

Ask the "experts": retina edition

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- Professor, SCCO@MBKU
- Mark Dunbar, OD, FAOD
- Bascom Palmer
- Mary Beth Yackey, OD
- Cincinnati Eye center

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Disclosures: ferrucci

- I serve on the speaker bureau or advisory board for the following companies
 - Apellis
 - Astellas
 - B&L
 - I-care
 - LENZ Therapeutics
 - LKC Technologies
 - Notal Vision
 - Science Based Health
 - Visible Genomics
- All relevant relationships have been mitigated

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Disclosures : Dunbar

- | | |
|--------------|------------------|
| • Orasis | • Thea |
| • Tarsus | • Glaukos |
| • Astellas | • Sight sciences |
| • Sun pharma | • B&I |
| • Visus | • Azura |
| • Topcon | • Sydnexis |
| • apellis | • Cloudbreak |
| | • tenpoint |

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Disclosures: Yackey

- | | |
|----------------|-------------------|
| • Apellis | • Orasis/Qlosi |
| • Astellas | • RgenexBio |
| • Glaukos | • Reliance |
| • Haag Streit | • Tarsus |
| • Notal vision | • Topcon |
| • Ocuterra | • Visible genomic |
| | • zeiss |

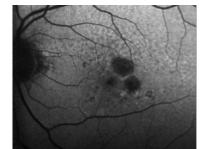
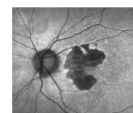
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WHEN WOULD YOU REFER A GA PT?

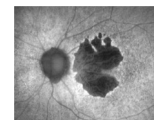
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When to Refer?

- GA that is **threatening** central visual function
- GA that is approaching the fovea
- Large extrafoveal lesions
- PROGRESSION OVER TIME!!!



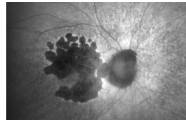
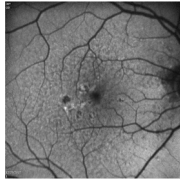
Progression to subfoveal
involvement 18 mo



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When NOT to Refer?

- Extrafoveal lesions that are not a threat to central VA
- Central GA lesions that have already have sig loss of visual function?



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HOW SOON DOES A WET AMD PT NEED TO BE SEEN BY RS?

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Importance of Early Treatment: CNV Lesion Size

- Evidence from many trials is clear: smaller lesions respond better to treatment
- MARINA study¹: larger CNV lesion size at baseline was associated with greater loss of letters in sham-treatment group and less gain of letters in ranibizumab-treated arms
- ANCHOR study²: smaller baseline CNVM lesion size was associated with greater gain of letters in those receiving ranibizumab
- CATT trial³: larger area of CNVM at baseline was associated with worse VA at 1 year, less gain in VA at 1 year, and lower proportion of patients gaining ≥ 3 lines of acuity

1. Royer GS, et al. Ophthalmology 2007;114:2040-2052. 2. Kaiser PM, et al. Am J Ophthalmol 2007;144:850-857. 3. Ying GS, et al. Ophthalmology 2011;120:122-129.

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Importance of Early Treatment: 2020 Analysis of IRIS Registry

- Real-world patients with neovascular AMD who underwent anti-VEGF treatment
- Study included 162,902 eyes
- Results
 - Patients who presented with VA of 20/40 or better at diagnosis maintained mean VA of 20/40 or better for 2 years after initiating treatment
 - Those who presented with VA worse than 20/40 never reached 20/40 at 1 or 2 years
- Conclusion: baseline VA at diagnosis of wet AMD predicts long-term VA outcomes

Early diagnosis before VA is adversely affected is a key factor in preserving vision in patients with wet AMD

Hu AC, et al. Ophthalmic Surg Laser Imaging Retina. 2020;51:639-649.

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When Should Patients Be Referred to Retinal Specialist to Consider Treatment?

- Any change in vision or metamorphopsia in patients with AMD should be taken seriously
 - Assume “wet” AMD until proven otherwise
- Unless able to determine no fluid/CNVM, patient should be referred to retinal specialist
- Any patient with “wet” AMD deserves prompt referral to retinal specialist for consideration of treatment
 - Data show patients exhibiting CNVM do better with early detection and prompt treatment!¹

1. Kaiser PM, et al. Clin Ophthalmol 2013;8:203-208.

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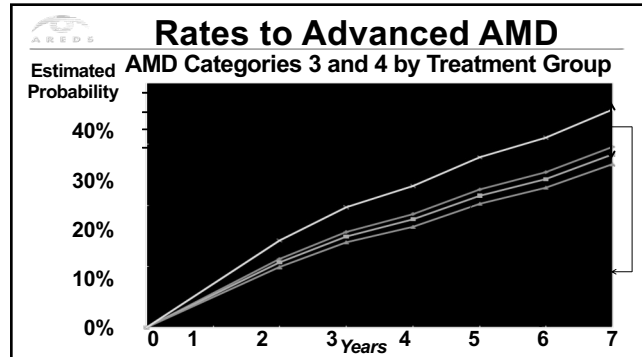
DO YOU BELIEVE IN AREDS SUPPLEMENTATION?

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AREDS

- First large-scale study looking at nutrition and ocular health
- 3640 pts followed on average for 6.3 years
 - Results released October 2001
- Results showed that 25% risk reduction to developing advanced AMD in pts with intermediate (stage 3) AMD or worse
 - 500 mg vitamin C
 - 400 IU vitamin E
 - 15 mg vitamin A (25,000 IU beta carotene)
 - 80 mg zinc
 - 2 mg copper

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AREDS: Shortfalls

- No apparent benefit in category 1 and 2
 - 80% fall into this group
- Unsure how long someone at risk should continue supplements
- Beta carotene associated with increased risk of lung cancer in smokers
 - substitution of other antioxidants (lutein) was unclear
 - how long a non-smoker was debatable

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AREDS: Shortfalls

- Did not evaluate the role of lutein/zeaxanthin, or omega 3's
- Benefit is modest, and all groups had progression despite treatment
- “The supplements are not a cure for ARMD, nor will they restore vision already lost from the disease”
 - AREDS press release 10/2001

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AREDS 2

- AREDS 2: Enrollment ended June 2008 with ≈4200 patients followed for six years
 - Effect of lutein, zeaxanthin and omega 3 on AMD
 - Effect of eliminating beta carotene on AMD
 - Effect of reducing zinc on AMD
 - Effect of supplements on cataracts
 - Validate the AMD scale from original AREDS
- Results released May 5, 2013

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JAMA The JAMA Network

ORIGINAL CONTRIBUTION

Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration: The Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial

Abstract

Background The Age-Related Eye Disease Study 2 (AREDS2) was a randomized clinical trial designed to evaluate the effects of lutein, zeaxanthin, and omega-3 fatty acids on the progression of age-related macular degeneration (AMD) in patients with intermediate or advanced AMD. The study also evaluated the effects of eliminating beta carotene and reducing zinc on AMD progression.

Design, Setting, and Participants The study was a randomized clinical trial conducted in the United States. Participants were enrolled between June 2008 and June 2011. The study included 4200 patients with intermediate or advanced AMD.

Interventions The study compared four treatment groups: 1) Lutein + Zeaxanthin + Omega-3 Fatty Acids; 2) Lutein + Zeaxanthin; 3) Omega-3 Fatty Acids; and 4) Placebo.

Main Results and Conclusions The study found that the combination of lutein, zeaxanthin, and omega-3 fatty acids significantly reduced the risk of progression to advanced AMD compared to the placebo group. The study also found that eliminating beta carotene and reducing zinc had no significant effect on AMD progression.

Published online May 5, 2013

Available at
www.jama.com

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AREDS 2

■ Major Conclusions:

- The addition of lutein and zeaxanthin, DHA and EPA or both to the AREDS formulation did not further reduce the risk of progression to advanced AMD
- Substituting L/Z (10 mg/2 mg) for beta carotene is an appropriate substitution, because of potential increased incidence of lung cancer in former smokers

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Additional findings

- Lutein and zeaxanthin did provide an additional 10% reduced risk over current supplements
 - In patients with lowest dietary intake of l/z, additional 26% reduced risk
- Decreasing zinc from 80 mg to 25 mg had no significant effect
 - No change recommended (?)
 - Deserves further study
- No benefit for omegas 3

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AREDS2 Formulation

- Vitamin C (500 mg)
- Vitamin E (400 IU)
- ~~Beta Carotene (15 mg)~~
- **Lutein (10 mg)/Zeaxanthin (2 mg)**
- Zinc (80 mg zinc oxide)
- Copper (2 mg cupric oxide)
- ~~Omega-3 fatty acids (DHA/EPA)~~

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AREDS 10 year

Combined Arms Main Effect Progression to Late AMD – Hazard Ratio

	5 years	10 years
Lutein/Zeaxanthin	0.91 (P = 0.05)	0.91 (P = 0.03)
DHA/EPA	0.98 (P = 0.74)	1.01 (P = 0.91)
Low Zinc	1.06 (P = 0.32)	1.04 (P = 0.48)
Beta Carotene	1.07 (P = 0.31)	1.04 (P = 0.50)

• Key Takeaways:

- Using a factorial study design, combining the arms that had Lutein/Zeaxanthin to increase sample size, the addition of Lutein/Zeaxanthin provided a similar ~10% reduction in progression to late AMD
- Addition of Omega-3 FA DHA/EPA had no effect on progression
- Reduction of Zinc level had no effect on progression
- These results were sustained through 10 years

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GA and AREDS2

- New analysis in *Ophthalmology* looked at pts with late stage GA in AREDS/AREDS 2 study
- Showed that taking AREDS supplements slowed down lesion growth in non foveal GA by 55% over 3 years
 - Not as helpful for pts with central GA
- Consider recommending AREDS 2 supplementation for extra foveal GA pts
- NEWER STUDY CONTRADICTION THIS

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Vitamins: Take Home

- Use AREDS 2 type formulation in suitable patients
 - Encourage proper dosing
 - Discourage use of similar products that differ from what you want
- Pick one or two products
- Review literature and additional AREDS 2 reports
- Discuss prevention in high risk patients

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Vitamins: Take Home

- The best intake is through diet/food
 - Not always realistic:
 - Average American gets only 2mg Lutein
 - Leading antioxidants for average American is coffee
 - French fries account for 25% of all vegetable intake in US
 - Vitamin E 13x, A and C 5x recommended daily dose
- Only 3% of Americans follow 4 basic health practices
 - No smoking
 - BMI 18.5 – 25
 - 5 or more FRUITS & VEGABLES daily
 - > 30 minutes physical activity/ 5x times wk

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My thoughts...

- Discuss vitamins/nutrition and lifestyle changes with ALL AMD pts
 - Smoking, increased BMI, UV light, exercise, diet
- Decide which you feel should start vitamin therapy
- Make SPECIFIC recommendations based on your knowledge
- **DO SOMETHING!!!**

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WHEN DO YOU REFER A NEVUS?

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Nevus

- TFSOM: To Find Small Ocular Melanomas (1995)
 - T: Thickness: lesions > 2 mm
 - F: Fluid: any subretinal fluid suggestive of RD
 - S: Symptoms of photopsia or vision loss
 - O: Orange pigment overlying the lesion
 - M: Margin touching the optic nerve head
 - No factor= 3% risk of converting to melanoma in 5 yrs
 - 1 factor=8% risk
 - 2 or more factors =50% risk

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Update 2019

- Incorporates imaging and re-evaluates risk factors
- TFSOM-DIM
 - To Find Small Ocular Melanomas Doing Imaging
 - T: Thickness > 2mm (US)
 - F: Fluid, subretinal (OCT)
 - S: Symptoms of vision loss (VA)
 - O: Orange pigment (FAF)
 - M: Melanoma Hollowness (US)
 - DIM: diameter > 5 mm (photos)

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Update 2019

- M: Tumor Margin replaced with ultrasound
- S: Vision loss (VA < 20/50) rather than flashes/floaters
- Most important:
 - Thickness, Fluid, orange Pigment, Hollowness
- Least important:
 - Symptoms, Diameter

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Update 2019

- Risk of converting to melanoma over 5 years
 - 0 factors: 1 % risk
 - 1 factor: 11%
 - 2 factors: 22 %
 - 3 factors: 34%
 - 4 factors: 51%
 - 5 factors: 55%
 - 6 factors: who knows?
- Bottom line: Increasing number of risk factors imparts greater risk for transformation

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Nevus

- TFSOM: To Find Small Ocular Melanomas (1995)
 - T: Thickness: lesions > 2 mm
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 - O: Orange pigment overlying the lesion
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Gardner's Syndrome

- Multifocal CHRPE have been associated with Gardner's Syndrome
 - AKA FAP: familial adenomatous polyposis
 - Familial condition of colonic polyps that may be precursor to colon cancer
 - However, these lesions are bilateral, have more irregular borders, and are often scattered throughout the fundus

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WHEN/HOW DO YOU FOLLOW UP ON A NEW PVD?

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AAO Preferred Practice Patterns : Retina Summary Benchmarks, 2023

- Posterior Vitreous Detachment, Retinal Breaks, and Lattice Degeneration (Initial and Follow-up)
- Evaluation)
 - Ophthalmic Exam (Key elements)
 - Confrontation visual field examination
 - Visual acuity testing
 - Pupillary assessment for the presence of a relative afferent pupillary defect
 - Examination of the vitreous for hemorrhage, detachment, and pigmented cells
 - Examination of the peripheral fundus using scleral depression. The preferred method of evaluating peripheral vitreoretinal pathology is with indirect ophthalmoscopy combined with scleral depression.

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AOA Optometric Clinical Practice Guideline Retinal Detachment and Related Peripheral Vitreoretinal Diseases

April 1995, review April 1998, revised June 18999, reviewed 2004

- Ocular Examination The examination for retinal detachment and related peripheral vitreoretinal disease may include, but is not limited to:
- Best corrected visual acuity
 - Pupillary responses
 - Biomicroscopy
 - Binocular indirect ophthalmoscopy, with scleral indentation if indicated
 - Tonometry
 - Visual field screening (confrontation)
 - Retinal drawing or photodocumentation, if indicated.
 - Scleral depression may be needed to detect small, asymptomatic peripheral retinal detachments.

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Study: American
Journal of
Ophthalmology

- 50 eyes, 25 pts with symptoms of flashes floaters
- 50 eyes, 25 pts with no symptoms
 - Examination with scleral depression did not provide any additional benefit to an examination vs without in any of the 100 pts
 - Scleral depression did significantly increase pt discomfort

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DO YOU NEED TO DO A SYSTEMIC WORKUP FOR RETINAL PLAQUES? VEIN OCCLUSION? ARTERY OCCLUSION

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RVO Risk factors

- Age: most common after 65
- HTN (46%)
- Hyperlipidemia (20%)
- Diabetes (5%)
- Others: smoking, glaucoma, obesity
- Younger pts: Hypercoagulability, inflammatory disorders like lupus, contraceptives

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RVO Systemic testing

- In office BP
- Lipid profile, HGBA1c, CBC
- Maybe Refer for complete vascular workup including carotid doppler, TEE
- Might consider: Sarcoid testing, Syphilis, SLE, etc in younger pts or if suspected on exam
- Thrombolytic factors, homocysteine, antiphospholipid if needed

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RETINAL PLAQUES

- Several different types of plaques can often be visualized in the retinal vasculature
- Often totally asymptomatic and found on routine exam
- Three different types of plaques, but all share strong association to significant cardiovascular disease
 - HOLLENHORST PLAQUE (CHOLESTEROL) 80% > FIBRINO-PLATELET 14% > CALCIFIC 6%

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RISK FACTORS

- Age
- HTN
- Vascular disease
- Past vascular surgery
- SMOKING
- High TOTAL cholesterol
- Men > women

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Retinal Plaques: Work up

- Assess risk factors with PCP
 - DM, HTN, LIPID PANEL
- Carotid auscultation in clinic for bruit
- Carotid ultrasound/Duplex
 - Identifies flow rate and % stenosis OF Common, internal, and external carotid arteries
 - ORDER WITHIN TWO WEEKS!!

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Work up, cont.

- TEE: trans esophageal echocardiogram
 - invasive, probe into esophagus to image heart valves
 - Helpful with calcific
- CTA: Computed Tomographic angiography
 - CT scan of arteries construct 3D images
 - Useful for atypical /confounding findings or if surgery indicated

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treatment

- <50% stenosis: medical management with blood thinner/antihyperlipidemics
 - Aspirin, clopidogrel, warfarin, statins
- >70% stenosis: Surgical intervention
 - CEA: Carotid endarterectomy
 - Carotid angioplasty
- 50-69% stenosis: Depends on other risk factors if medical or surgical
 - ONLY 7-20% of Asymptomatic retinal plaques have significant stenosis

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Artery occlusion

- If acute, straight to ER
- **DO NOT SEND TO RS FOR CONSULT BEFORE OBTAINING STROKE WORK UP**
- Needs close follow up for NV

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WHEN DO YOU FOLLOW UP ON CSR? WHEN DO YOU REFER?

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Central Serous Retinopathy

- 80-90% of pts will undergo spontaneous resolution and return to normal (or near normal) VA within 1-6 mos.
 - >60% resolve back to 20/20
 - Rare to have vision remain < 20/40
- Approx 40% will get recurrence
- CNVM is VERY rare occurrence, but possible

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CSR

- **When to worry/refer**
 - If VA worse than 20/70
 - If pt demographics do not support
 - If does not resolve in 6 mos
 - If gets worse rather than better
 - FA/ OCT does not support diagnosis
 - “Just doesn’t feel right”
 - Pt is unable to accept vision/prognosis

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Treatment

- Observation
- PDT
- Anti-VEGF
- Anti-corticosteroids
 - Rifampin
 - Mifepristone
 - Ketoconazole
 - Spironolactone/eplerenone
 - Finasteride
- Acetazolamide
- Aspirin
- Metoprolol
- H.pylori treatment
- Methotrexate
- Behavior Modification!

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WHEN WOULD YOU REFER AN ERM??

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Epi-retinal Membrane

- AKA macular pucker, cellophane maculopathy
- Can be secondary to peripheral retinal disease, such as detachment or tear; a retinal vascular disease such as BRVO; inflammation; trauma or idiopathic
- Idiopathic tend to be more mild and non-progressive vs. those after retinal tear

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Epi-retinal Membrane

- VA can range from 20/20 to 20/200 or worse
 - Studies show > 5% have worse than 20/200
- Often metamorphopsia is only complaint with idiopathic ERM
- Fewer than 20% of cases are bilateral
- Surgical removal is considered if severe vision loss or distortion

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ERM

- Consider surgery if:
 - VA 20/40-ish or worse
 - Symptomatic
 - Visual need of patient
- Make sure you have an experienced surgeon!!

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AT WHAT STAGE DO YOU REFER A PT WITH DR TO A RETINAL SPECIALIST? HOW ABOUT DME??

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When to refer: DR

- Worse than Moderate NPDR: 2 weeks
 - Moderately severe to severe NPDR
 - 4/2/1 rule
- PDR: 1-2 weeks
- High risk PDR: 48 hrs
- However, really anytime exceeds your comfort level!
- REFER TO PCP AS NEEDED FOR A1C/HTN CONTROL

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DME

- Old definitions being replaced with newer ones based on OCT findings
 - Center involved
 - Non-center involved
 - OCT best way to evaluate retina for DME
- Can Occur at ANY level of DR

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When to refer: DME



- NON-CI DME, PT CAN BE MONITORED Q4-6 MOS
 - REFER IF NOT COMFORTABLE BUT RS MAY DEFER TX
- CI-DME WITH REDUCED VA, REFER TO RETINAL SPECIALIST 2-4 WEEKS
 - MOST COMMON TREATMENT IS ANTIVEGF
 - LASER STILL USED SPARINGLY
 - STEROID IMPLANTS IF NO RESPONSE
- CI-DME WITH GOOD VA (20/25 OR BETTER)
 - CONSIDER REFERRAL BUT TX MAY BE DEFERRED

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DO YOU BELIEVE IN GENETIC TESTING FOR AMD PATIENTS?

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Why do genetic testing?

- Increased surveillance for those at higher risk
 - Sooner/more frequent appointments
 - More diligent home monitoring
- More diligence with modifiable risk factors
- Consider earlier vitamin supplementation
- Potential treatments in the future

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Is AMD in our DNA?

- AMD is a genetic disease with known markers accounting for at least 70% of the population attributable risk
- Other 30% is environmental/lifestyle
- Risk factors
 - Non-modifiable: age, race, gender
 - Modifiable: Smoking, increased BMI, poor diet/nutrition, UV exposure

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AMD Genetic Testing: Arctic DX

Macula Risk NXG

Looks at 15 SNPs as well as smoking, BMI, age and AMD status to determine AMD patients who may progress to advanced AMD and vision loss in

- 2 years
- 5 years
- 10 years

Cheek Swab

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AMD Risk Testing for a Full Spectrum of Patients

AMDiGuard DNA Progression Assessment

For people ≥ 55 yo with or without AMD findings

For people < 55 yo WITH AMD findings

- Assesses a patient's risk of progression to advanced AMD within 2, 5, 10, 20 and 30 years
- Delaying progression to advanced AMD with secondary prevention including AREDS vitamins, increased surveillance (home monitoring)

AMDiGuard DNA Risk Assessment

For people < 55 yo without AMD findings

- Assesses a patient's lifetime risk of developing advanced AMD (GA or CNV) allowing preventive lifestyle changes at younger age
- Delaying onset of disease with primary prevention including lifestyle modifications, supplementation (i.e. nutrition) and nutritional intervention

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Visible Genomics AMD Gene Panel

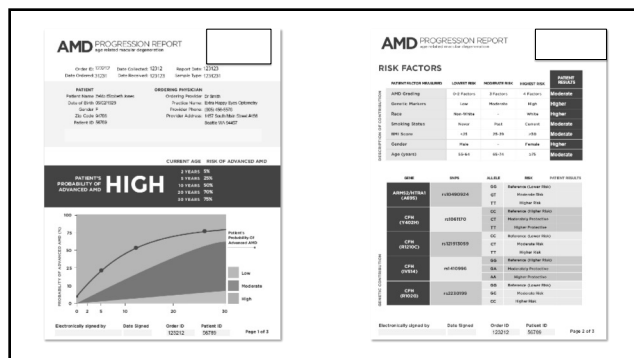
- Based on the latest in AMD Genetics research
- Clinically Proven and Clinically Actionable to be the most impactful variations on AMD progression
- Combines both genetic + non-genetic markers

23andMe SNPs

Gene	SNP No.	Allele Variants	AMD Risk	Chromosome	Pathway
ARMS2/HTRA1 (HTRA1 Serine Peptidase 1)	R1108922A (A59)	GG	Lower Risk (Reference)	10q26	Immune/inflammatory
		GT	Moderate Risk		
		TT	Higher Risk		
CFH (Complement Factor H)	R11081170 (R402N)	TT	Highly Protective	1q31	Complement
		CT	Moderately Protective		
		CC	Higher Risk (Reference)		
	R1121913059 (R1210C)	CC	Lower Risk (Reference)		Complement
		CT	Moderate Risk		
		TT	Higher Risk		
C3 (Complement Component 3)	R11410996 (V514)	AA	Highly Protective	19p13	Complement
		GA	Moderately Protective		
		GG	Higher Risk (Reference)		
	R122301199 (R102G)	GG	Lower Risk		
		GC	Moderate Risk		
		CC	Higher Risk		

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WHAT NEW RETINAL DEVELOPMENT ARE YOU MOST EXCITED ABOUT?

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Referral for Diabetic Eye Exam for Macular Edema

Updated HPI Details
The 61 year old patient presents for evaluation of MAC EDEMA. Pt states vision is fine as long as she is wearing glasses. Pt denies pain and irritation. Pt denies new flashes of light and floaters. Patient is pre-diabetic and states that she does not check her BGL.
meds: no gtt's

HPI Completed By: Mary Beth Yackey

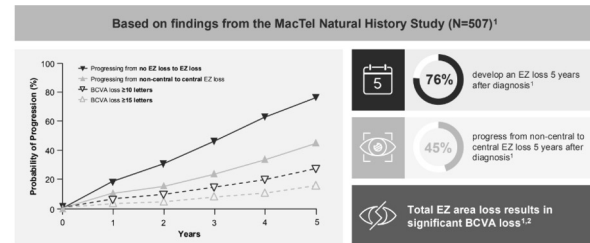
- Systemic Health: Pre Diabetes, HTN, High Cholesterol
- Meds: Lisinopril and Atrovastatin
- BCVA at distance: OD 20/40 OS 20/125
- BCVA at near: OD J3 OS 20/400
- IOP: 17mmHg OD and 18mmHg OS
- SLE: normal, 1+ milky NS OU
- Fundus exam:
 - Clear Vitreous OU
 - 0.3 C/D OU
 - No Diabetic Retinopathy OU
 - Normal Periphery OU

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So What the heck is this???

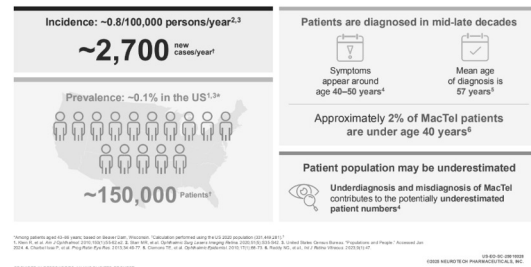
- **MacTel 2: Perifoveal Telangiectasia**
 - A neurodegenerative retinal disease that may start in one eye, but it almost always affects *both eyes*
 - Characterized as nonproliferative or proliferative
 - Nonproliferative stages: inner retinal thickening and cysts, loss of retinal transparency, and foveal involvement
 - Proliferative stages: presence of telangiectatic vessels and subretinal vascular complex
 - Photoreceptor loss occurs in MacTel 2 and leads to central vision loss and functional impairment

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MacTel 2 is underdiagnosed!



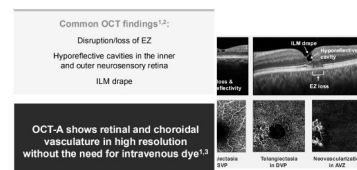
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Who gets MacTel 2?

- Slightly increased prevalence in *women*
- Possible *genetic* component
 - Although no inheritance pattern has been found, it has been observed in familial clusters and among monozygotic twins
 - Risk loci for MacTel 2 have been identified across the genome
- Certain *systemic conditions* are commonly seen in patients with MacTel 2
 - Hypertension or prehypertension
 - Diabetes mellitus or impaired fasting glucose
- Being a current or former *smoker* may increase the risk of MacTel

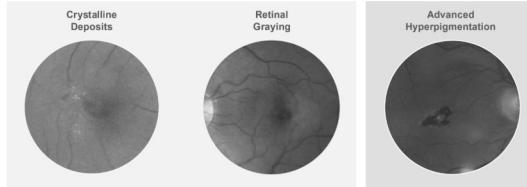
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How to diagnose MacTel 2



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Fundus Changes can be quite subtle



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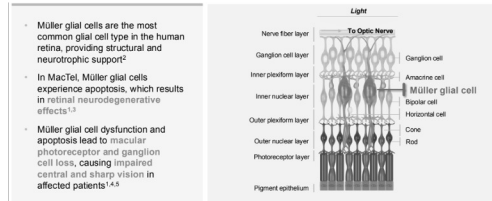
EXCITING NEWS!!

- March 6, 2025: FDA approves ENCELTO (revakinagenetaroretcellwey) a surgically implanted device implant designed to preserve sight in people by slowing vision loss in MacTel2
- “The Lowy family’s commitment to finding a treatment through their extraordinary support of the MacTel Project and the Lowy Medical Research Institute—combined with the work produced by Scripps Research, Neurotech, and an international consortium of scientists and clinicians—is a testament to the power of collaboration and the importance of basic science in developing effective treatments for debilitating diseases,” says Friedlander, whose research, along with that of others, helped pave the way for ENCELTO.

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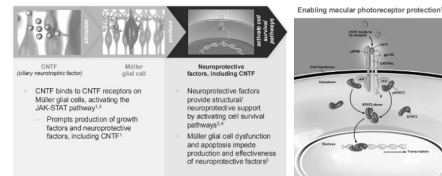
How does it work?

- Dysfunction in Müller glial cells and apoptosis leads to vision impairment



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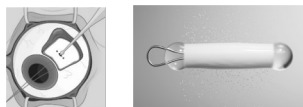
ENCELTO delivers a steady dose of ciliary neurotrophic factor (CNTF), a naturally occurring protein that supports the survival and health of nerve cells—including photoreceptors in the retina. CNTF acts as a neuroprotectant, meaning it helps shield these cells from damage to delay the degenerative process.



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How is revakinagenetaroretcellwey (ENCELTO) administered?

- One-time treatment, reducing the need for repeated injections or ongoing therapy.
- The surgical implant provides continuous, long-term delivery of the therapeutic protein directly to the retina, helping preserve vision and prevent further decline.
- This not only offers greater treatment stability but also minimizes the burden on patients and caregivers.



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In summary...let's help those with MacTel2 preserve vision

- Photoreceptor loss in MacTel leads to functional vision loss
- Most MacTel patients develop ellipsoid zone loss with a subsequent impact on vision
- BCVA often does not reflect disease burden
 - patients may develop a scotoma, but visual acuity may remain stable
- Visual symptoms have a significant impact on daily life, including work productivity (central visual distortion, scotoma)
- Patients with MacTel experience significant emotional and psychosocial burdens

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TKI Inhibitors

- Tyrosine Kinase Inhibitors
 - Small molecules that can act intracellularly to inhibit multiple pathways involved in the pathogenesis or retinal disease
 - May be a more durable treatment approach, reducing treatment burden over anti-VEGF
 - Early studies show promise
- AIV007 (Aiviva BioPharma): Phase 1, single periocular injection for DME and nAMD,
- D-4517.2 (Ashavattha Therapeutics): Phase 2 TEJAS study, subcutaneous or oral for DME and nAMD
- EYP-1901 (EyePoint Pharmaceuticals): LUGANO and CLUCIA trials in AMD; VERONA in DME
- OTX-TKI (Ocular Therapeutix): Apaxli, bioresorbable intravitreal implant for AMD and DR
- CLS-AX (Clearside Therapeutics): suprachoroidal injection of axitinib for nAMD
- PAN-90806 (Zhaoke Ophthalmology): Topical KI eye drop for AMD