Clinical Decisions in Retina

(Random Thoughts of a Cluttered Mind)

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Mark Dunbar: Disclosure

- Optometry Consultant and Advisory Board for:
  - Allergan
  - Carl Zeiss
  - Regeneron
  - Genentech

Mark Dunbar does not own stock in any of the above companies

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From the second a patient walks in the door we are faced with making clinical decisions and ultimately solving problems

- **Arise from the chief complaint**
- **Or identified through the course of the exam**

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The Clinical Decisions

- Why is their vision blurry?
- Are the cataracts responsible for their 20/40 Va?
- Do we need to increase the minus or increase the add?
- Why do they have sandy, burning eyes?
- Do they have diabetic retinopathy?
- Is this ON glaucomatous?
- Is this ON swollen?

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Paying attention to the key fundamentals of the eye exam

- Good case history
  - Ocular and medical
- Detailed and organized exam addressing the key elements
  - Skipping any steps can result in missing a key finding
  - Use technology as an adjunct to the exam
    - But do NOT substitute technology for doing the exam
- Make sure the clinical findings explain and fit the "Assessment/Plan"

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55 yo Caucasian Male

- **Presents with sudden onset of floaters RE**
  - "Feels like I am looking through an oil slick or water"
- BCVA: 20/20 each eye
- CVF: FTFC OU
- Dilated patient with 1% Tropicamide, 2½% Neo
- Examines with 90 D and peripheral retina with BIO and 20 D lens
- Notes Weiss Ring and attached retina

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55 yo Caucasian Male

- Diagnosis: PVD
- Educated regarding signs and symptoms of retinal detachment
- Explains need to **return immediately** if he should see these symptoms
- RTC 1 yr

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Clinical Decisions…

- Did the OD manage this patient correctly?
- Was there anything else they **should have** done?

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Clinical Decisions…

- Was he obligated to do scleral depression?
- Should he have referred this patient to a retinal specialist?

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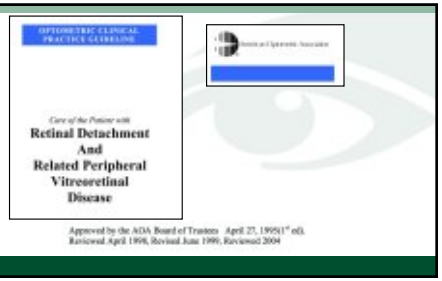
OPTOMETRIC CLINICAL PRACTICE GUIDELINE

Care of the Patient with

Retinal Detachment And Related Peripheral Vitreoretinal Disease

Approved by the AOA Board of Trustees April 27, 1995(1st ed).
Reviewed April 1998, Revised June 1999, Reviewed 2004

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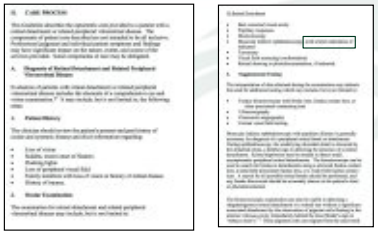

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the detached retina, a helpful sign in detecting the presence of a retinal detachment. Scleral depression may be needed to detect small, asymptomatic peripheral retinal detachments. The biomicroscope can be used to search for breaks in detachments using a mirrored fundus contact lens, a hand-held precorneal fundus lens, or a wide-field fundus contact lens. A search for all possible retinal breaks should be performed, and

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65 yo Caucasian Male PVD

The rest of the story…

- Patient return about 5 weeks later complaining he can't see out of his right eye for th past 4 days
- Has a macula-off RD
- RD repaired but VA 20/200

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Anatomy of a Malpractice Suite

- Professional care rendered must be below the generally accepted standard of care.
- The patient must suffer a loss.
  - Visual
  - Emotional
  - Financial.
- A connection must exist between what the clinician failed to do and the subsequent loss suffered.

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Avoiding Malpractice Suites

- You have to be able to explain why the vision is not 20/20
  - Amblyopia is a diagnosis of exclusion
- When in doubt do an automated visual field
- IOP should be done on all visits
- Make sure patients understand how to take care of their contact lenses

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PVD

- 65% of individuals > 65 have PVD
- More common in women
- More common following intraocular surgery
- More common following inflammation
- More common in aphakes

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PVD

- Retinal tears occur **8-15%** of eyes with symptomatic PVD
  - 90% are superior
- VH occurs in **13-19%** of symptomatic PVD's
- **VH + PVD -> 70% will have a retinal break**
- PVD No VH -> 2-4% will have retinal break

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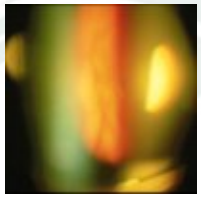
PVD – Weiss ring



Courtesy of Leo Semes, OD

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Exam of a Pt with Symptomatic PVD

- Should have a high suspicion of detecting Weis ring
- Should have a high index of suspicion of a possible retinal break
- Clinical exam should be conducted with these suspicions

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Clinical Exam of a Patient with A Symptomatic PVD

- All the testing and procedures that you would normally do with any patient
- Dilated fundus exam
- Look specifically at the anterior vitreous
  - Note presence or absence of pigment or cells in the anterior vitreous -> tobacco dust, schafer's sign
- Peripheral extended ophthalmoscopy including scleral depression

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Symptoms of Flashes… PVD NOT Seen

What is your management?

Return with in 3-4 weeks

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Symptoms of Flashes… PVD is Seen

What is your management?

Do you bring him back for follow up?

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Management of Acute PVD

With Symptoms

- Educate about the Si/Sx of RD
- Return in 4-6 weeks, then 3-4 months, then annually

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What is the time frame that she needs to be treated before it affects the final visual outcome?

A. Within 24 hours
B. Within 3 days
C. Within 7 days
D. Within 14 days

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Predictive Factors for Poor Visual Outcome

- Initial presenting visual acuity – worse visual acuity
- Duration of the macular detachment
  - Longer the mac-off RD -> worse the visual outcome
- Height of the retinal detachment

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Timing of Macula-Off RD Surgery

- Best visual outcomes are when the surgery is performed within 7 days of the macular detachment
- Meta-analysis have shown that a delay of more than 3 days was associated with statistically worse final visual outcome
  - Eyes that had surgery within 3 days averaged a final visual acuity of around 20/30
  - Eyes that were operated between 4-7 days averaged a final visual acuity of around 20/70.

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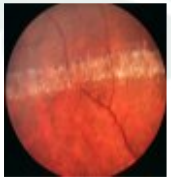
Lattice Degeneration as a Routine Finding?

Is this any cause for concern?

How do you manage it?



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Lattice Degeneration

- Present 5-20% of the general population
- Localized area of retinal thinning associated with a fluid pocket in the overlying cortical vitreous

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Lattice Degeneration and Risk of RD

- RD develop in 0.7% of eyes with lattice degeneration followed for 10.8 yrs
- Eyes with lattice that developed tractional retinal tears
  - 40% occurred in areas not associated with lattice…normal-appearing retina

Byer NE. Ophthalmology. 1989; 96:1401-1402

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Indications for Prophylactic Treatment of Peripheral Retinal Tears and Holes in Symptomatic Patients

	Treat
• Horseshoe tears	Yes
• Operculated holes	Rarely
• Atrophic holes	No

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Examining the Retina

The peripheral retina

- It has to be done through a dilated pupil
- Don't substitute imaging for indirect ophthalmoscopy
  - Use Imaging as a compliment, but not substitute
- Be systematic in your examination
- You should be able to see ora on "all" gazes

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How About This One…

- 37 y/o Hispanic female presented with a recent onset of blurred vision OU **X 1 mo – 3 episodes**
- Currently taking Rifampin, Ethambutol, Clarithromycin **5 mo** prior for MAC (Mycobacterium avium complex)
  - **PCP recommended eye exam when starting meds**
- VA: 20/20 RE; 20/25 – corrects to 20/20 LE
  - Very low hyperopic correction (+0.25)
- CVF: FTFC OU, Pupils: Normal
- **Normal fundus exam**

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37 y/o Hispanic Female

- OD recommends patient get glasses

"Present meds do not document any visual problems."

(No return appointment given)

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How Did the OD Do?

- Is there anything else he/she should have done?

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The Rest of the History

Returns to the OD 7 months later

- Patient continues to have progressive painless loss of vision (PPLOV) – she says for 2 months
- **VA: 20/160 RE; 20/300 LE**
- Color vision – "normal"
- Optometrists thinks there is diabetic macular edema (Patient not diabetic)
  - Orders diabetes work up – comes back as (-)
  - RTC 1 week

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37 y/o Hispanic Female

- OD sends patient to retinal specialist
- Ret specialist can't find anything but suspects Ethambutolol toxicity
- Refers to Neuroophthalmologist
- Diagnosis is confirmed

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What Do You Think?

- Was the OD negligent at the time of the initial exam?
  - Never did a visual field
  - Color vision not recorded but the Dr. claims he did it
- Was he obligated to do any of these things?

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What Do You Think?

- Was he even aware of the ocular side-effects of this drug?
- Just because you can't see any ocular problems doesn't mean it's not there….

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Ethambutol Toxic Neuropathy

- 1st described by Leibold in the 1960's
- Dose dependent
- Risk is 6-18% for pts with dose > 30 mg/kg/day (18% at 35 mg/kg/day)
- Develops in 1-3% at dose 15-25 mg/kg/day

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Anti-tuberculosis drugs

Ethambutol HCL (Myambutol),
Isoniazid (Laniazid)
Rifampin (Rimactane)

Chelates copper, so the decreased levels impair mitochondrial activity of axonal transport in optic nerve leading to optic neuropathy

Ocular side effects

- Optic neuritis/neuropathy and blindness.
- Change tears, sweat, saliva, urine, feces and contact lenses a red-orange color.

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Ethambutol

- TB regimens begin at either **50 mg/kg/day** (maximum 4 grams) for 2 weeks or **25-30 mg/kg/day (maximum 2 grams) for 3 weeks**, and then maintained at 15-20 mg/kg/day (max 2 grams)
- For MAC regimens the maintenance dose is 15 mg/kg/day (maximum 2.5 grams).
  - Depending on the species of mycobacteria pts, may be treated with a loading dose of 25 mg/kg/day for the first two months of therapy (Mandell et al., 2005; Micromedex 2007).

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Anti-tuberculosis drugs

- Ophthalmic examinations are recommended by the PDR **every month** for doses of ethambutol greater than 15mg/kg/day.
- No official standard of care exists in dosages less than 15 mg/kg/day.
- Optic neuropathy can occur at any dose despite regular ophthalmic exams: **vision loss can be severe and irreversible**.
- Obtain a baseline exam to include a visual field test, color vision test, dilated fundus and optic nerve exam, and visual acuity.
- If any visual symptoms occur, patients should discontinue the medication and see an ophthalmologist.

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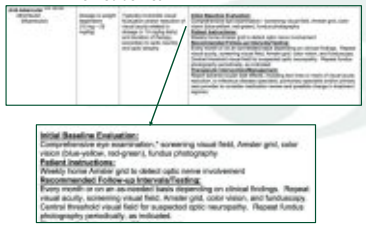
AOA Guidelines



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What are your/our obligations in deciding if certain medications that a patient is taking are affecting the patient's vision?

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Systemic Interactions

- At least **76 classes** of systemic drugs have been associated with ocular side effects
- Drug can interact with and disrupt any step of the biochemical process resulting in negative effects to the ocular tissues
- Drugs may incite an **exaggerated immune** response within the eye
  - Uveitis or retinitis
- Solidified form of the medication may **deposition** in the tissue

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Systemic Interactions

- Medications may cause **alteration of the pigment**
  - Plaquenil -> Bull's eye maculopathy
- **Pharmacologic toxicity** can occur leading to cell death and loss of function
  - Can affect the optic nerve
- **Patient variability** may influence and cause unexpected effects
  - Pharmaceutical studies provide statistical evidence supporting appropriate dosage for meds, however individual variation can result in unexpected results

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51 y/o White Female

- 1st presented to OD practice 11/24/09 with blurred vision distance and near
  - Also typical dry eye symptoms
- Was noted to be on plaquenil 100 mg bid
- **BCVA: 20/40** each eye with myopic correction
  - (~ -2.50)
- Color Vision: 3/5
- CVF: FTFC OU – screening perimetry done
- Fundus: Normal, screening photo done

Patient Refused Dilation…

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51 y/o White Female

Impression

- Dry eye
- Myopia, astigmatism, presbyopia
- Amblyopia, unspecified
- Long-term use of hgh risk medication (plauquenil)
- RTC 1 yr

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51 yo Patient on Plaquenil

- The patient was seen almost yearly over a **3 ½ year period**
  - A few times she came in early because she felt like glasses were not correct – or just not seeing well
- It is really not clear why VA was 20/40
- Was never dilated
- Never had an OCT
- Never had a visual field

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11/29/10

Impression

- Amblyopia (368.0)
- Long-Term use of high risk medication Plaquenil (V58.69)
- Dry eye (375.15)

Plan

- Pt counseled on the importance of monitoring as directed. Advised to wear sun protection out doors, **consider OCT at next exam with DFE**
- **RTC 1 year**

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6/14/2012

Impression/Plan

- Patient counseled on importance of monitoring as directed
- Advised to wear sun correction
- Consider OCT at next exam with DFE
- …Glasses given, dry eye treated
- RTC 1 year

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5/23/2013

- See's other OD in community
  - VA: 20/30 OU
- Orders VF for the next week – 6/10/2013
  - Patient returns as directed

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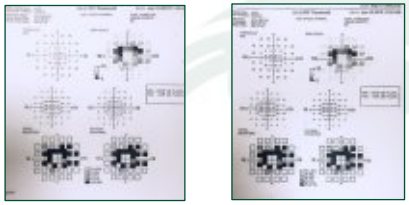

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What Went Wrong?

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What are your obligations for managing a patient on plaquenil?

- What is the risk of having ocular problems from plaquenil?
- What testing is necessary?
- How often do you need to follow her?

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Is there Fluid?

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Clinical Decision in AMD:

Is there fluid?
What level of AMD is this?
When should I start a supplement?
(Zinc, low Zinc, no Zinc)

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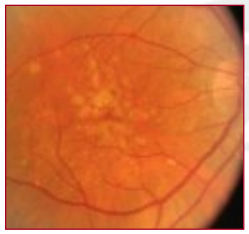

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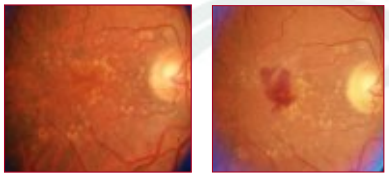
Drusen: Increased Risk of CNV



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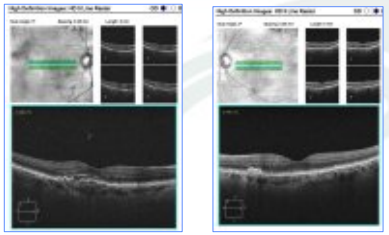

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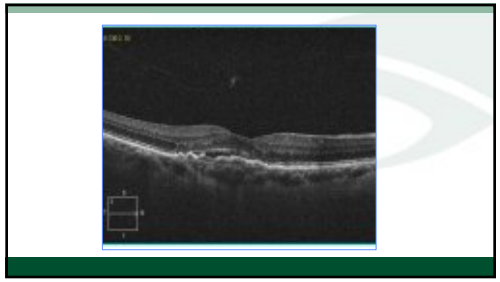

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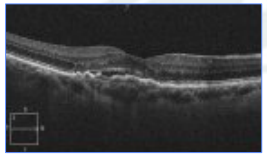
Is there fluid?

- Without an OCT it can be a very difficult question to answer



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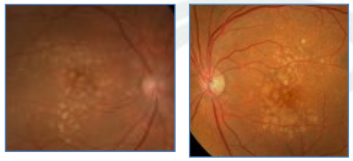
Olga: 80 y/o Hispanic Female



20/20 each eye

After Cataract Surgery

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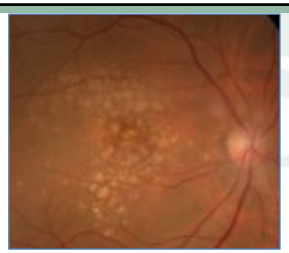

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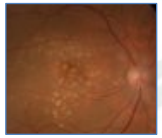

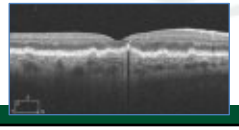

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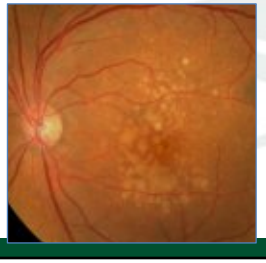

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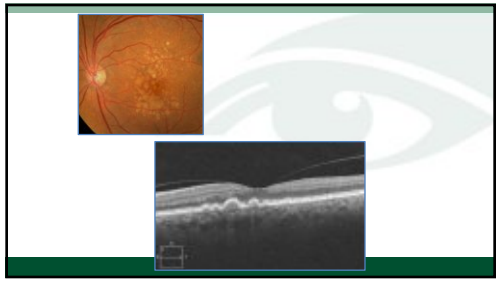

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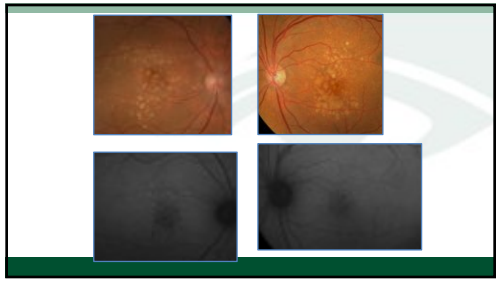

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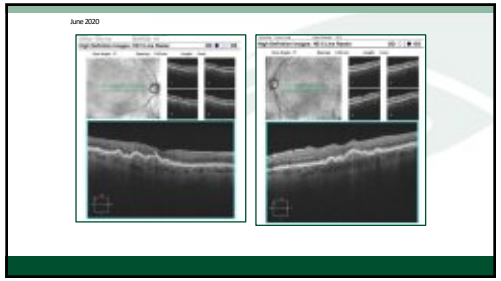

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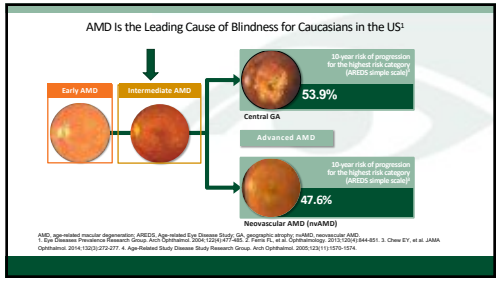

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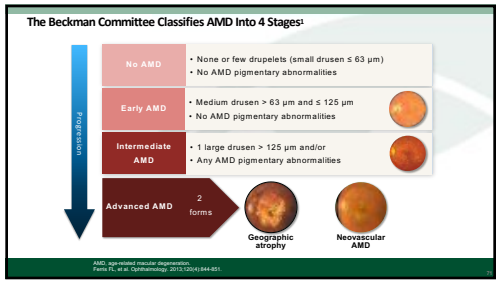

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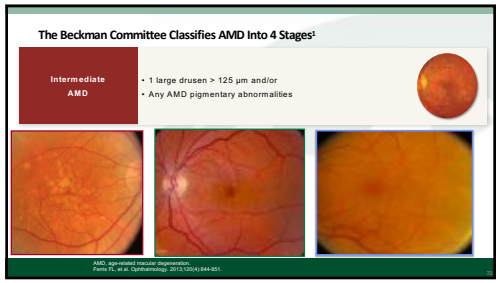

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Home Monitoring of AMD

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ForeseeHome®

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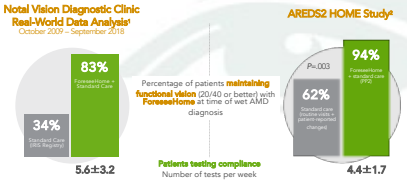
ForeseeHome helps physicians detect wet AMD earlier: Real-world performance resembles pivotal trial results



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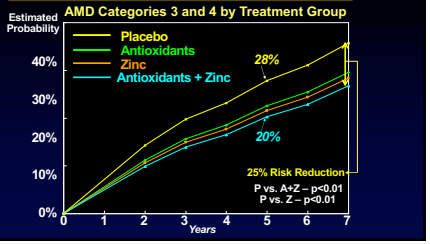
Rates to Advanced AMD



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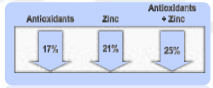
AREDS

- AREDS 1 constituents:
  - 500 mg vitamin C
  - 400 IU vitamin E
  - 15 mg beta-carotene (25,000 IU)
  - 80 mg zinc
  - 2 mg copper



- 25% decrease risk reduction in developing advanced AMD (groups 3 and 4) with antioxidants plus zinc

Age-Related Eye Disease Study Research Group. Report No. 8. *Arch Ophthalmol*. 2001;119(10):1417–1436.

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AREDS Results
Arch of Ophthalmol Oct 2001

- AREDS was unable to determine potential treatment benefits among early AMD pts
  - Slow progressive trend
  - Not likely to progress to an advance stage of AMD
  - These groups make up a large number of our pts

http://www.nei.nih.gov/amd/

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AREDS Results

Arch of Ophthalmol Oct 2001

- 592 Developed CNV, 257 developed geographic atrophy
- Group 1: Early AMD (1063 Pts)
  - Only **15 progressed over 5 yrs** due to CNV or geographic atrophy: **1.3% probability**
    Projected 50
- Group 2 and group 3: 834 total developed CNV

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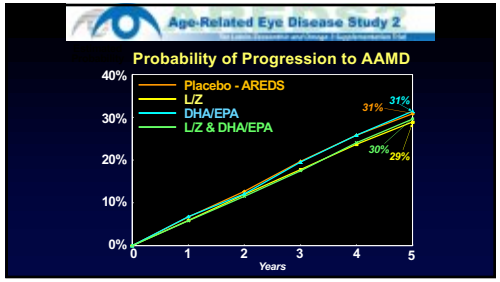

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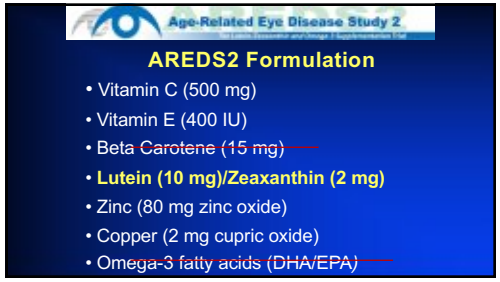

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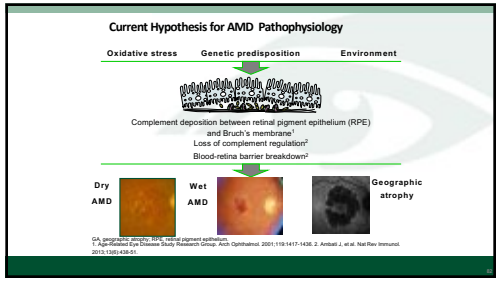

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What is the Relationship between Genetics, AMD and AREDS Supplement?

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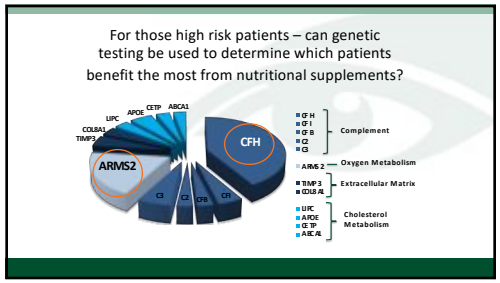

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Genetic Testing for AMD

- Artic Dx is the only commercially available genetic test for identifying high-risk AMD patients
- For those high risk patients – can genetic testing be used to determine which patients benefit the most from nutritional supplements?
- No **prospective** clinical trials showing the value
  - There are retrospective studies but the data analysis varies

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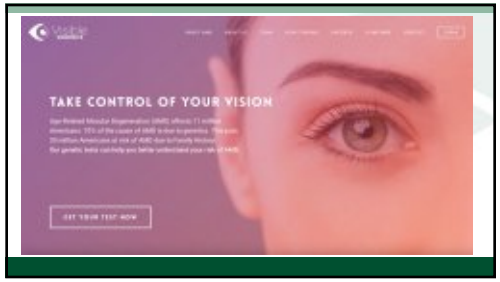

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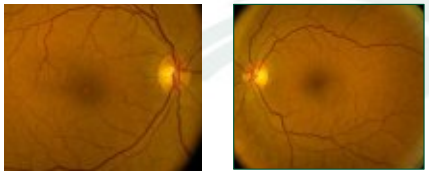
87

Why Isn't My Patient Seeing Better…?

88

66 yo Hispanic Female: Intermittent episodes of stabbing pain in the RE related to computer use



20/80 20/25

89

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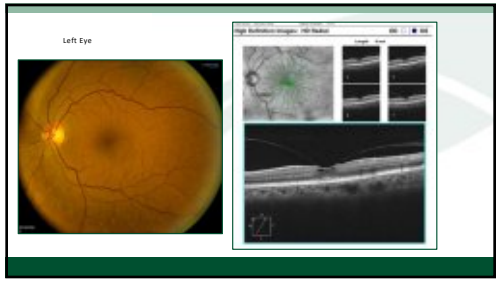

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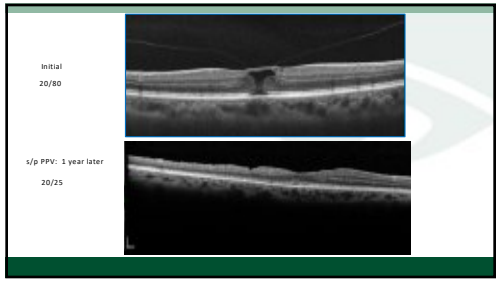

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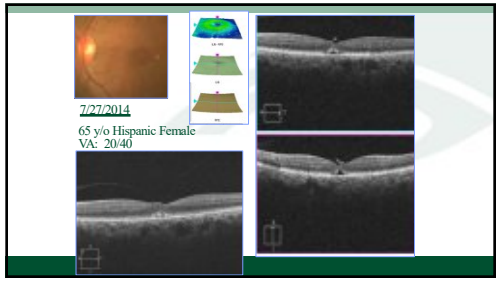

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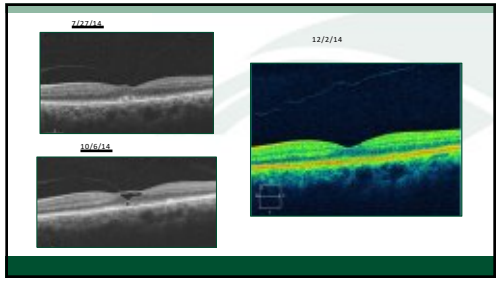


94

What is the OD's Role in Managing Patients with ERM?

- Immediate referral
- Follow for resolution

- When do these patients get treated?

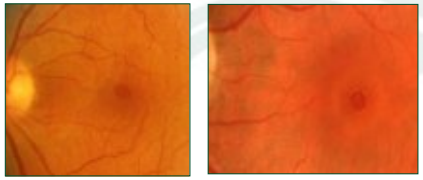
95

Managing ERM

- Determine how symptomatic
- The presence of **metamorophsia, distortion** is a good gauge for determining when to refer for consideration of vitrectomy
- OCT very helpful in quantifying the amount of retinal thickening
  - The presence of CME

96

When is a Hole a Hole?

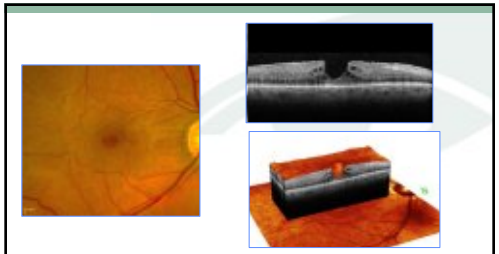


97

Differential diagnosis of Full Thickness Macular Hole

- ERM with pseudo hole
- Lamellar hole
- Solar maculopathy

98



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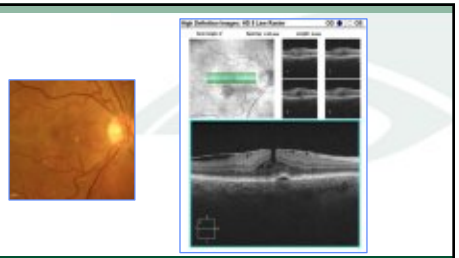
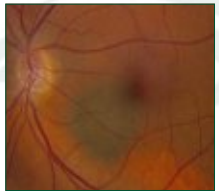


100

48 y/o Asymptomatic Pilot

- No Sx
- VA 20/15 OU
- Anterior Segment: Unremarkable
- Fundus



101

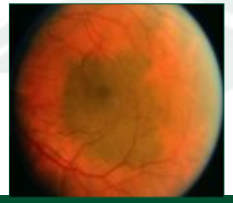
48 y/o Pilot

- No Sx
- VA 20/15 OU
- Anterior Segment: Unremarkable
- Fundus

102

48 y/o Asymptomatic Pilot

- VA 20/15 OU
- Anterior Segment: Unremarkable
- Fundus



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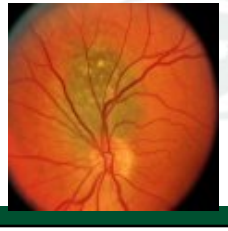
48 y/o Asymptomatic Pilot



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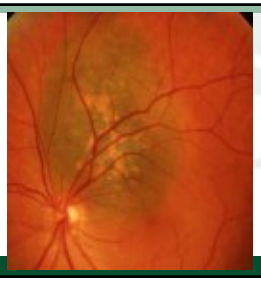
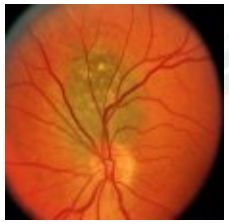
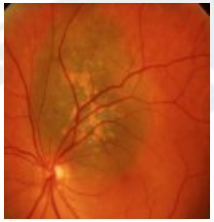


105

What is Correct Diagnosis?

1. Choroidal nevus
2. Choroidal melanoma
3. Melanocytoma
4. I don't really care, I am going to refer it regardless of what the diagnosis is?

106

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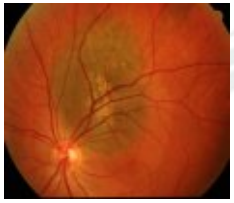
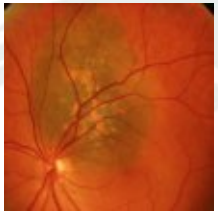
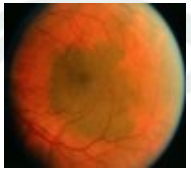



Growth over 7 ½ months

108

Choroidal Nevi

- < 3 mm elevation
- < 3 DD in size
  - 95% are less than 2 DD
- Slate gray
- Drusen
- SRF associated with drusen
- CNVM



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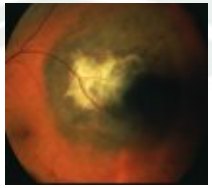
Features Suggesting Nevi

- Drusen
- Overlying neurosensory detachment
- Choroidal neovascular membrane
- Circinate exudate
- Bony pigment spiculing
- Zones of RPE atrophy



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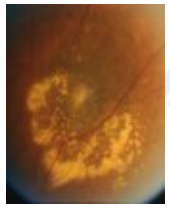

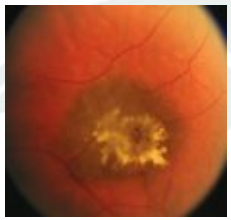

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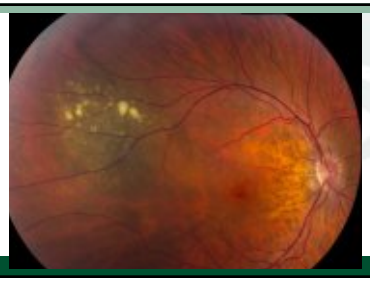

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Choroidal Melanoma

- >3 mm elevation
- Variable pigment
- Multiple areas of orange pigment (lipofuscin)
- Serous fluid (detachment) in absence of drusen
- **Unequivocal evidence of growth**

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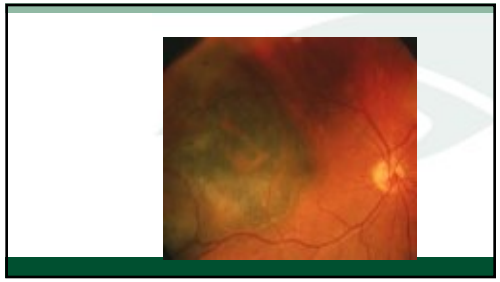

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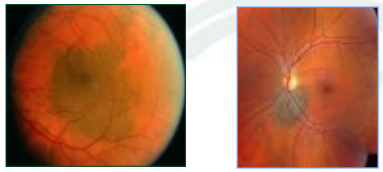
Do Choroidal Melanoma's Develop from Pre-Existing Choroidal Nevus



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Long term ultrasonic follow up of choroidal nevi and their transformation to melanomas

Br J Ophthalmol 2006;**90**:8 994-998 Published Online

- 659 consecutive eyes with choroidal nevi examined between 1984 and 2004
  - 165 clinically suspicious nevi were followed clinically w ultrasound
- 17 choroidal nevi (2.6% of all nevi, 10.3% of suspicious nevi) converted to small choroidal melanoma
- 1.5 years of follow up were necessary to statistically distinguish between premalignant and benign nevi
- **No nevus smaller than 1 mm thickness converted to melanoma**
- A thickness of ≥2 mm and a LBD ≥7 mm were most predictive of conversion to melanoma

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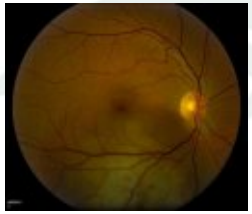
37 y/o Middle Eastern American Radiologist

Presented on Monday for a refraction

Blurry vision OU



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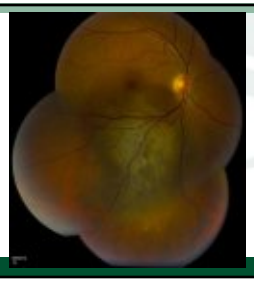

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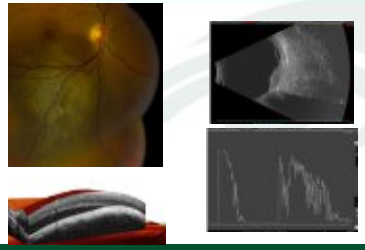
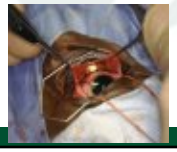


120

Plaque Radiation (Ionizing Radiation)

- Iodine-125
- Seeds of radioactive material implanted into a plaque
- Sewn onto the globe and left on for 3 d
- Dosage: 8-10 rads reach apex, 40-50,000 reach the base



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COMS Results: Small Tumors

- 204 patients with small choroidal melanomas
- 8% were immediately treated at the time of diagnosis
- 33% were treated during the follow-up
- 6 deaths due to metastatic melanoma
- Small choroidal have a low 5 yr mortality

COMS report no. 4. The Collaborative Ocular Melanoma Study Group. Arch Ophthalmol. 1997 Jul;115(7):886-93.

122

COMS Results: Medium Tumors

- Enucleation vs I_{125} Brachytherapy
- 1317 Enrolled: 660 Enucleation 657 plaque
- 1072 (91%) followed for 5 yrs
  - 416 (32%) 10 yrs
- **364 patients died:**
  - 188 Enuc (28%); 176 (27%) Plaque

Arch of Ophthalmol July 2001 119(7):969-982

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COMS Results: Medium Tumors

- Unadjusted 5 yr survival: 81% vs 82%
- 5 year **adjusted rate of death** from metastatic melanoma:
  - **11% Enucleation**
  - **9% Plaque**
- Conclusion: Mortality rates do not statistically differ b/w the 2 treatments for up to 12 years

Arch of Ophthalmol July 2001 119(7):969-982

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Large Choroidal Melanomas

Pre-enucleation Radiation vs Enucleation

- Randomization 11/86 to 12/94: 1003 Pts enrolled
  - 506 Enucleation alone vs 497 Pre-enucleation Radiation
  - 5-year outcome known for 80%
- 5 Year survival
  - 57% Enucleation alone vs 62% Pre-Enuc Radadiation
    - Includes all causes of death

Initial Mortality, COMS Report # 10 AJO June 1998

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Large Choroidal Melanomas COMS Report # 10

Pre-enucleation Radiation vs Enucleation

- Total 435 deaths classified by Mortality Coding Committee
  - 269 had histologically confirmed melanoma metastases (166 died from other causes)
- **5 yr survival = 72% Enuc vs 74% PERT**
  - No statistical survival difference b/w 2 groups

Initial Mortality, COMS Report # 10 AJO June 1998

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Assessment of Metastatic Death: Large Tumors

- 1003 enrolled in trial
- 457 deaths – disease status avail on 435
  - Median survival from time of enrollment 7.4 yrs
- 361/435 **(83%) confirmed death metastatisis**
  - 62% Histopathologic confirmed, 21% suspected
- **93% Liver, 24% lung, 16% bone**

Arch of Ophthalmol May 2001 119(5):670

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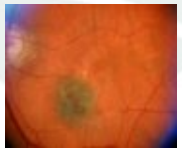
Management

- Flat choroidal nevi: follow yearly
- Suspicious nevi:
  - photo
  - follow in 6 wks, 3 mo, then 6 mo
  - evidence of growth -> early melanoma
- Lesions > 3 mm thickness: probably early melanoma



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Molecular Genetics of Ocular Melanomas

- Discoveries in molecular genetics have established that there are 2 classes of tumors with distinct molecular signatures
- Class 1 -> carries a low risk of metastasis - less than 10%.
- Class 2 -> greater than 90% chance of spreading to the liver.

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Molecular Genetics of Ocular Melanomas

- Via fine needle biopsy transcriptomic profiling can be done which can accurately predict which tumors will likely go on to develop metastic disease and which won't…
- This risk may be independent of what type of treatment that patient may have had

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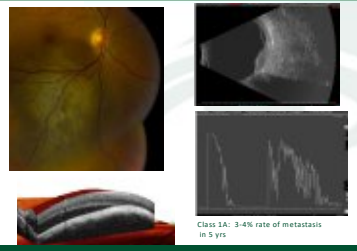

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