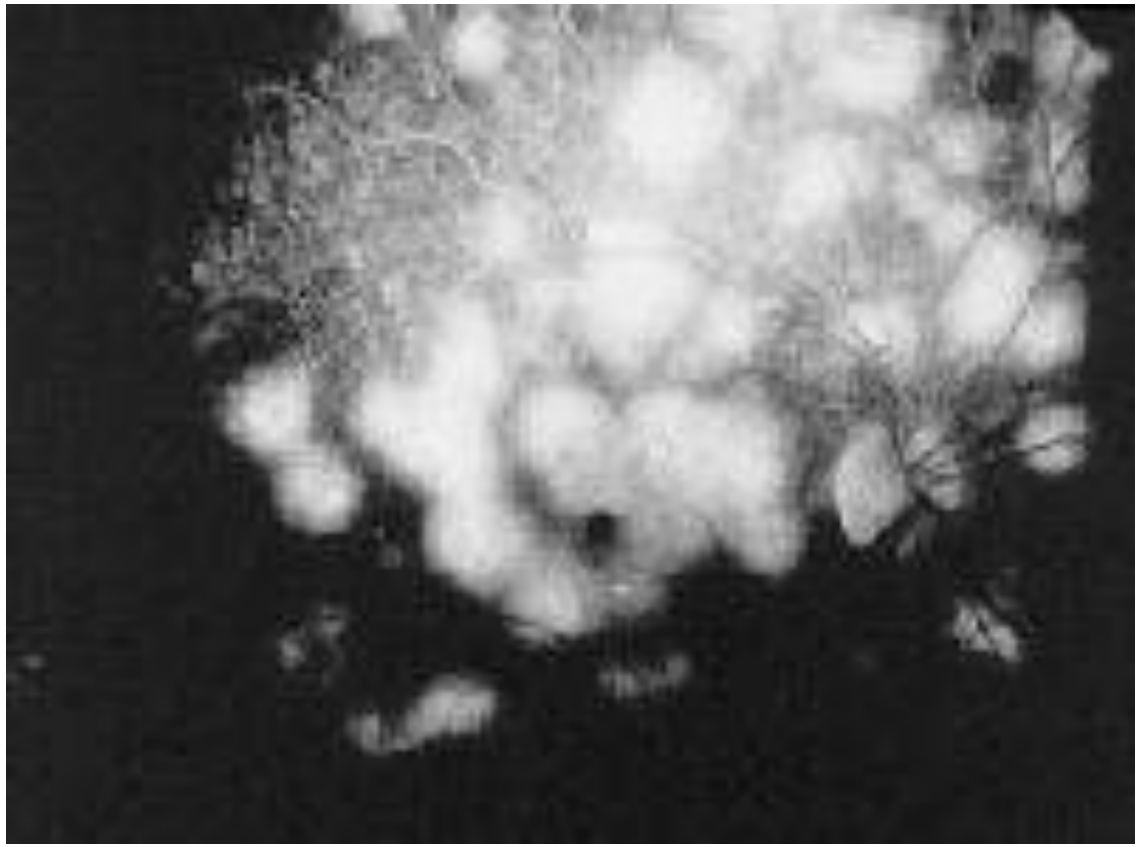
Case 1

- 23-year-old Caucasian male
- Sudden reduction in vision over last 2 days
- Just recovered from mild cold; final exams
- No systemic disease; no known drug allergies
- BCVA 20/200- OD, OS; PH no improvement
- Pupils reactive and equal OU
- Ocular motilities full OU with no pain
- Ocular pressures, anterior segment normal OU









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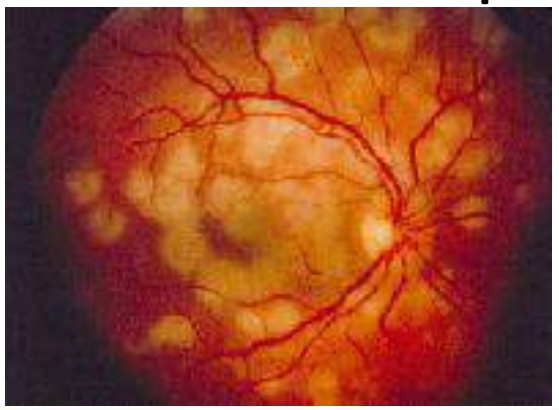
Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)

- Multifocal idiopathic inflammatory disorder
- Yellow-white-gray circumscribed flat lesions
- At level of RPE and choroid
- Choroidal non-perfusion in the posterior pole
- Leads to ischemia of overlying RPE and receptors
- Age 15-42 yo; 80% Caucasian
- Incidence and prevalence unknown

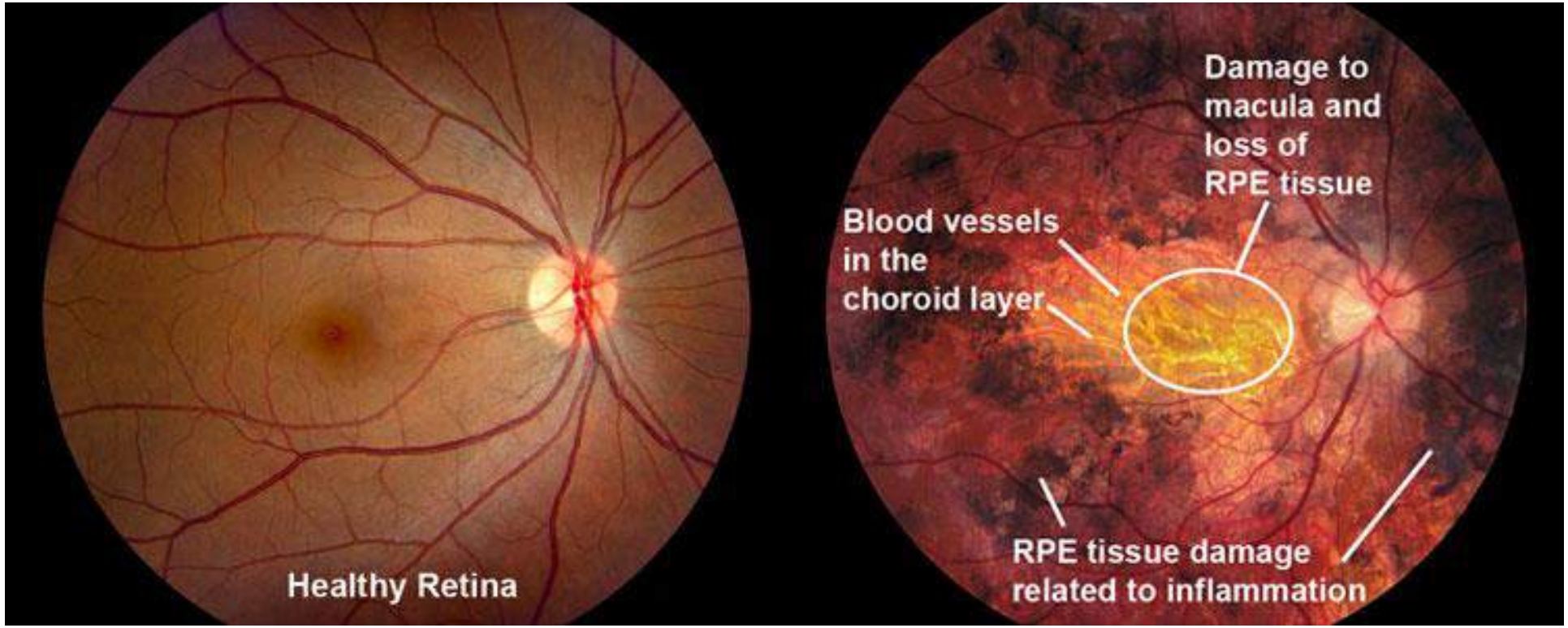


APMPPE Symptoms

- Recent immune system ‘trigger’ – i.e. flu, treatment for infection, medications, etc.
- Bilateral, painless vision loss over several days with preceding viral illness
- Scotomas, metamorphopsia, floaters, red eye
- Possible HA
- VA decrease or scotomas may persist for several weeks to months

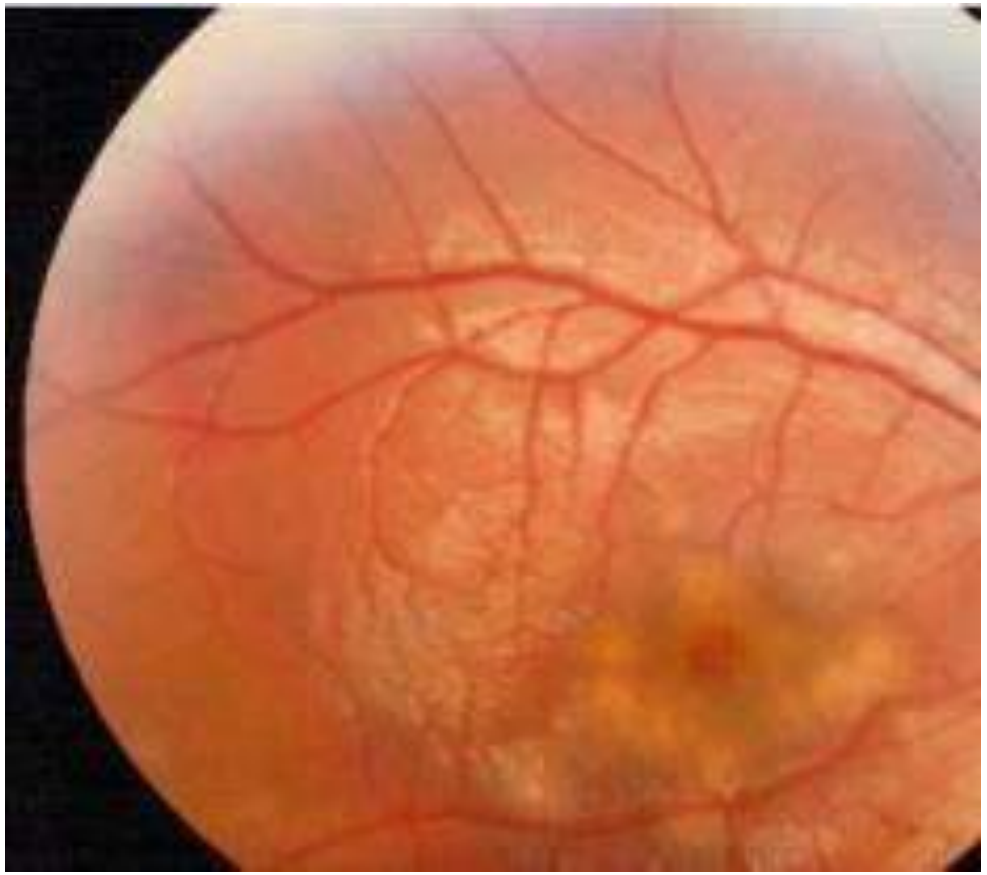
APMPPE Signs

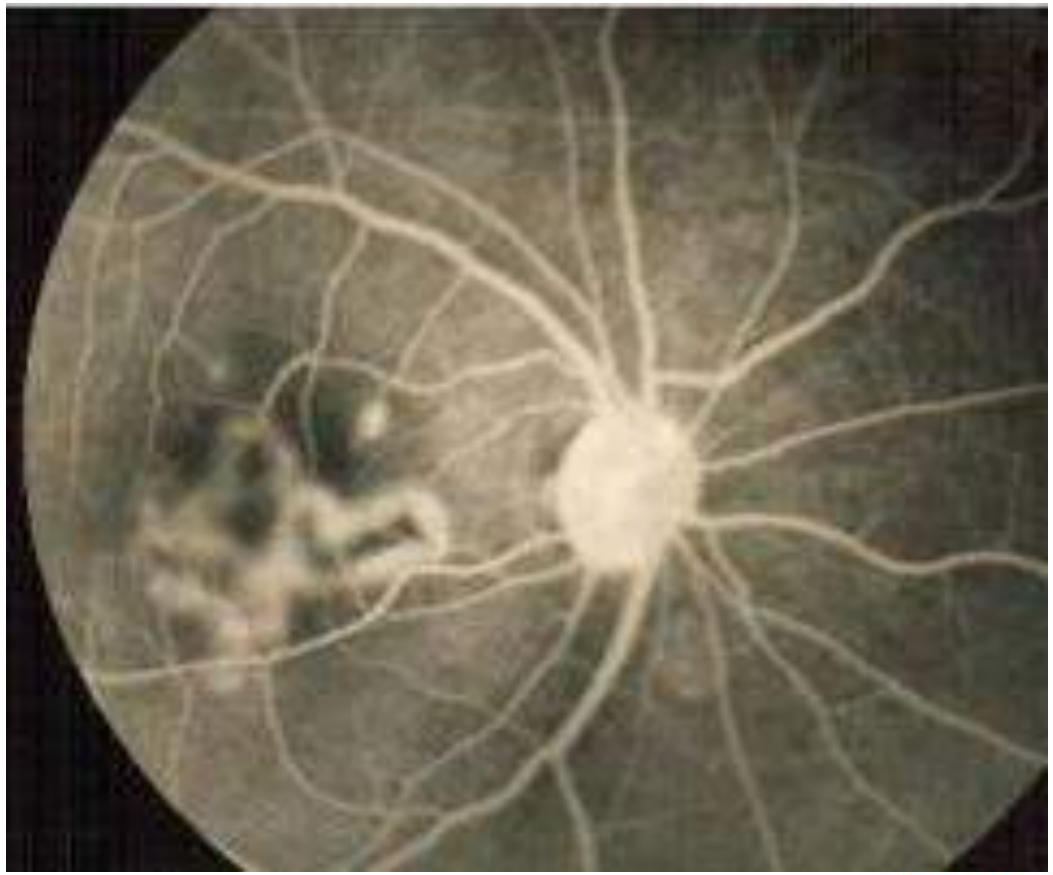
- Vitritis = 35%
- Lesions resolve in 9-14 days, leaving residual RPE mottling



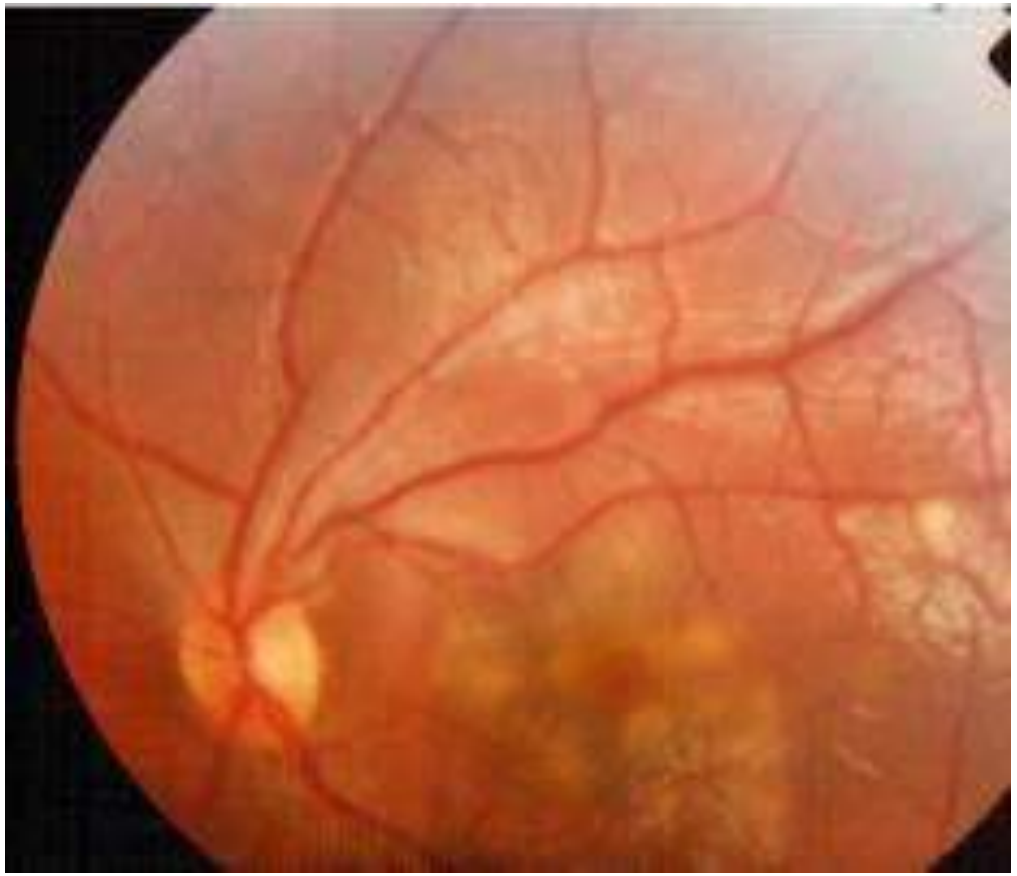
http://www.your-eye-sight.org/apmppe.html

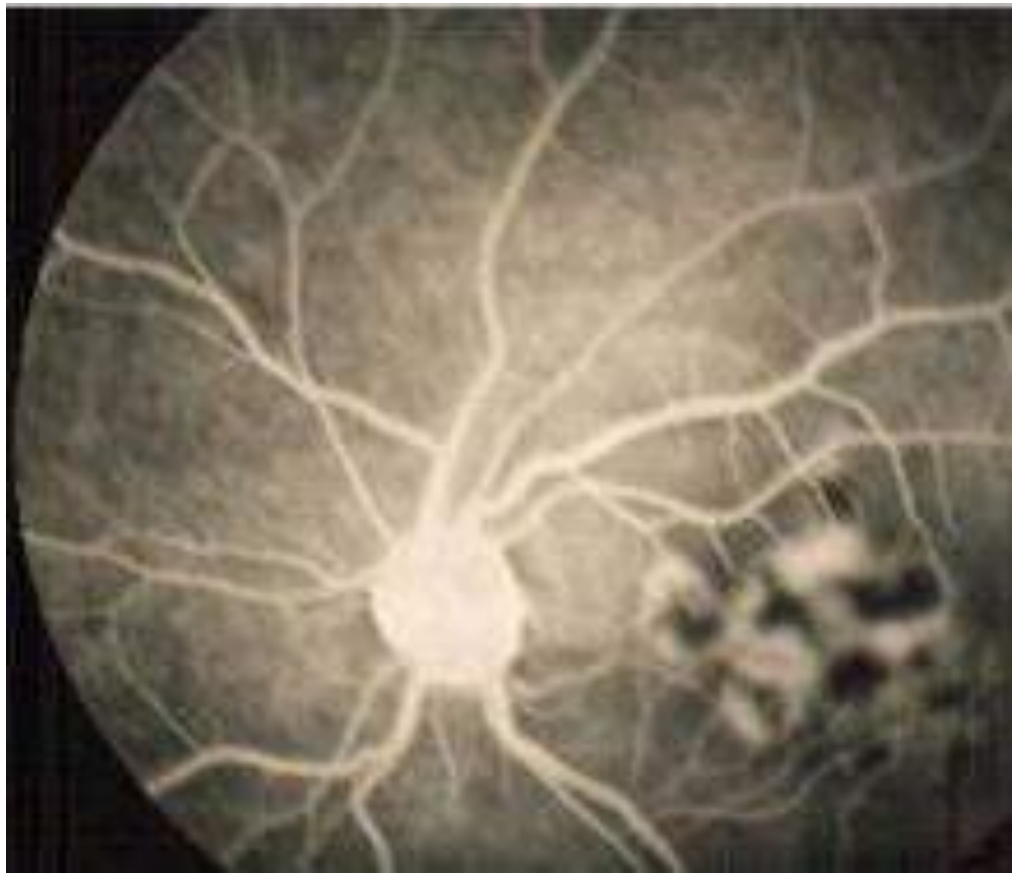
APMPPE





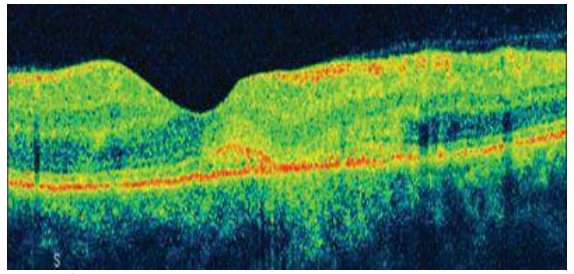
APMPPE





APMPPE Management

- HLA-B7 and HLA-DR2
- Angiography crucial!
- FA – early hypofluorescence, late hyperfluorescence
- ICG - delayed choroidal filling (hypofluorescent lesions); hypofluorescent in early and late phases
- OCT – hyper-reflective areas above RPE; nodular hyper-reflective lesion within RPE
- ERG – may be abnormal
- 80% may recover vision to 20/40 or better



APMPPE Complications

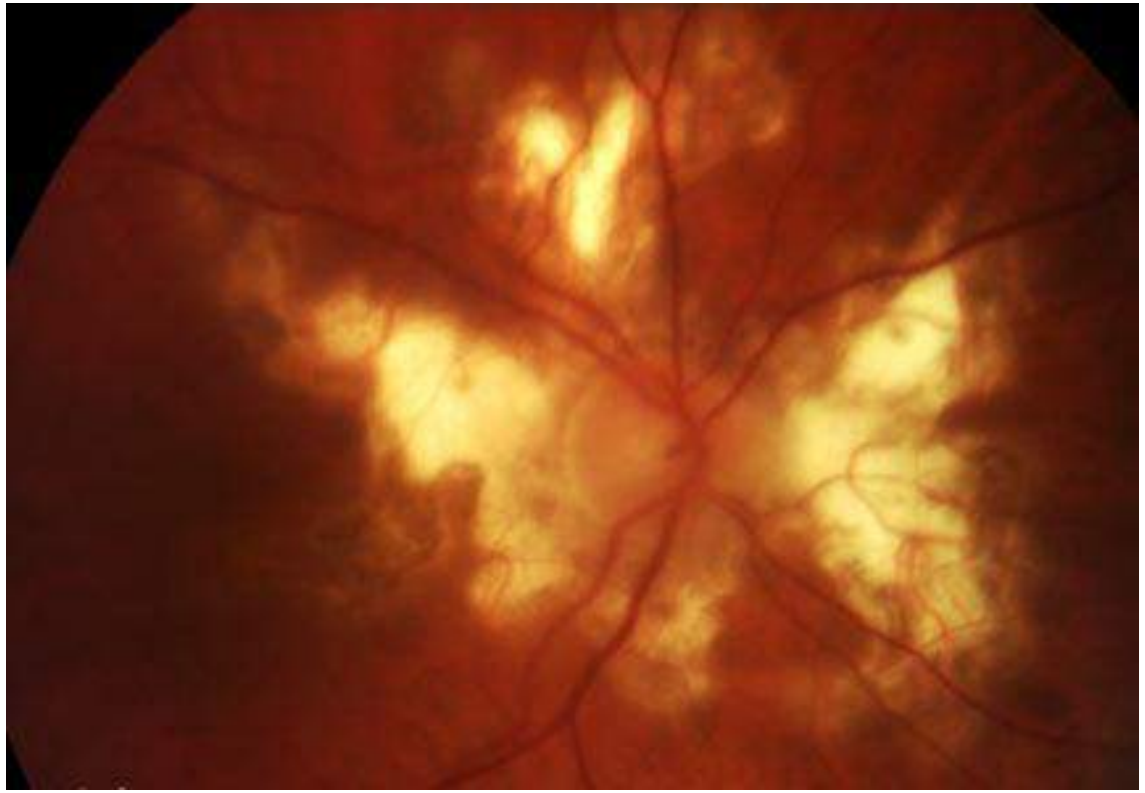
- CNVM
- Central serous RD
- Choroidal vasculitis
- CRVO
- Hemorrhagic maculopathy
- Optic neuropathy
- Meningoencephalopathy
- Cerebral vasculitis → muscle paralysis, permanent hearing loss → Death

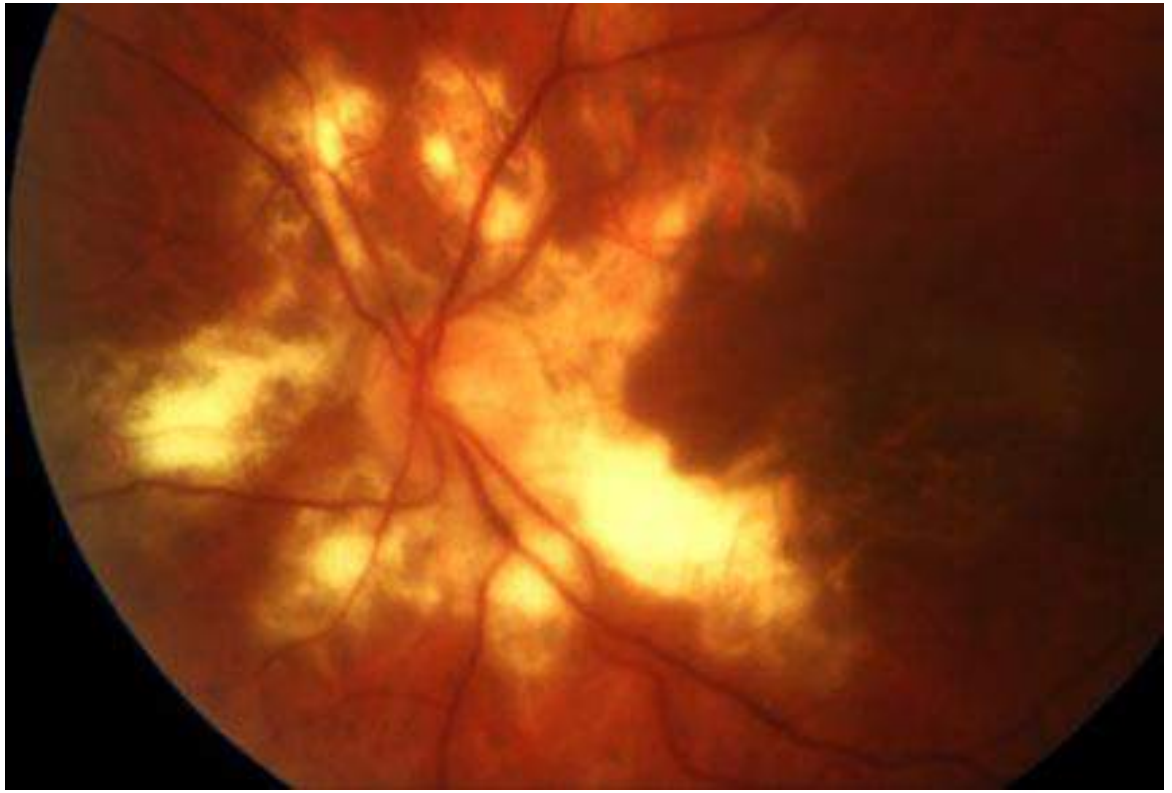
APMPPE Treatment

- Residual chorioretinal scarring associated with few visual symptoms – none
- Most patients (80%) recover with 20/20 to 20/40 vision
- Corticosteroids (various types) to may be used to control other ocular inflammations related
- Query re: headaches/hearing/motoric problems
- Monitor every 1-2 weeks; resolution up to 6 mo

Case 2

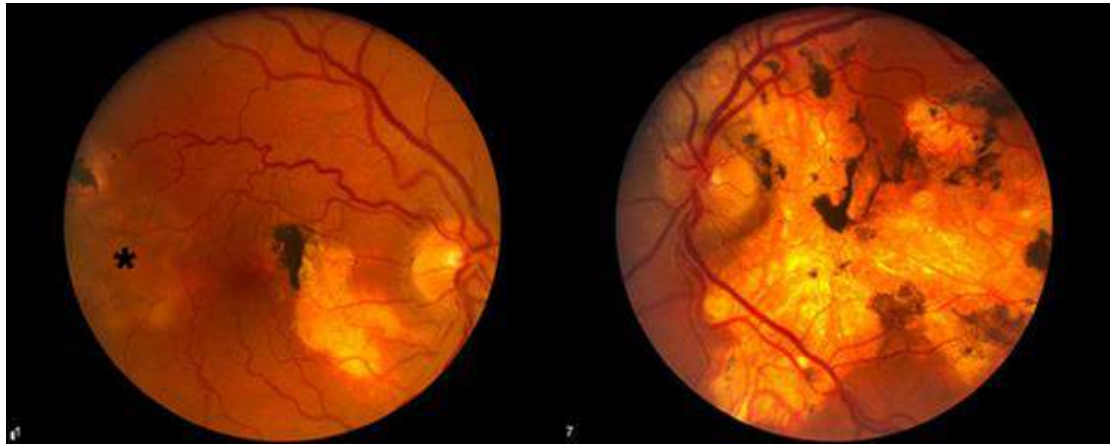
- 52-year-old Asian male
- History of ‘inflamed eyes’ 10 years prior
- Feels like distorted vision returning again
- Borderline hypertension; no meds currently
- No known drug allergies
- BCVAs 20/30+2 OD, 20/25-3 OS
- Pupils, motilities, IOPs, normal OU
- Visual fields show large scotomas nasal to blind spot OD, OS





Serpiginous Choroiditis

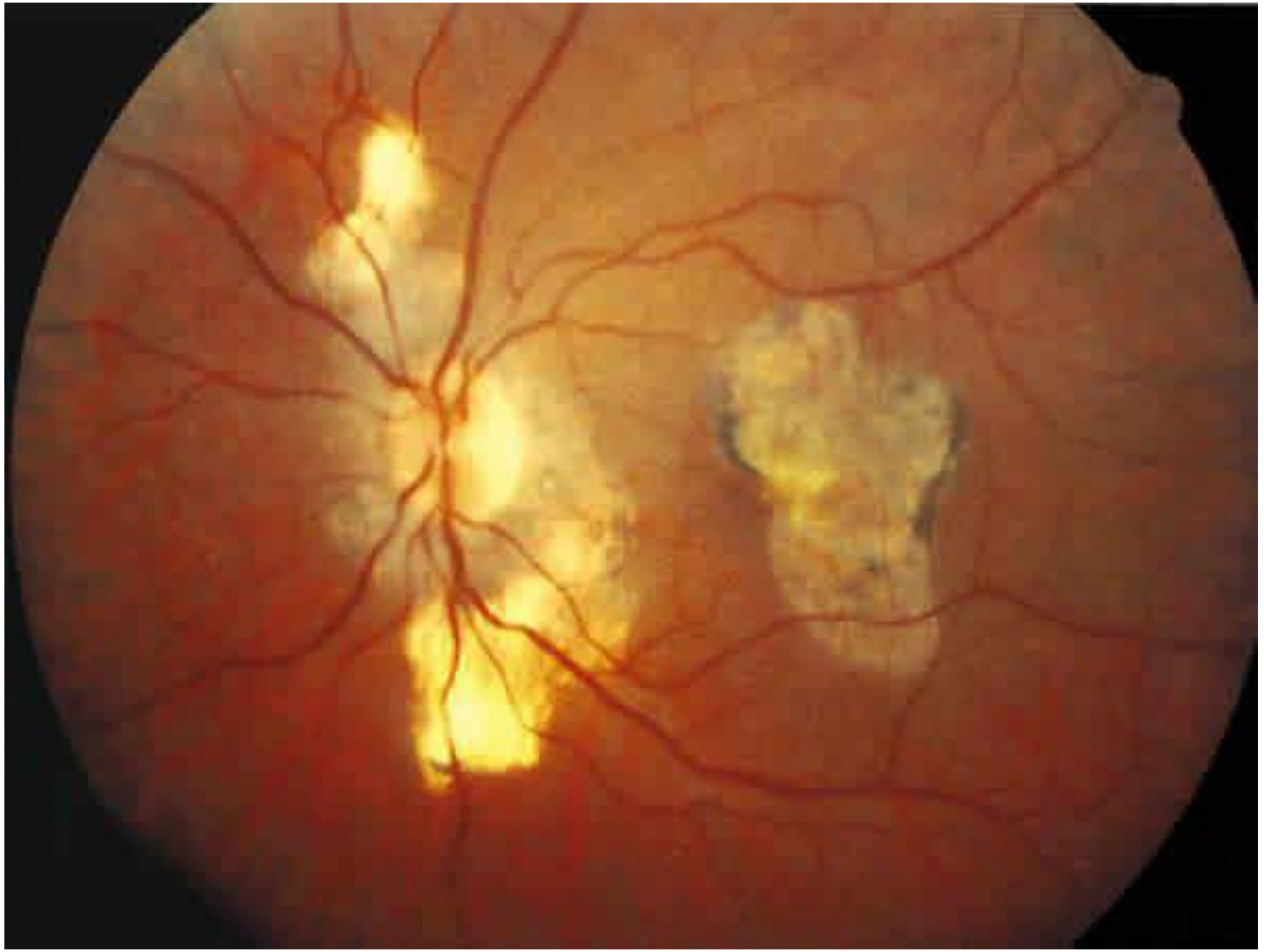
- aka geographic helicoid peripapillary choroidopathy (GHPC)
- Bilateral, recurrent, inflammatory disease of the RPE and choroid
- Blurry vision, metamorphopsia, central scotomas
- 30-70 yo
- HLA-B7



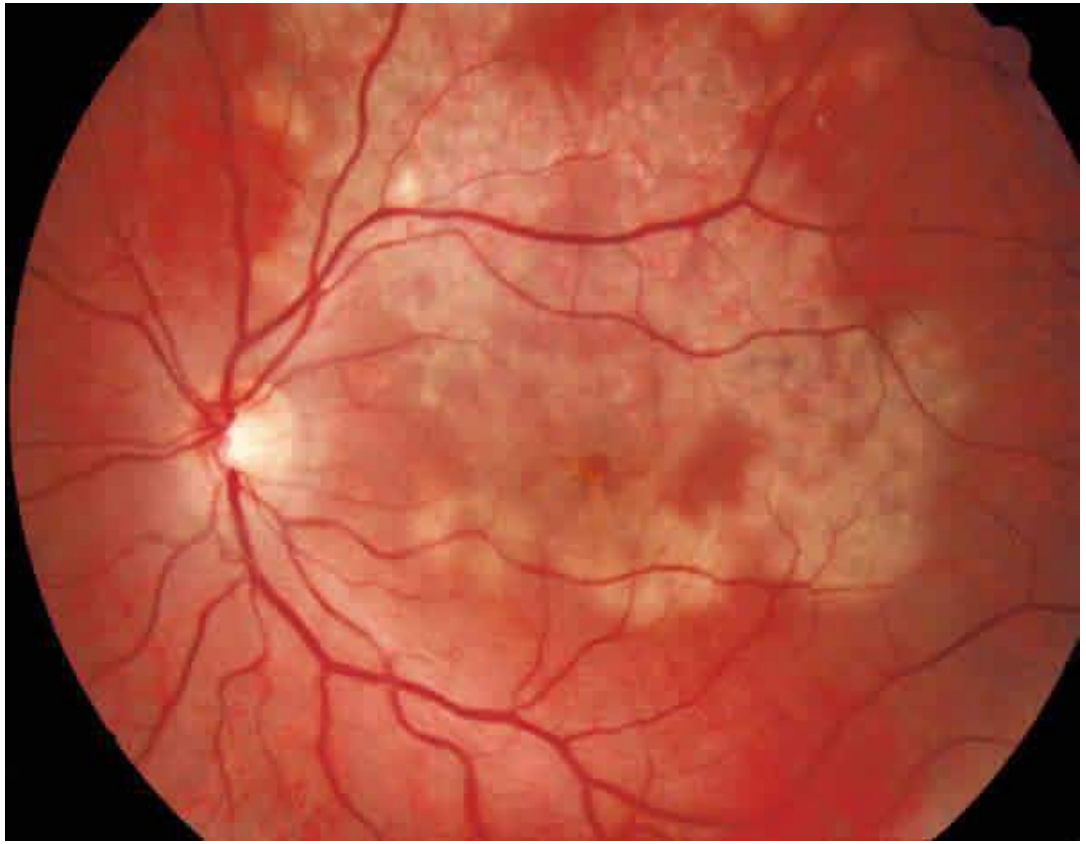
Serpiginous Choroiditis Signs

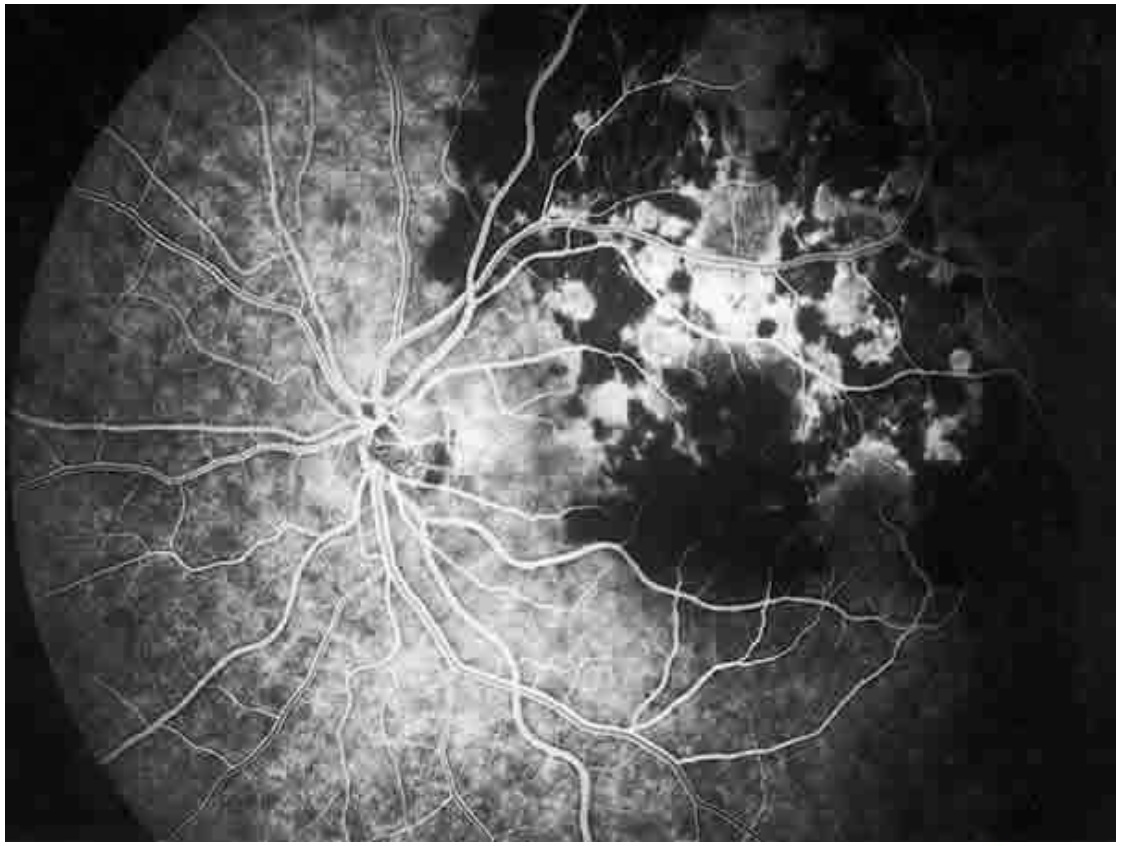
- Acute phase – “propeller-like pseudopods” extend out from ONH
- Creamy lesions develop at edges of pseudopods, persisting for several weeks → relentlessly progressive
- Vitritis = 30%
- FA shows early hypofluorescence of central scar and hyperflurescence early in active creamy lesions
- ICG helpful to identify choroidal involvement

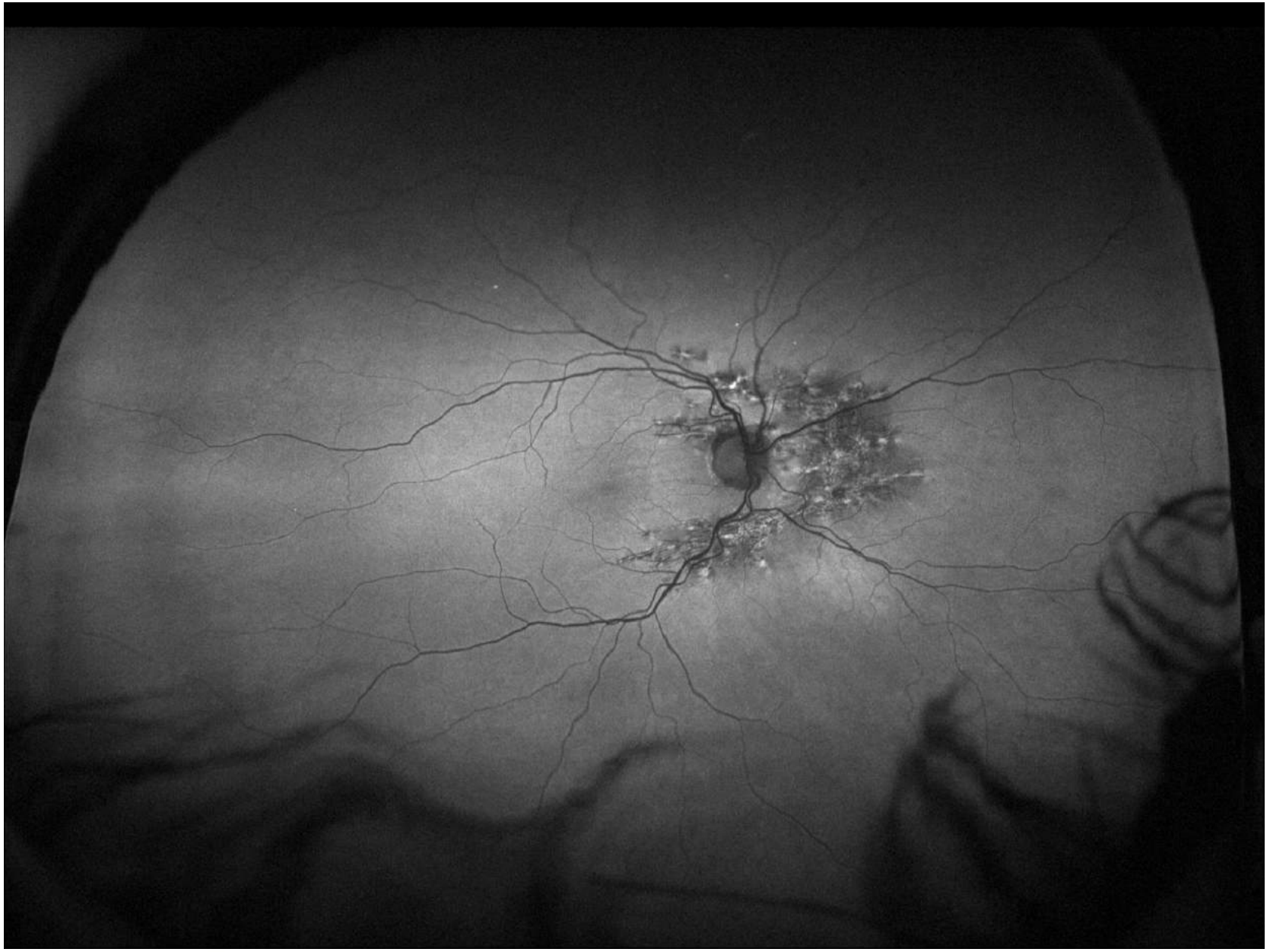
Serpiginous Choroiditis



Serpiginous Choroiditis







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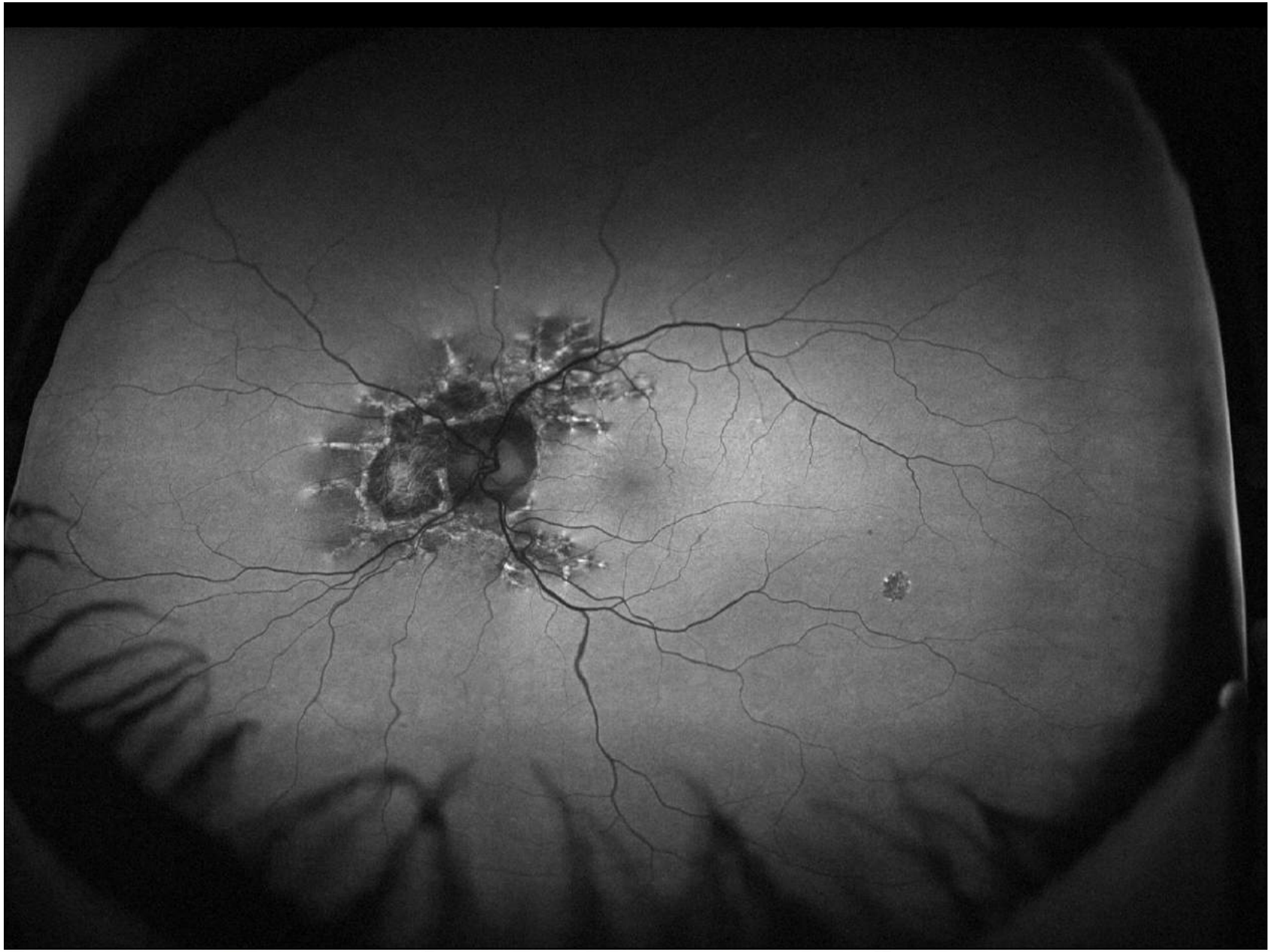

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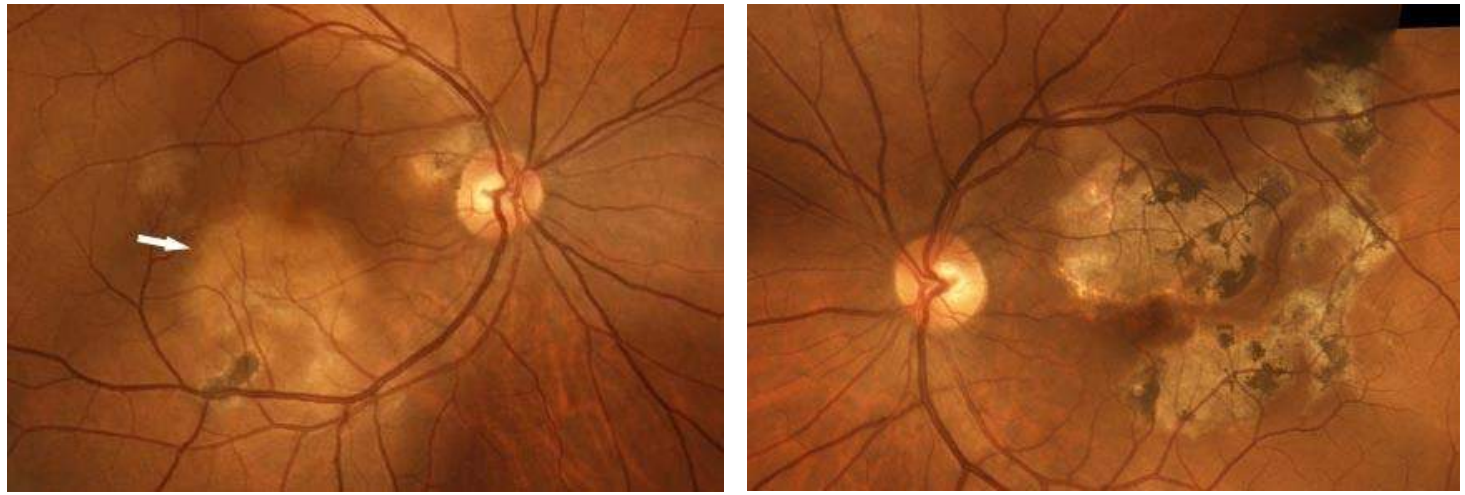
Serpiginous Choroiditis Management

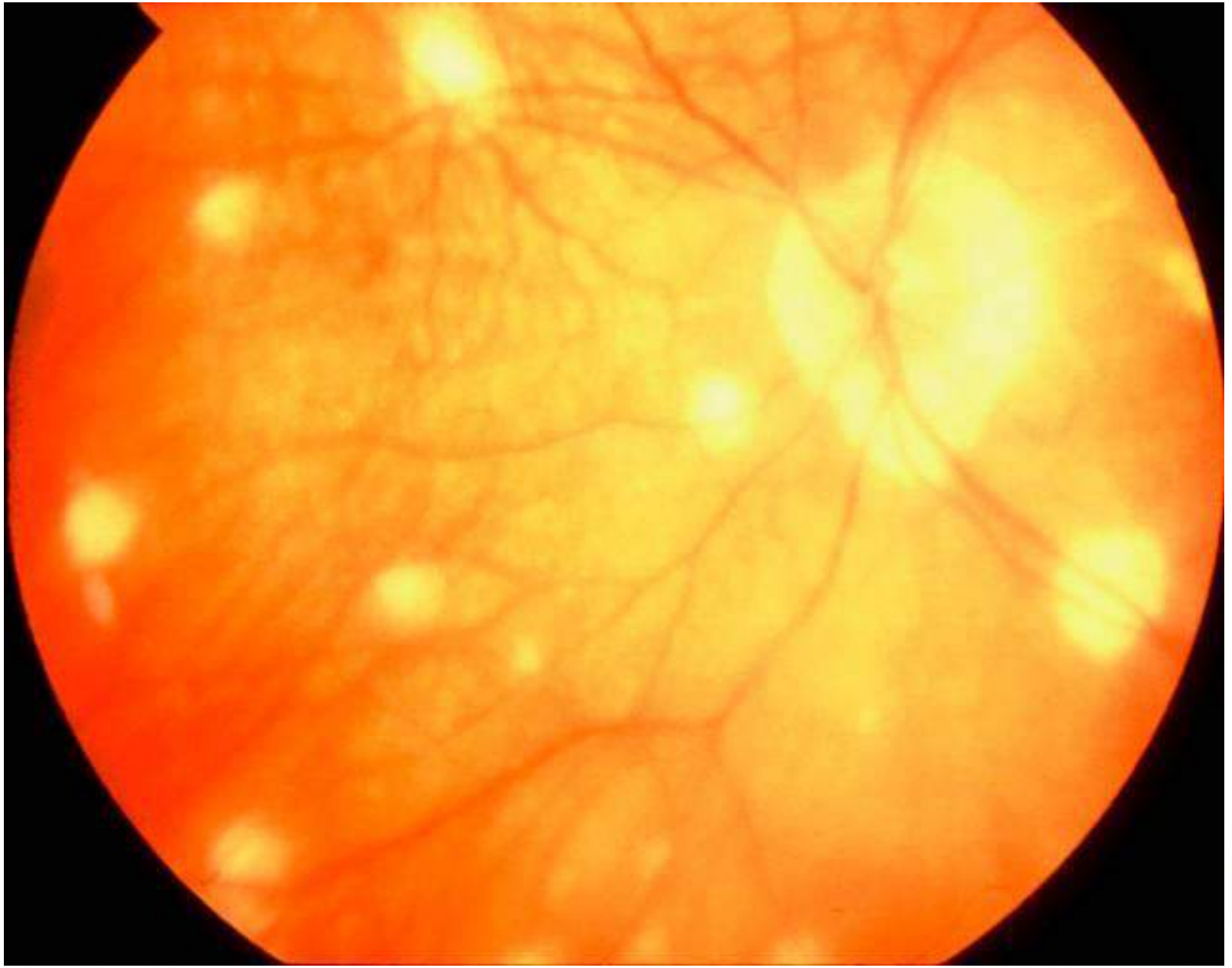
- Immunosuppressive agents
  - cyclosporine
- Oral steroids
- Complications:
  - CME
  - CNVM 25%



- Home monitor with Amsler
- RTC q 6 months if quiet

Case 3

- 31-year-old Caucasian female
- Noticing ‘spots’ and blur in both eyes x 1 week
- Eyes sensitive to light
- Had mononucleosis a few weeks ago
- No medications, penicillin allergy
- BCVA 20/80 OD, 20/70 OS (-1.00 sph OU)
- 1+ cells in anterior chambers OU
- Pupils slowly responsive to light OU
- Mild diffuse vitreal haze OU



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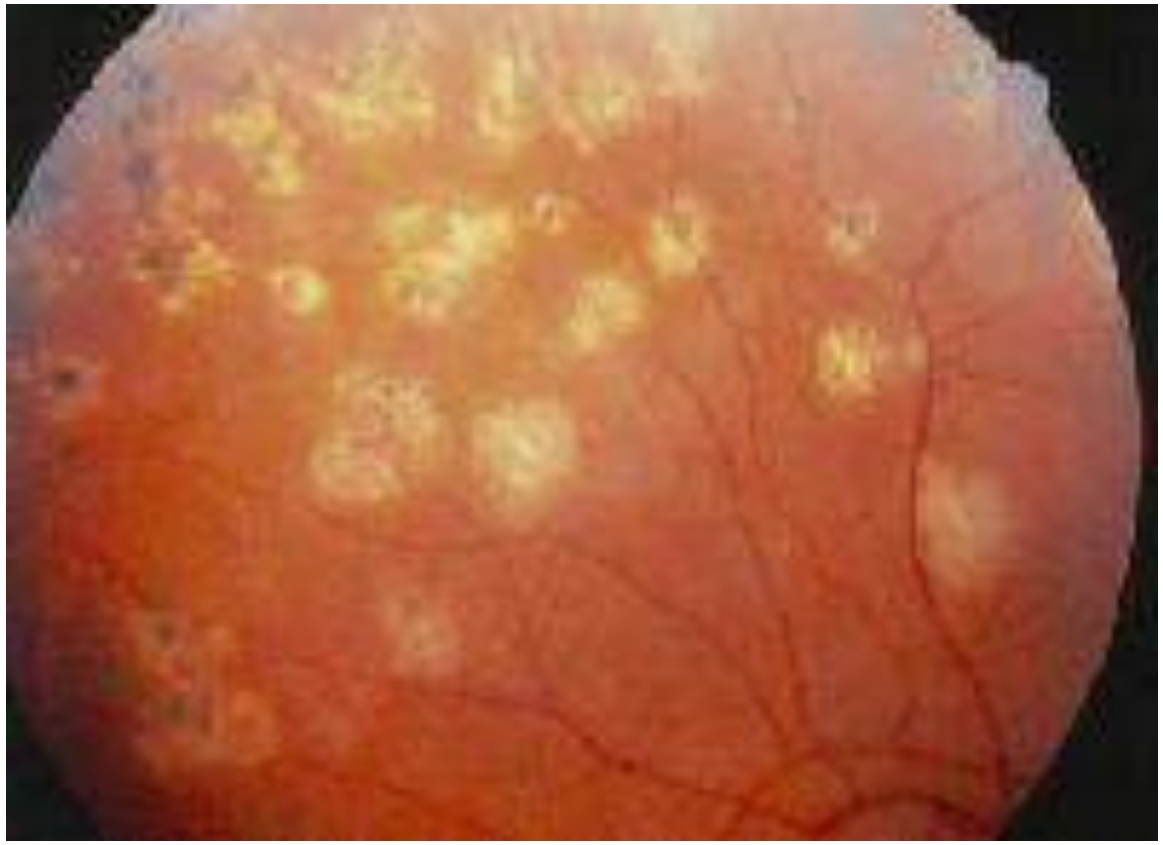
MFC (Multifocal Choroiditis)

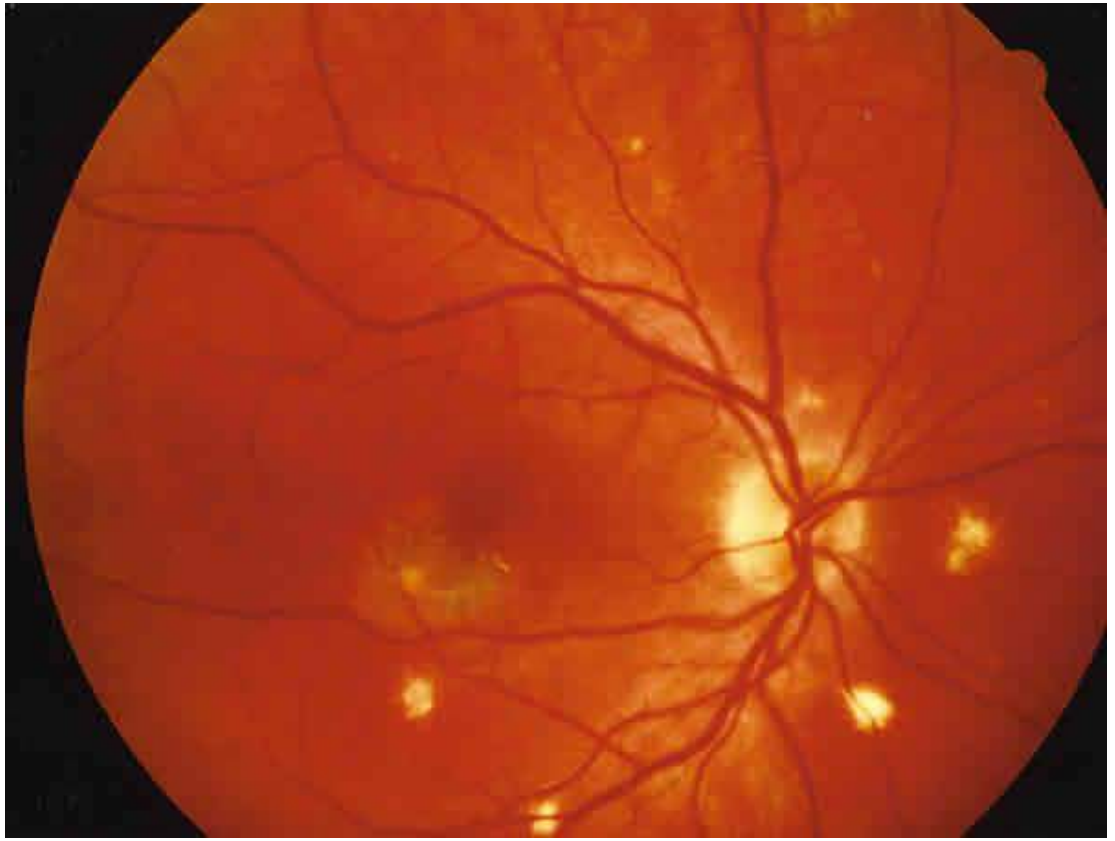
Progressive RPE and choroidal inflammatory disorder with multiple relapses

Known by many names:

- **Punctate inner choroidopathy (PIC)**
- Multifocal choroiditis with panuveitis (MCP)
- Multifocal choroiditis with disciform macular degeneration
- Chorioretinopathy with anterior uveitis
- Subretinal fibrosis
- Pseudohistoplasmosis

Multifocal Choroiditis





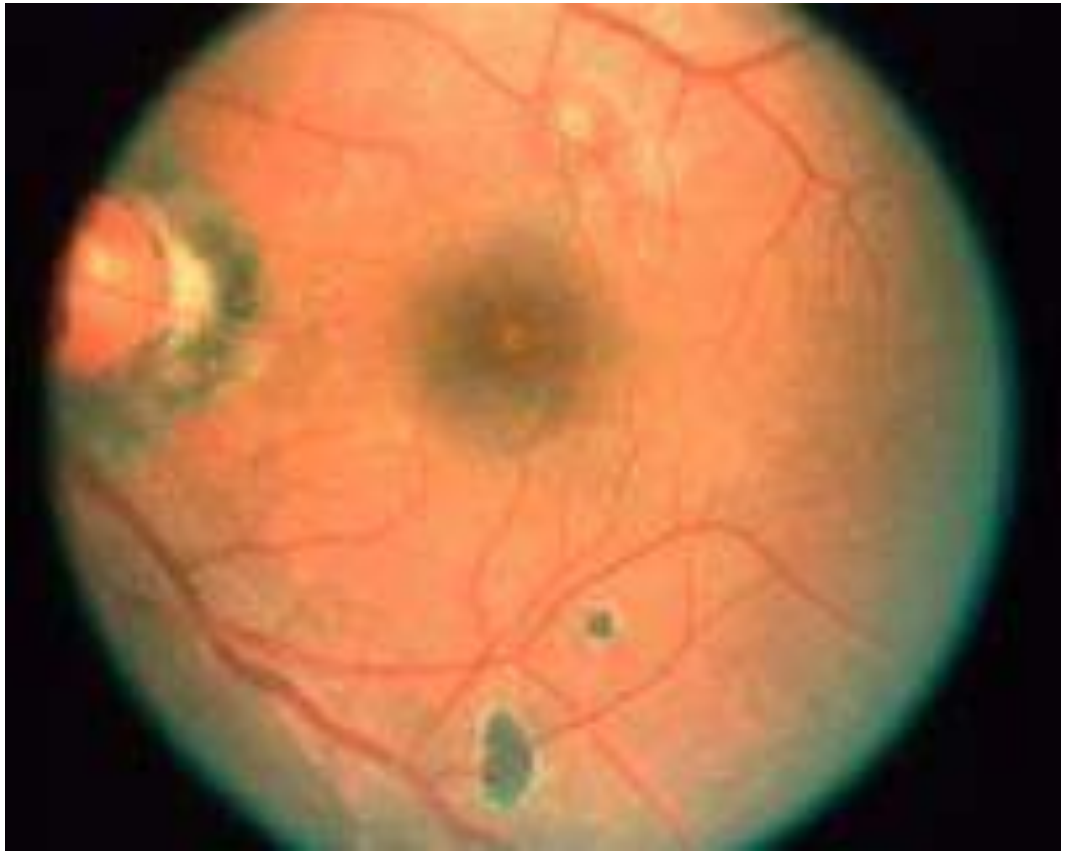
Multifocal Choroiditis Symptoms

- 14 – 34 yo
- 85% mildly myopic
  86% females, 66% White
- Possible viral prodrome
  associated with EBV (Epstein-Barr Virus)
- Bilateral 80% of time
- Blurry vision, metamorphopsia, floaters, scotomas, photopsia:
- Presenting VA may vary from 20/20 to LP, with average of 20/100

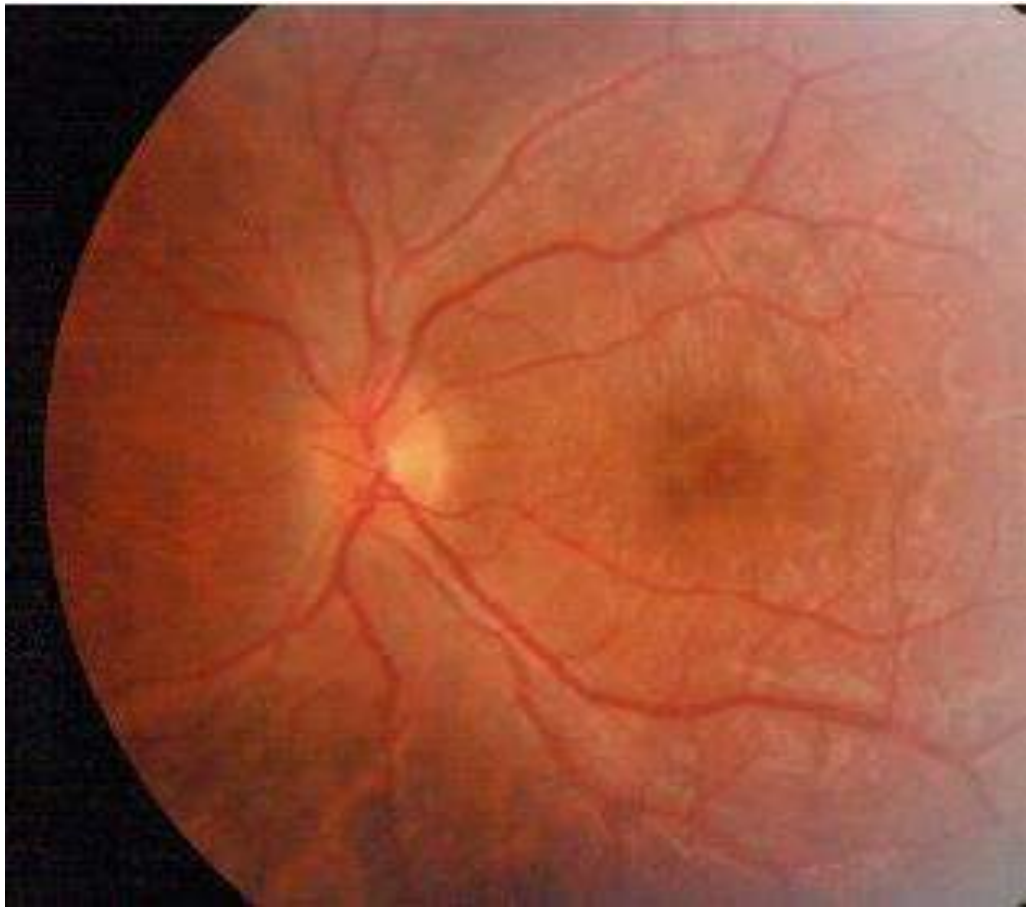
Multifocal Choroiditis Signs

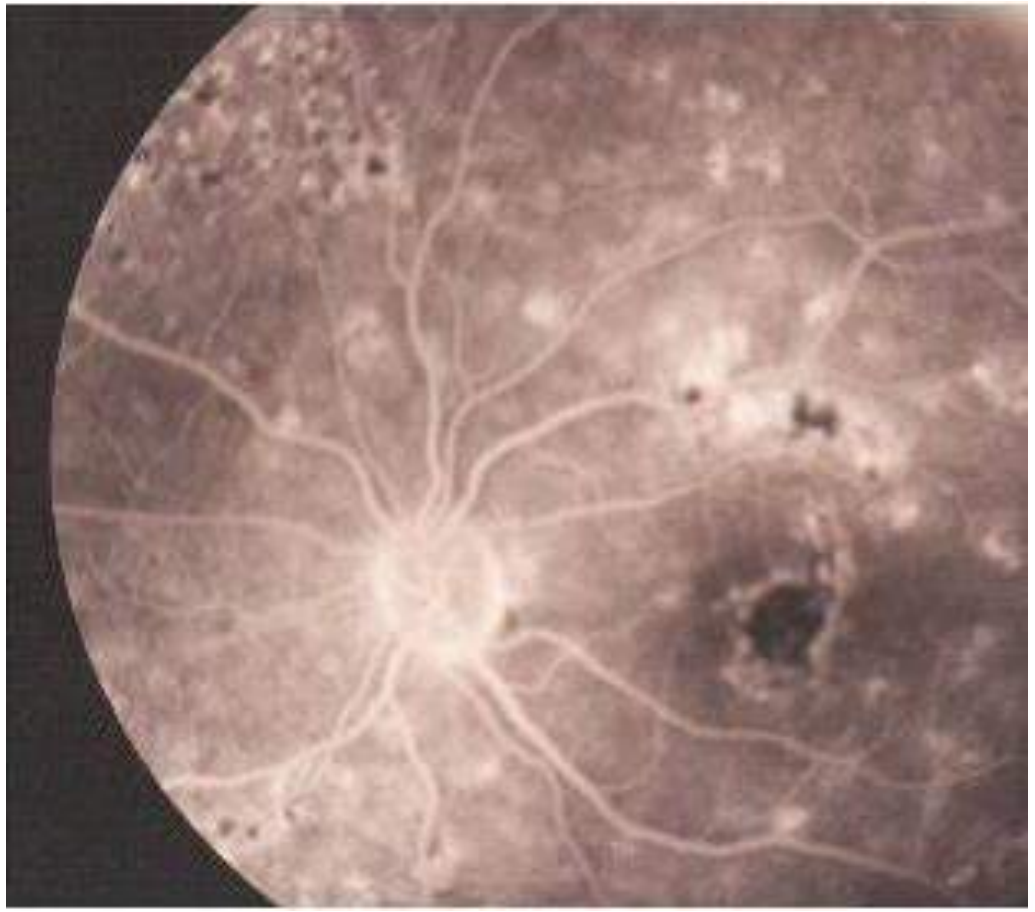
- Small multiple gray to yellow-white lesions
- Become gray and fuzzy during active phase
- At level of RPE and choriocapillaris
- Mostly in periphery rather than macula
- Vitritis (90%), anterior uveitis (50%), optic disc edema (acute phase)
- FA - Early hyperfluorescence of active lesions
- Complications – CNVM (25-40%), CME, Subretinal fibrotic scarring

Multifocal Choroiditis

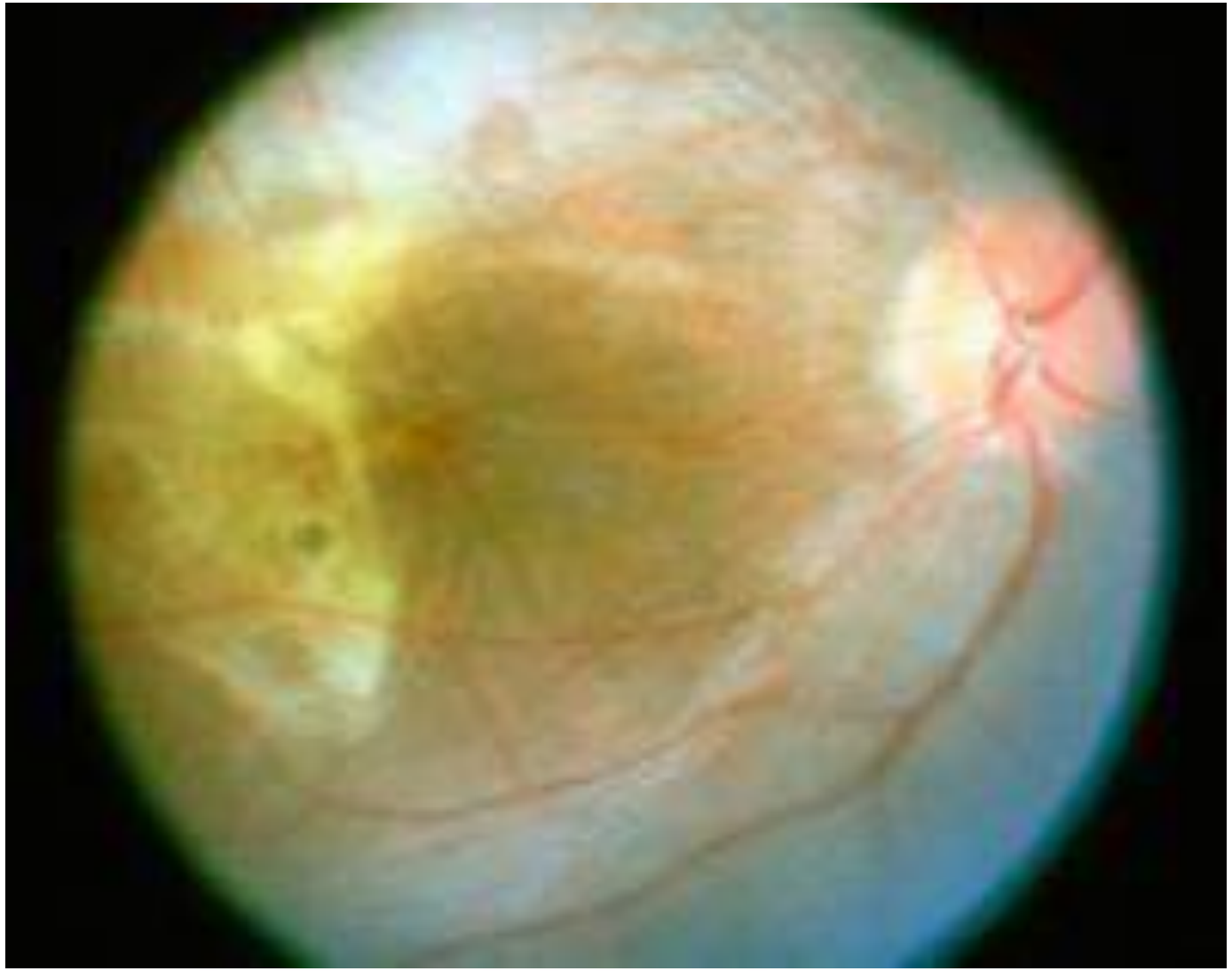


Multifocal Choroiditis



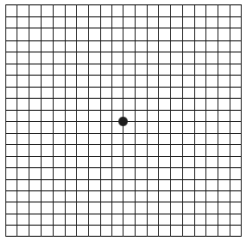


Multifocal Choroiditis: subretinal fibrosis



Multifocal Choroiditis Management

- Idiopathic (possible virus)
- Home Amsler



- Oral steroids
- Immunosuppressives
  - azothioprine, cyclosporine, methotrexate, others
- Laser/Anti-VEGF for CNVM
- RTC q 6 months if quiet
- Recurrence high; visual prognosis poor

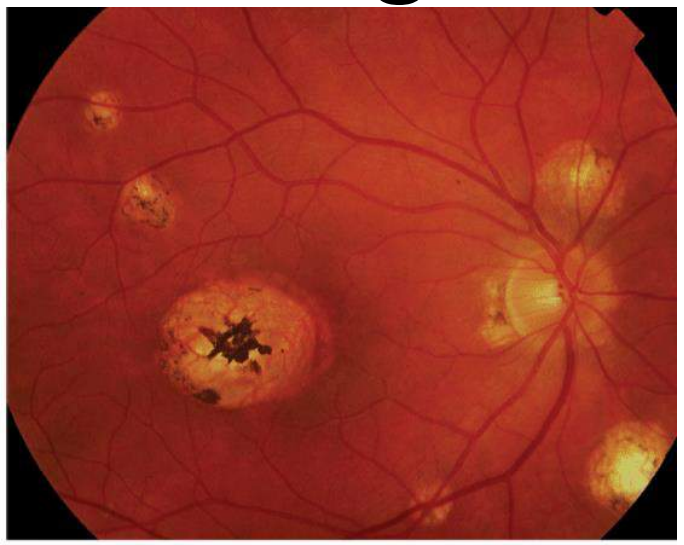


Figure 2. Multifocal choroiditis and panuveitis. A 30-year-old woman with MCP demonstrating punched-out, atrophic chorioretinal lesions in the peripapillary and posterior pole region. Numerous others were present in the mid and far periphery. The atrophic scar temporal to the fovea represents an old focal laser scar from treatment of previous choroidal neovascularization.

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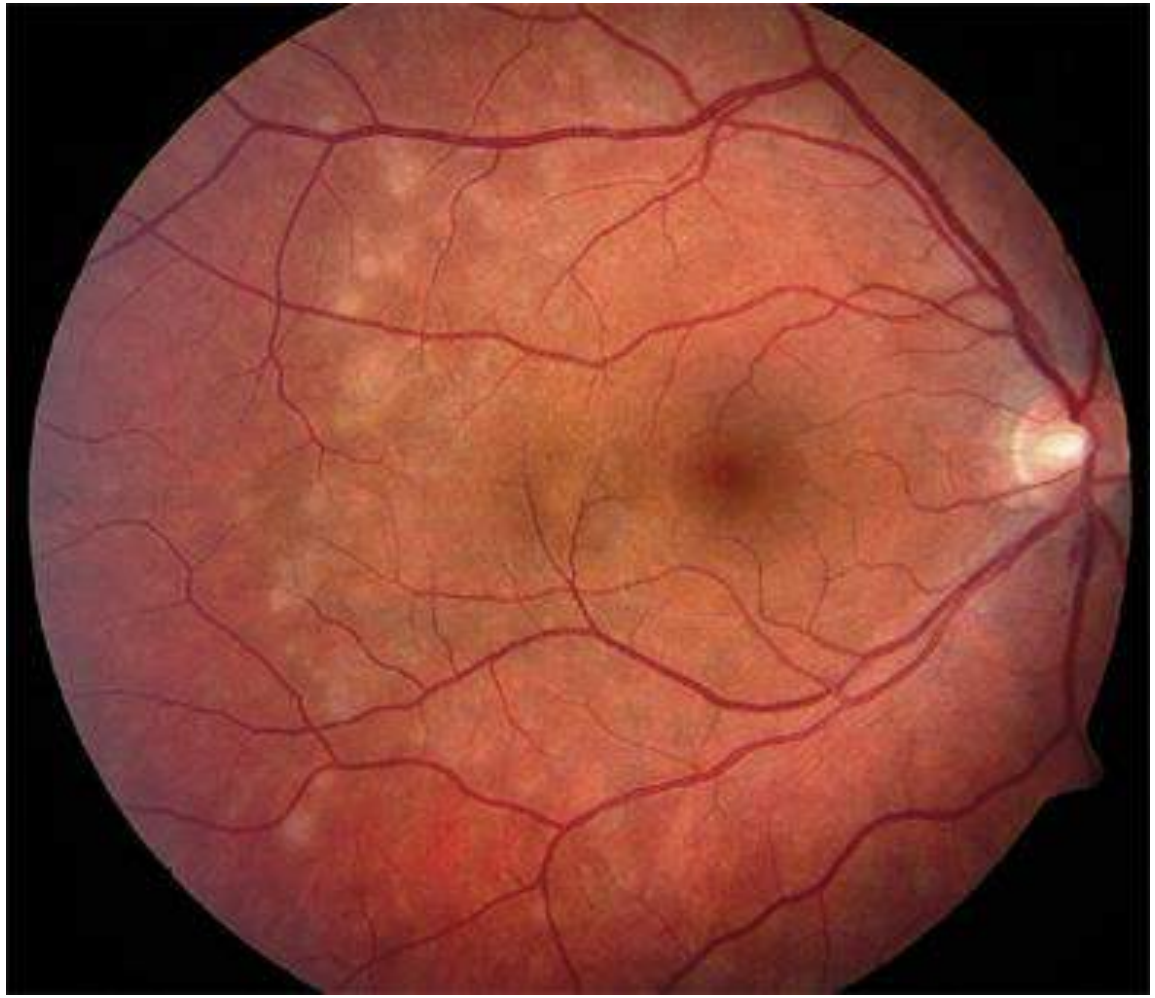
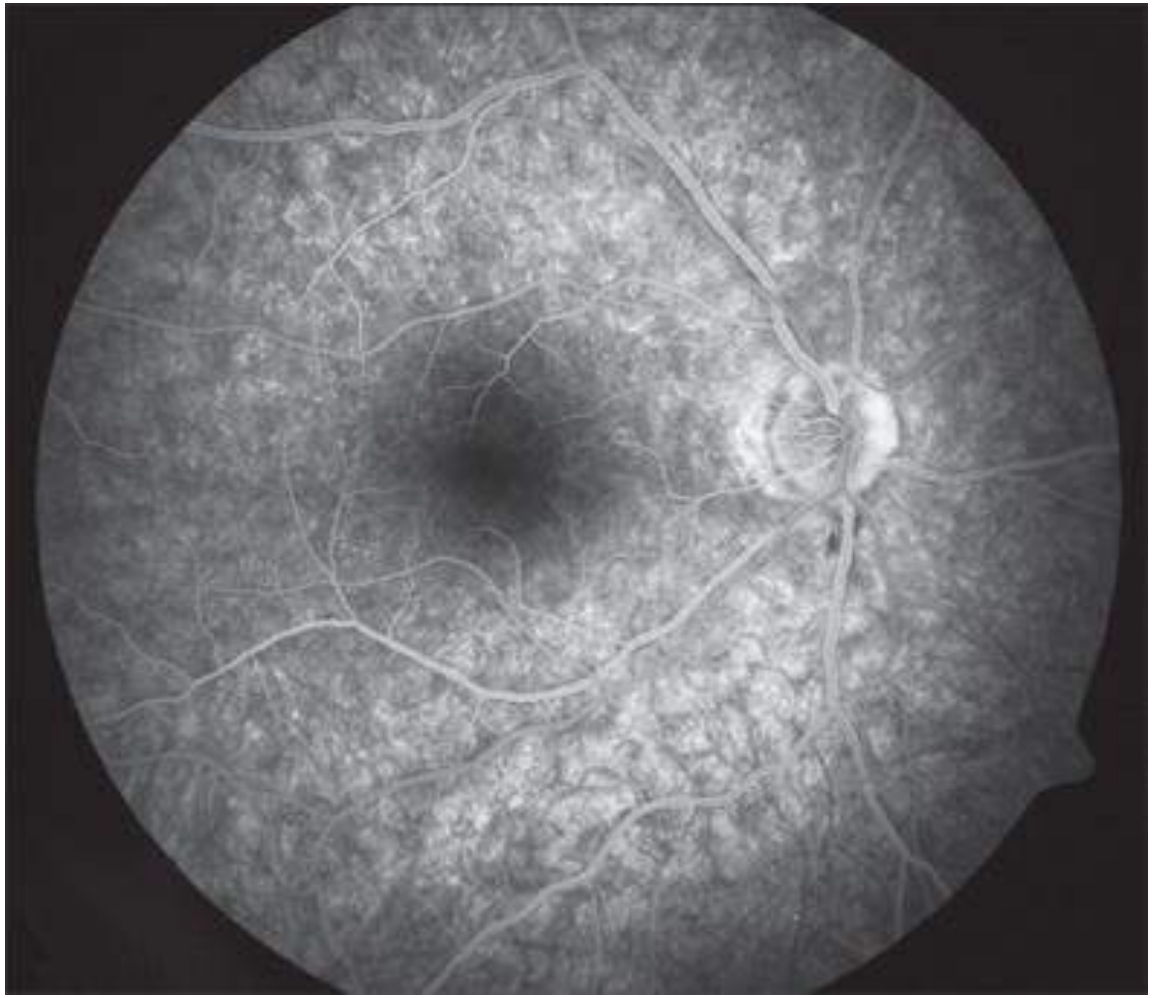
https://www.reviewofophthalmology.com/article/recognizing-the-white-dot-syndromes

Case 4

- 32-year-old Caucasian female; family friend
- Lives across country, out of state
- Called with complaints of blurry vision OD
- Onset 5 days prior
- Sees ‘numerous little spots’…migraine?
- Other eye fine
- Under stress (son undergoing heart surgery)
- Referred for fluorescein angiography





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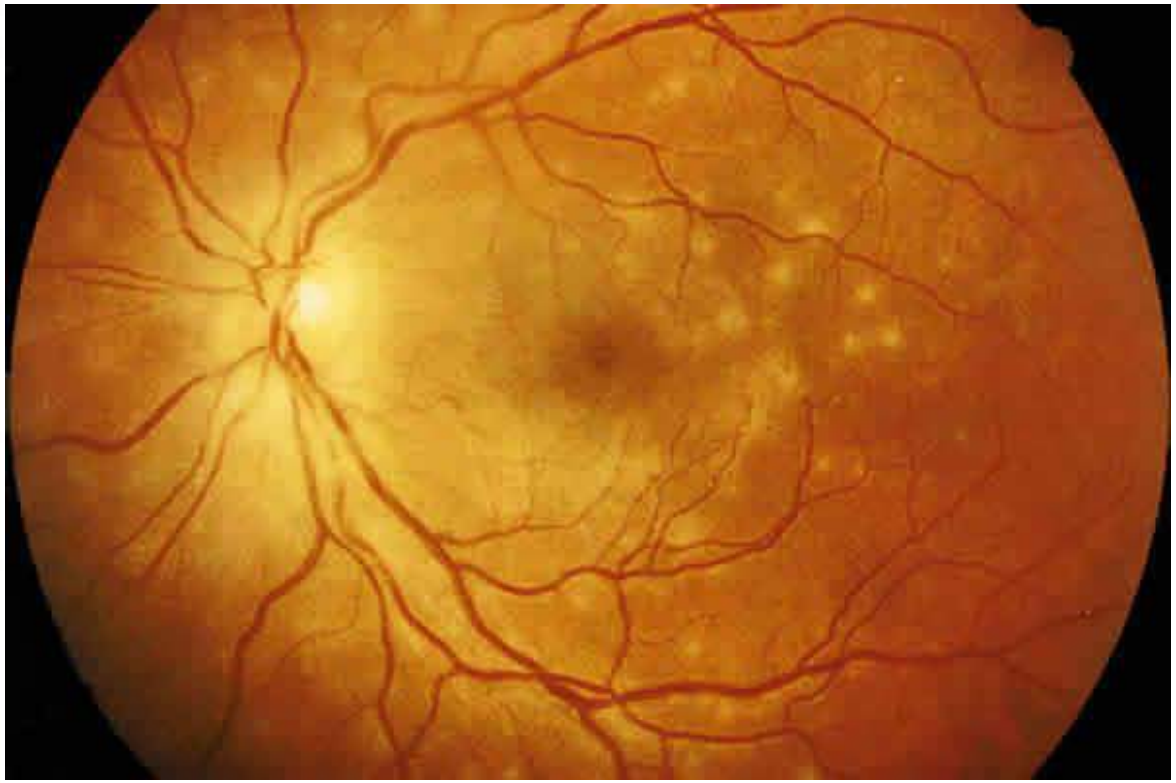
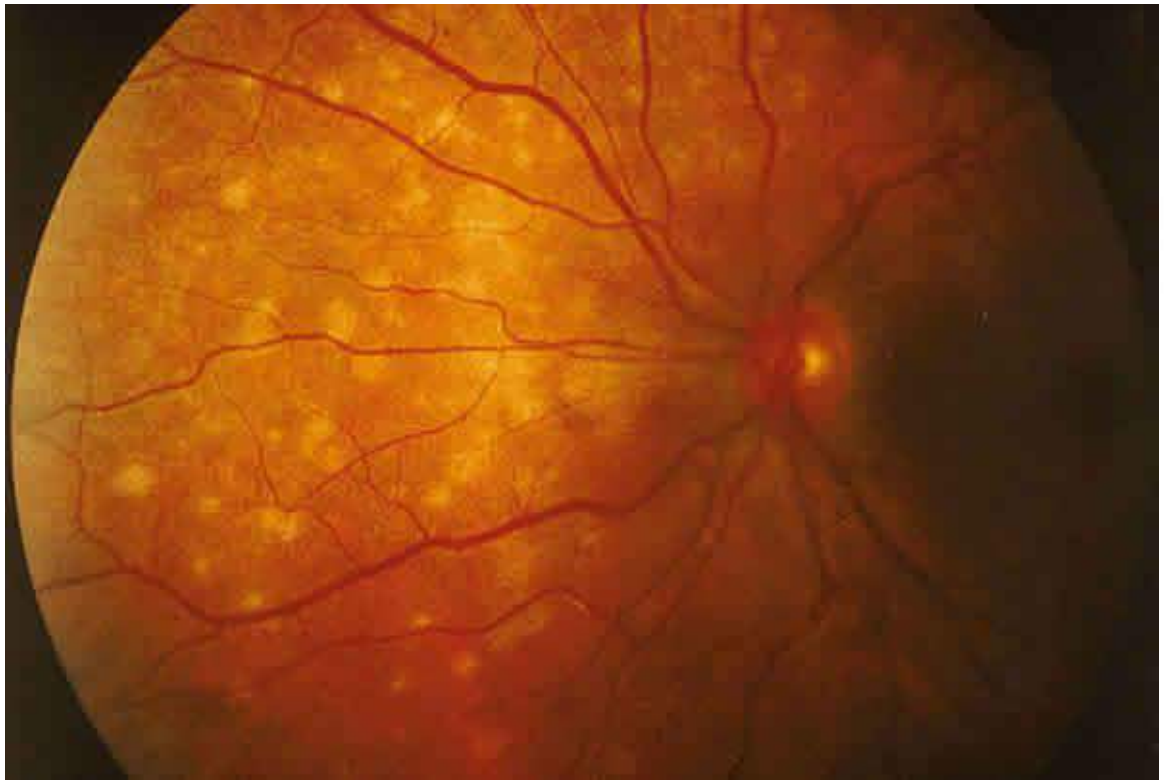
Multiple Evanescent White Dot Syndrome (MEWDS)

- Acute, multifocal retinopathy involving RPE and outer retina
- 17 – 38 yo
- Young females with prodromal flu-like syndrome (35%)

- Acute unilateral vision loss, photopsia
- May see spots (that don't move) in vision

MEWDS





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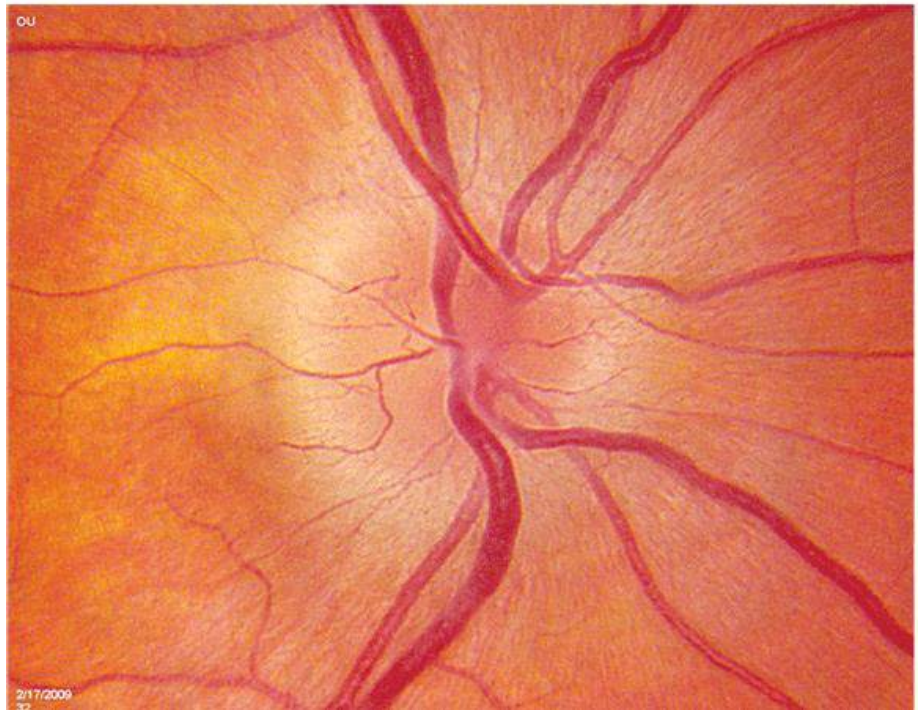
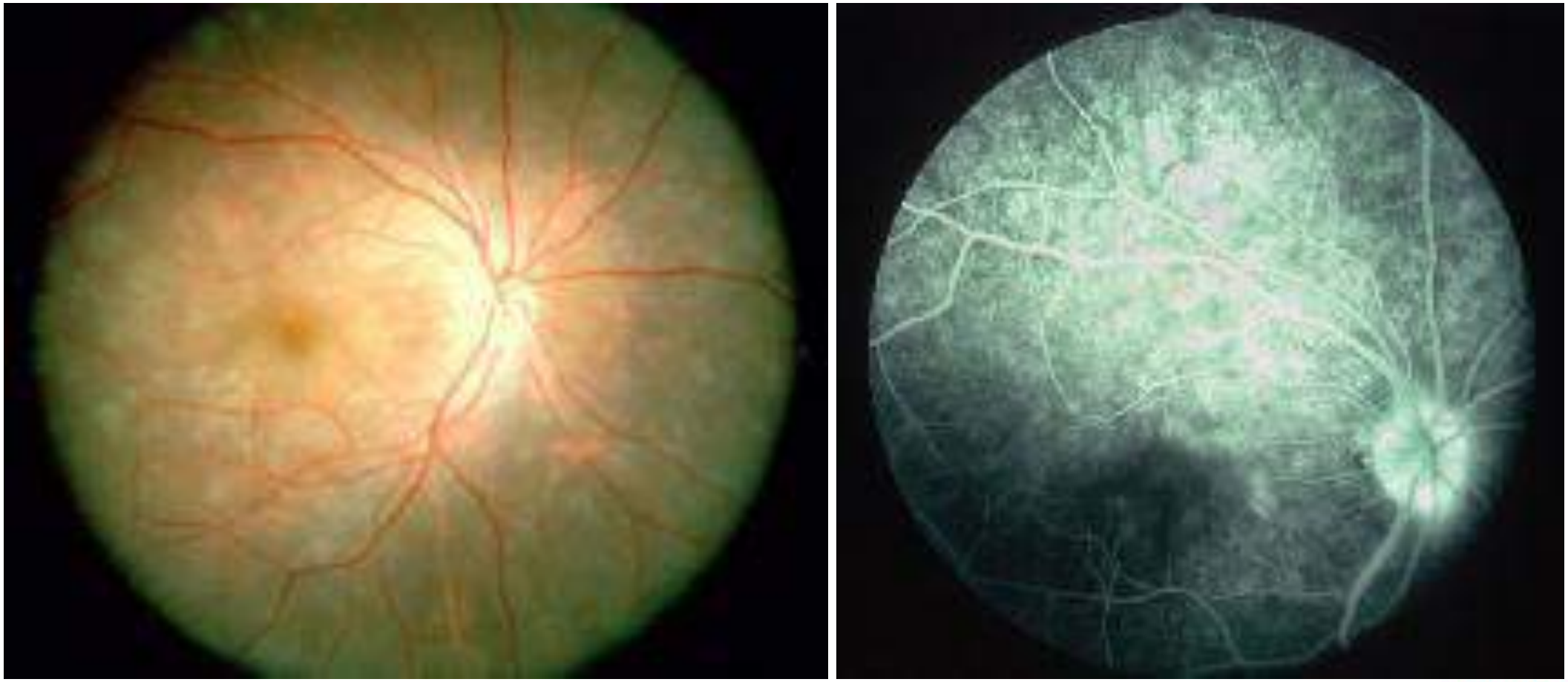
MEWDS Signs

- Unilateral
- Multiple creamy flat grey-white dots in posterior pole (spare fovea)
- Granular appearance of macula
- Possible optic disc edema (possible RAPD)
- Possible vitritis



MEWDS



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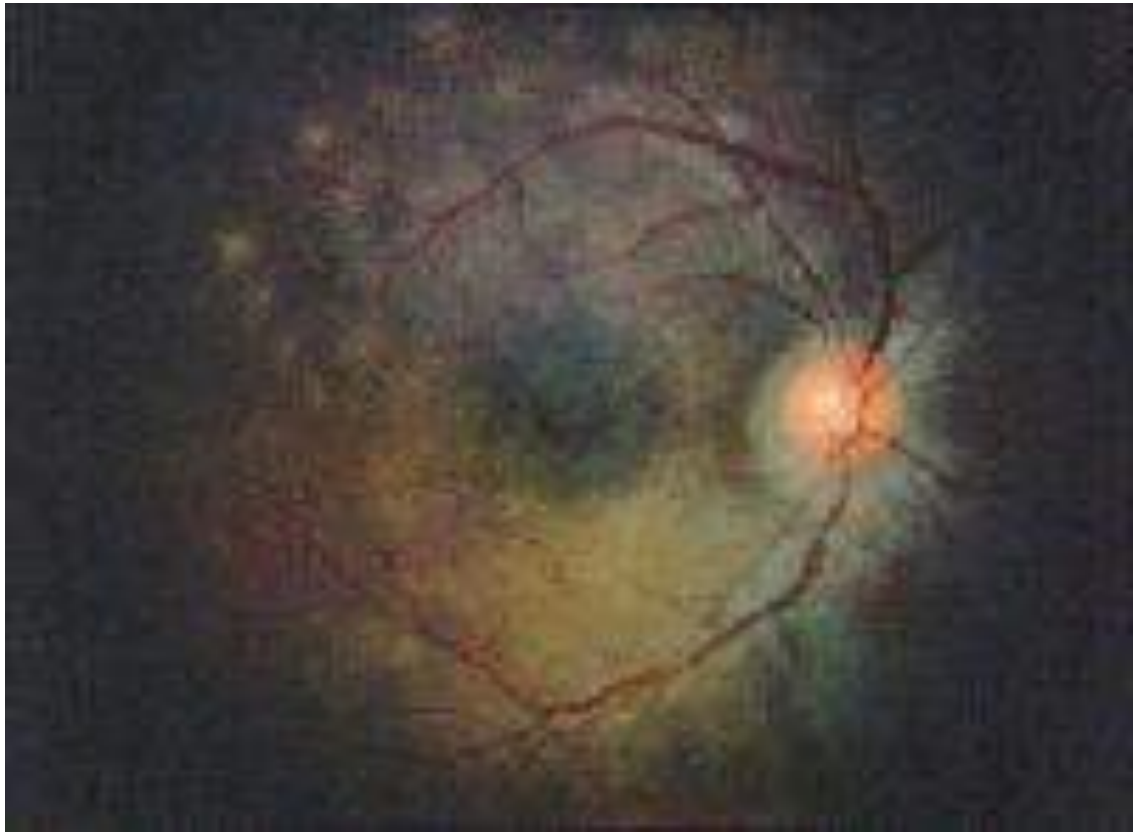
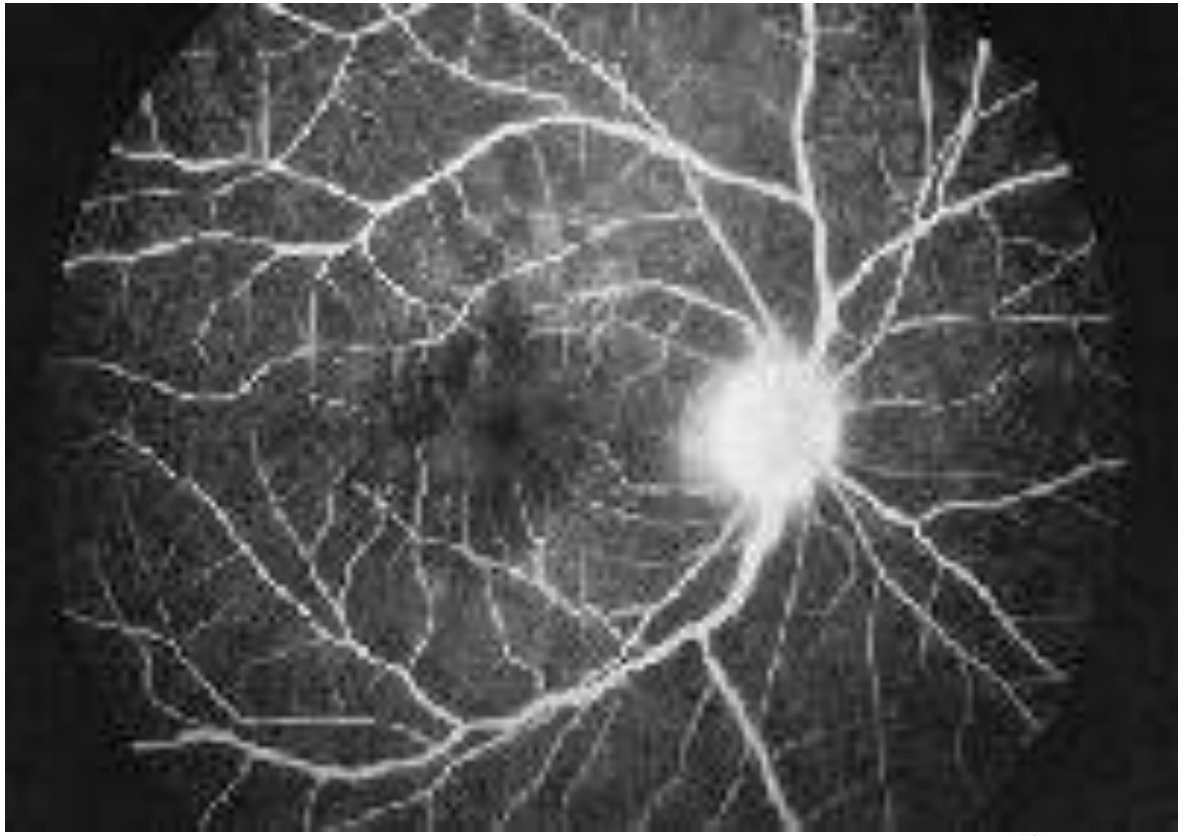
MEWDS Angiography

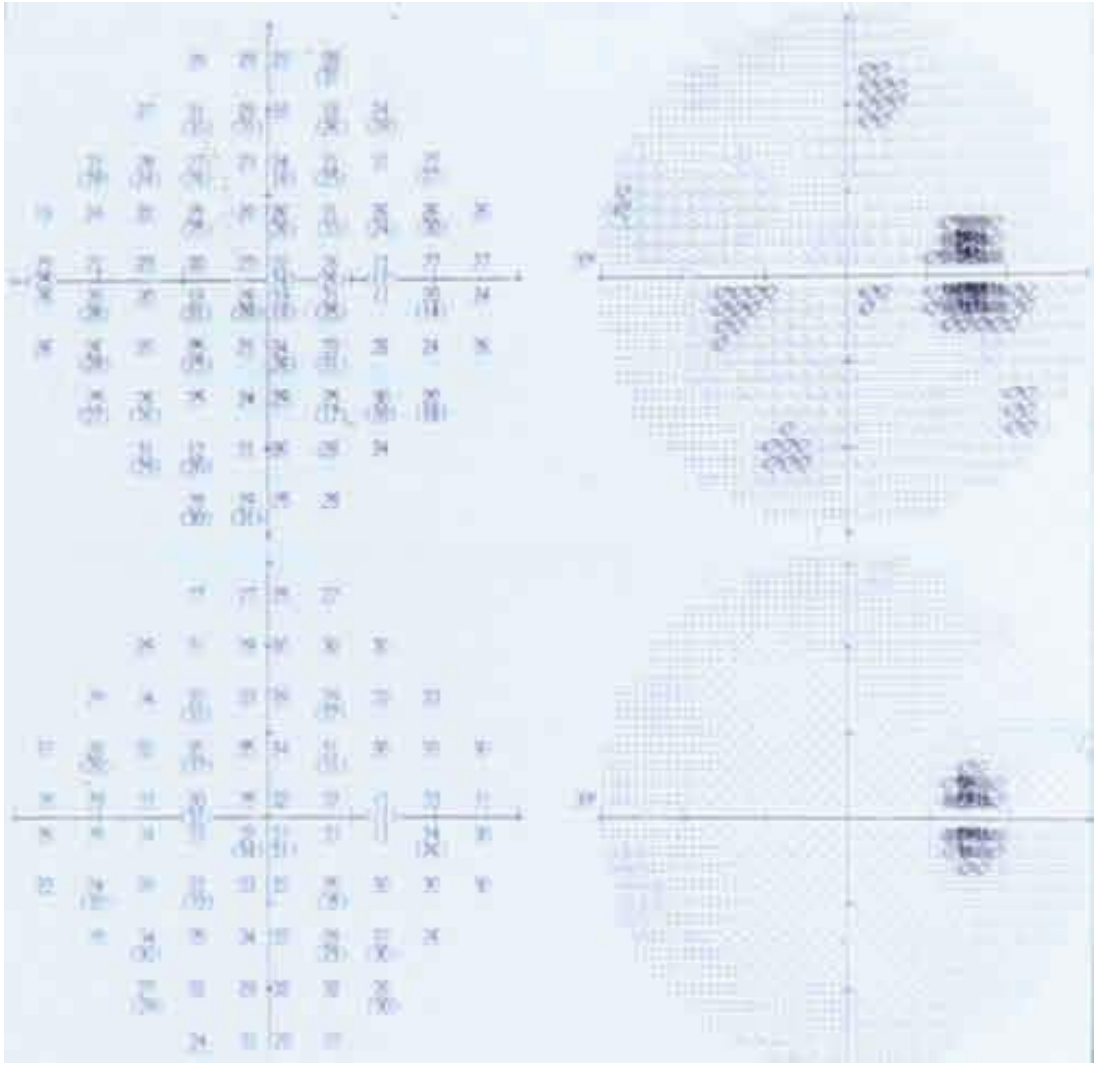
- FA shows ‘wreath-like’ hyperfluorescence and late focal staining, disc hyperfluorescence
- ICG shows hyperfluorescent spots in posterior pole and around disc
- Possible enlarged blind spot
- Possible abnormal ERG

MEWDS





MEWDS: enlarged blind spot

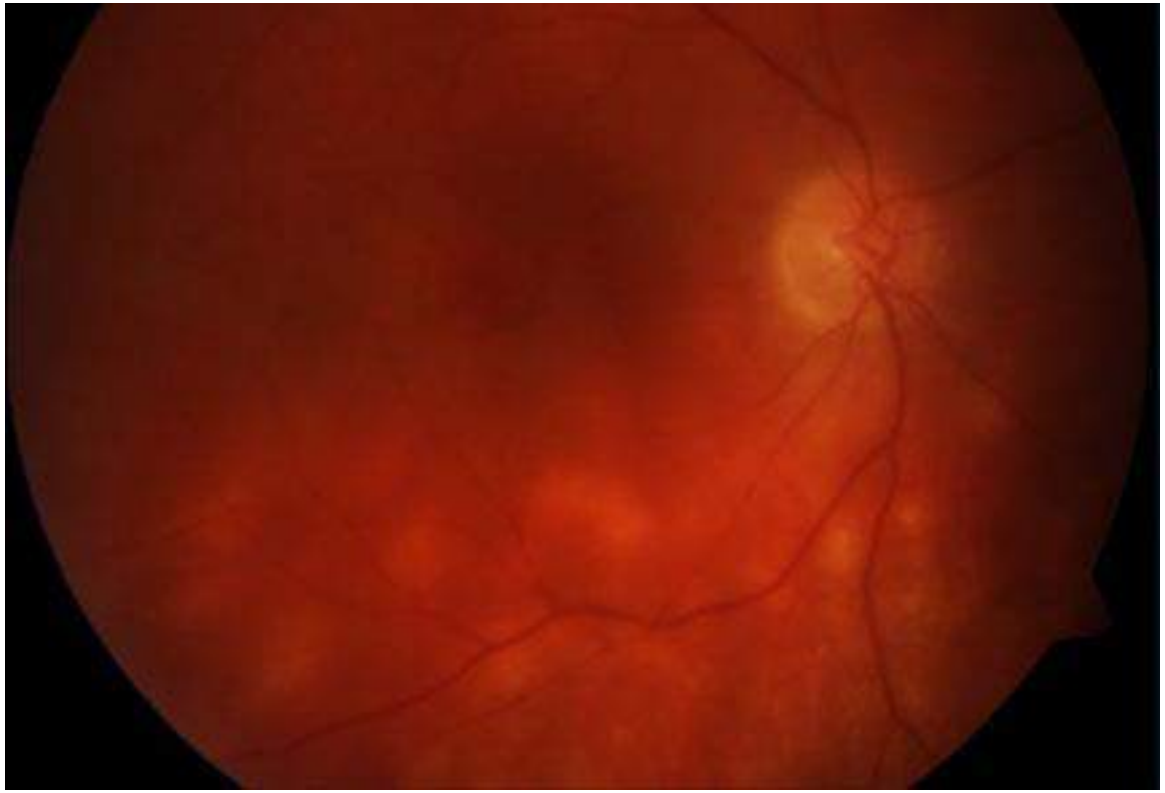


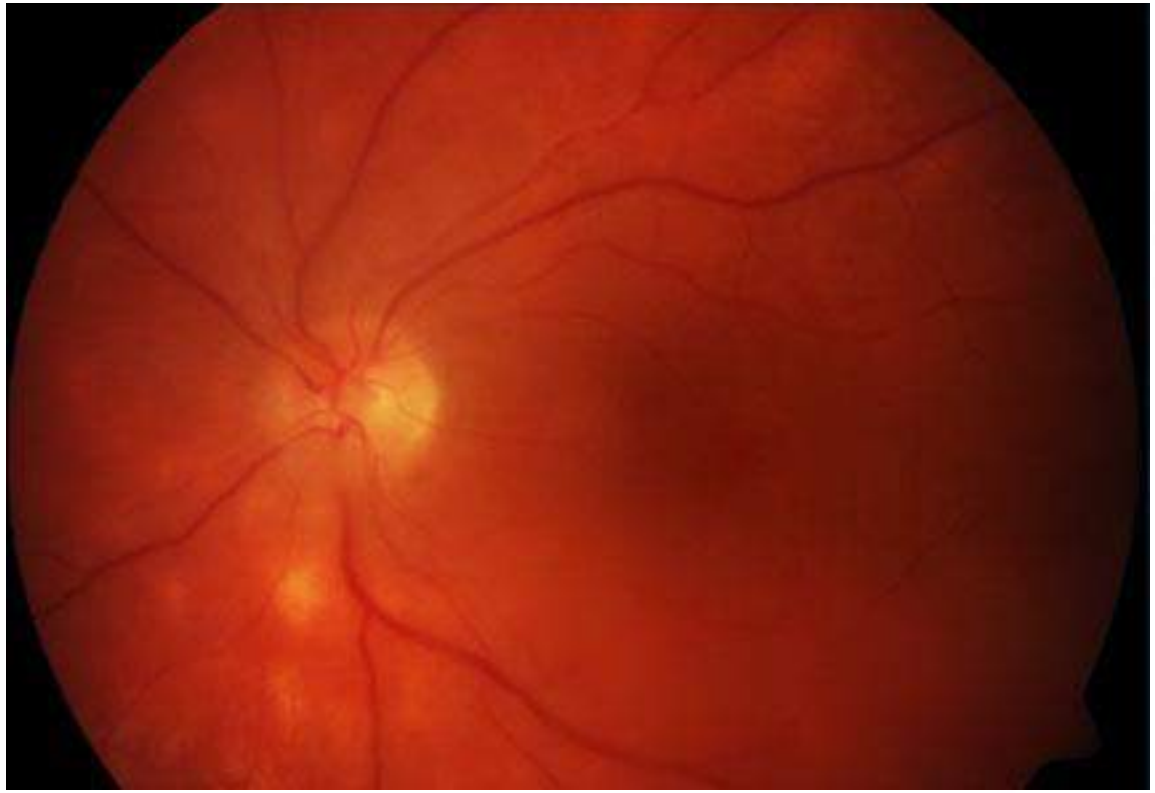
MEWDS Management

- Self-limiting; monitor only
- Vision usually recovers well in 6 – 12 weeks
- No further visual deterioration with recurrence
- Enlarged blind spot may persist
- Pt education
- Complications - CNVM (rare)
- RTC yearly

Case 5

- 49-year-old Caucasian female
- Fuzzy vision last 2 weeks; both eyes
- Noticed harder to see at night x 1 month
- Family history of MS; however no PMHx of MS
- Asthma; takes Singulair, Flovent inhaler PRN
- Allergic to sulfa meds
- BCVA 20/40 OD, 20/30 OS
- Color plates 8/14 correct OD, 9/14 correct OS





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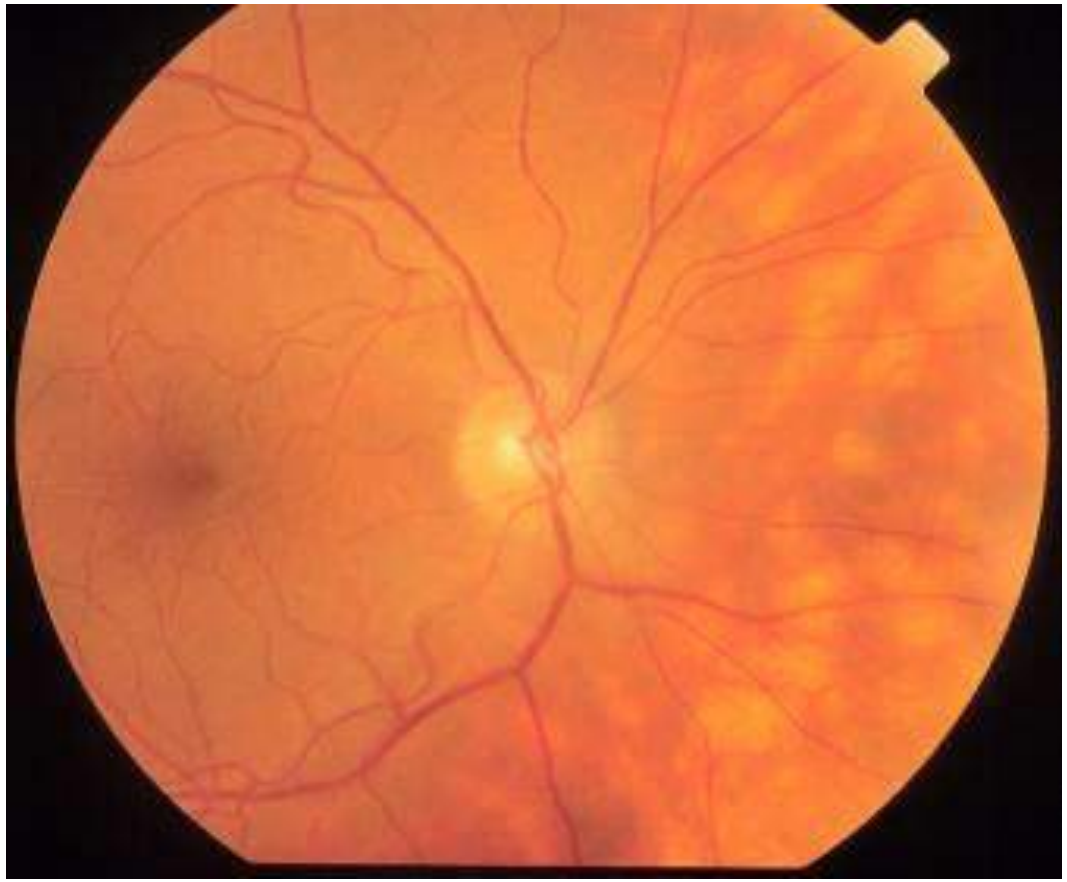
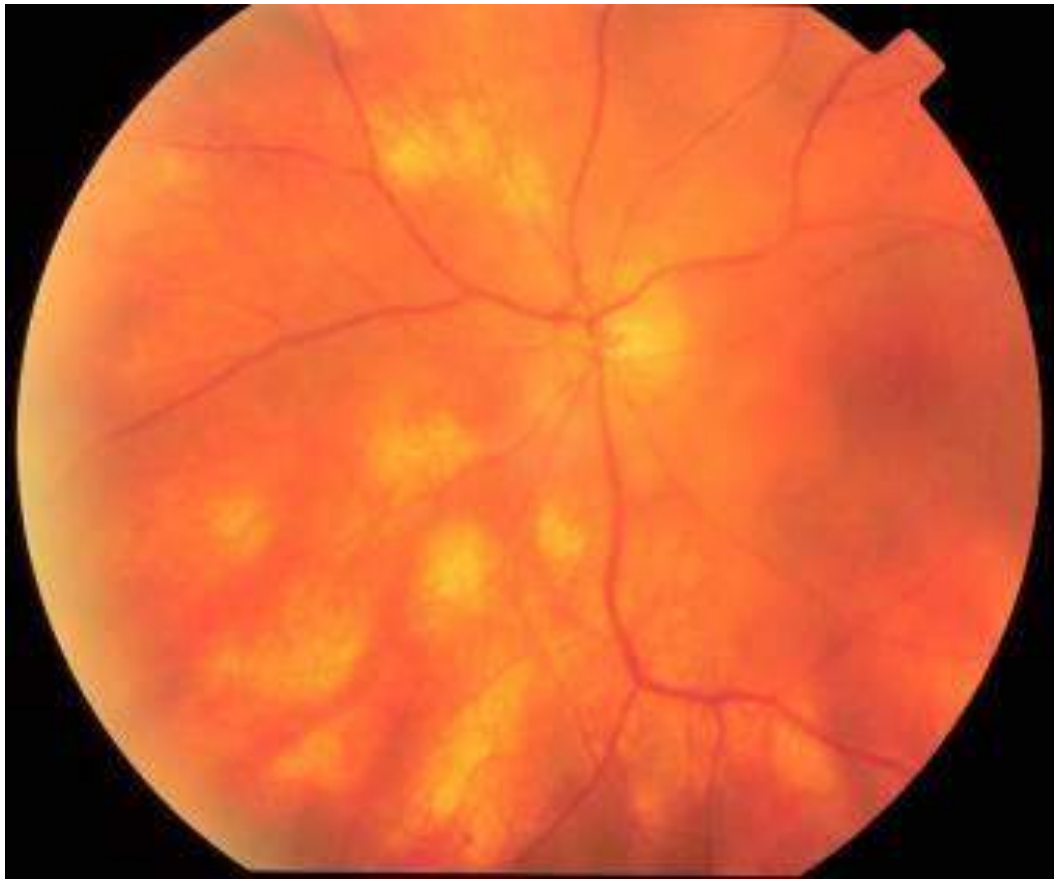
Birdshot Retinochoroidopathy aka Vitiliginous Choroidopathy

- Bilateral, inflammatory disease
- Multiple oval yellow-white spots
- In deep retina and choroid
- Vascular predilection for posterior pole
- 40 – 60 yo
- White, middle aged adults (women > men)
- Blurry vision, floaters, photopsia, night blindness, decreased color vision
- HLA-A29

Birdshot Retinochoroidopathy

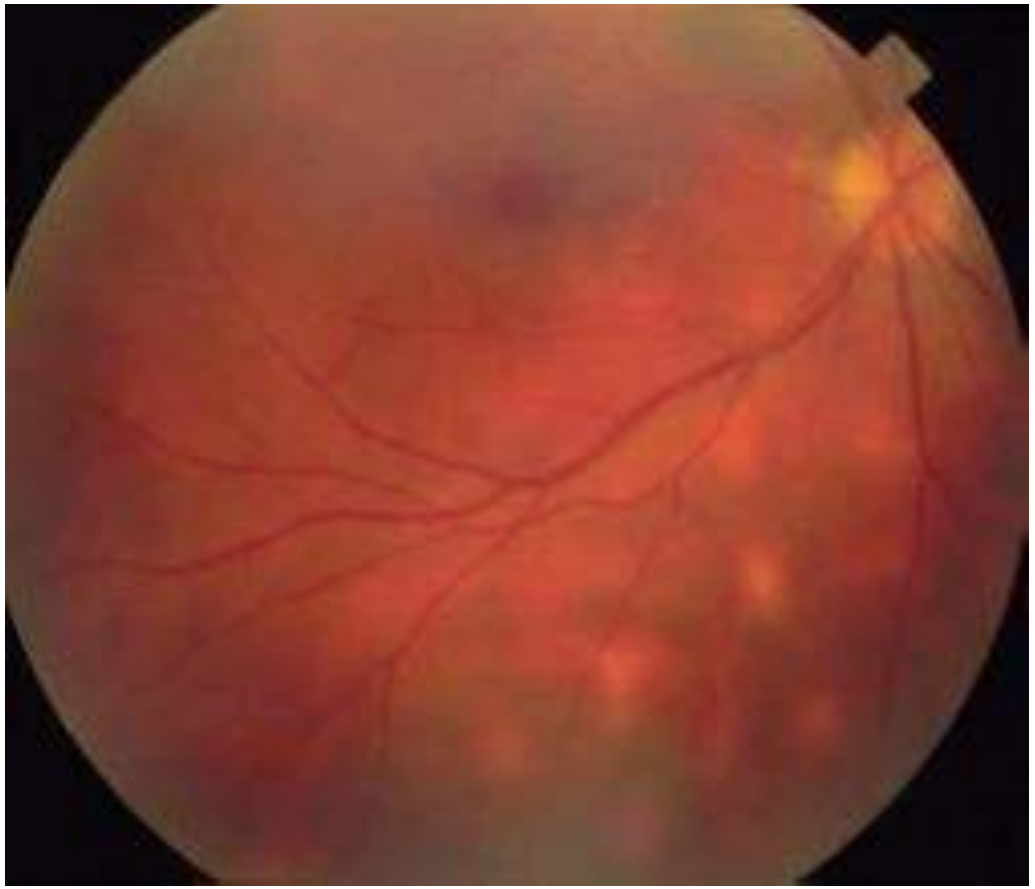


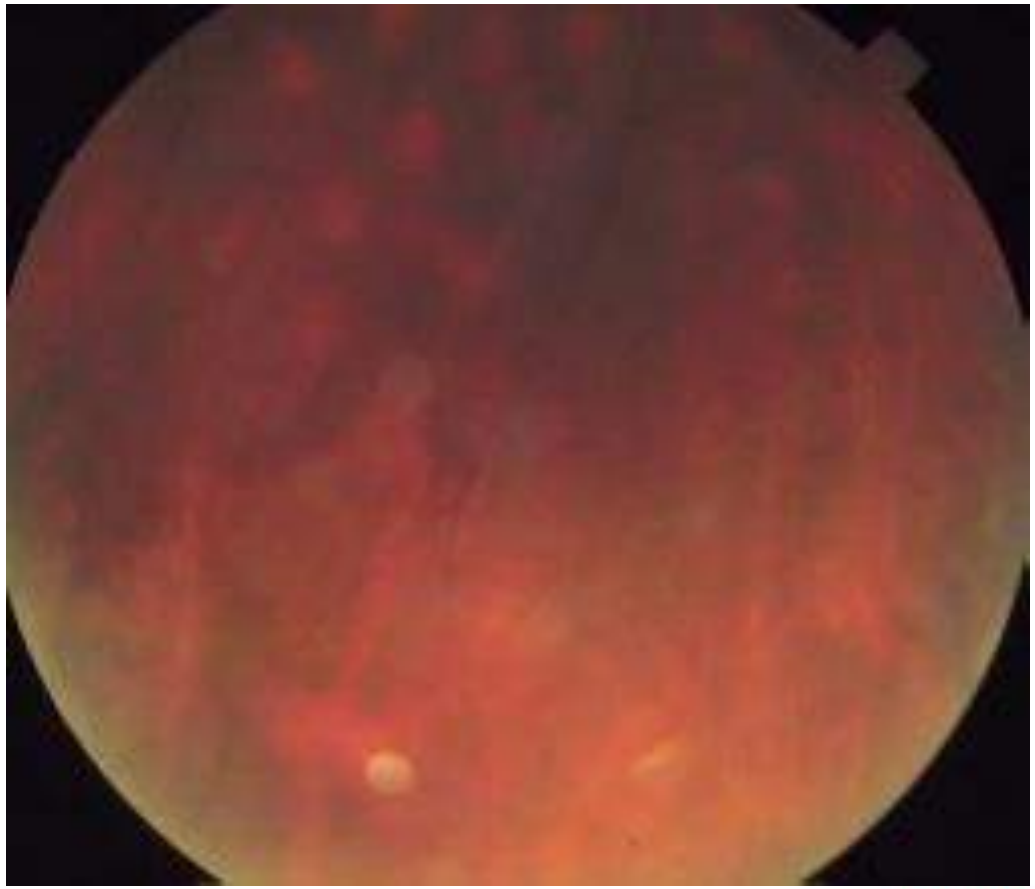


Birdshot Retinochoroidopathy signs

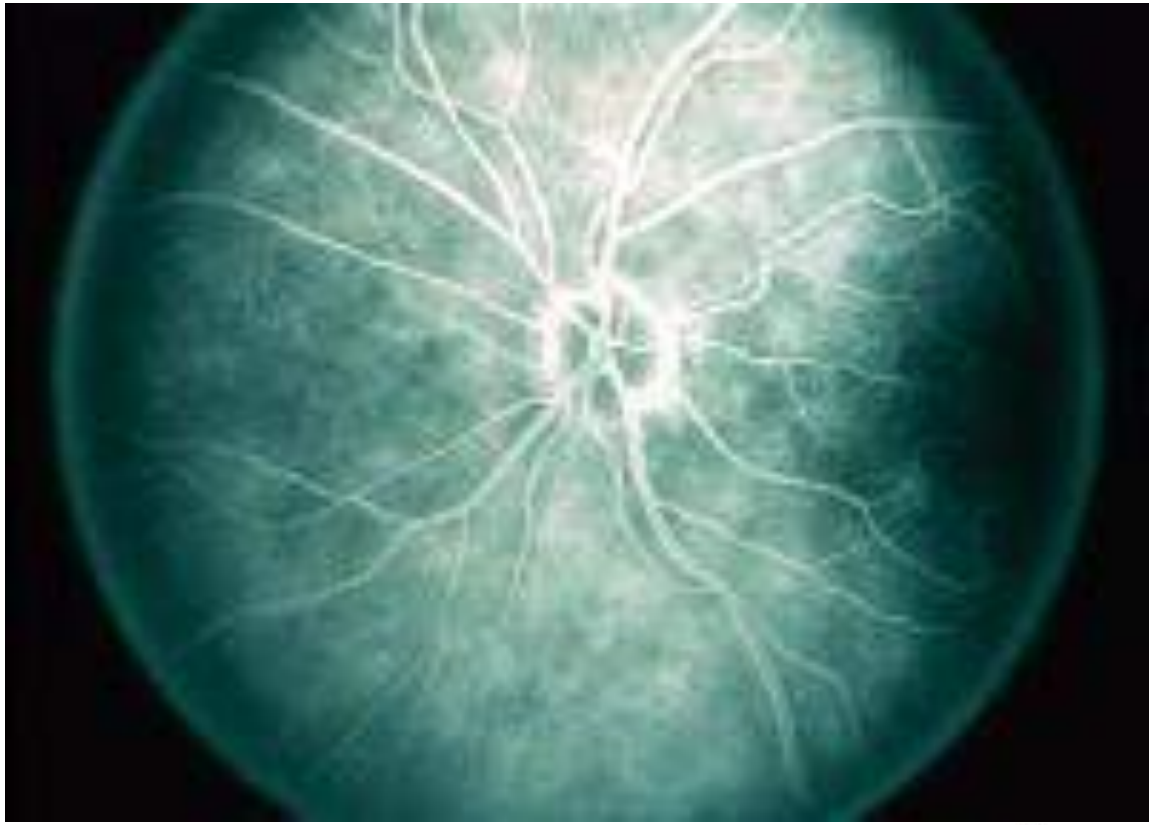
- Initial multiple depigmented areas develop into creamy spots in mid-periphery to posterior pole
- Pattern of lesions look like ‘shotgun blast’ of scattered birdshot
- FA - early hypofluorescence with late accumulation of dye and vascular leakage in larger veins
- Chronic vitritis, retinal vasculitis, AION, CME (50%)
- Abnormal ERG (90%)
- Complications - ERM (epiretinal membranes), retinal neo, CNVM, optic atrophy

Birdshot Retinochoroidopathy

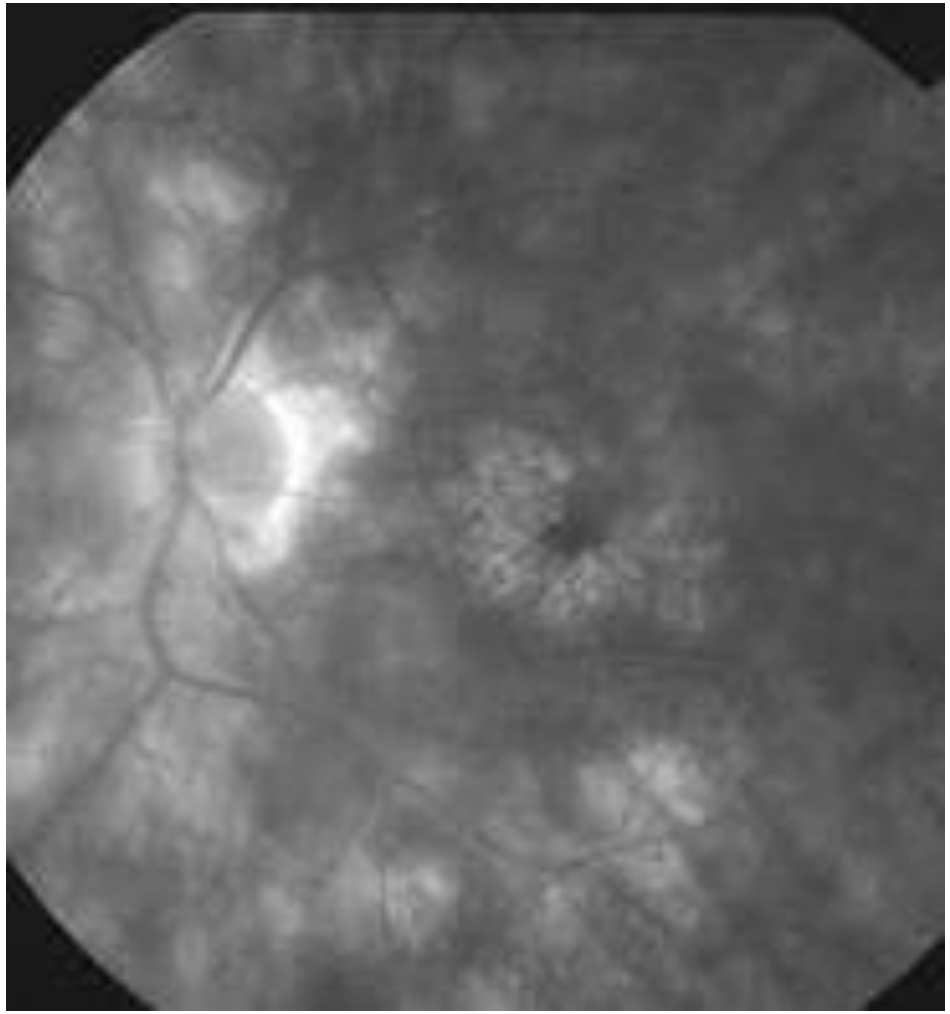




Birdshot Retinochoroidopathy

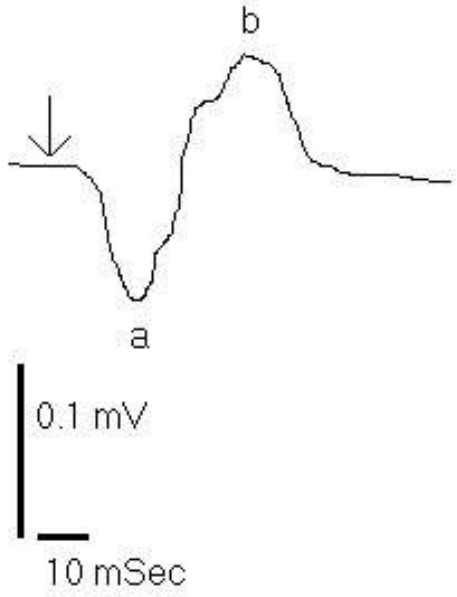


Birdshot Retinochoroidopathy: CME



Birdshot Retinochoroidopathy: abnormal ERG

- Birdshot retinochoroidopathy electroretinogram response to scotopic white light stimulus (arrow). Tracing demonstrates slight disproportionate reduction of the b-wave response in comparison to the a-wave.



- Moderate-to-severe abnormalities of both rod and cone function (less than or equal to 80% of patients)

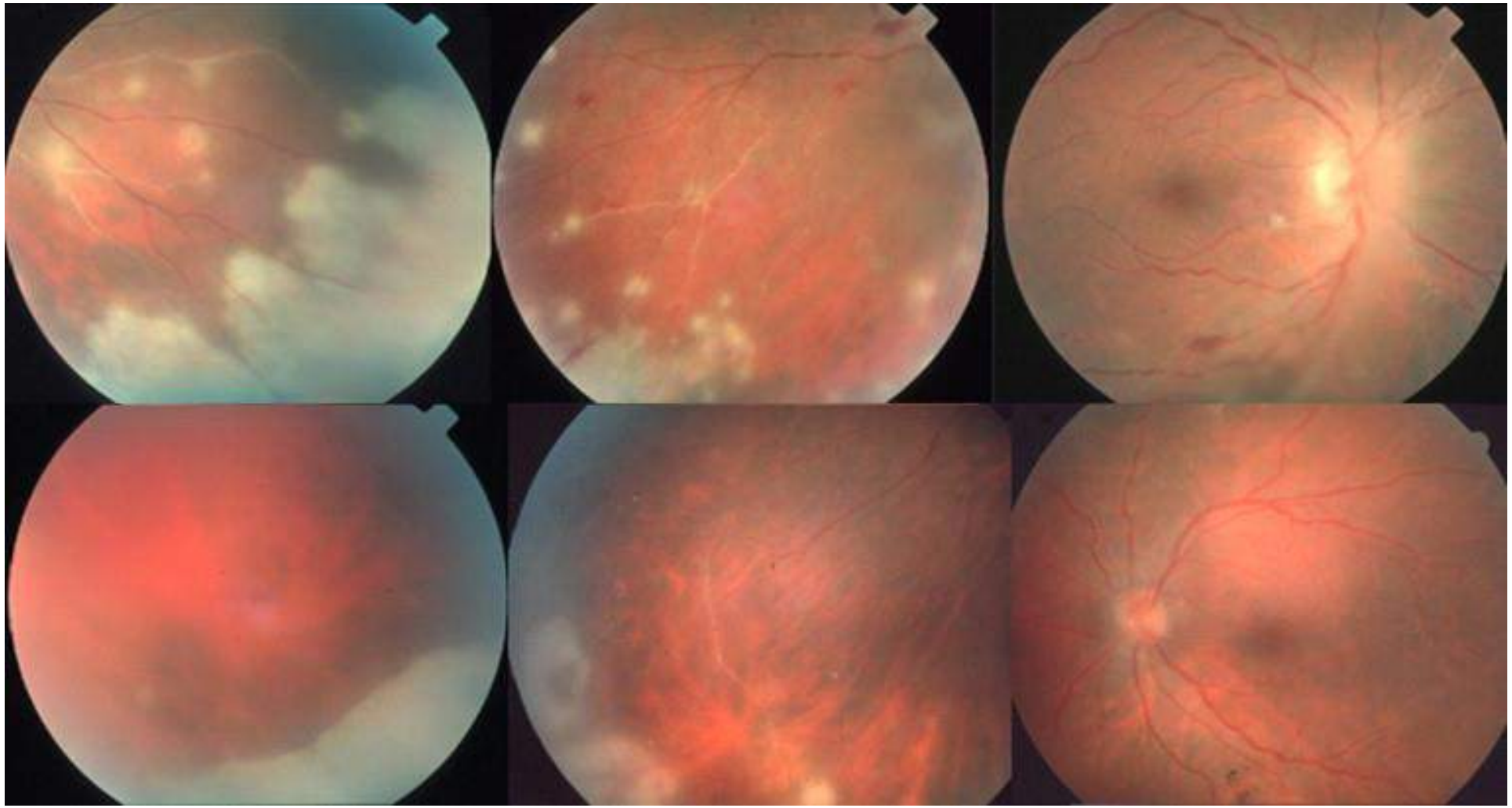
From Hirose T, Katsumi O, Pruett RC, et al. Retinal function in birdshot retinochoroidopathy. *Acta Ophthalmol (Copenh)*. Jun 1991;69(3):327-37.

Birdshot Retinochoroidopathy Management

- Cause unknown
- Possible autoimmune etiology
- Low dose steroid therapy (oral, local)
- Immunosuppressive agents
- Best spectacle Rx, LV devices
- Chronic disease (unlike MEWDS); prognosis guarded

Case 6

- 57-year-old Hispanic male
- Blurry vision OD > OS
- Gradually worsening over last few weeks
- Light bothers eyes during the last week
- History of past shingles
- No medications or known med allergies
- BCVA 20/25-3 OD, 20/25+2 OS;
- Pupils responsive OU, motilities full OU
- Mild NS OU; trace cells (?) OU



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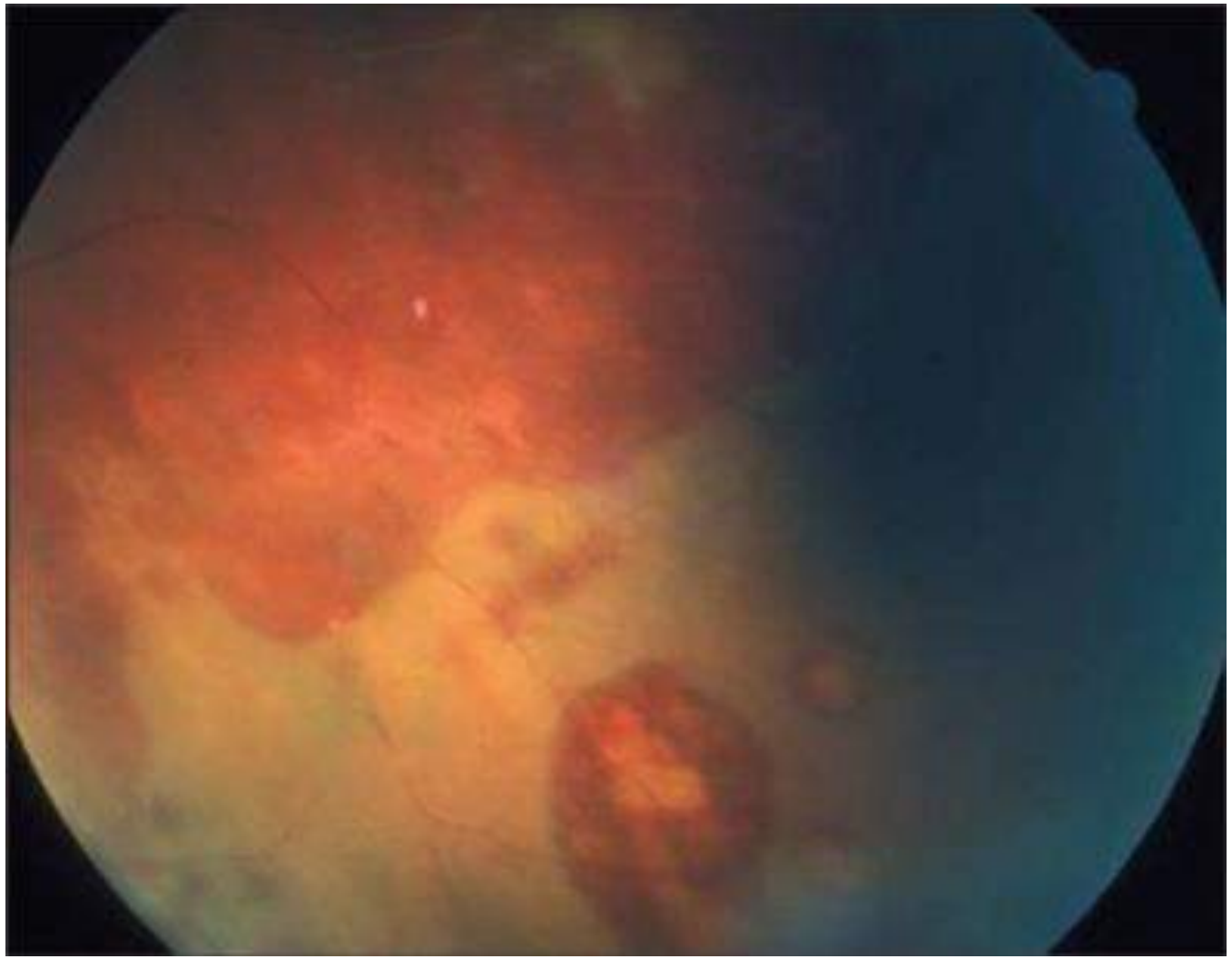
Acute Retinal Necrosis (ARN)

- Varicella zoster virus (VZV) and herpes simplex virus (HSV) types 1 and 2 implicated causes
- Anterior uveitis, vitritis, and retinal vasculitis
- Patchy or confluent areas of cream-colored retinal necrosis
- Necrosis starts peripherally → moves centrally
- Serous retinal detachments can occur
- Healthy patients; 1 or both eyes involved

Acute Retinal Necrosis (ARN)



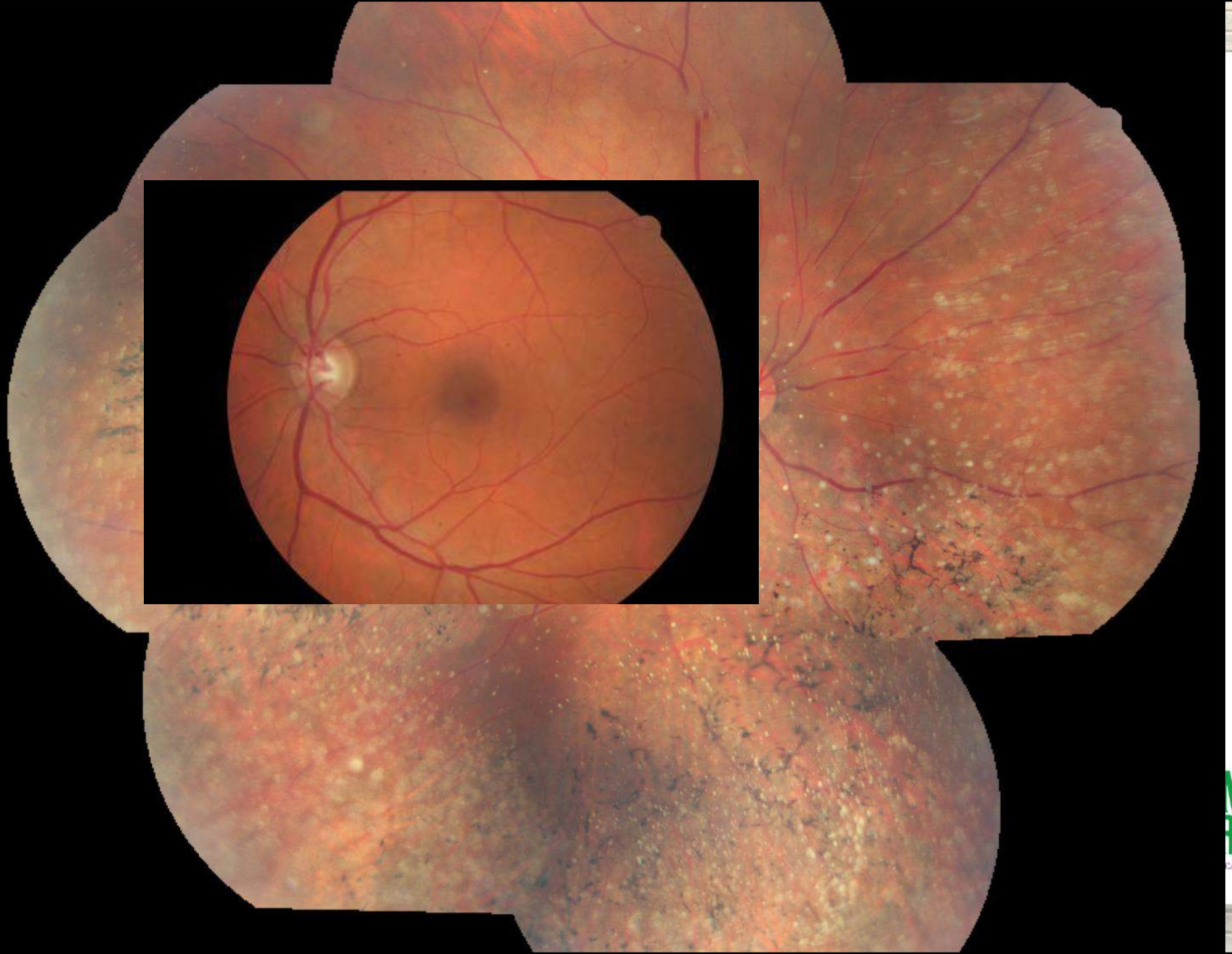
Showing an advancing border of necrosis with atrophic areas and holes

Acute Retinal Necrosis Treatment

- Full dilation for r/o retinal detachment → surgical RD repair if needed
- Treat uveitis, vitritis (steroids, cycloplegia)
- IV or oral antivirals (acyclovir, valacyclovir, famcyclovir)
- Low dose aspirin to prevent/treat occlusive vasculitis
- Prognosis is poor (especially if VZV is cause)

Case 7

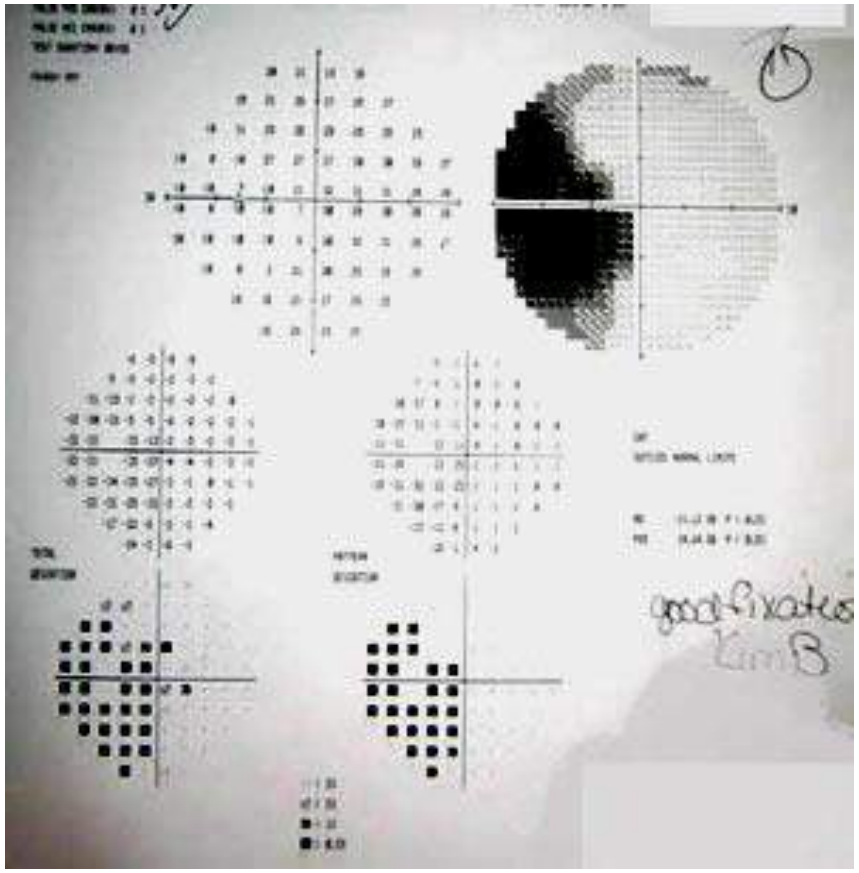
- 65-year-old Caucasian female
- Was told had RP in ‘one eye only’ (right eye)
- Had vision loss in the eye years ago; improved since then
- Things seem ‘dimmer in that eye, especially at night
- Systemic health good; taking HTN meds
- BCVAs 20/25 OD, OS

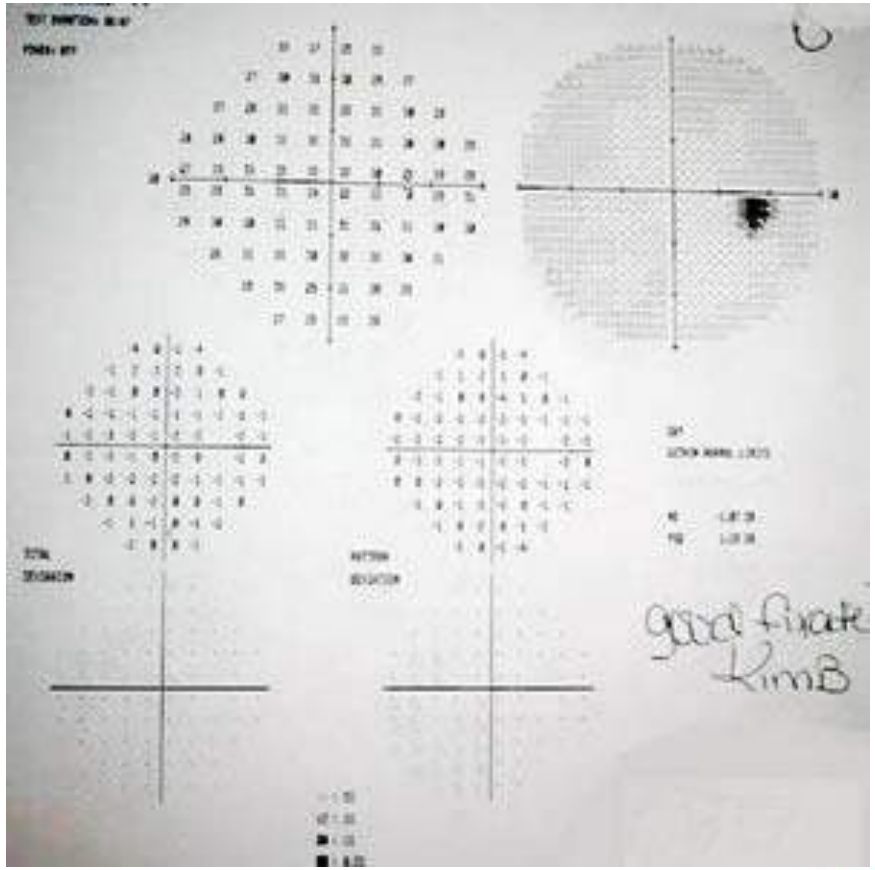


AZOOR Acute Zonal Occult Outer Retinopathy

- Young Caucasian (90%) women (3:1 over men)
- Etiology unknown (possibly viral or *Candida*)
- Strange multicolored lights/sudden vision loss
- 85% unilateral; about 40% pupil defect
- No observable fundus findings common
- Possible disc edema, RPE changes, retinal dots
- 85% self-improve; 65% enlarged blindspot

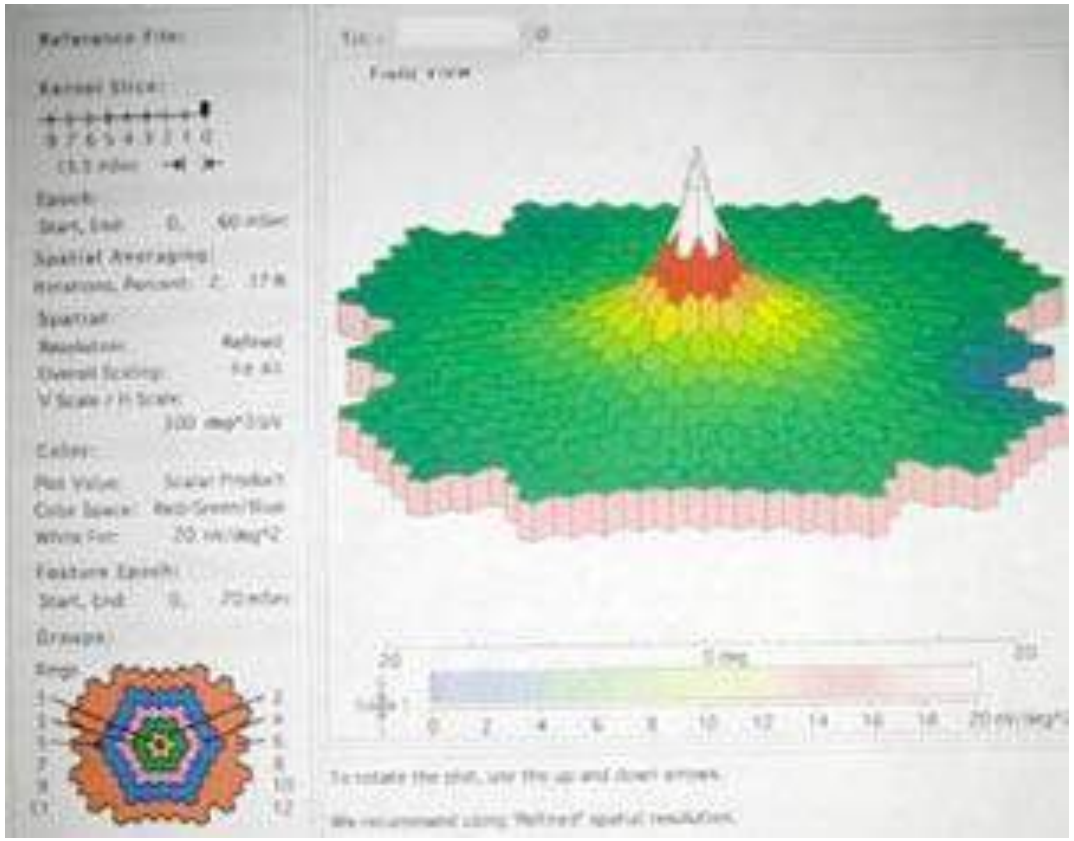
AZOOR

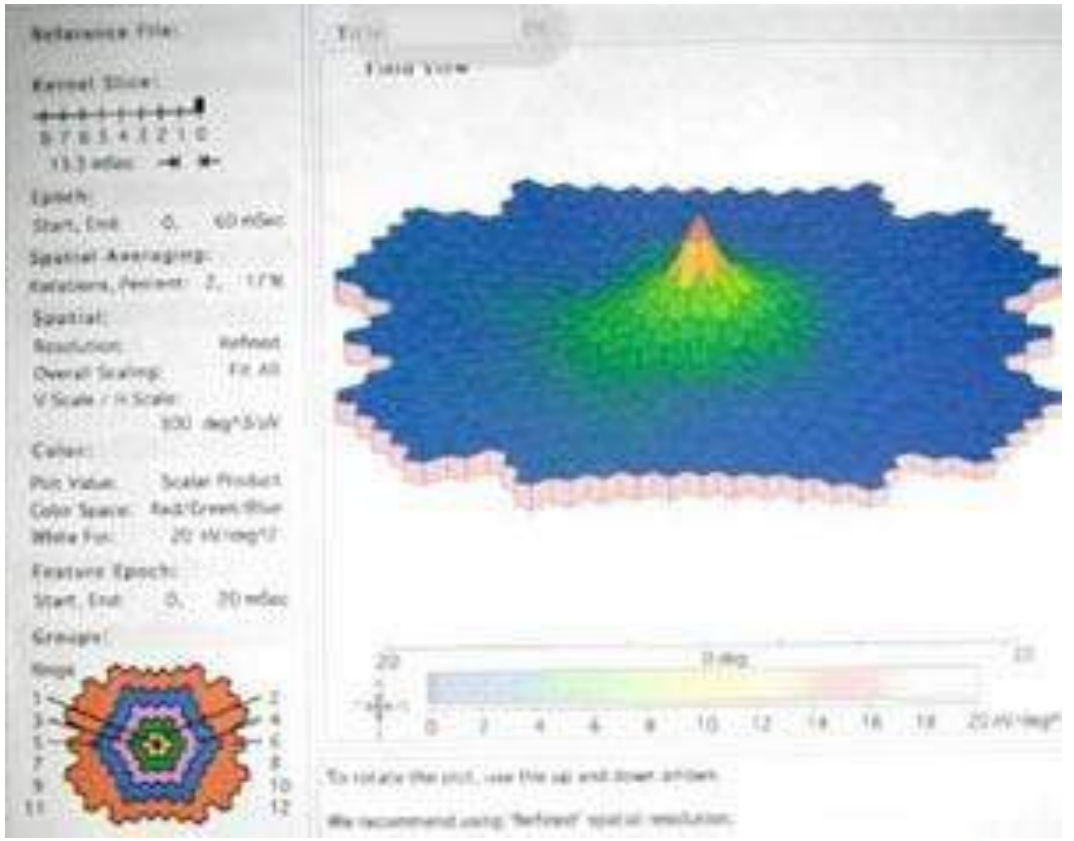




Doan A, Lee AG, Boldt HC: Acute Zonal Occult Outer Retinopathy (AZOOR) and Acute Idiopathic Blind Spot Enlargement Syndrome (AIBSE): 34 y.o. woman awoke with painless loss of vision OS 3 weeks prior to presentation. February 21, 2005; Available from: http://www.EyeRounds.org/cases/case18.htm.

AZOOR





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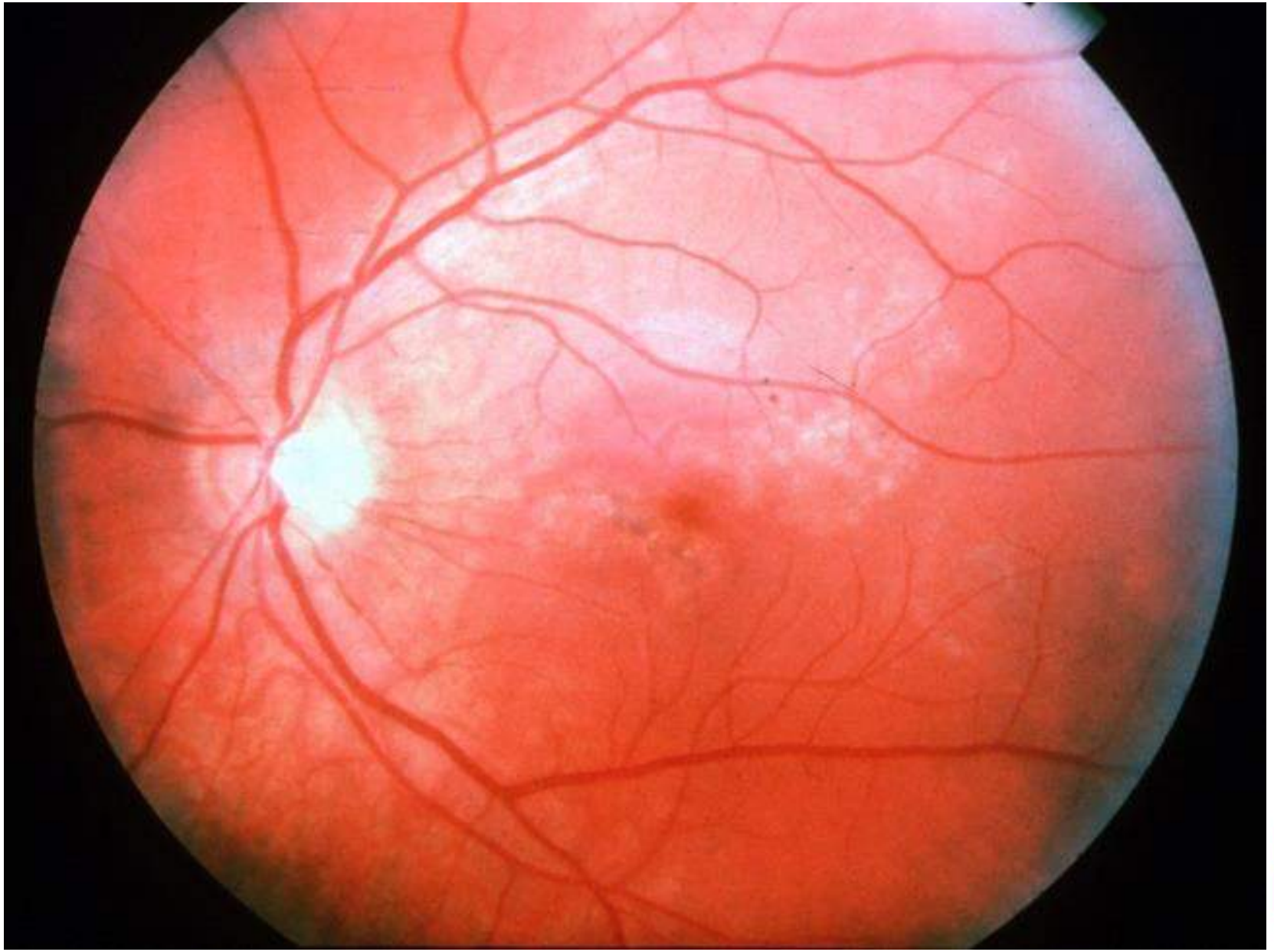
Case 8

- 47-year-old African American male
- Gradual mild blur in left eye over a year
- No health problems; no known med allergies
- BCVA 20/20 OD, 20/30 OS
- Pupils, motilities normal OU
- Anterior segment normal OU
- IOPs normal OU



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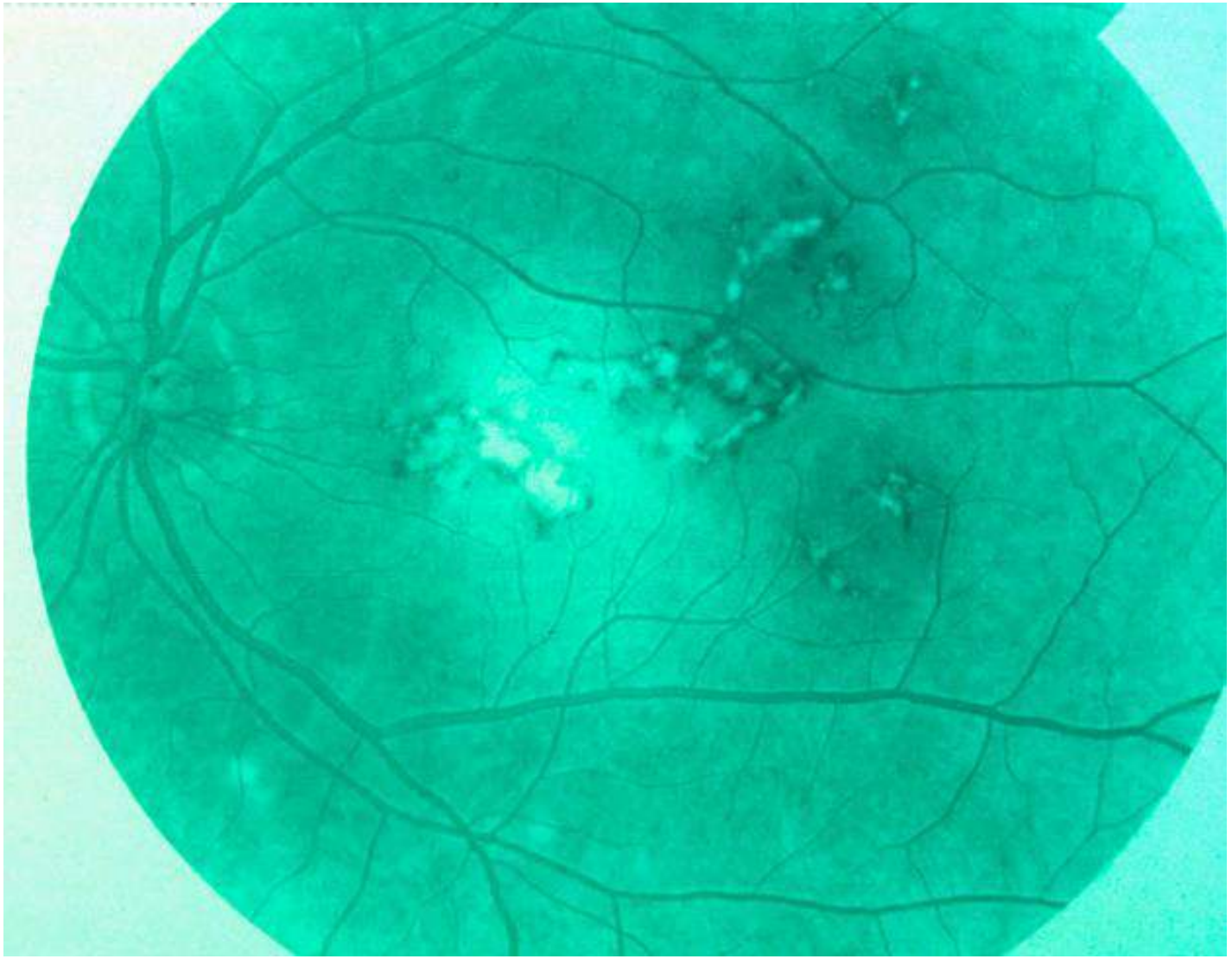
Acute Retinal Pigment Epitheliitis (ARPE)

- aka Krill Disease
- Very rare
- Self-limited RPE disease
- Young, otherwise healthy adults
- Mean age 45 years (range 16-75 yrs)
- 2/3 males
- No racial predilection
- unilateral ~60%

Acute Retinal Pigment Epitheliitis (ARPE)



Emedicine.com

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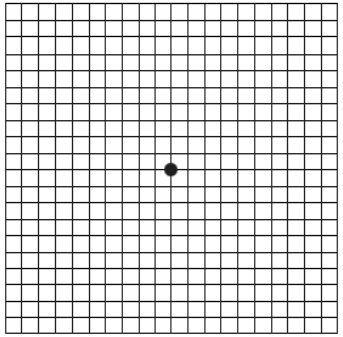
Acute Retinal Pigment Epitheliitis (ARPE)



- Half asymptomatic; half sudden mild VA decrease
  - Possible (para)central scotomata, metamorphopsia
- Unlike APMPPE, many patients (75%) VAs ~20/30
- Gray-black 50-100µm lesions with yellow-white halo
- Resolution → spots darken or lighten; halos remain
- Often 1-4 golden colored spots around macula
- Very rare macular edema or vitritis
- Extramacular lesions rare
- “Cockade-like” lesions

Acute Retinal Pigment Epitheliitis (ARPE)

***cock·ade*/kä-kād/:**

Noun:A rosette or knot of ribbons worn in a hat as a badge of office or party, or as part of a livery

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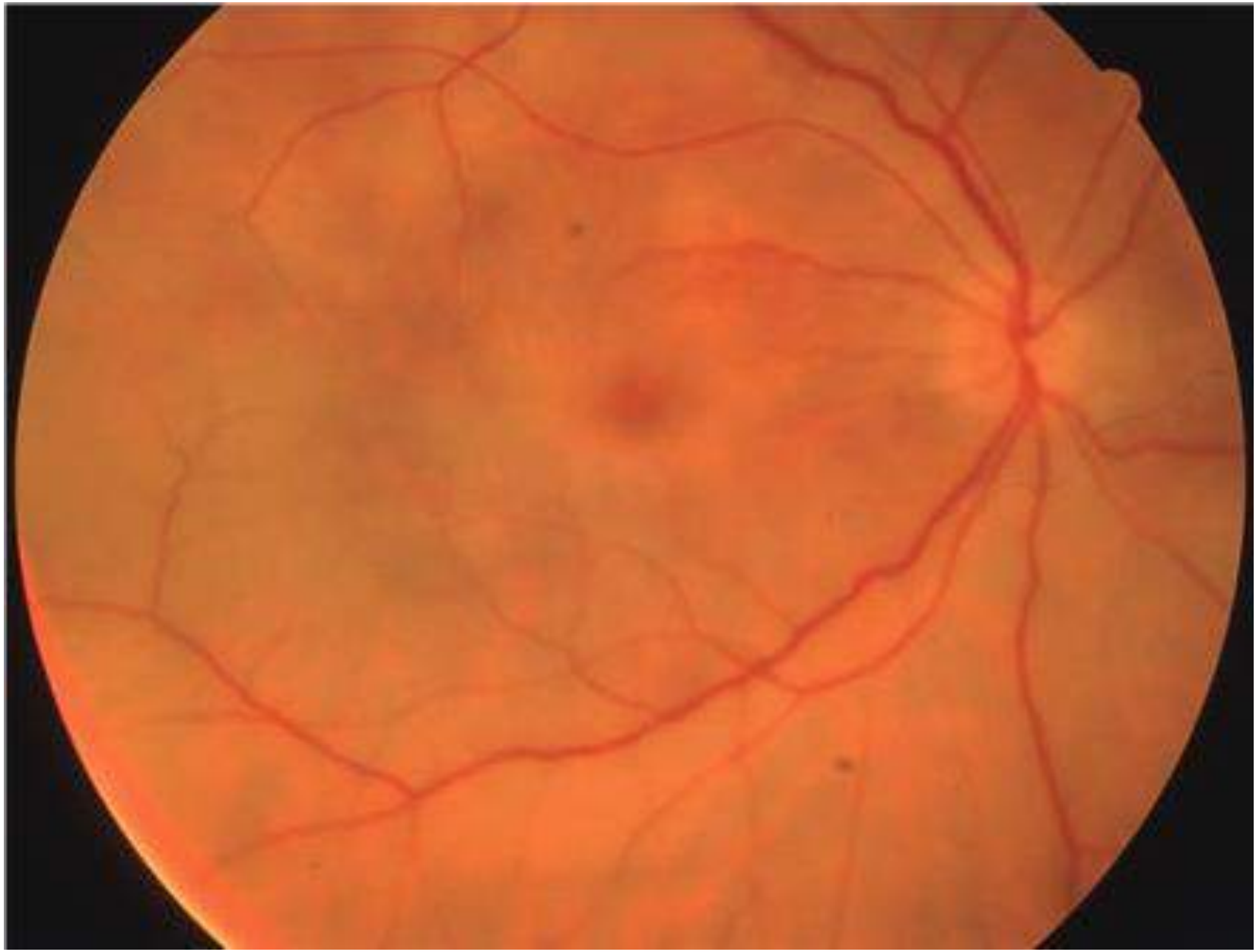
Acute Retinal Pigment Epitheliitis (ARPE) Management

- Baseline and subsequent photos/OCT/FAF
- ERG normal, EOG mixed results
- Etiology unknown – possibly virus
  - rubella, *Borrelia burgdorferi* (Lyme disease), influenza, and hepatitis C infection possibilities
- Amsler grid monitoring (variable scotomas)
- ARPE usually self-limited (6-12 weeks) and generally resolves without treatment

Case 9

- 41-year-old Caucasian male
- Advanced AIDS; CD4 count < 100
- On HAART cocktail, anti-herpetic meds
- Noticing visual blur over last 5 days, OD > OS
- BCVAs 20/40-1 OD, 20/30 OS
- Pupils sluggish but responsive to light OU
- Anterior segment shows no abnormalities
- IOPs and ocular motilities normal OU



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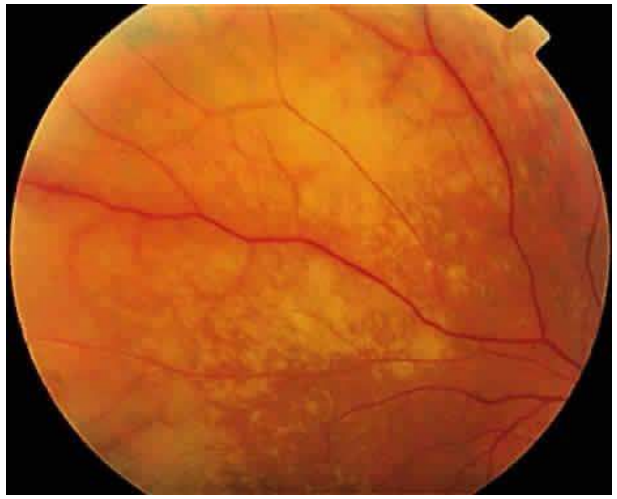
Progressive Outer Retinal Necrosis (PORN)

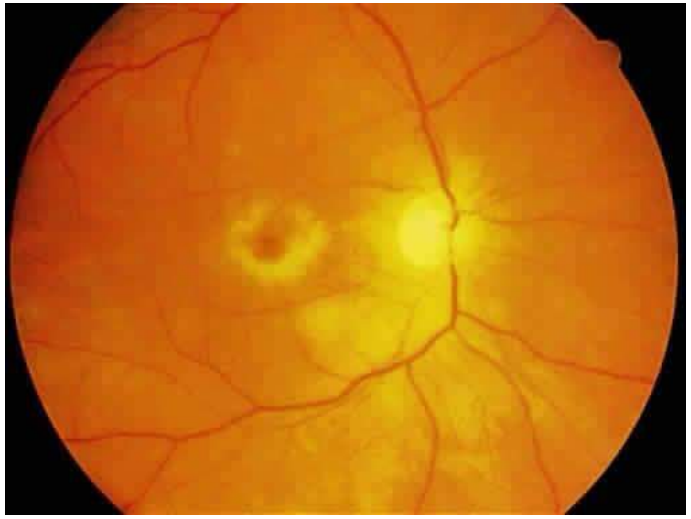
- aka Varicella zoster virus retinitis (VZVR)
- Opportunistic viral retinal infection
- Decreased Immunity (i.e. terminal AIDS, cancer)
- Bilateral 70% of time
- Differentials: ARN, CMV retinitis, diffuse toxo retinitis
- May lead to VZV encephalitis
- 3 Stages:
  - Early – peripheral multifocal plaques, +/- papillitis, maculitis
  - Middle – full thickness retinal whitening over days
  - Late – 'cracked mud' retinal and disc atrophy, RD

Progressive Outer Retinal Necrosis (PORN)



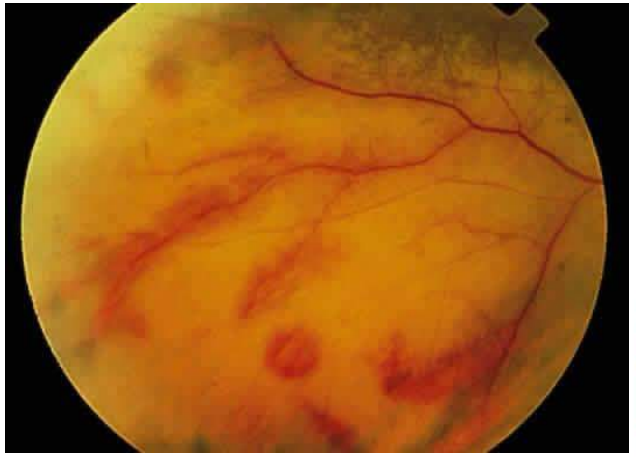
Early lesions

Cherry red macula



Confluence of lesions

Perivenular lucency



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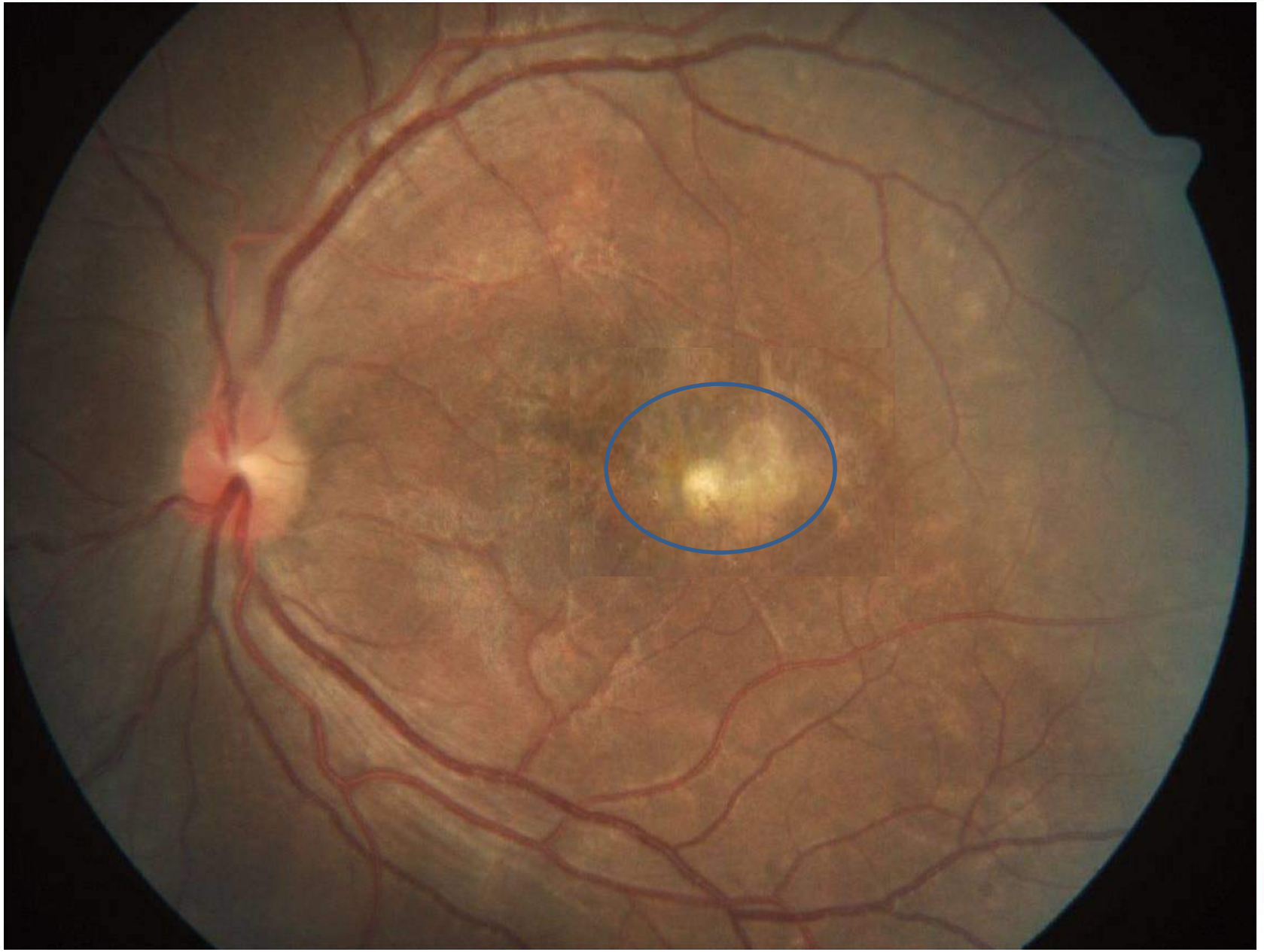
Progressive Outer Retinal Necrosis (PORN) Management

- Chorioretinal biopsies questionable
- Chronic acyclovir use may predispose getting it!
- Aggressive acyclovir or foscarnet may help
- Ganciclovir may provide synergistic benefit
- Anticoagulants not recommended
- May recur within 2 months of initial presentation
- Treat retinal detachments (laser, cryo, vitrectomy)
- Prognosis poor

Case 10

- 60-year-old Central American male
- Patient model for lab
- Reduced VA OS; unsure how long
- OD 20/25-, OS 20/200-
- Pupils, ocular motilities, IOPs normal OU
- Heavy arcus OU corneas
- Mild-moderate nuclear/cortical cataracts OU
- Macula OD normal. Macula OS…
- …is moving (!)



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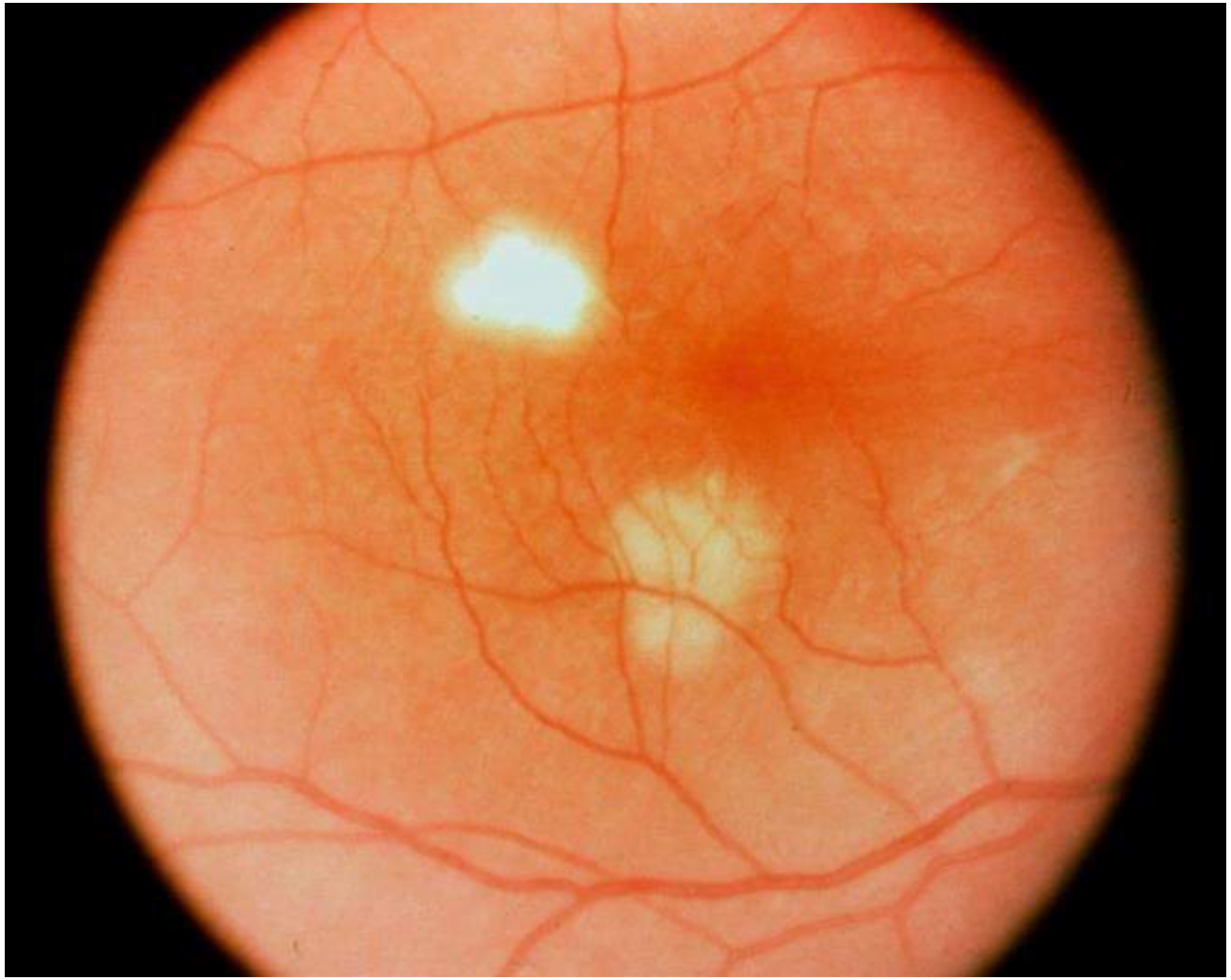
Diffuse Unilateral Subacute Neuroretinitis (DUSN)

- Chronic subretinal migration of nematodes
  - *Toxocara canis* (dog roundworm)
  - *Ancylostoma caninum* (dog hookworm)
  - *Baylisascaris procyonis* (raccoon intestinal nematode)
- Toxic tissue reaction from worm's by-products
- Usually involves children or young adults
- Slight male preponderance
- Patients otherwise healthy/asymptomatic
- Late in disease VA drops to < 20/200

Diffuse Unilateral Subacute Neuroretinitis (DUSN)

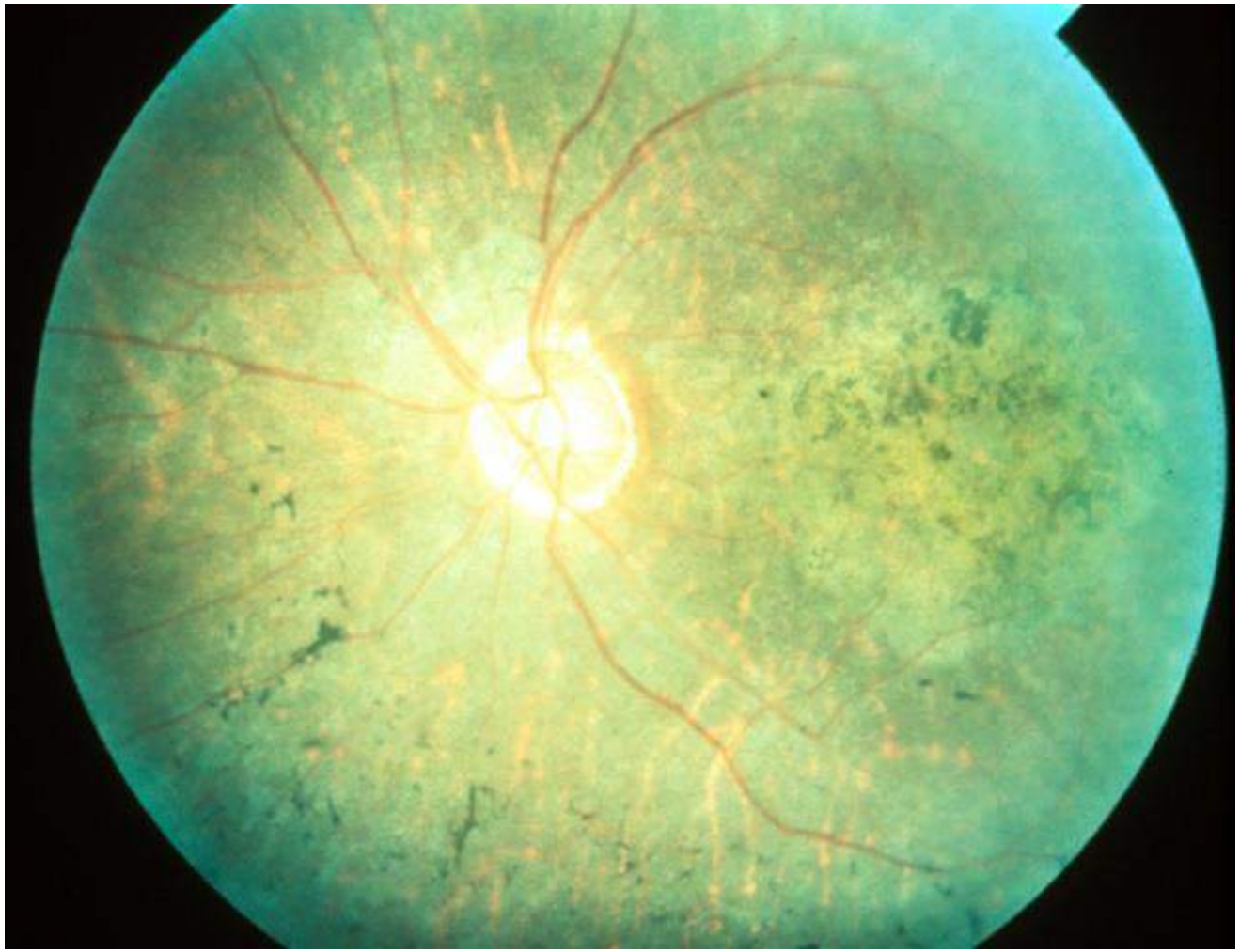
- Moderate vitritis
- Optic disc swelling
- Variable anterior chamber reaction
  - with or without hypopyon
- Focal, gray-white or yellow-white spots
  - deep layers of retina and RPE
  - develop days to weeks from symptom onset
  - tend to cluster in macula or juxtamacular region
  - typically last several days before fading
- Occasionally, a subretinal worm (500-2000 µm length, 25 µm in width) can be seen

Diffuse Unilateral Subacute Neuroretinitis (DUSN)



Diffuse unilateral subacute neuroretinitis. Attempted focal laser photocoagulation of a subretinal nematode suspected of being *Baylisascaris procyonis*. Courtesy of Everett Ai, MD, San Francisco, Calif.

Diffuse Unilateral Subacute Neuroretinitis (DUSN)



Late stage disease showing pseudo-RP like features

Diffuse Unilateral Subacute Neuroretinitis (DUSN)

- Lab tests, biopsies limited value
- Argon laser photocoagulation
  - effective in destroying the worm
- Surgical (transvitreal, PPV) removal of worm
- Antihelminthics
  - Thiabendazole
  - Diethylcarbamazine
- Antifilarial agents
  - Ivermectin

Other White Dot Syndromes and 'Occult' Retinal Diseases

- AIBSE (Acute Idiopathic Blind Spot Enlargement)
  - Peripapillary inflammation; APD, permanent VF loss
- PIC (Punctate Inner Choroidopathy)
  - may be milder form of MFC; unlike MFC does not recur
- AMN (Acute Macular Neuroretinopathy)
  - red-brown wedge-shaped macular lesions; VF loss
  - Possibly related to oral contraceptives, decr. immunity
- Pigmented Paravenous Retinochoroidal Atrophy
  - Males, RPE atrophy around vortex veins, rare VA loss

Summary

- Group of rare chorioretinal disorders
- Pathology at or near level of RPE
- Etiology often unknown; autoimmune or viral
- Features of each overlap, causing confusion
- Lab, imaging, functional tests limited benefit
- Many other differential diagnoses
  - Toxo, histo, VKH, RP, rod-cone dytrophies, etc.
- Management challenging for many disorders

THANK YOU!

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