White Dot Syndromes

Noninfectious Chorioretinopathies
Update 2019

Kelly T. Mitchell, MD
Retina Service
TTUHSC

Definition

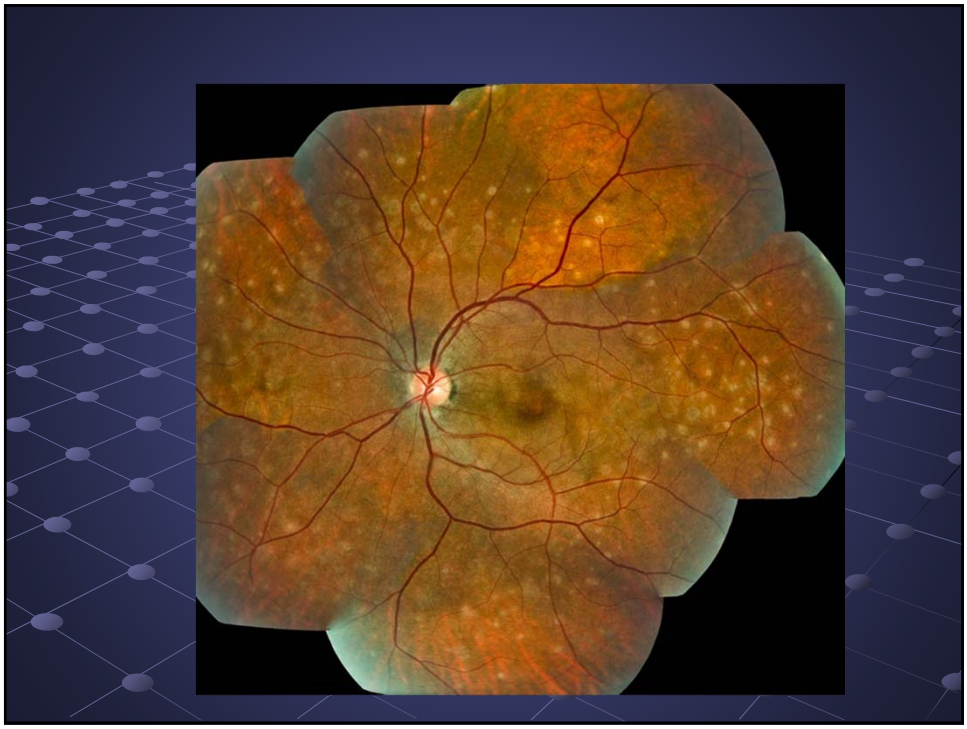
Noninfectious disease

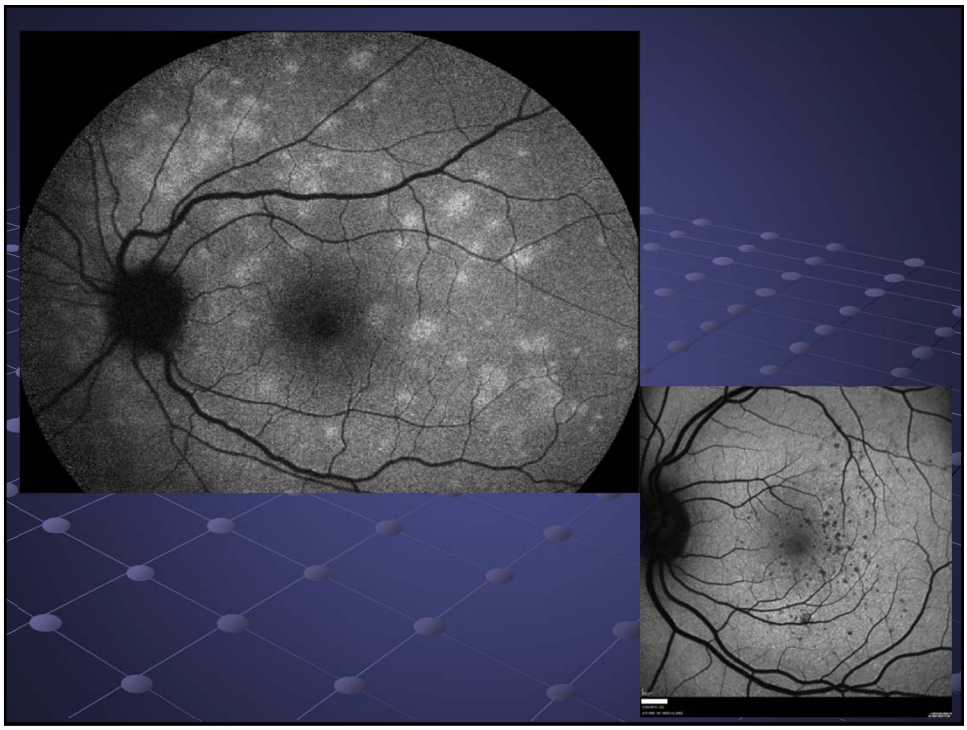
Inflammation of choroid, choriocapillaris, RPE, and Retina

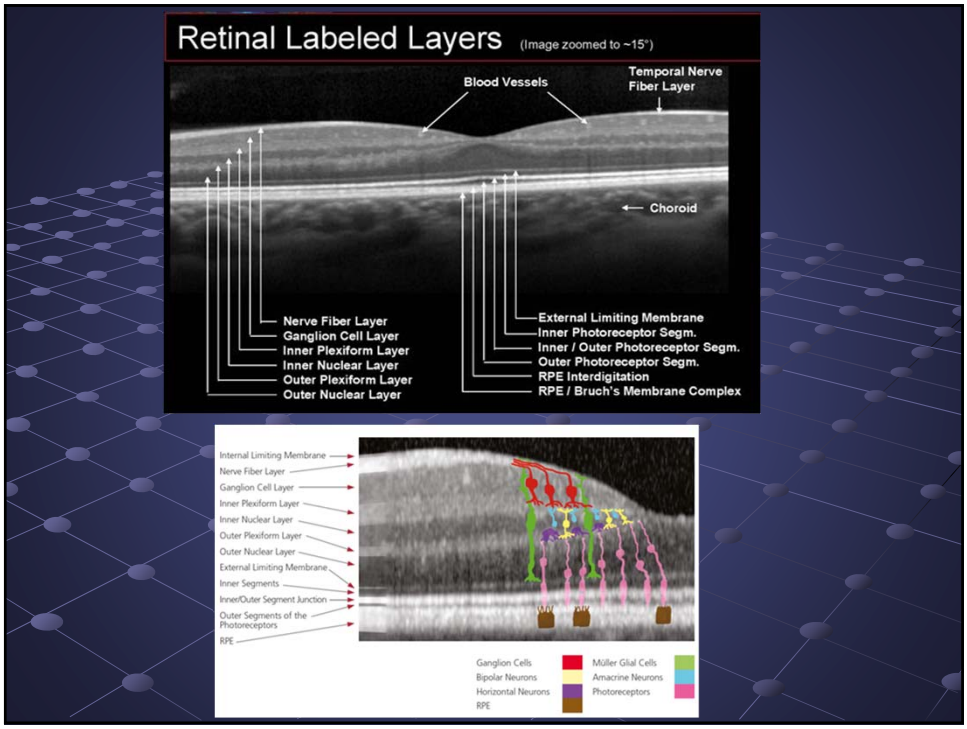
"GENERALLY"

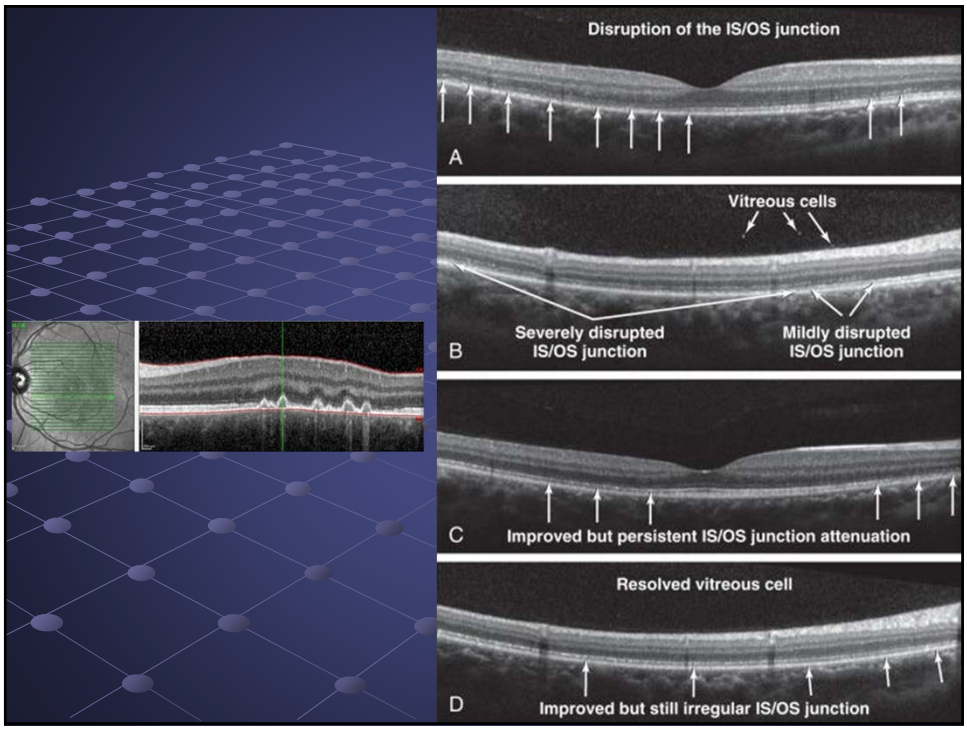
- SX: blurred central vision, scotomata
- PE: A/C and PS inflammation variable, single or multiple white, yellow or gray areas deep in retina
- Imaging will be helpful

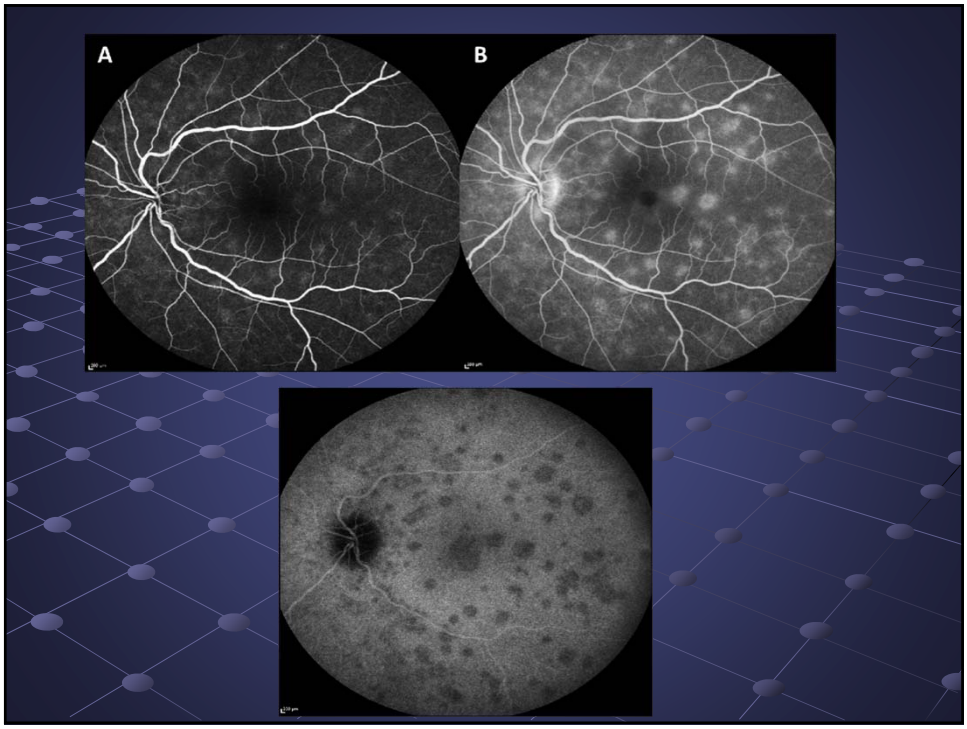
DX of exclusion: syphilis/Toxo/TB/sarcoid/VKH






Retinal Labeled Layers
(Image zoomed to ~15°)
Blood Vessels
Temporal Nerve Fiber Layer
Choroid
Nerve Fiber Layer
Ganglion Cell Layer
Inner Plexiform Layer
Inner Nuclear Layer
Outer Plexiform Layer
Outer Nuclear Layer
External Limiting Membrane
Inner Photoreceptor Segm.
Inner / Outer Photoreceptor Segm.
Outer Photoreceptor Segm.
RPE Interdigitation
RPE / Bruch's Membrane Complex
Internal Limiting Membrane
Nerve Fiber Layer
Ganglion Cell Layer
Inner Plexiform Layer
Inner Nuclear Layer
Outer Plexiform Layer
Outer Nuclear Layer
External Limiting Membrane
Inner Segments
Inner/Outer Segment Junction
Outer Segments of the Photoreceptors
RPE
Ganglion Cells
Bipolar Neurons
Horizontal Neurons
RPE
Müller Glial Cells
Amacrine Neurons
Photoreceptors


Disruption of the IS/OS junction
A
Vitreous cells
Severely disrupted IS/OS junction
Mildly disrupted IS/OS junction
B
C
Improved but persistent IS/OS junction attenuation
Resolved vitreous cell
D
Improved but still irregular IS/OS junction



MEWDS

Multiple Evanescent White Dot Syndrome

Who:
- Young (20-40s ave 28), female 75%, viral trigger 50% (to include vaccinations HB)
- Usually myopic

SX:
- Acute/abrupt
- Unilateral loss of acuity, scotomata, photopsia

PE:
- Yellow-white spots consisting of 100-200 micron spots in wreath shape, posterior pole and round disc,
- Orange granularity of fovea
- +/- papillitis/vitritis
  - VF: enlarged blind spot or cecocentral scotomata

FAF: HyperAF more than hypo

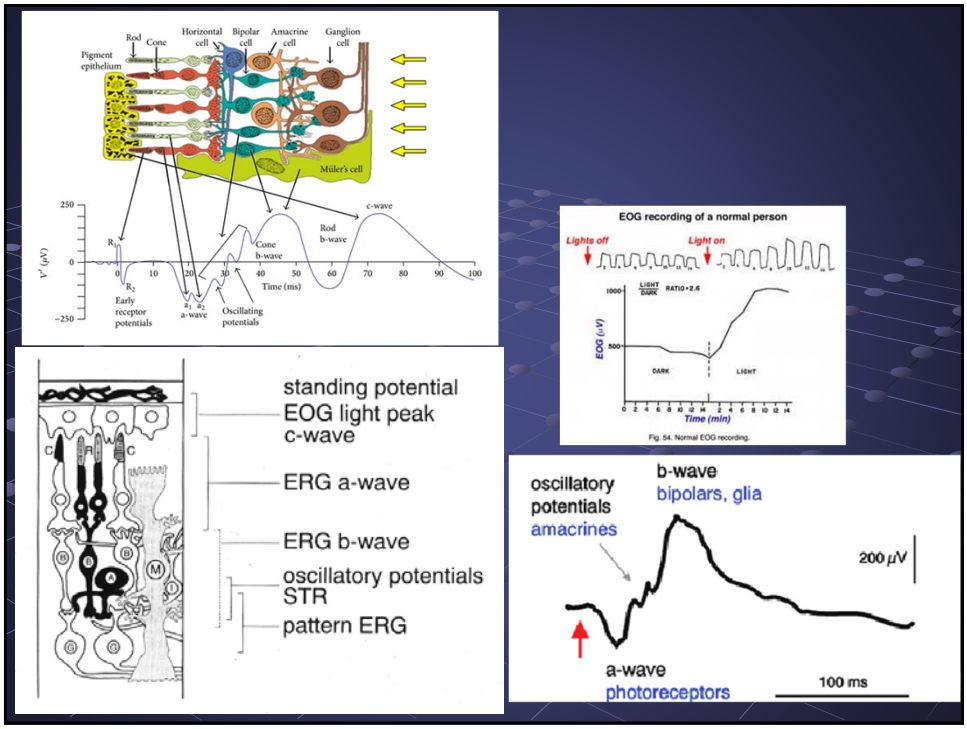
OCT: focal disruption of IS/OS junction//RPE

FA: Early blocking, late staining, can see staining of ONH

ICG: Early, barely visible lesions; late hypofluorescence more than visible lesions

ERG: loss of A wave and abnormal EOG (impact at Photoreceptors/RPE)

Clinical Triad: **big blind spot, papillits/vitritis, orange fovea**



MEWDS

Multiple Evanescent White Dot Syndrome

Pathology: photoreceptor and RPE junction
- ERG: A wave abnormality
- EOG: Abnormal

Associations: none except viral exposure

Prognosis:
- Good (rare VF defects or CNVM)→ no TX
- Rare (less than 10%) recur

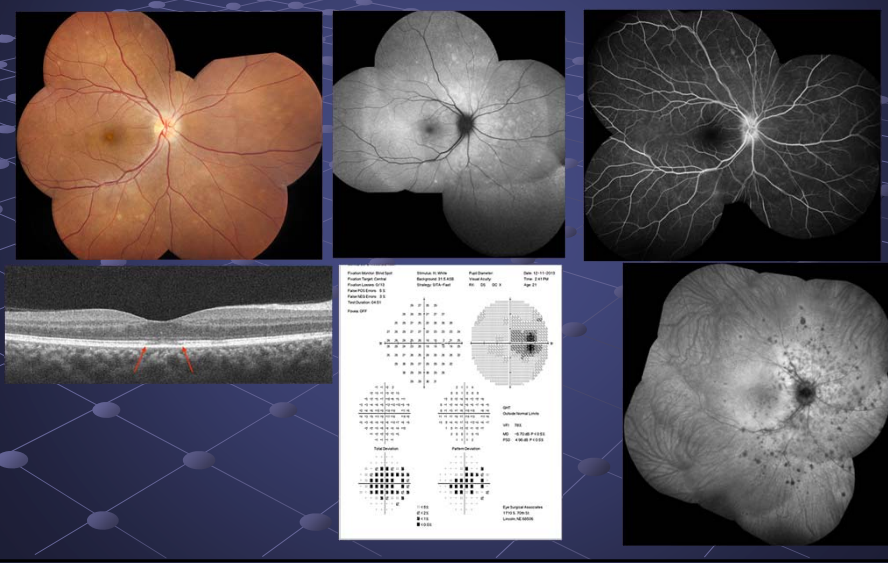
MEWDS

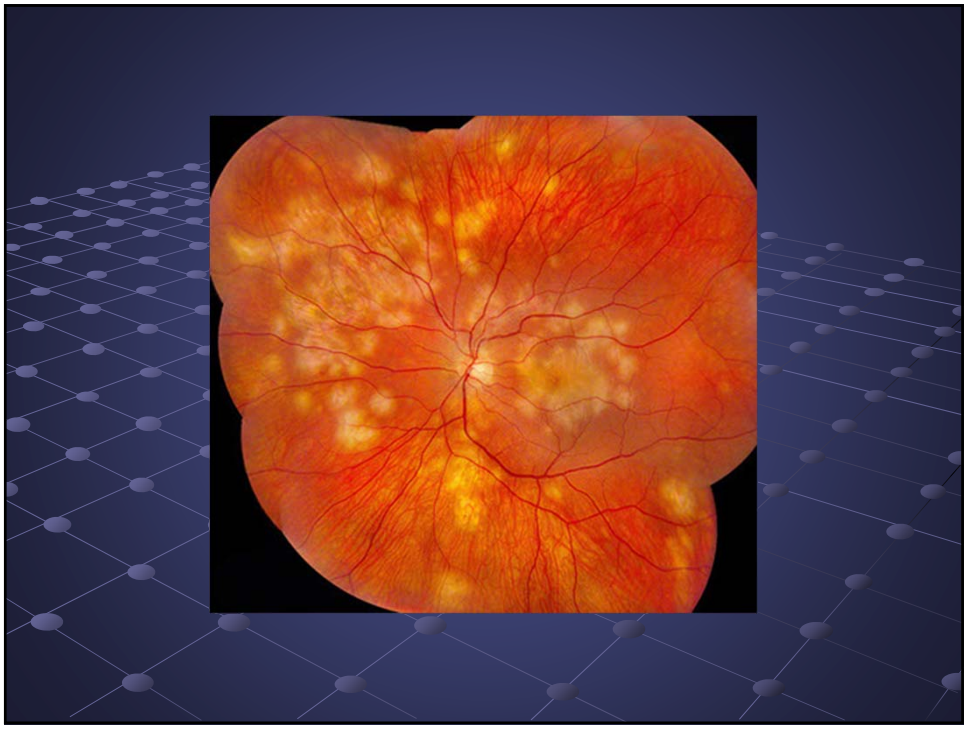
Multiple Evanescent White Dot Syndrome

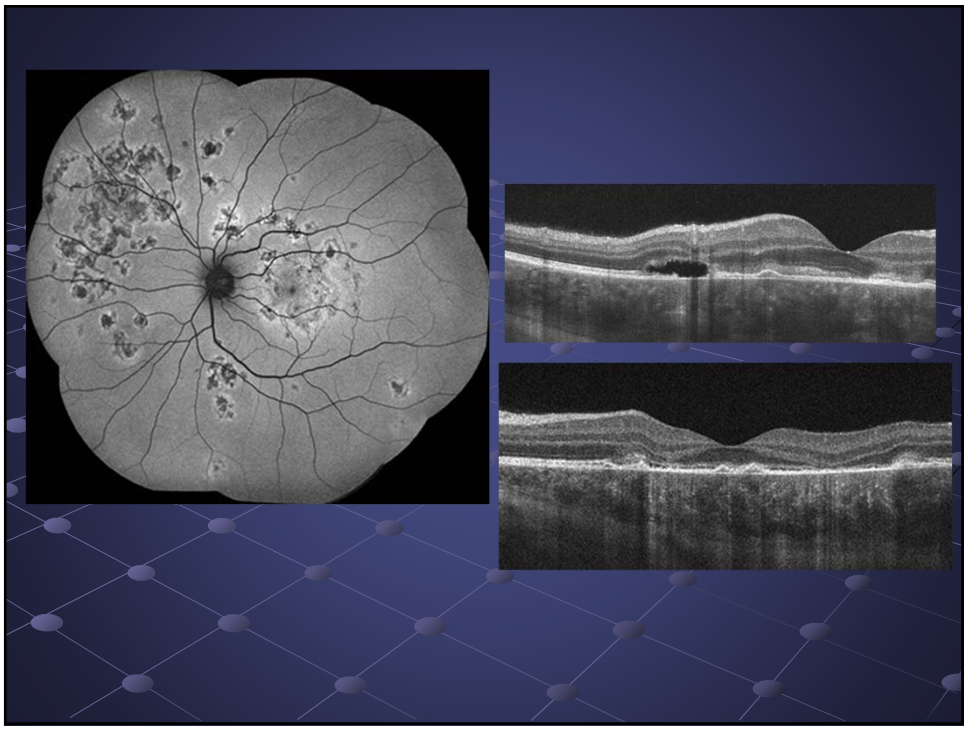
- Summary
  - Unilateral disease of young women most with viral prodrome
  - Small spots (tiny spots in wreath pattern)
  - Orange granularity of fovea
  - Papillitis → visual field changes
  - **Clinical triad: big blind spot, papillits/vitritis, orange fovea**
  - Impact at Photorecptor & RPE layer = abn a wave EOG
  - **BRIEF AND BENIGN COURSE → NO TX**

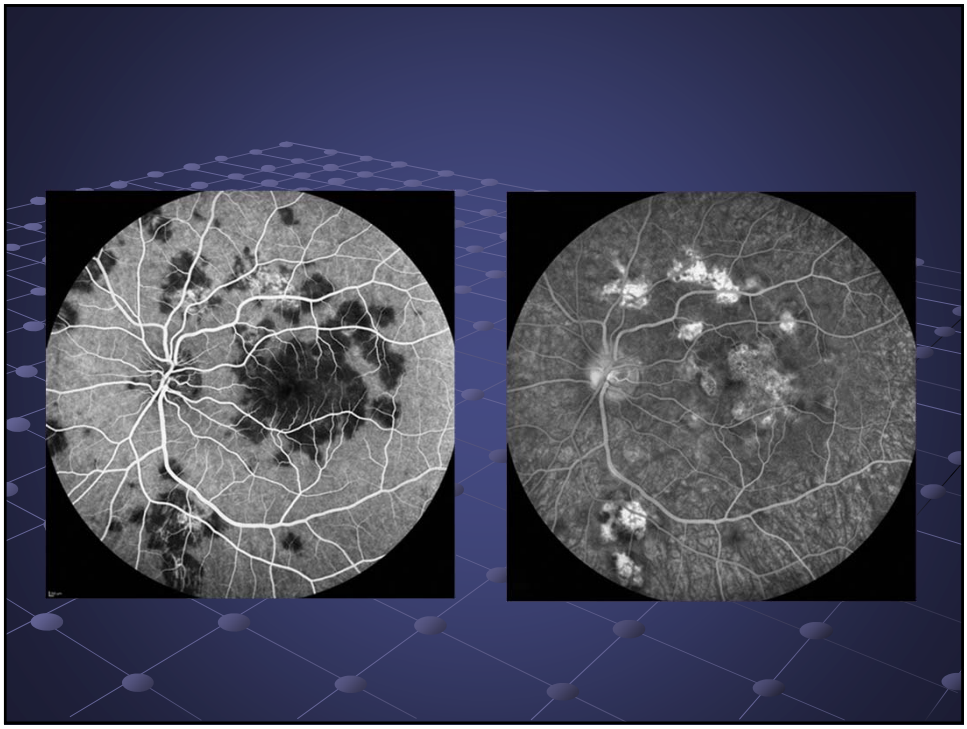
MEWDS

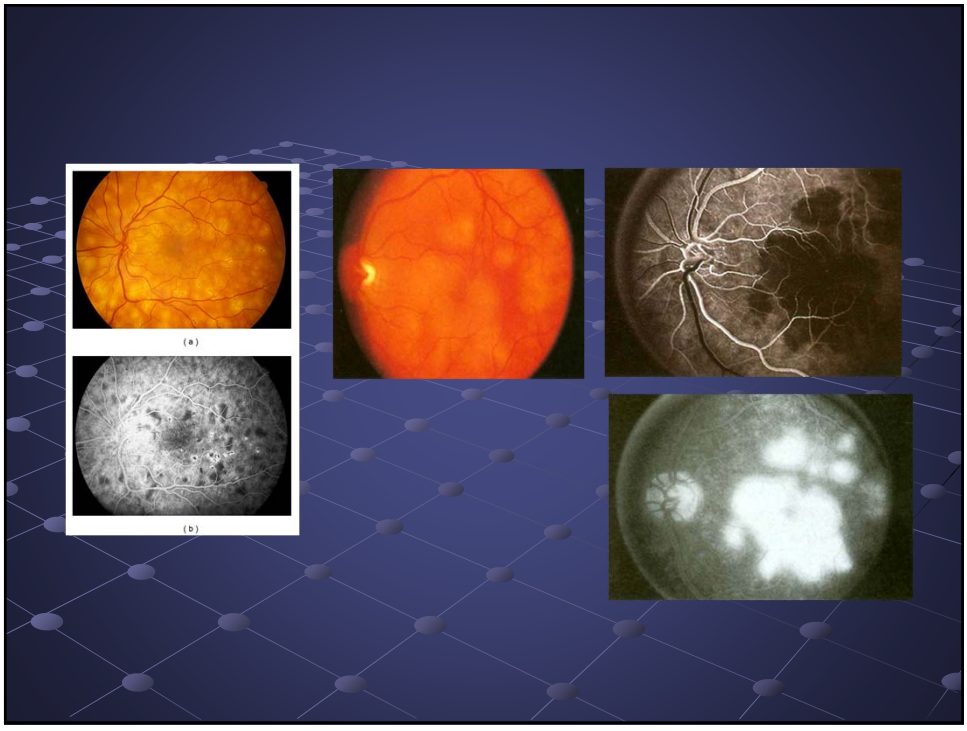
Multiple Evanescent White Dot Syndrome

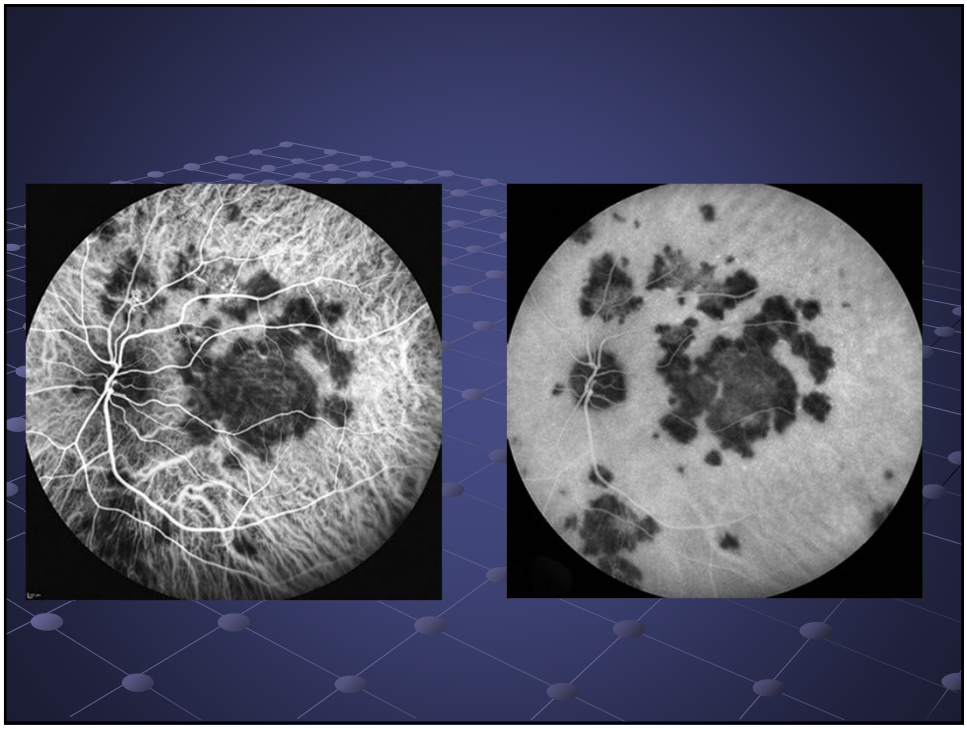


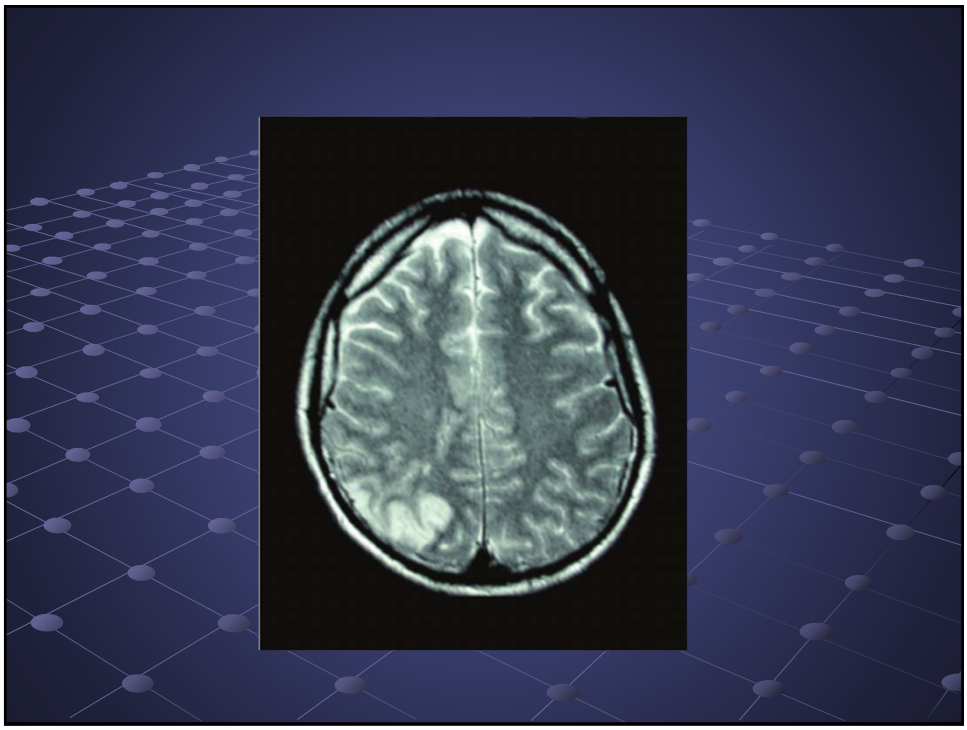







(a)
(b)





A(p)MPPE

Acute posterior Multifocal Placoid Pigment Epitheliopathy

Who:
- Young adults (20-40 ave 28), M=F
- 30% viral prodrome

SX:
- Acute/abrupt Bilateral, asymmetric acuity loss, photopsia

PE:
- large (1-2DD), cream colored spots in posterior pole and around arcade and disc move toward equator, at RPE level, 50% vitritis, papillitis

FAF: Early hyperAF then mixed areas of hypoAF

OCT: Irregularity at outer retina/RPE/inner choroid layer

FA: Early blockage, late staining

ICG: hypofluorescence

ERG → mild, transient abnormality and **EOG → marked persistent abnormality**

A(p)MPPE

Acute posterior Multifocal Placoid Pigment Epitheliopathy

Associations:
- HLA B7 and DR2

A P M P P E Associations

Non-Infetious	Infectious
Erythema Nodosum	Group A Streptococcus
Wegener's Granulomatosis	Adenovirus Type 5
Polyarthritis Nodosa	TB
Cerebral Vasculitis	Lyme Disease
Scleritis & Episcleritis	Mumps
Ulcerative Colitis	Hepatitis B vaccination

Ocular
- Corneal thinning, episcleritis, retinal vasculitis, serous RD

Systemic
- **Cerebritis, TIA**, Erythema nodosum, thyroiditis, hearing loss

Prognosis:
- Good (most >20/30 rare cnvm)→ no TX
- If neurologic sx are present then treat

A(p)MPPE

Acute posterior Multifocal Placoid Pigment Epitheliopathy

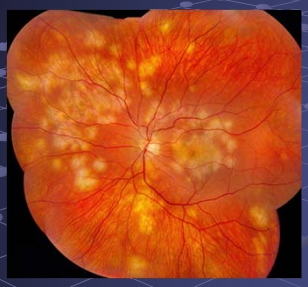
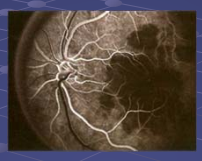
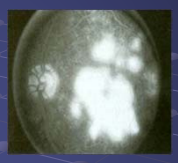
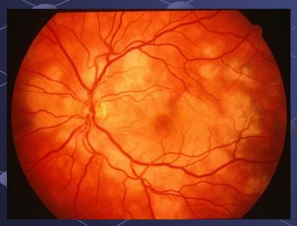
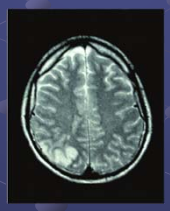
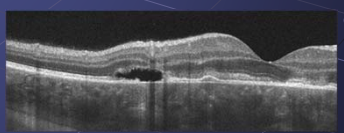
Summary

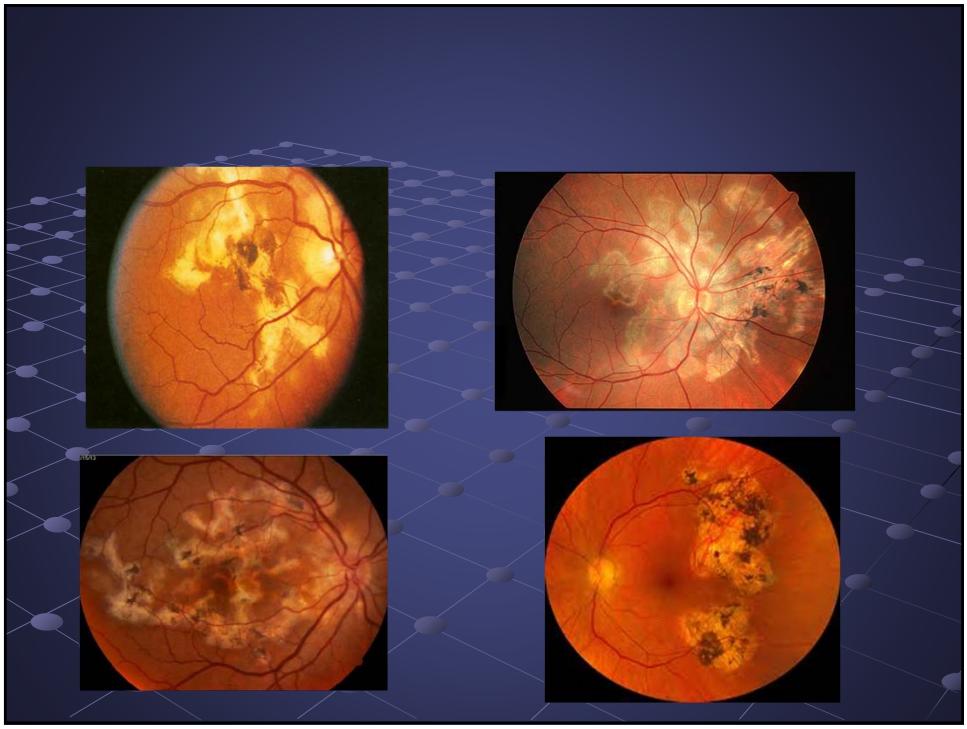
- Bilateral disease in young adults, some with viral prodrome
- Large spots→areas of RPE atrophy
  - Most like Serpiginous
- EOG abnormalities are persistent

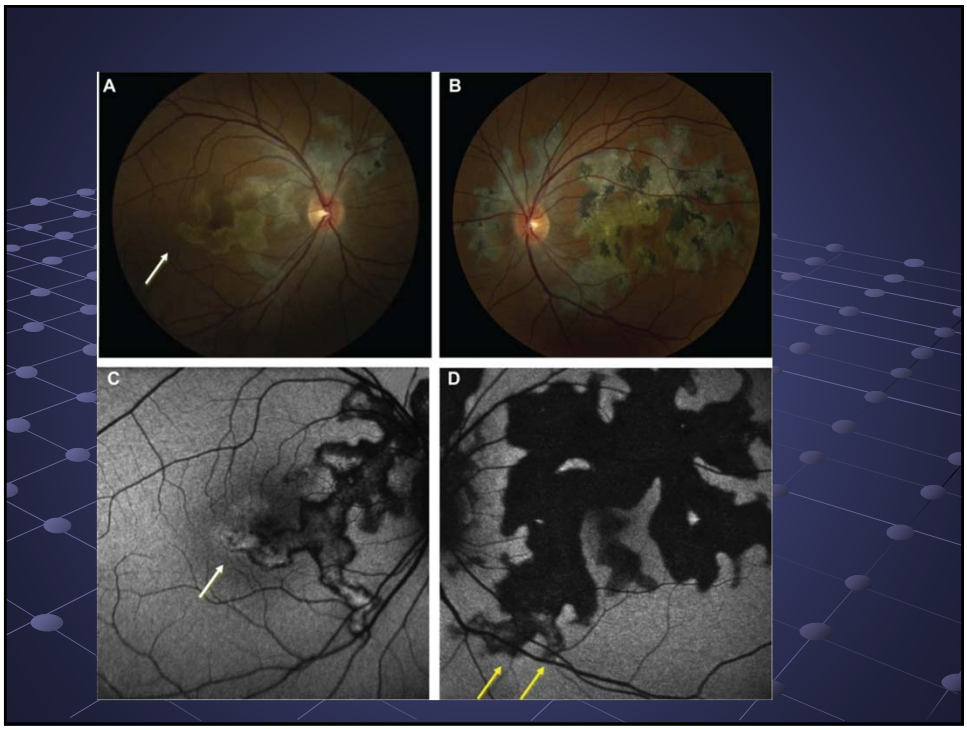
- Most have brief and benign course→ **NO TX**
- **Unless extensive macular involvement:**
- Oral corticosteroids have been recommended to speed resolution, especially in cases with extensive macular or foveal involvement; its efficacy has not been proven; high dose corticosteroid treatment suggested if cerebral vasculitis is present
  - Rare cause of cerebritis, and CNVM, hearing loss
  - high dose corticosteroid treatment if cerebral vasculitis is present
  - TX CNVM with AntiVEGF

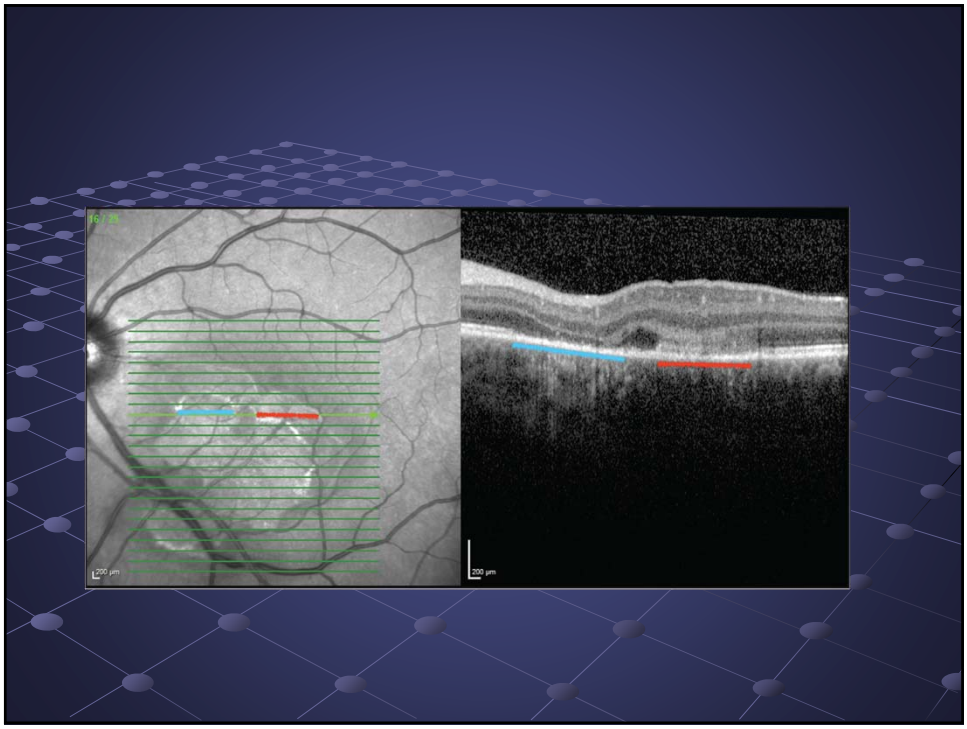
A(p)MPPE

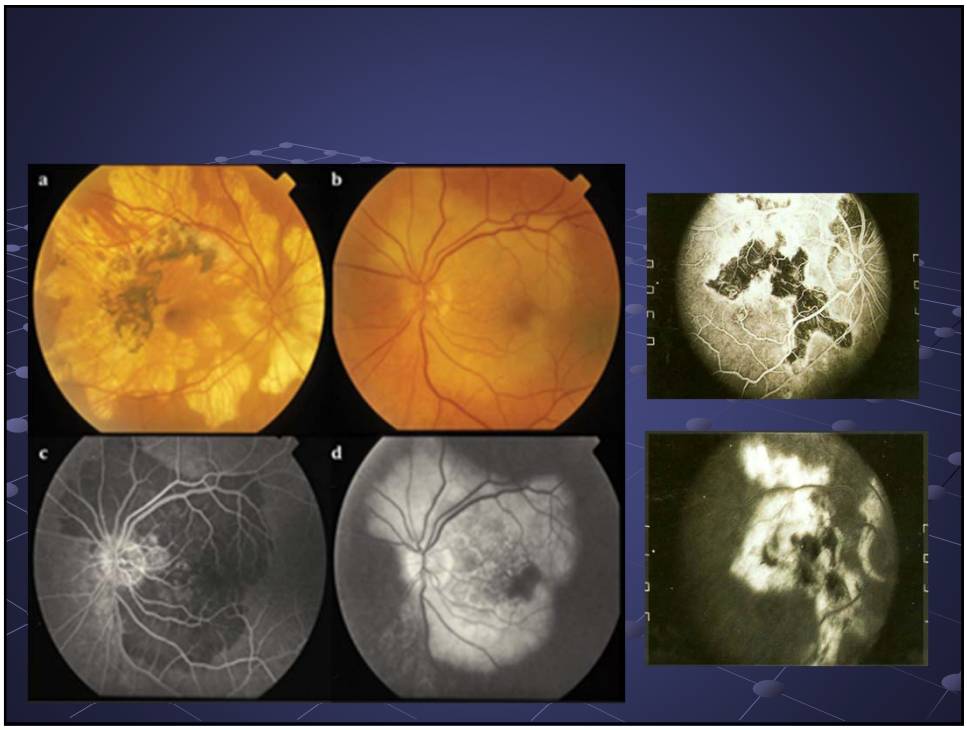
Acute posterior Multifocal Placoid Pigment Epitheliopathy

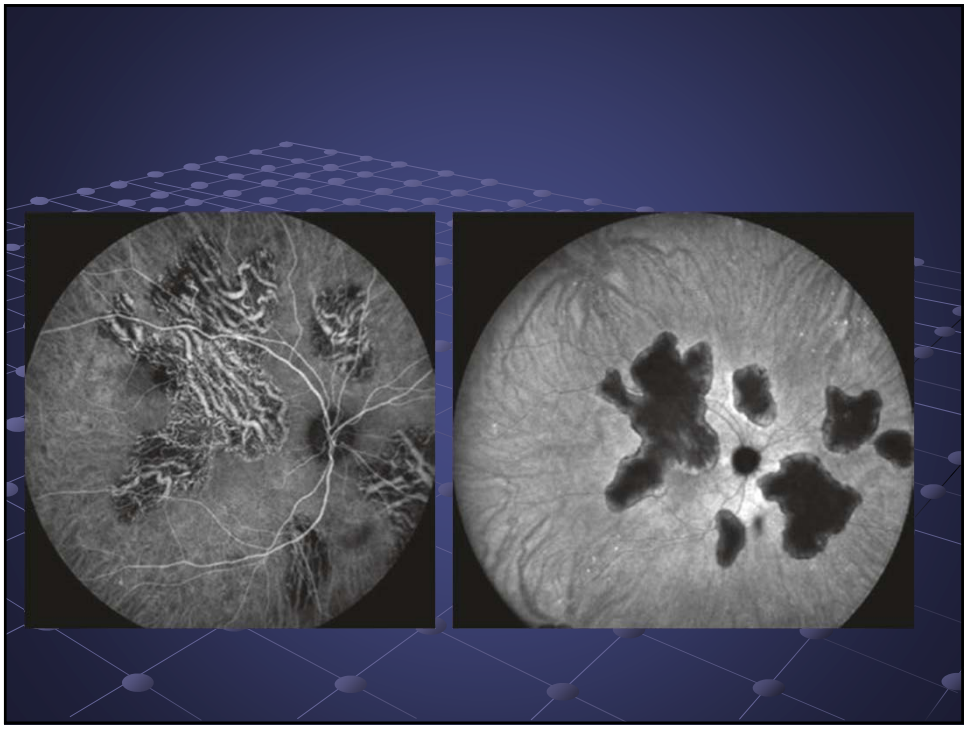










A
B
C
D




a
b
c
d



Serpiginous Choroiditis

Geographic Helicoid Peripapillary Choroidopathy

Who: (20-60 ave 40s), M=F or M>F
SX: Variable onset of Bilateral vision loss, scotomata
PE: Gray-white, fingerlike projections at edge of previous atrophy → usually spreads out from disc
Macular lesion only in 20%, vitritis 30%
FAF: early hyperAF, late hypoAF
OCT: loss, fluid, extra reflective band IS/OS junction/RPE
FA: early blocking and late staining
ICG: early can show hyper; late hypo
ERG is usually normal and the EOG abnormal since pathology is at RPE/choriocapillaris

Serpiginous Choroiditis

Geographic Helicoid Peripapillary Choroidopathy

Associations:

HLA B-7 (55%), nongenetic dystonia, hypoglycemia, elevated factor VIII-vwf, TB/HSV history

Prognosis: Poor (one eye with useful VA)

Recurrences, cnvm (25%-33%),

TX: steroids/immunosuppression

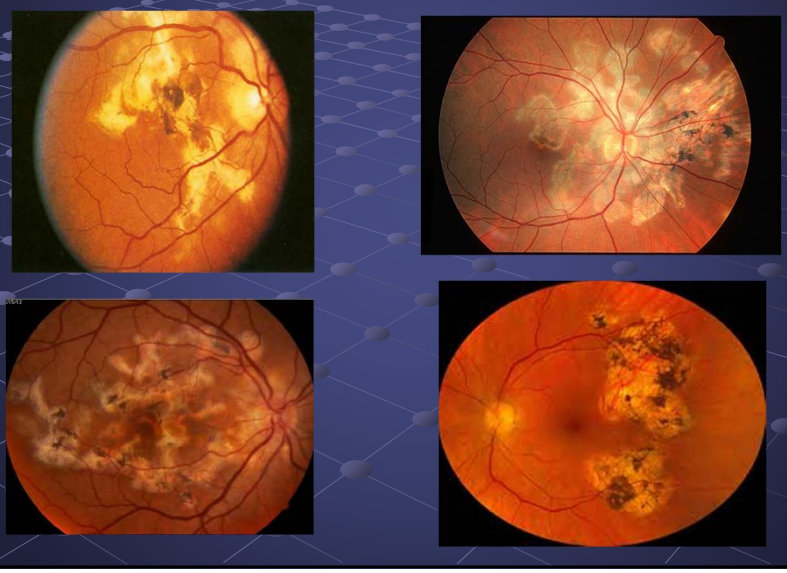
Serpiginous Choroiditis

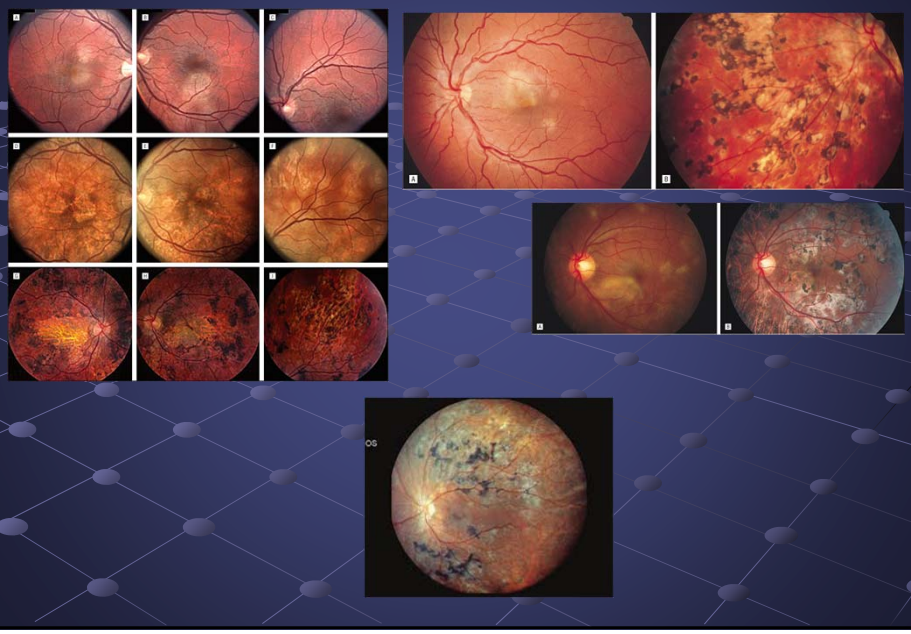
Geographic Helicoid Peripapillary Choroidopathy

- Summary
  - Bilateral disease of middle aged adults
  - Usually lesions start from the disc and spread both confluently and outwardly
    - Most like AMPPE
  - Associations: HLA B-7 (55%) , ↑ factor VIII (VWF), may have history of TB/HSV
  - Prognosis: **Poor**
    - Progressive, recurrent→ poor vision→ **TX**

Serpiginous Choroiditis

Geographic Helicoid Peripapillary Choroidopathy





Relentless Placoid Chorioretinitis (RPC) "ampiginous"

Resembles both APMPPE and Serpiginous
Who: 2nd to 6th decades M=F Rare
SX: Bilateral, Decreased vision, Scotoma, Floaters, Photopsias
PE:
Active lesions
Smaller than APMPPE (1/2 disc area).
May affect the mid- and far periphery first
Then involvement of the posterior pole (unlike APMPPE or serpiginous)
Lesions heal over weeks, resulting in chorioretinal atrophy
New lesions occur in all patients.
Presence of fifty or more lesions throughout the fundus
Subretinal fluid may be seen in association with the acute lesions.
Lesions heal - visual acuity is often preserved even with macula involved

Relentless Placoid Chorioretinitis (RPC)

Diagnostic Testing
FA/ICG (like APMPPE and Serpiginous)
Early hypofluorescence & late staining of acute lesions
SDOCT
Early Lesions
retinal photoreceptor disruption in the ellipsoid zone
surrounding areas of central subretinal fluid
Healed lesions (RPE atrophy with patchy hyperplasia)
FAF
lesions different zones:
of hypoautofluorescence (sick RPE)
and of hyperautofluorescence (dead RPE and RPE scaring blocking)

Laboratory evaluation is not helpful.

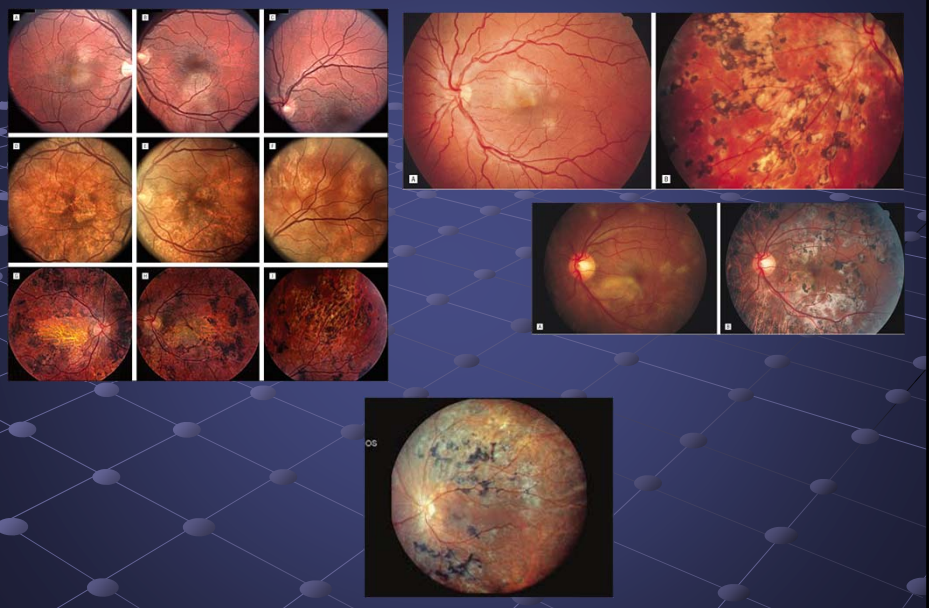
No consistent systemic association has been found.

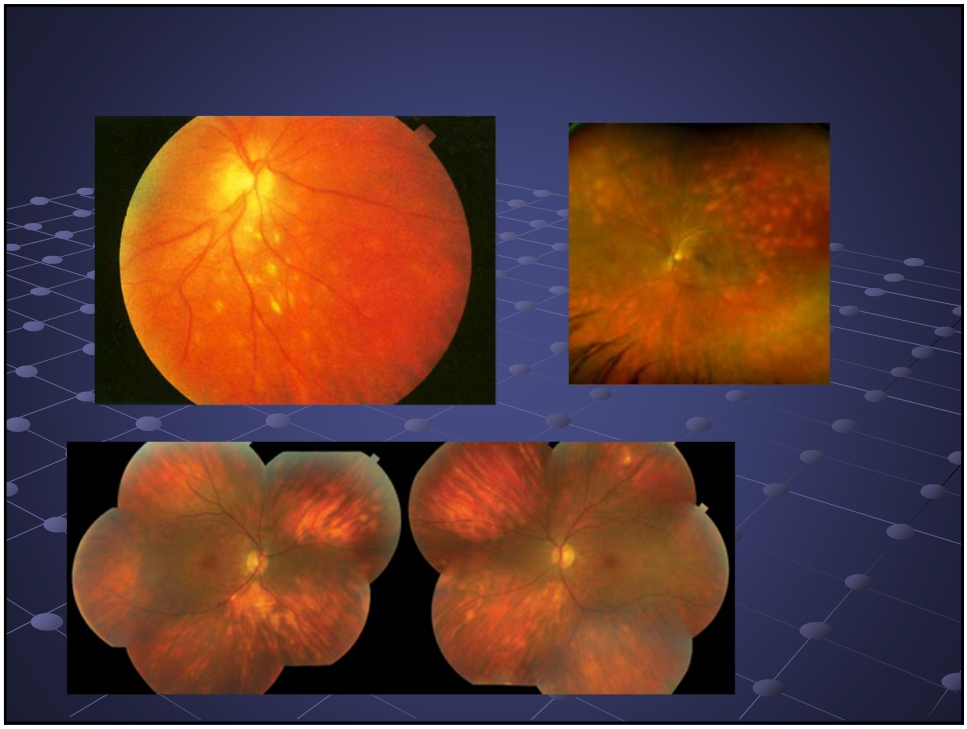
Relentless Placoid Chorioretinitis (RPC)

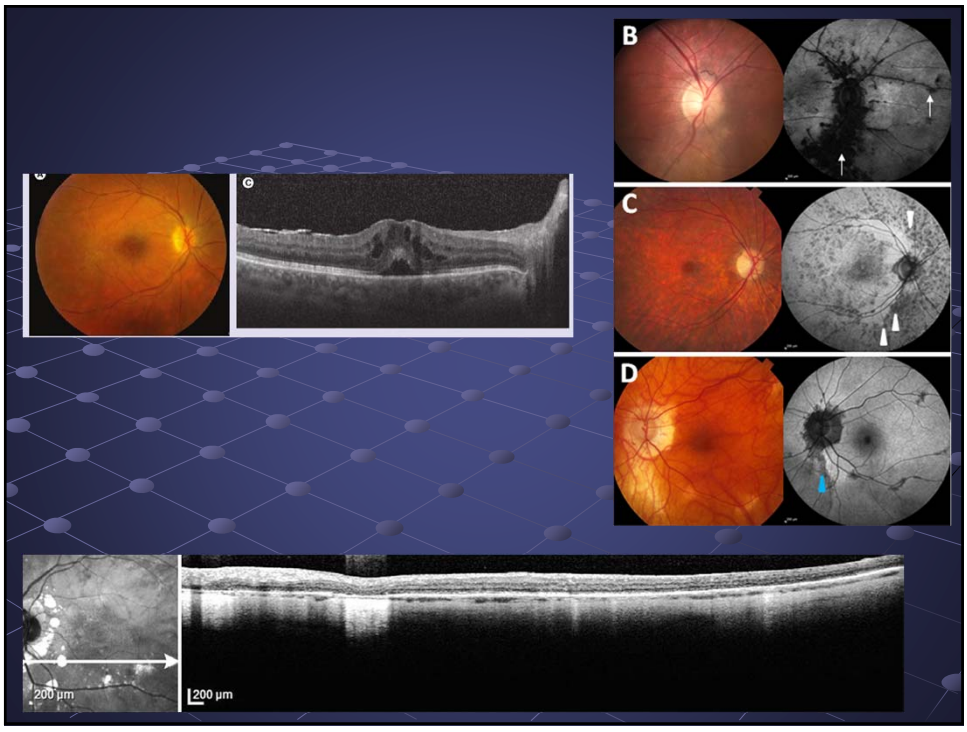
Treatment

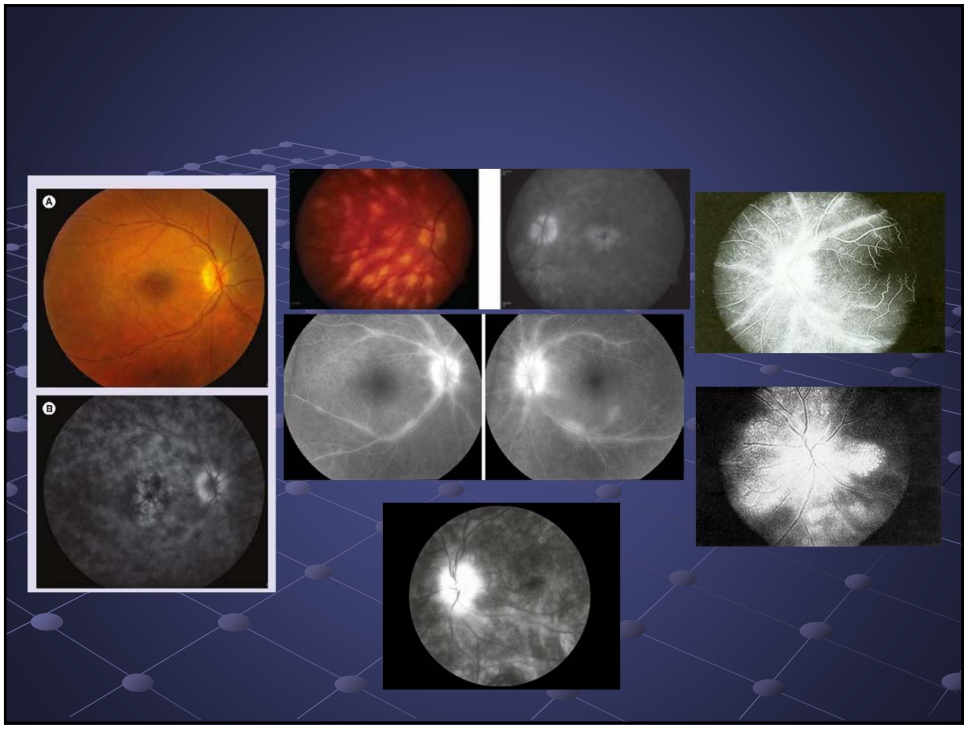
- Oral corticosteroids
- Steroid Sparing IMT • Course
- Healing with treatment
- Relapses common
- Preserved central vision despite 100s
- Of lesions and macular involvement

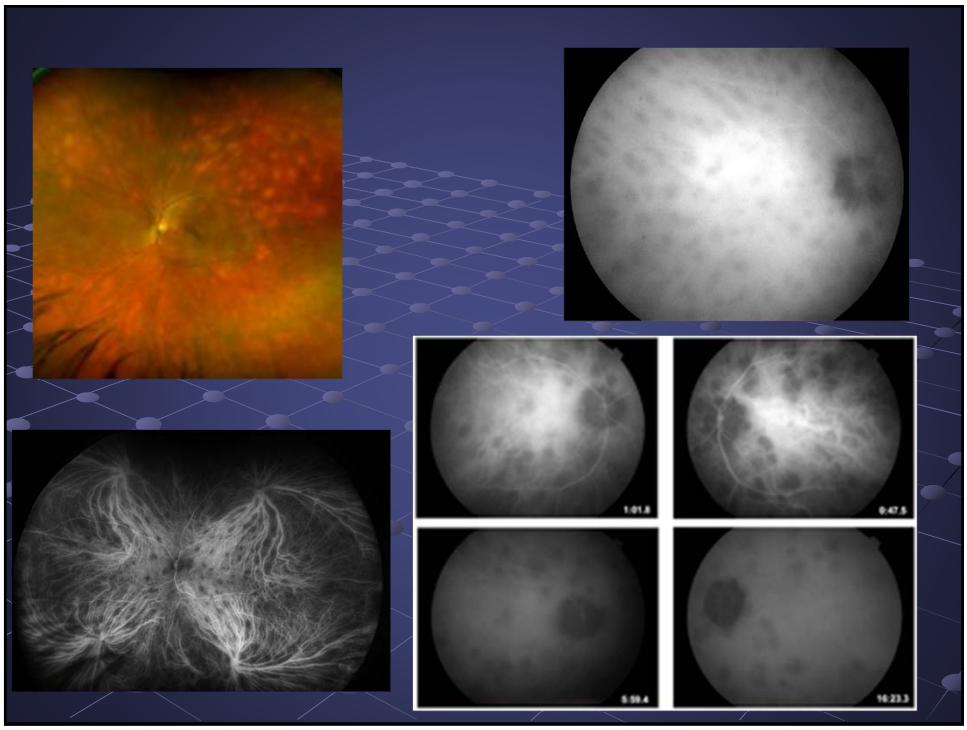
Relentless Placoid Chorioretinitis (RPC)






B
C
D
200 µm
200 µm


A
B



Bird Shot Chorioretinopathy
Vitiliginous Chorioretinitis

WHO: Middle aged (40-60 ave 53) white, W>F

SX: EARLY Bliateral decrease of acuity, floaters
LATE nyctalopia, color vision problems, VF compalints

PE: Smaller than disc, cream colored, round-oval spots at choroidal level
Swirl out from disc, nasal>temporal, do not pigment over time, vitritis 90-100%, a/c cells 30%

FAF: hypoAF lesions

OCT: focal loss of is/os junction and RPE layer (late CME)

FA: Quenching – dye rapidly disappears from retinal circulation
later see leakage at vessels/ONH and CME
can be normal

ICG: early and late hypofluorescence

ERG is abnormal, Lymphocyte proliferation to S antigen

Bird Shot Chorioretinopathy
Vitiliginous Chorioretinitis

Associations:
- HLA A29 90%
- depression, abnormal sleep cycle
- Hearing loss and vertigo

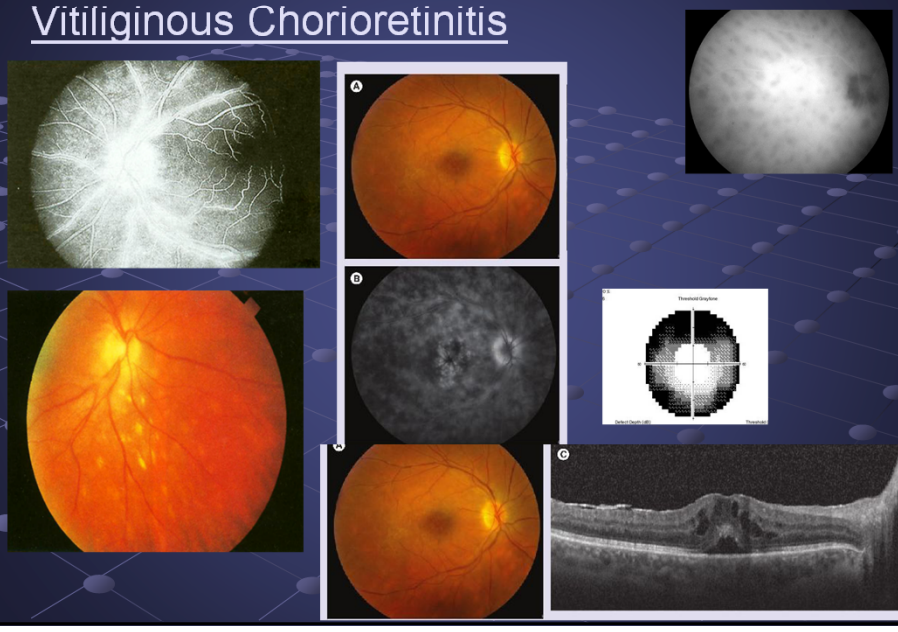
Prognosis: Fair (50% have > 20/60)
- Usually due to CME, can see CNVM

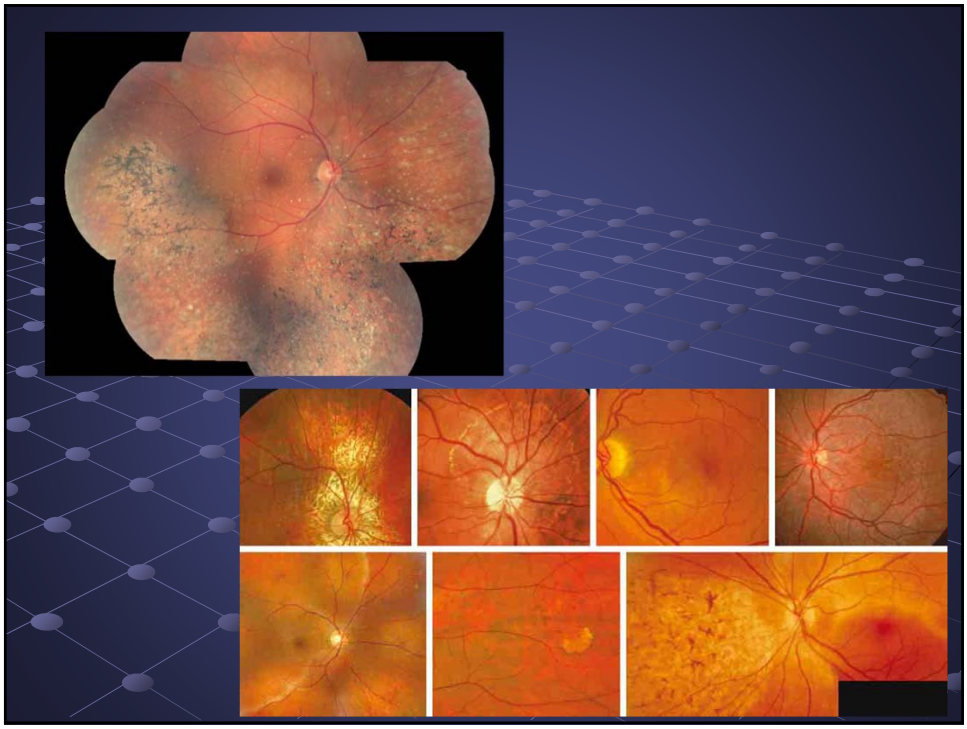
TX: If VA worse than 20/40

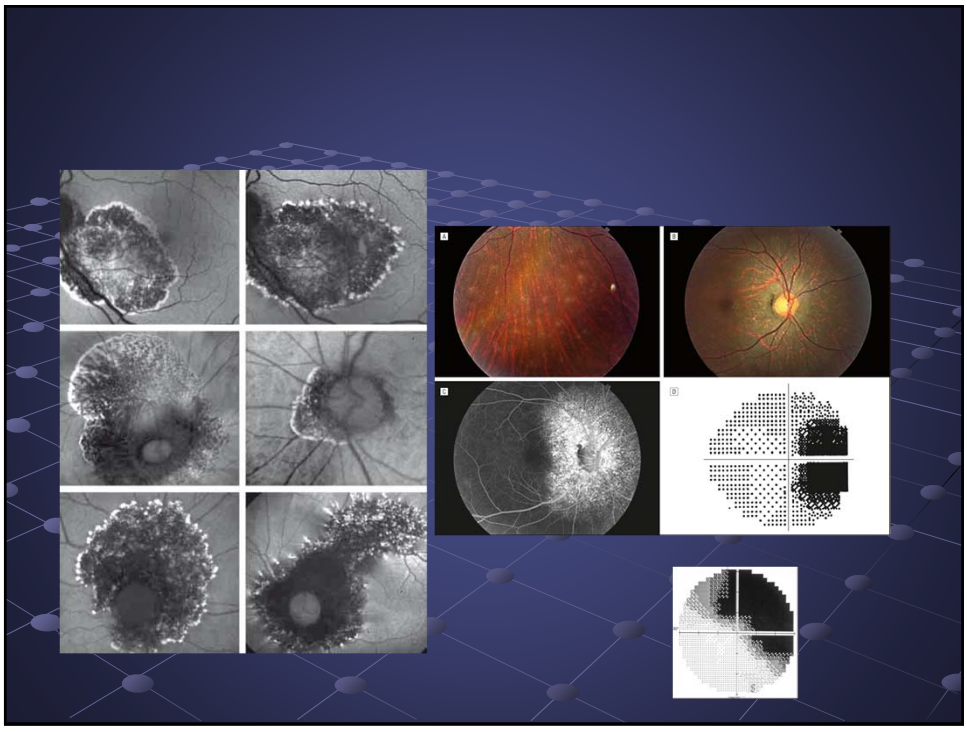
Bird Shot Chorioretinopathy
Vitiliginous Chorioretinitis

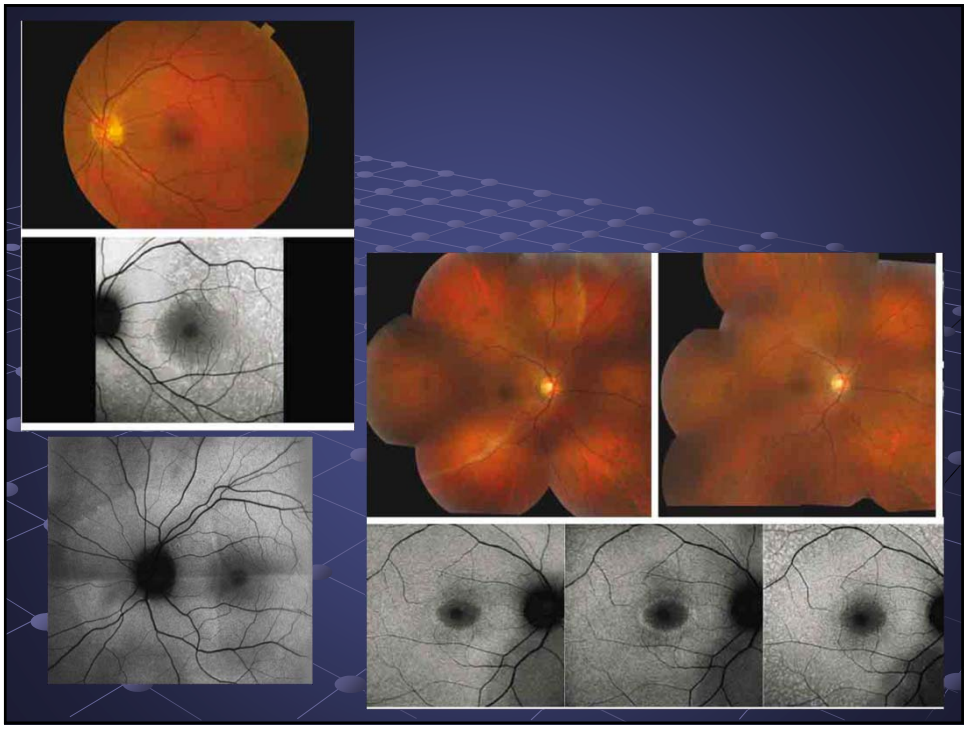
- Summary
  - Bilateral, middle aged, white women
    - **Early** acuity loss,
    - **Late** night and/or color vision problems
  - Spots swirl out from disc, do not pigment
  - Vitritis and HLA A29 in 90%!
    - May see iritis, depression and sleep problems
  - Prognosis: FAIR
    - Vision Loss (<20/40) usually due to CME/CNVM →**TX**

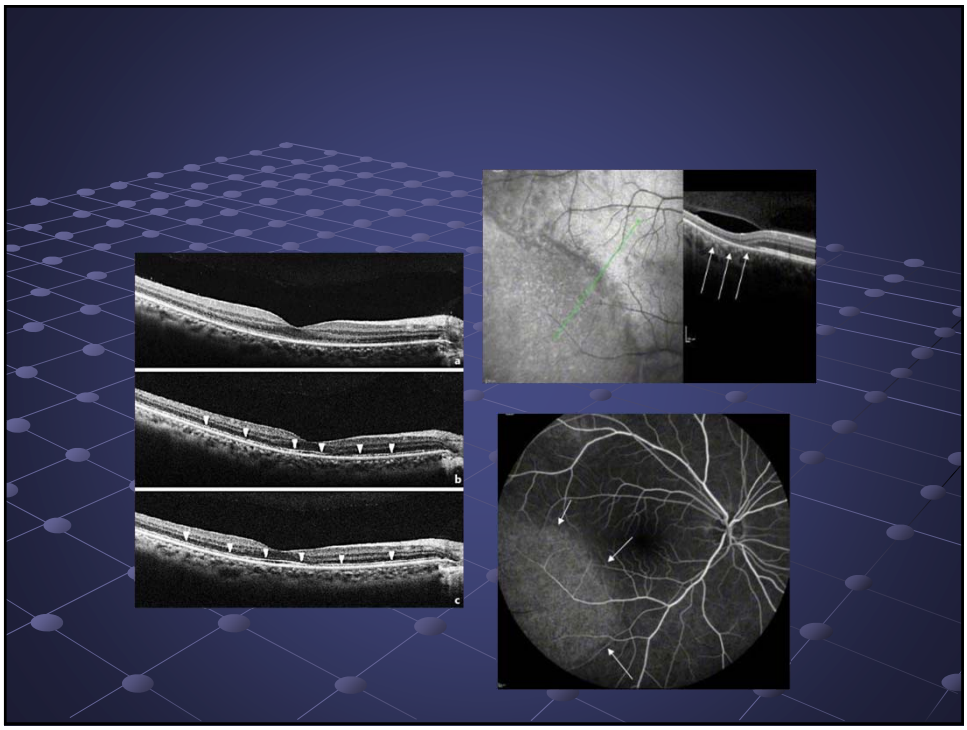
Bird Shot Chorioretinopathy
Vitiliginous Chorioretinitis











AZOOR
Acute Zonal Occult Outer Retinopathy

Who: (Teens -60s **ave 38**) young women 75%
SX: Subacute Bilateral (75%), asymmetric, large peripheral scotomata, photopsias,
PE: Early, mild vitritis (50%), minimal retinal changes
Late, seen RPE changes, large gray rings around ONH, in mid-periphery or periphery
FAF: early hyperAF then mottled hyper/hypoAF
OCT: early focal loss of IS/OS then broader loss of outer retina
FA: Late leakage at retinal vessels/ONH
Especially in patients with vitritis
without vitritis FA can be normal
ERG: abnormal, pathology is in the outer retina

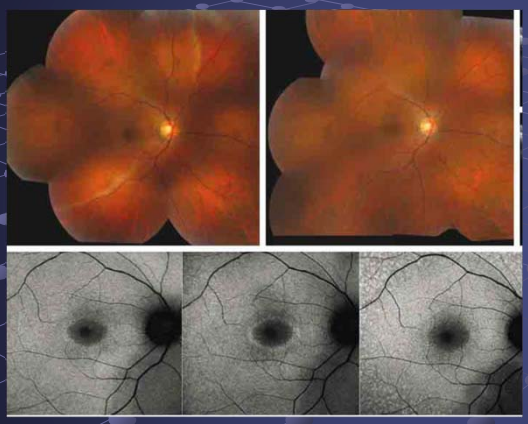
AZOOR
Acute Zonal Occult Outer Retinopathy

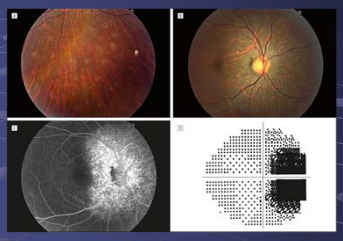
Pathology: outer retina
ERG: abnormal
EOG: normal
Associations: none
CAR and RP should be in DDX
Prognosis:
Good for central VA
Peripheral field loss stabilizes in 6 months
TX:
Steroids for significant vitritis

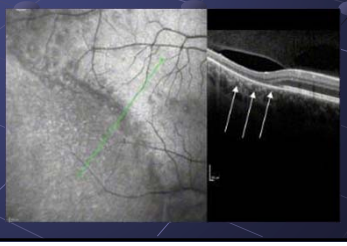
AZOOR
Acute Zonal Occult Outer Retinopathy

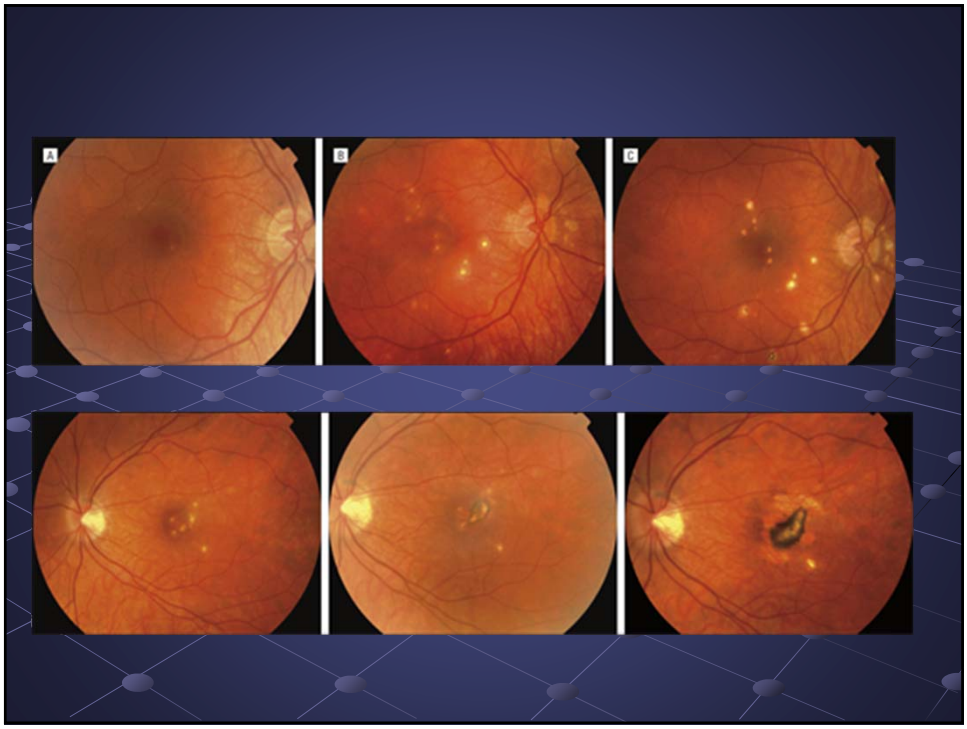
- Summary
  - Bilateral disease in young women
  - Complaint is peripheral field loss
  - Initial retina normal/mild vitritis
  - Prognosis: Fair
    - Some have mild central acuity loss due to CME
    - Peripheral Field Loss can be moderate but is non progressive
    - **TX based on level of vitritis/CME**

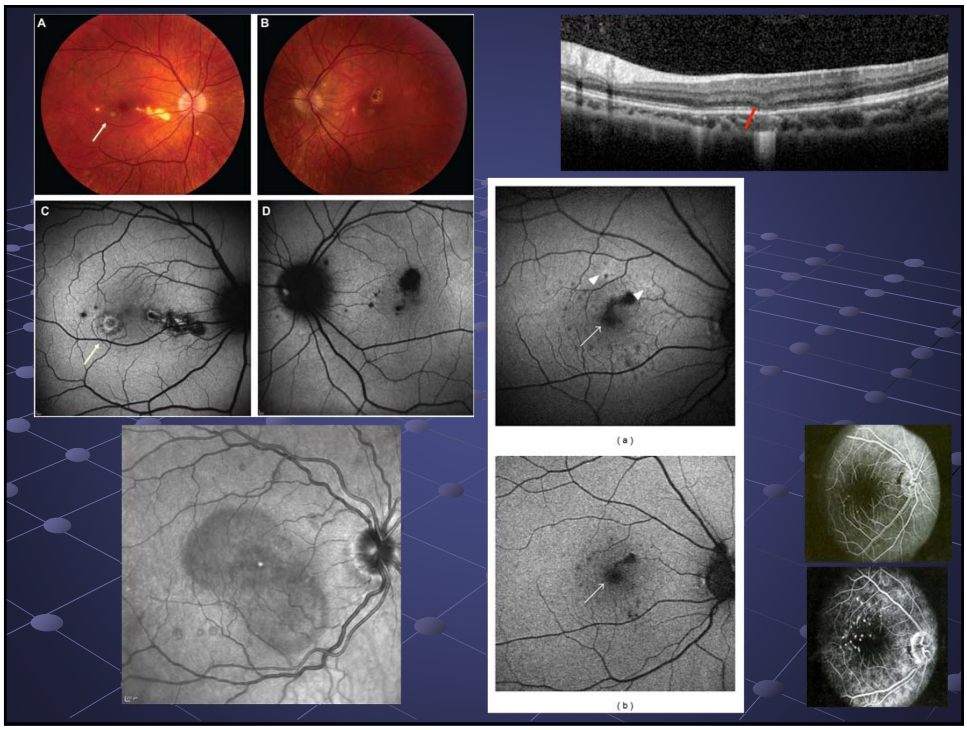
AZOOR
Acute Zonal Occult Outer Retinopathy

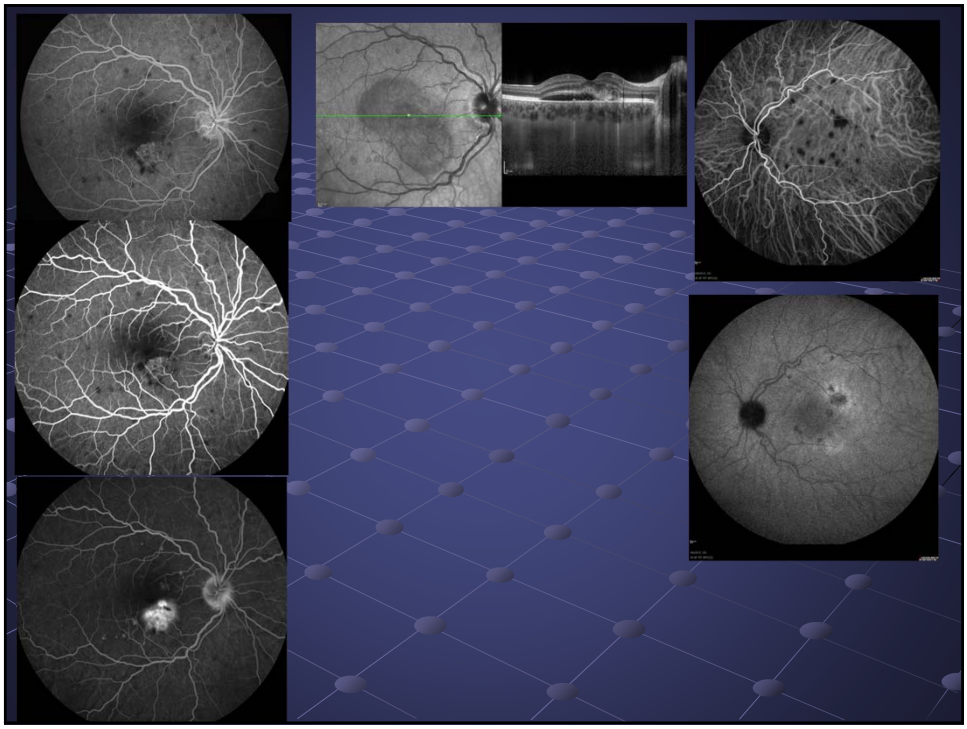







A
B
C


A
B
C
D
(a)
(b)



PIC

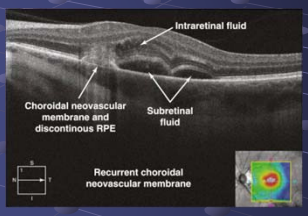
Punctate Inner Choroidopathy

Who: Young (20-40s, ave 33), myopic women (90%)
SX: Acute/abrupt Bilateral (can be unilateral) decrease in acuity, metamorphopsia, scotomata, photopsia
PE: Bilateral smaller than disc yellow spots, → like OHS
- Usually in posterior pole
- Rare Serous RD, NO a/c or vitreous cell

FAF: mix of hypo and hyperAF
OCT: focal loss at RPE level and then signs of CNVM
FA: Early blockage, late staining, leakage of CNVM
ICG: early and late hypo, with hyper think CNVM
ERG: either normal or borderline abn depending on amount of pathology at RPE choroid junction

PIC
Punctate Inner Choroidopathy

Associations: none or possible EBV



Prognosis:
- Good most return to 20/20
- CNVM (20-40%) worse acuity, but some resolve

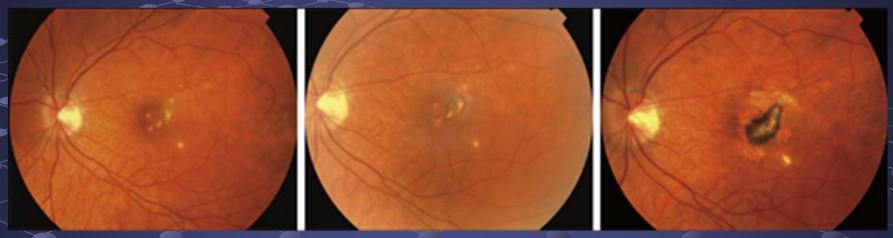
TX:
- Usually none, treat cnvm, consider steroids
- Amsler grid

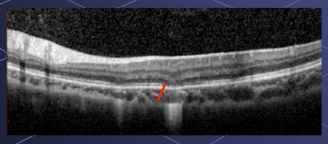
PIC
Punctate Inner Choroidopathy

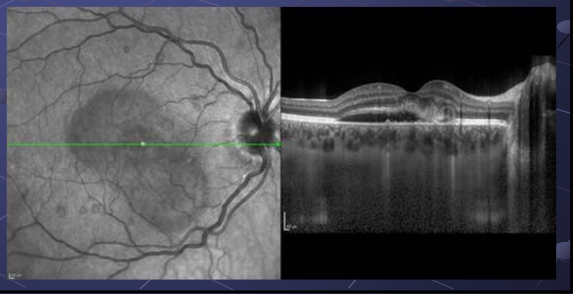
- Summary
  - Bilateral young myopic women
  - Spots in periphery
    - Most like MCP
  - Pathology is in choroid → ERG/EOG are nl
  - NO vitiritis/iritis
  - Lower association with EBV
  - Prognosis: GOOD no TX
    - **(except for 40% CNVM)**→Amsler → TX as needed

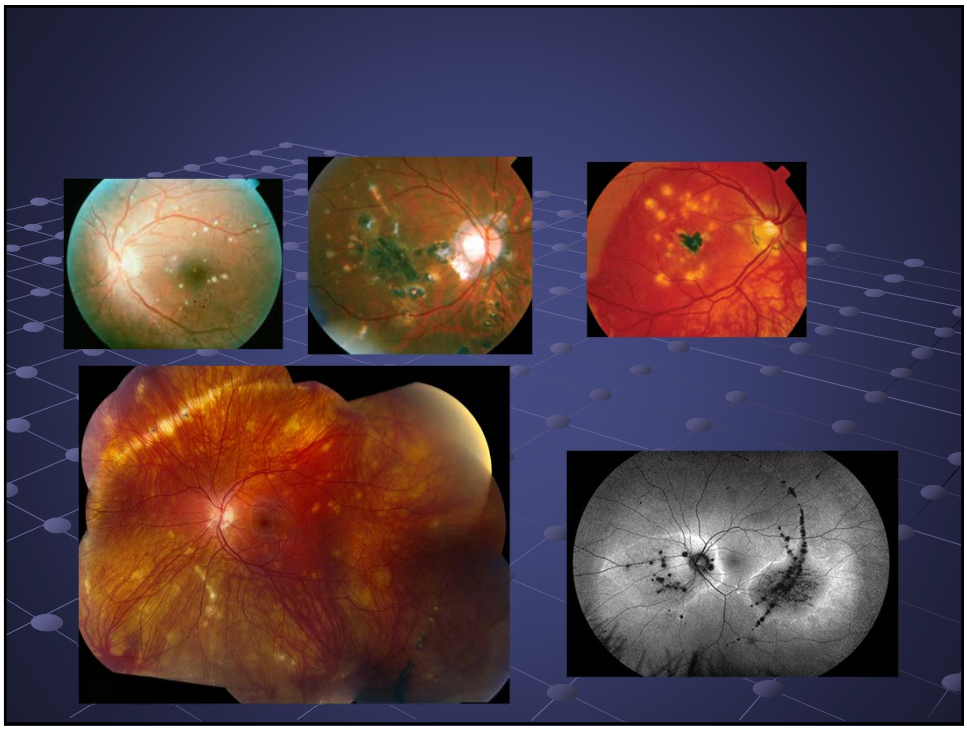
PIC

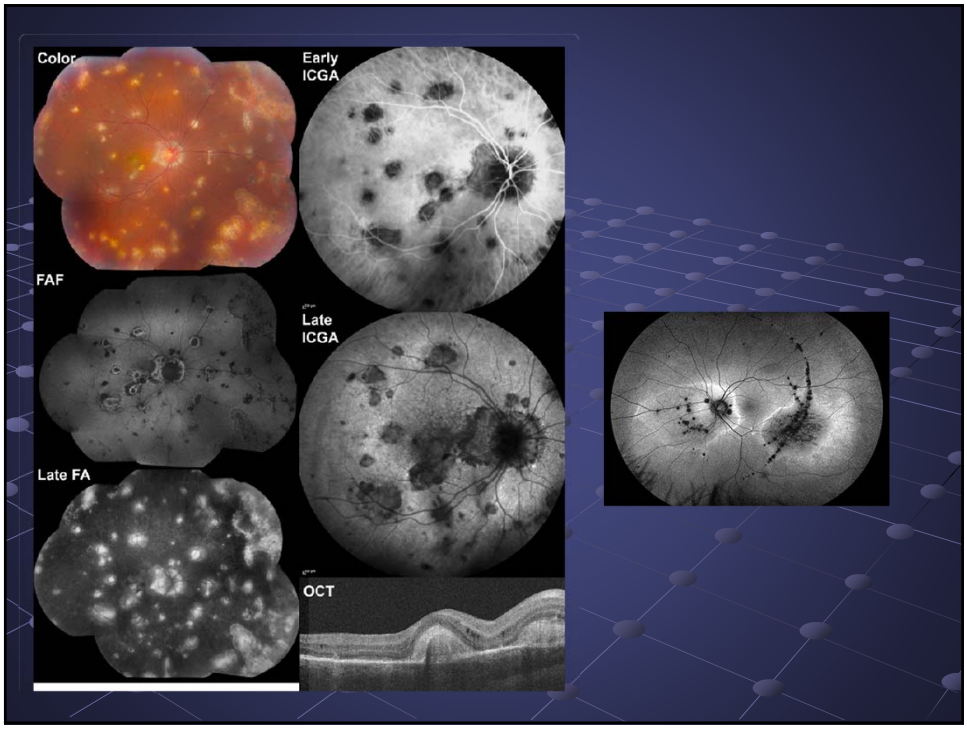
Punctate Inner Choroidopathy

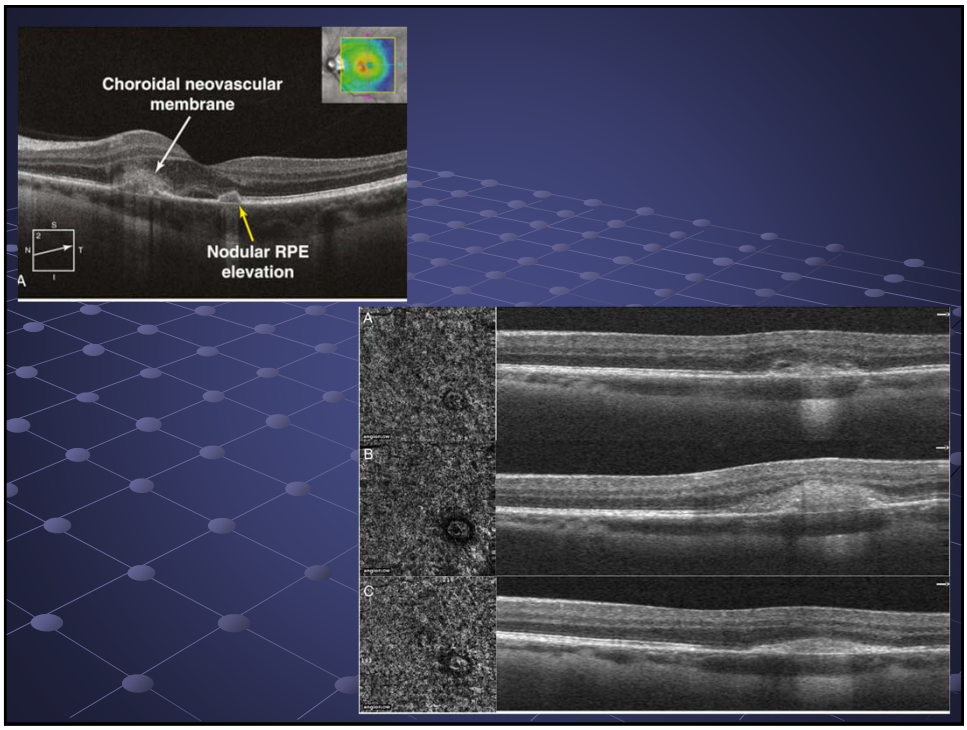









Color
Early ICGA
FAF
Late ICGA
Late FA
OCT


Choroidal neovascular membrane
Nodular RPE elevation
A
B
C

MCP

Multifocal Choroiditis and Panuveitis
(pseudo histoplasmosis syndrome)

Who: Young (30's ave 39) women (75%), myopic,+/- viral trigger

SX: Subacute bilateral decrease in acuity, floaters

PE: Smaller than disc gray-white spots

Inferior and nasal → late punched out lesion (like OHS)

Vitritis 100%, iritis 50%, CME 30%, CNVM 33%

FAF: mix of hypo and hyperAF

OCT: RPE subretinal space

FA: early blocking, later staining, old lesions→window defects

ICG: hypofluorescence

ERG: variable because of focal lesions at RPE/choroid level

MCP

Multifocal Choroiditis and Panuveitis
(pseudo histoplasmosis syndrome)

Associations: Epstein Barr Virus

Prognosis:

Poor: Recurrent, CME common (CNVM 30%)

TX:

Steroids, cyclosporine

Acyclovir in patients with elevated EBV titers

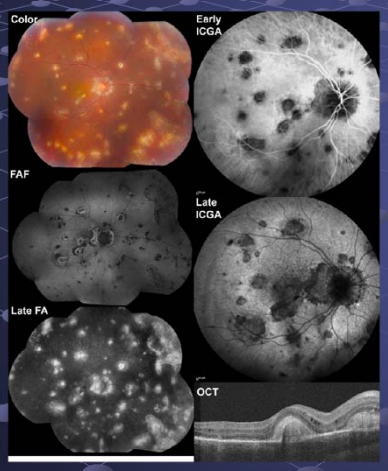
MCP

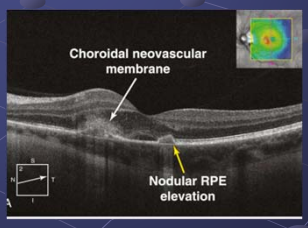
Multifocal Choroiditis and Panuveitis
(pseudo histoplasmosis syndrome)

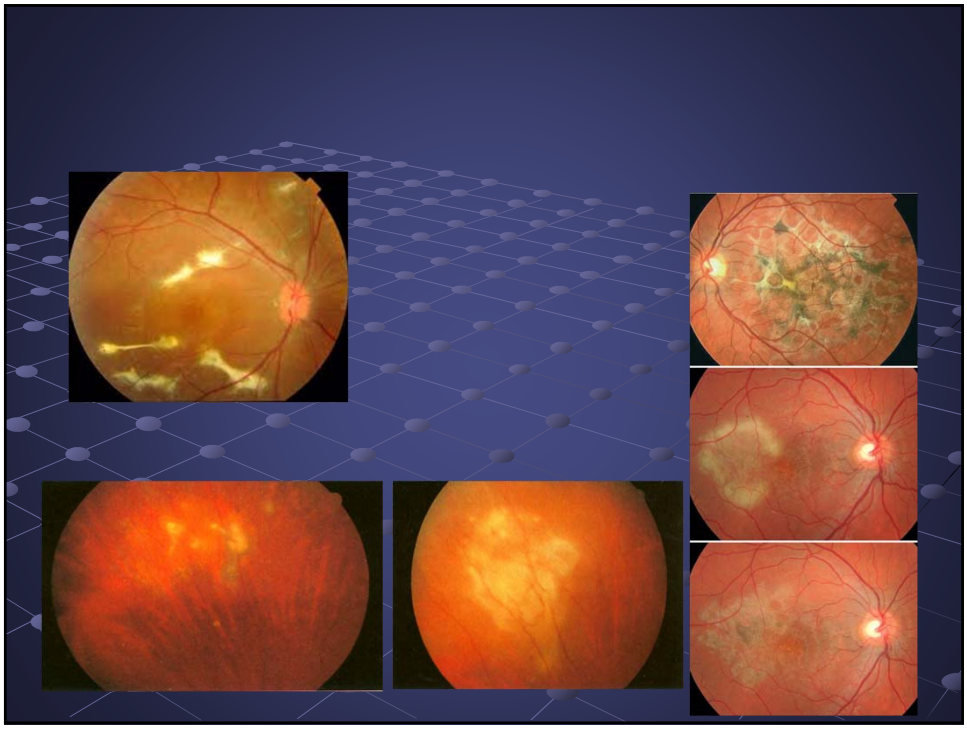
- Summary
  - Bilateral in young, myopic women
  - Spots are usually nasal or inferior
    - Late lesions are areas of atrophy "punched out"
  - All have vitritis, half have iritis
  - Associations: EBV
  - Prognosis: Poor
    - Vision loss due CME >CNVM → **TX**
      - Acylovir for pt with ↑ EBV titers

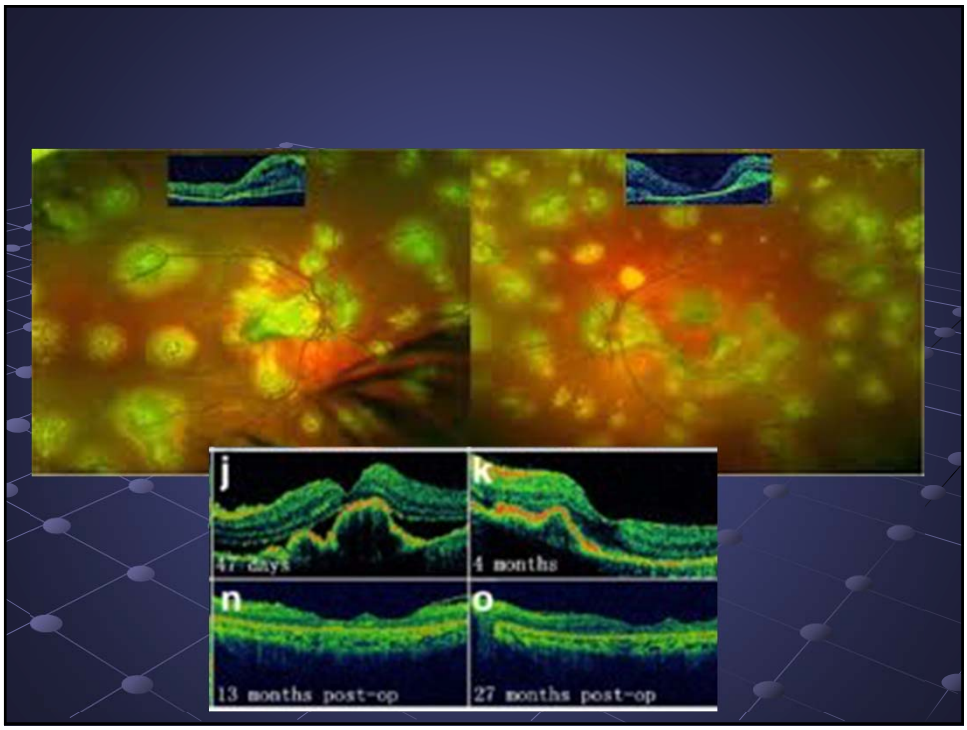
MCP

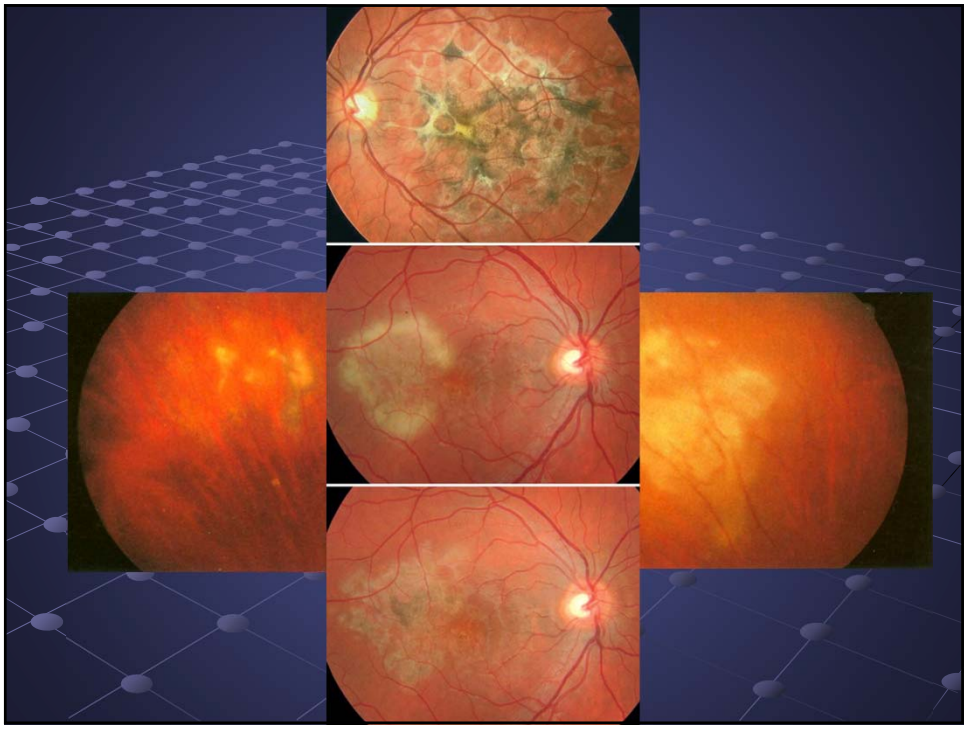
Multifocal Choroiditis and Panuveitis
(pseudo histoplasmosis syndrome)








j
47 days
k
4 months
n
13 months post-op
o
27 months post-op



PSFU

Progressive Subretinal Fibrosis and Uveitis

Who: Young (teens-30's) women 100%, BLACKS > WHITES

SX: Chronic/recurrent, bilateral asymmetric loss of acuity
1-2 months many separate eyes

PE: Smaller than disc white dots, temporal > nasal
Iritis 30%, vitritis 50-70%
Later spots resolve, subretinal fluid →stellate fibrosis, CME, CNVM, RD

FA: early blockage or sometimes see window defect,
late hyperfluorescence staining of scars

ERG/EOG: decreased
impact is in Sub retinal space (b cells/plasma cells)

PSFU

Progressive Subretinal Fibrosis and Uveitis

- Associations: none
- Prognosis: POOR (CF-HM months-years)
  - Recurrences, CNVM, RD
- TX:
  - steroids, immunosupressives, acyclovir
  - Treat CME, CNVM, RD

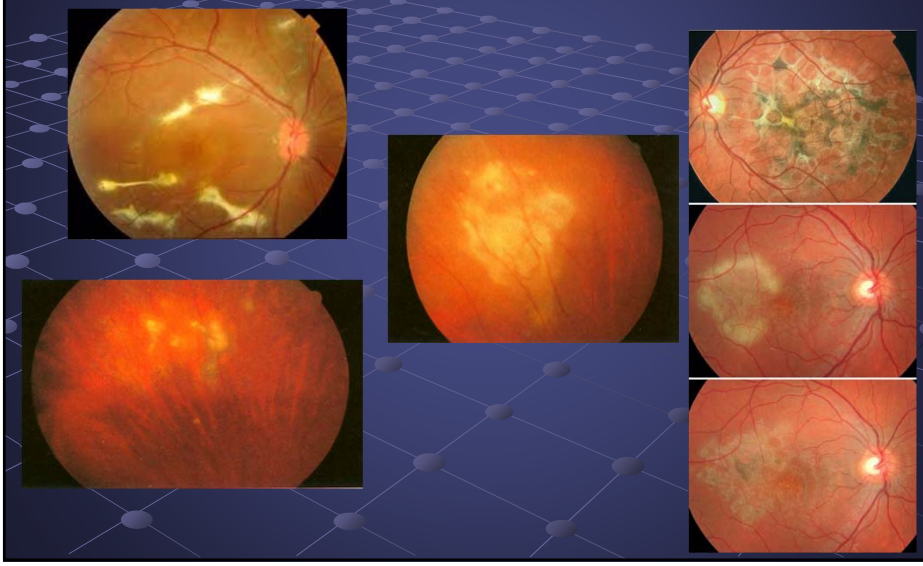
PSFU

Progressive Subretinal Fibrosis and Uveitis

- Summary
  - Bilateral disease in young, black women,
  - Dots associated with subretinal fluid, fibrosis, RD
    - Temporal > nasal, a bad end of MCP spectrum
  - Vitritis >> iritis
  - Prognosis: POOR →**TX**
    - progressive (CNVM/RD)

PSFU

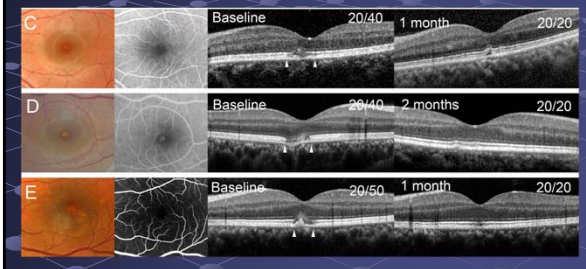
Progressive Subretinal Fibrosis and Uveitis

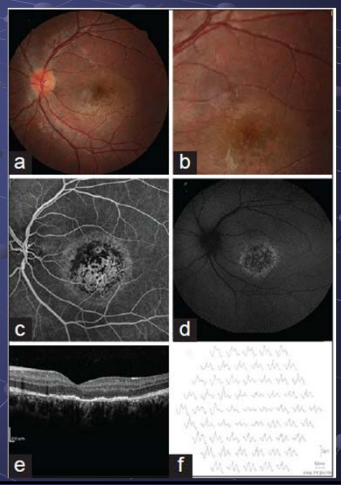


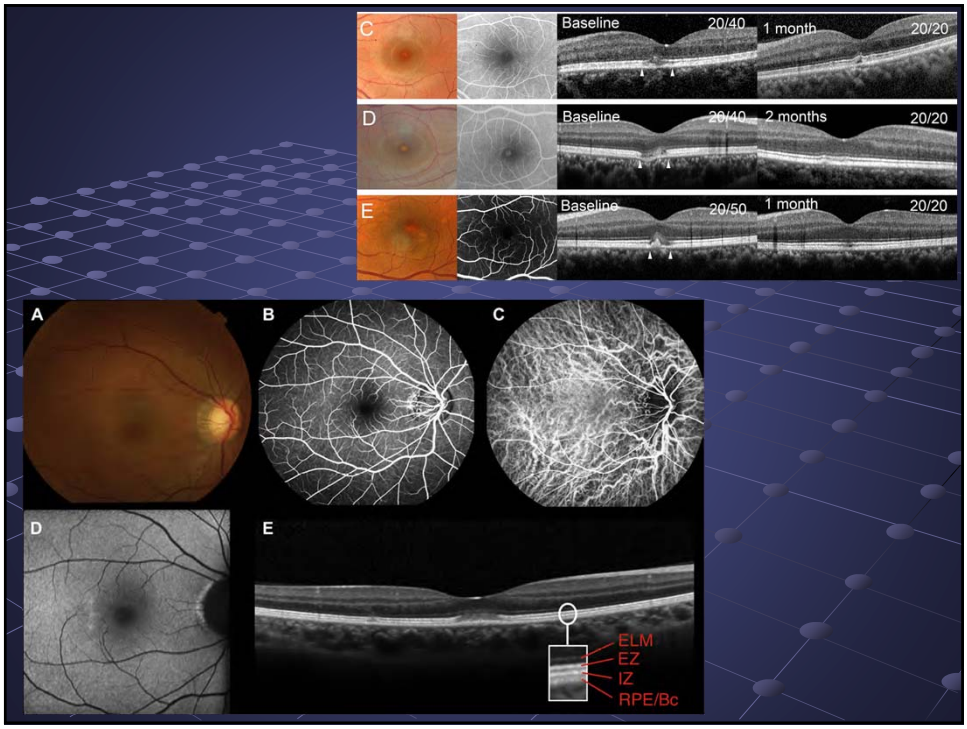
ARPE

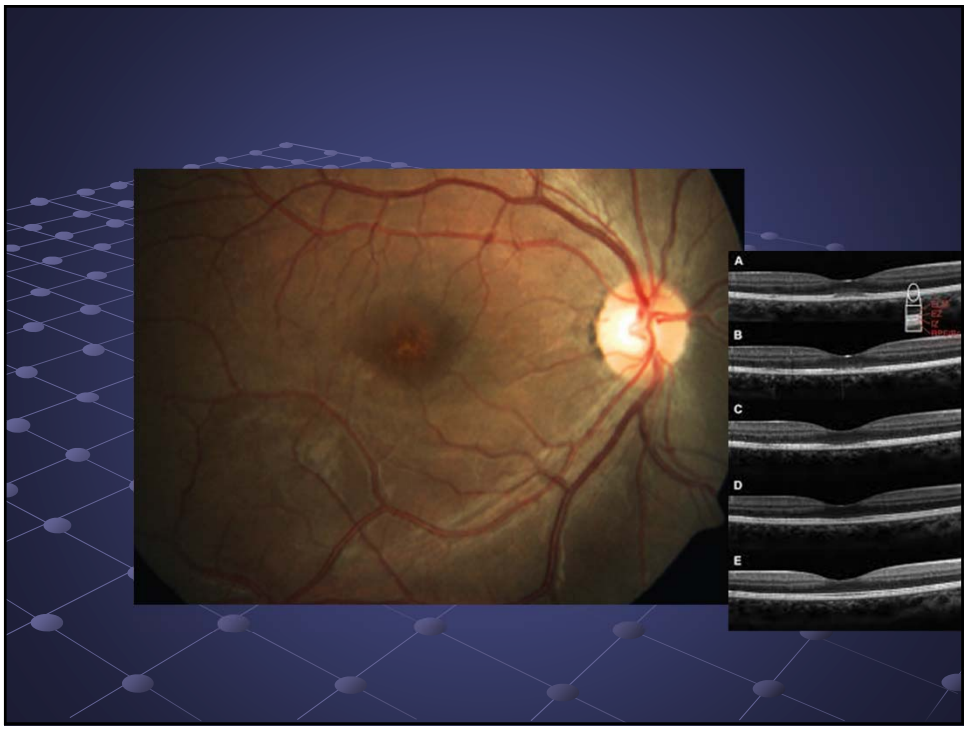
Acute Retinal Pigment Epitheliitis

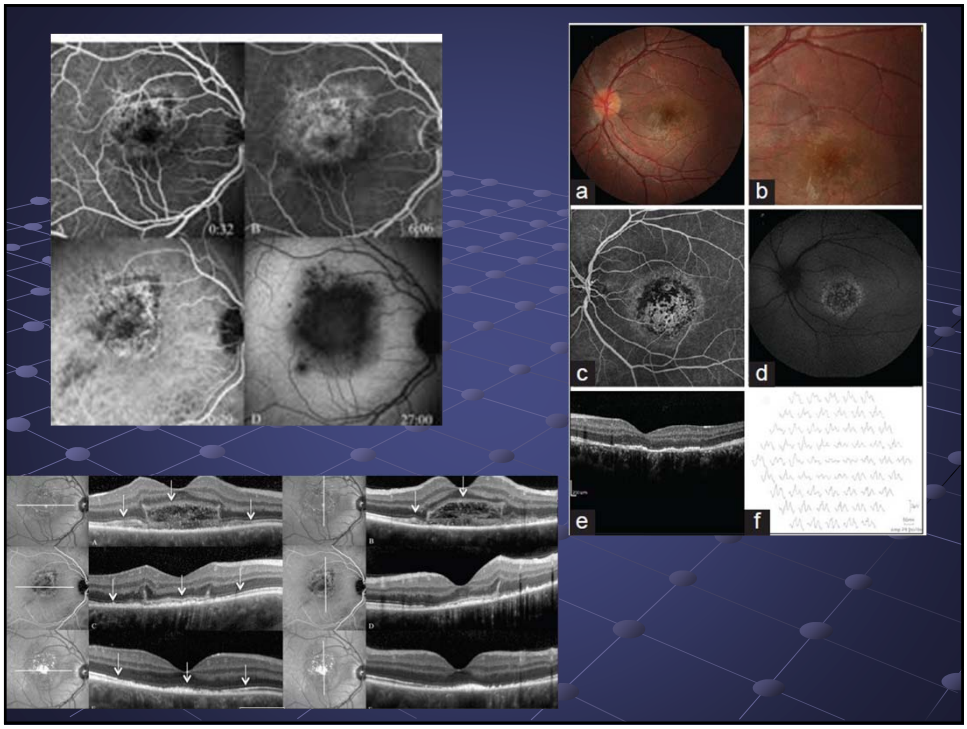
(Krills Disease)






C
Baseline
20/40
1 month
20/20
D
Baseline
20/40
2 months
20/20
E
Baseline
20/50
1 month
20/20
A
B
C
D
E
ELM
EZ
IZ
RPE/Bc


A
B
C
D
E



ARPE

Acute Retinal Pigment Epithelitis

(Krills Disease)

Who: Young (teens -40) adults, rare disease

SX: Acute Unilateral 75%, mild drop in acuity,
metamorphosia

PE: 2-4 clusters of small black spots + halo at macula
Later spots darken, halo fades

FAF: nonspecific area of hyopAF or focal hyper

OCT: a range of sublte change at RPE to more significant outer retinal findings that seem to fade away

FA: Honeycomb pattern (hyperpigmented center/halo stains)
"bulls eye pattern" No leakage

ERG/EOG: normal and abnormal; pathology is at RPE

ARPE

Acute Retinal Pigment Epitheliitis
(Krills Disease)

Associations: none or possibly virus

Prognosis: Good, recovery over 2-3 months

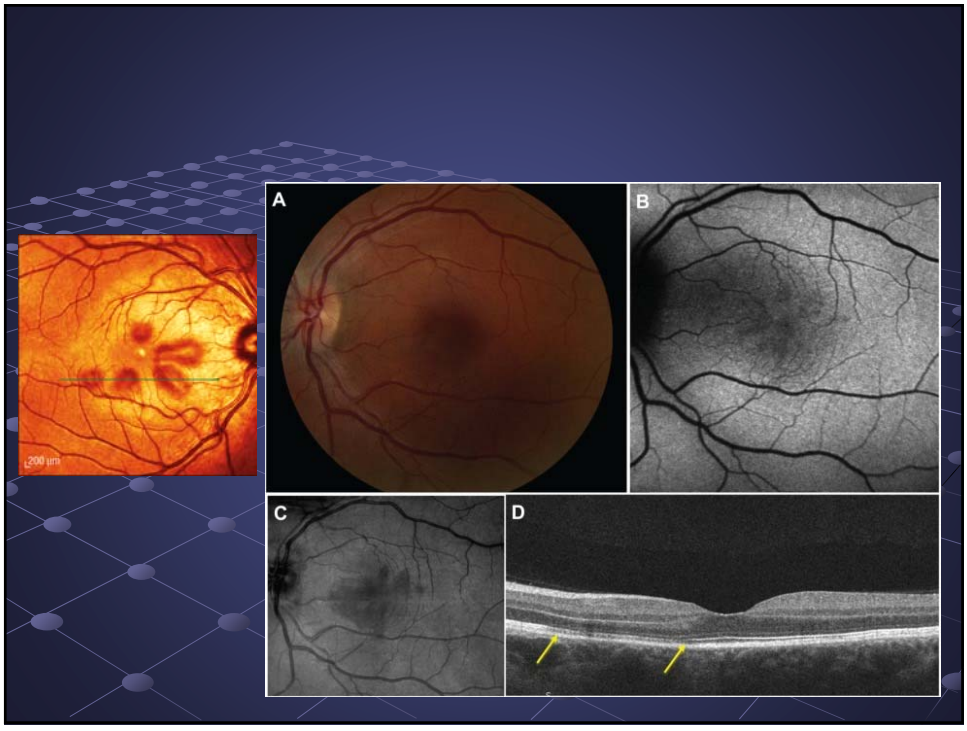
TX: none

ARPE

Acute Retinal Pigment Epithelitis
(Krills Disease)

- Summary
  - Rare unilateral disease in young adults
  - Dark spots with halo
  - FA: bulls eye or honeycomb pattern
  - Good Prognosis→ **NO TX**

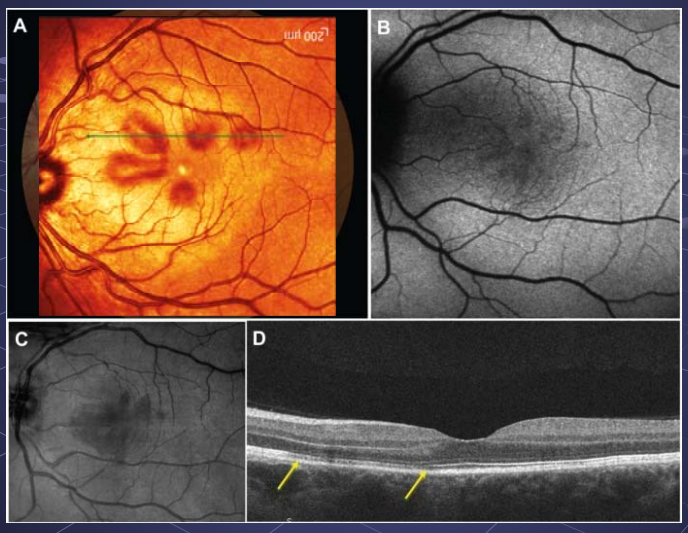

200 µm

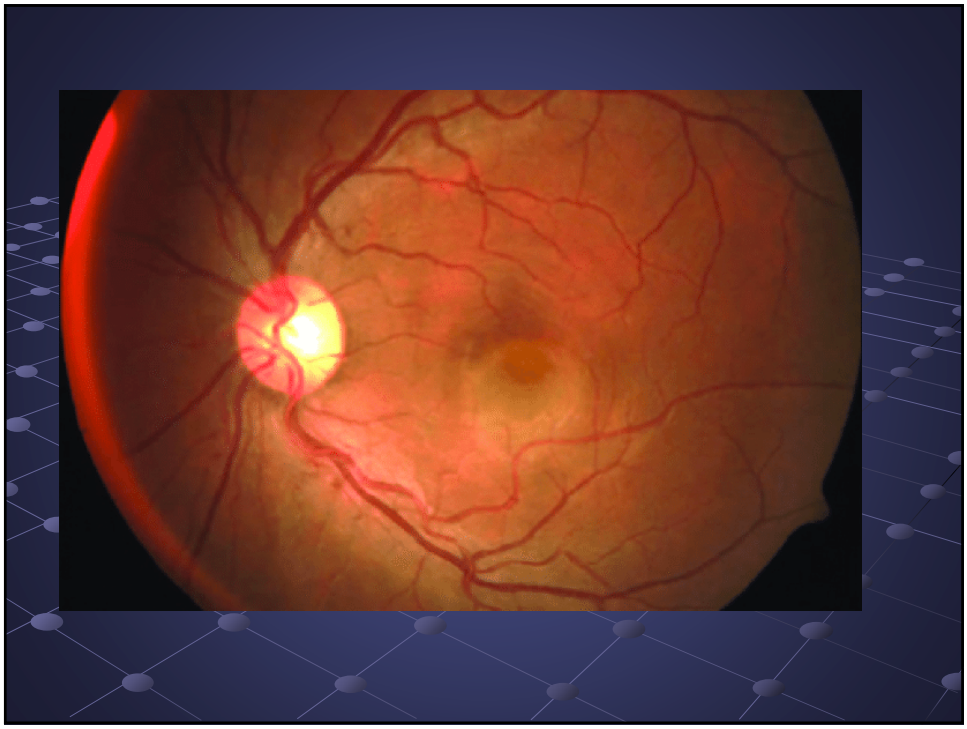

A
B
C
D

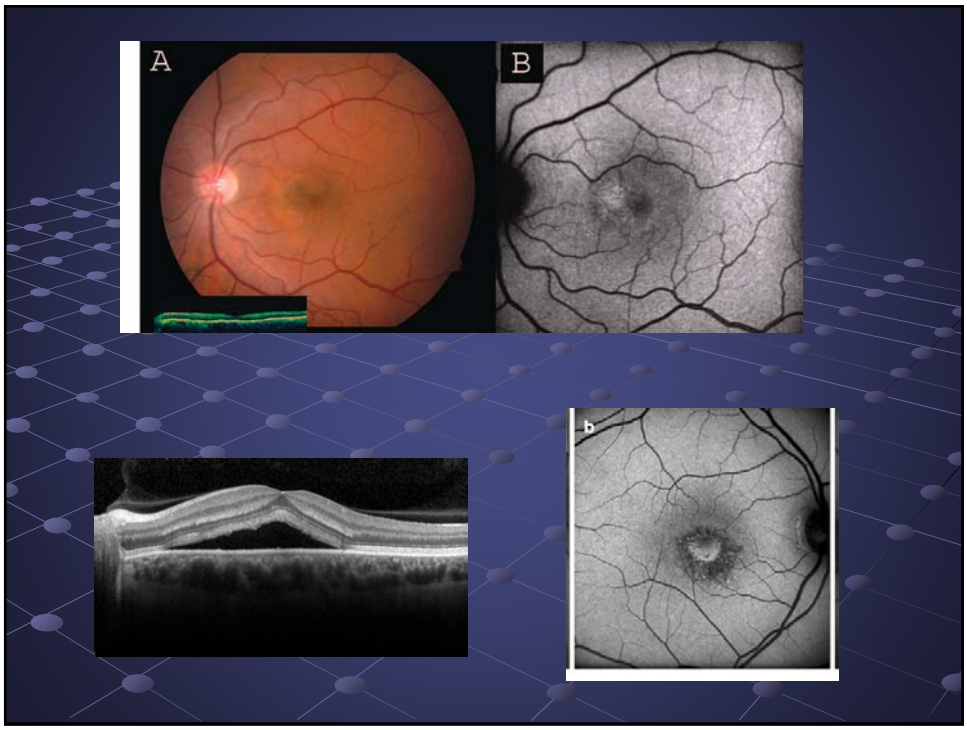
AMN Acute macular neuroretinopathy

Who: young women >85%
SX: acute paracentral scotomas in one or both eyes
PE: reddish-brown tear-drop wedge shape lesions pointing toward the fovea sometimes hard to seen on exam Retina vesseles and ONH are unaffected and no vitritis
These can look similar to those seen blunt or whiplash trauma
Redfree/FAF: show areas affected more clearly as darker areas/blocking
OCT: either in middle or outer retina see focal areas of abn
Pathology: ischemia of deep plexus of the capillary plexus
Association:
Preceding flulike illness, use of OCP, caffeine, injection of adrenline or epinephrine.
Usually complete recovery in weeks to months

ANM Acute Macular Neuroretinopathy



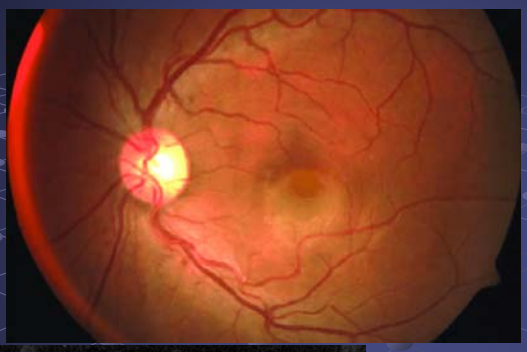


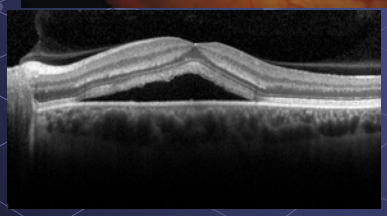

A
B
b

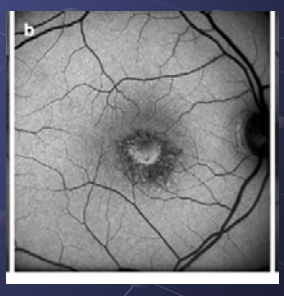
AIM Acute idiopathic maculopathy

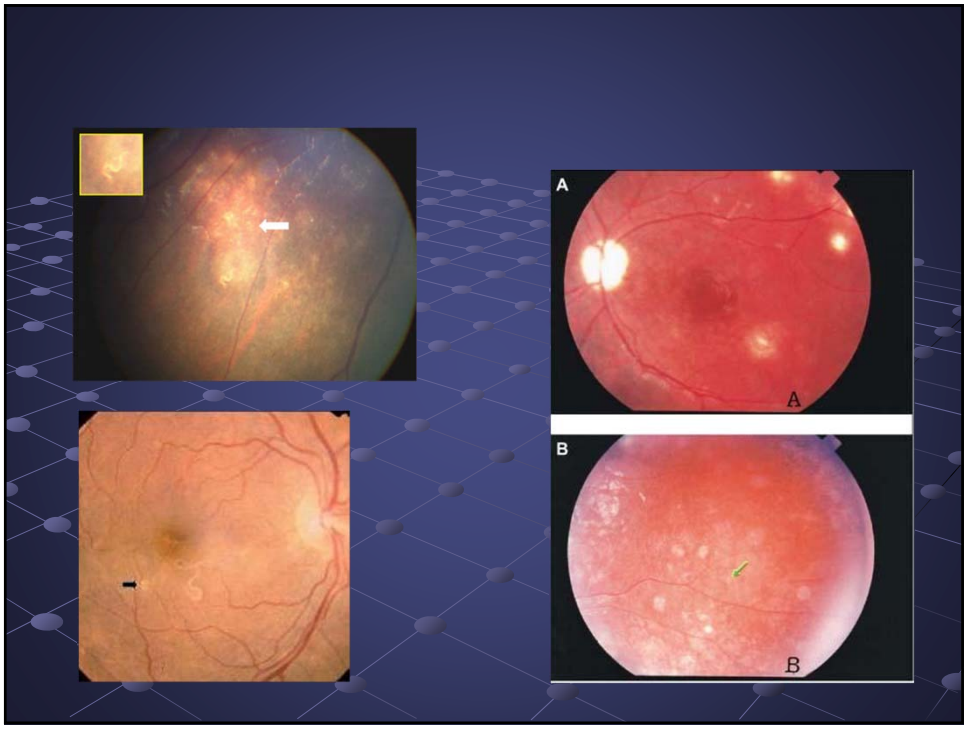
Who: young adults after a flu (coxackievirus)
SX: acute severe central or paracentral vision loss
PE: exudative macular neurosensory detachment
little or no vitritis, but may seen disc swelling & vasculitis
FAF: areas of mottled AF in NSD usually hyper
OCT: shows NSD
FA:
Early shows irregular hyperfluorescence at RPE and late pooling
Late shows bullseye pattern of RPE alteration
ICG: shows early and persistent blocking/hypofluorescence
Prognosis is good with near complete recovery of vision
Cause is not known but

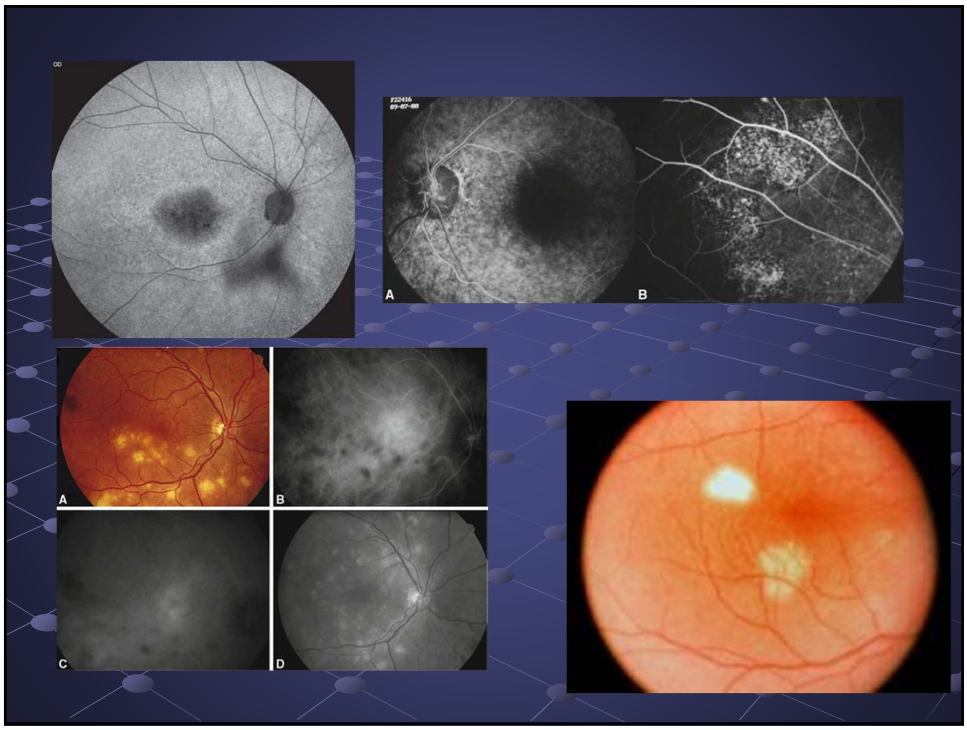
AIM Acute idiopathic maculopathy







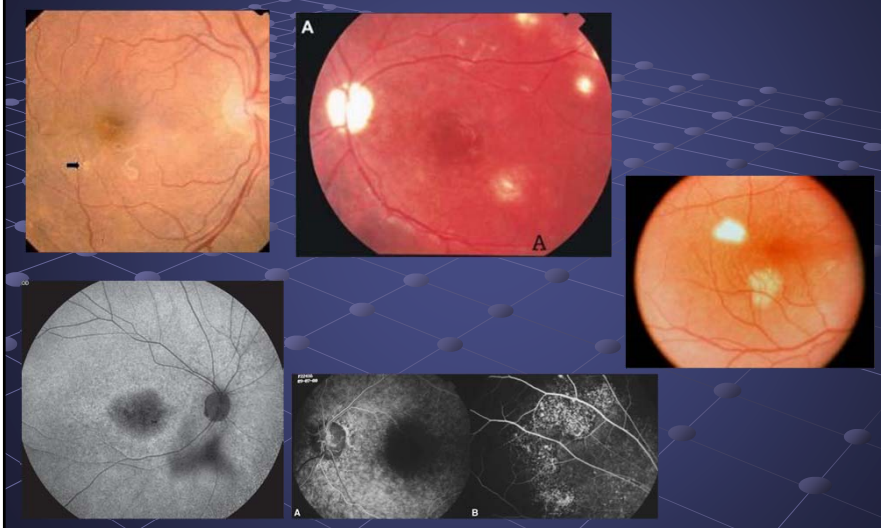

A
A
B
B

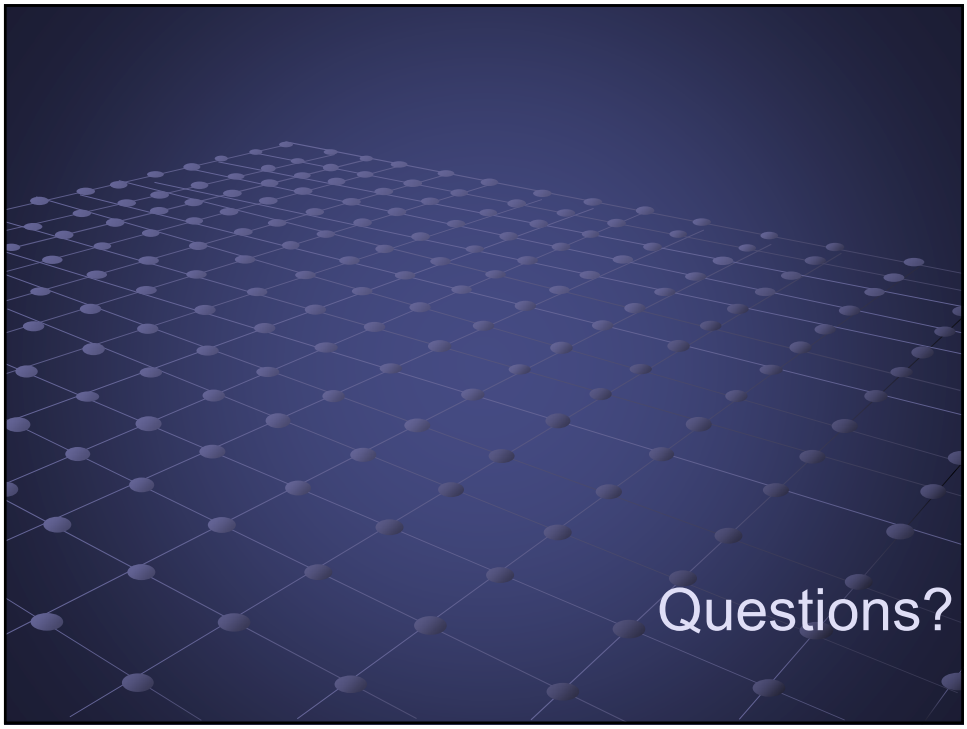

A
B
A
B
C
D

DUSN Diffuse Unilateral Subacute Neuroretinitis

- Usually young – 14 years (11-65yrs)
- Symptoms:
  - Unilateral decrease in acuity
- PE
  - EARLY
    - Evanescent crops of grayish white dots (400-1500 microns) usually posterior to equator
    - Motile Nematode (400-2000micron)
      - Baylisascaris procyonis, Ancylostoma caninum
  - LATE
    - Diffuse atrophy due to toxic/immunologic reaction to nematode
    - Retinitis Pigmentosa Like:
      - Optic nerve, retina, and RPE atrophy
- Prognosis: Poor without Treatment
- Treatment: Find and laser worm (no toxic reaction), if unable to find worm then treat with oral albendazole 400mg QD for 30 days and and as needed IVT

DUSN
Diffuse Unilateral Subacute Neuroretinitis





Disease	Presentation	White dot description	Other findings
Multiple evanescent white dot syndrome (MEWDS)	• Young females most common • Usually unilateral • Decreased vision, scotomata photopsias • Prodromal flu-like illness	• Numerous small white spots throughout mid peripheral retina • Orange specks at fovea	• Mild vitreous cells • Hypofluorescence on fluorescein angiography • Decreased a wave on ERG • Most patients obtain full recovery
Punctate inner choroiditis (PIC)	• Healthy young women • Bilateral • Decreased vision, scotomata, photopsia	• Mid peripheral/posterior pole spots at RPE and choroid • Serous detachment over lesions	• No anterior or posterior cells • Early hyperfluorescence with leakage on fluorescein angiography • Most patients recover but 33% can develop CNV
Acute multifocal placoid pigment epitheliopathy (AMPPE)	• Young male OR female patients most common • Prodromal flu-like illness common • Bilateral	• Large yellow placoid lesions throughout posterior pole in both retinas	• Mild anterior and posterior cells • Early hypofluorescence with late staining on fluorescein angiography • Self limiting in 6 months • Consider cerebral vasculitis if associated neurological signs
Serpinginous choroiditis (SC)	• Rare • Older patients • No prodromal illness • Bilateral	• Peripapillary yellow/grey contiguous large placoid lesions spreading out to peripheral retina	• Poor visual prognosis • 33% develop CNV • Early hypo- and late hyperfluorescence on fluorescein angiography
Birdshot chorioretinopathy (BC)	• Bilateral • Decreased vision, floaters, photopsia, decreased colour vision	• Cream coloured rice shaped dots starting at disc then scattering throughout entire posterior pole	• Slow chronic disease • No anterior cells but persistent vitritis present • Disc staining, leakage, and CME on fluorescein angiography • HLA-A29 positive in 90% of patients
Acute zonal occult outer retinopathy (AZOOR)	• Various ages • Bilateral • Photopsias • Rapid loss of visual field	• Large, thin grey rings in peripheral retina	No anterior or posterior cells • Reduced ERG in both eyes • Central vision often remains good • Normal fluorescein angiography
Multifocal choroiditis with panuveitis (MCP)	• Women > men • Decreased vision, floaters, photopsias	• Variable sized white/grey/yellow dots, single or in clumps, in posterior pole and peripheral retina	• Variable anterior and posterior cells angiography • 33% develop CNV • Chronic and recurrent with guarded visual prognosis

	APMPPE	Birdshot Chorioretinopathy	DUSN	MEWDS	Multifocal Choroiditis with Pan Uveitis	Serpiginous Choroiditis
Age	20-50s	40-60s	Variable	20-40s	Young – possibly children	30-60s
Sex	Men=women	Women>men	Men=women	Women > Men	Women > Men	Men > Women
Laterality	Bilateral	Bilateral	Unilateral	Unilateral	Bilateral	Delayed Bilateral
Viral Illness	+/-	-	-	+/-	+/-	+/-
Onset	Abrupt	Insidious	Variable	Abrupt	Insidious	Variable
Duration	Weeks – Months	Chronic /Recurrent	Months – Years	Weeks – Months	Chronic recurrent	Months – years
Symptoms	Blurred Vision Scotomas Photopsia	Blurred Vision Floaters Difficulties with Night or Colour Vision Photopsia	Severe loss of vision following subacute loss	Blurred vision Scotomas Photopsia	Blurred Vision Floaters Scotomas Photopsia	Blurred Vision Paracentral or Central Scotomas
Vitreous Cells	Mild	Moderate	Mild	Mild	Moderate	Mild
Findings	Multifocal flat, grey/ white placoid lesions at RPE which fade. May have mild disc swelling	Multiple ill-defined cream coloured lesions at outer retina / RPE with depigmentation. Possible vascular leakage, CMO, Disc Swelling Atrophy	Disc Oedema RAPD Clusters of yellow white spots at location of worm Optic atrophy RPE Atrophy	Myopia +/- RAPD Small white dots outer retina / RPE which may coalesce Orange granular fovea Disc oedema / BS enlargement	Myopia Anterior uveitis Active yellow grey choroidal lesions which form punched out scars Possible disc oedema or CMO	Geographic zone of grey/ white discolouration or RPE in Peripapillary / macula region spreading out. Active edge with wake of atrophy
FFA	Acute - early block late stain	Normal – may have vascular leakage / CMO	Acute – early non fluorescence, late stain – possible disc staining	Early hyperfluorescence, late staining	Acute block early then late stain with window defects	Early hypofluorescence with late staining of borders
ERG/EOG	+/- abnormal EOG	Abnormal rod/cone ERG	Mod to severe unilateral reduction ERG	Abnormal ERG	Normal / subnormal ERG	Normal
Sequelae	RPE mottling / depigmentation	CMO Rare CNV	Optic atrophy Vessel attenuation RPE atrophy	Mild RPE alterations	Punched out scars CNV	RPE Mottling Scarring Loss of Choriocapillaris CNV
HLA	HLA B7 HLA DR2	A29	n/a	n/a	n/a	HLA B7
Other	? CNS Vasculitis	+/- hearing loss Vertigo	n/a	n/a	n/a	n/a
Treatment	Observation Corticosteroids	Corticosteroids Cyclosporin	Direct photocoagulation	Observation	Corticosteroids Photocoagulation Treatment of CNV	Immunosuppresion ? Antivirals Treatment of CNV
Prognosis	Good	Guarded	Poor unless worm destroyed	Very good	Poor	Guarded
Aetiology	? Viral	? Autoimmune	Nematodes	? Viral	? Viral	? Autoimmune or infection

Table 1: Differential diagnosis of more frequently occurring White dot syndromes[8]

	APMPPE	Birdshot chorioretinopathy	MEWDS
Age	Young (20-50)	Old (30-70)	Young (10-45)
Sex	M=F	F>M	F>M
Laterality	Bilateral	Bilateral	Unilateral
Systemic association	Viral prodrome HLA B7/ DR2	HLA A29 (80-98%)	Viral Prodrome
Pathogenesis	Viral	Autoimmune	Viral
Onset	Acute	Insidious	Acute
Course	Self-limiting	Chronic recurrence	Self-limiting
	Blurred vision Scotoma photopsia	Blurred vision Floaters Distorted night & colour vision	Blurred vision Scotoma Photopsia
Vitritis	Mild	Moderate	Mild
IV Morquio syndrome	Multifocal flat yellowish-white lesion at the level of RPE	Numerous creamy/white indistinctly bordered foci at level of RPE, atrophy of the optic disc	Numerous small ill-defined deep grey-white patches sparing the fovea
V or IH Scheie syndrome	Early phase: hypofluorescence, which passes into hyperfluorescence recovery	Normal, progressively grading vascular hyperfluorescence, cystoid macular oedema may appear	early hyperfluorescence of the dots with late staining
VI Maroteaux-Lamy	Good	variable	Variable

	APMPPE	Birdshot	PIC	MEWDS	MFC	GHPC	POHS
Age	Young (20–40) Rarely-children	Middle-aged (40–60)	Middle aged (myopes)	Young (20–40) myopes	Myopic (20–60)	Variable (30–60)	Middle aged
Sex	M=F	F>M	F>M	F>M	F>M	M>F	M=F
Laterality	Bilateral, asymmetric	Bilateral	Bilateral	Unilateral	Bilateral; asymmetric	Bilateral; asymmetric	Bilateral
Viral illness	+	-	+	+	+/-	-	+/-
Onset	Abrupt	Insidious	Abrupt	Abrupt	Insidious	Variable	Abrupt
Duration	Weeks–months	Chronic	Weeks–months	Weeks–months	Chronic	Chronic	Chronic
Recurrence	Rare	Recurrent	Recurrent	Rare	Recurrent	Recurrent	Rare
Vitritis	Mild	Moderate with disc edema, CME	Absent	Mild	Moderate and anterior uveitis	Mild	Absent/mild
ERG/EOG	Abnormal EOG	Abnormal ERG	Abnormal	Abnormal ERG	Abnormal ERG	Normal	Abnormal
HLA	B7, DR2	A29	-	-	-	B7	HLA-DR2 HLA-B7
Fundus - active	Multifocal, flat gray-white placoid lesions primarily-posterior pole at the level of RPE and chorio capillaries	Multiple depigmented yellow-white patches scattered throughout fundus in the post-equatorial region. These lesions radiate from optic nerve and follow larger choroidal vessels	Multiple, discrete, flat, yellow, round lesion (50–300 microns) at the level of RPE and inner choroid. Concentrated at posterior pole	Multiple small (100–200 μ), round, slightly indistinct, white/yellow-white spots distributed over posterior fundus, especially at perifoveal and peripapillary regions at the level of RPE	Multiple yellow or gray lesions at the level of choroid and RPE. Mid periphery (50–100 μ)	Macular, peripapillary or ampigenous -irregular, gray-white or cream-yellow subretinal infiltrates at the level of the chorio-capillaries and RPE -snake-like pattern	Peripapillary atrophy, atrophic chorioretinal lesions, CNV, punched out yellow lesions Linear streaks-midperiphery
Fundus-healed	RPE clumping and hyper-pigmentation	Lesions have a hyperpigmented edge but are frequently hypopigmented in the center		Heals rarely by scarring	Punched-out atrophic scars that develop pigmentation over time	Heals from center towards periphery	Scars
Pathogenesis	DTH	Auto immune	-	?Hormonal	-	Idiopathic/ ?infective	-

Wks–Weeks, DTH–Delayed type of hypersensitivity

TABLE 7: Summary of gathered data

Disease	Average age (years)	Gender analysis (% women)
BCR	53.5	F > M (58%)
APMPPE	27.1	M > F (46%)
MEWDS	28.7	F > M (74%)
MFC	39.2	F > M (75%)
PIC	33.1	F > M (85%)
AZOOR	38	F > M (79%)

BCR: birdshot chorioretinopathy, APMPPE: acute posterior multifocal placoid pigment epitheliopathy, MEWDS: multiple evanescent white dot syndrome, MFC: multifocal choroiditis and panuveitis, PIC: punctate inner

Summary of white-dot chorioretinal inflammatory syndromes

	Acute posterior multifocal placoid pigment epitheliopathy	Multifocal evanescent white-dot syndrome	Birdshot chorioretinopathy	Multifocal choroiditis with panuveitis	Punctate inner choroidopathy
Unilateral or bilateral	Bilateral	Asymmetric	Bilateral	Bilateral	Variable
FFA	Early hypofluores-cence; late hyperfluorescence	Early hyperfluores-cence of lesions; disc hyperfluorescence	Subtle stain of lesions; disc stain	Early block; late stain; CME	Early hyperfluores-cence of lesions
ICG-V	Hypofluorescent lesions	Multiple hypofluores-cent lesions	Hypofluorescent lesions	Hypofluorescent lesions	Hypofluorescent lesions
Choroidal neovascularization	Rarely	Rarely	Rarely	Yes	Yes

Source: Arevalo JF