AMD from A to Z: Innovations in Management and Treatment

COPE# 89609-TD

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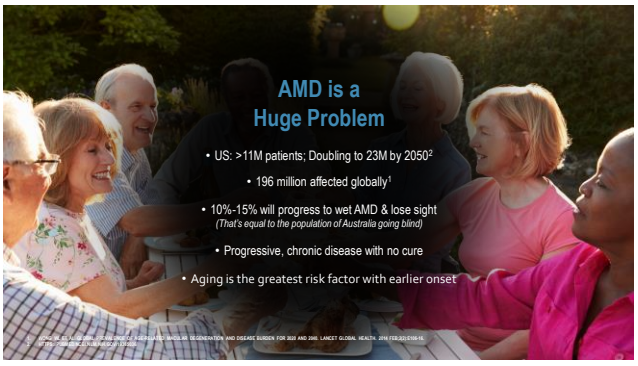
Disclosures:

Dr. Earley is a Paid Consultant and Key Opinion Leader (KOL) for Alcon Vision Care, Notal Vision, MacuHealth, Lumithera (pending) and LKC Technologies. He also serves on their Speakers Bureau.



A Brief History of AMD Diagnosis and Management

- I graduated from PCO in 1998 – no dry treatment; focal laser for wet
- I was trained to monitor dry disease, dispense Amsler, discuss UV protection
- PDT (PhotoDynamic Therapy) approved in 1999 – treatment for wet AMD
- AREDS findings released 2001 – intermediate dry or worse; role of supplements
- First OCT in 1996; OCT-2 in 2000; Stratus OCT in 2006
- First anti-VEGF in 2005 (off-label), first on-label use in 2006
- AREDS2 – began in 2006; results in 2013 – safer/more effective supplements
- Use of PHP for the detection of metamorphopsia in dry to wet conversion (2009)
- Discovery of Dark Adaptation as earliest biomarker for AMD (ALSTAR 2016)

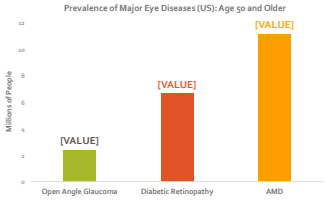
And the Innovations Continue…

- Use of Anti-VEGf medications that are longer-lasting
- Introduction of Home-Based Testing for conversion from Dry to Wet AMD
- FDA approval for the use of injectables to treat Geographic Atrophy (GA)
- Use in Europe of photobiomodulation to treat early and intermediate AMD
- Oral medications in FDA clinial trial show promise
- MANY OF THE NEW THERAPIES ARE LIKELY TO BE OPTOMETRY DRIVEN!

Leading Cause of Legal Blindness in the US *

Do you diagnose AMD as often as DR and POAG combined in your practice?

Clinical AMD **is more prevalent** than glaucoma and diabetic retinopathy combined



Primary Eye Care is Missing Visible Disease Using Today's Standard Workup

1288 eyes from 644 people
- Mean age of 69.4
- 36% male
- 64% female

- ✓ **25%** of "normal patients" had findings consistent with AMD
- ✓ **30%** of missed AMD eyes had large drusen (Intermediate AMD)
- ✓ MDs and ODs miss AMD diagnosis equally

Care. *JAMA Ophthalmol.* 2013;131(6):726–732.

As Clinicians, it is Frustrating That Our Patients are Still Presenting for Anti-VEGF Treatment Having Already Suffered Irreversible Vision Loss

Mean VA at diagnosis of nAMD in the 1st eye:

20/85

Mean VA at diagnosis of nAMD in the 2nd eye:

20/79

SOURCES: CERVANTES-CASTAÑEDA RA, ET AL. EYE (LOND). 2008;22(6):777-791. | OLSEN TW, ET AL. OPHTHALMOLOGY. 2004;111(2):250-255. | HO, ET AL. OPHTHALMIC SURG LASERS IMAGING RETINA. 2015;51:832-839.

source: AMD, age-related macular degeneration. Ferris FL, et al. Ophthalmology. 2013;120(4):844-851.

The Beckman Classification

4 Stages of AMD

PROGRESSION

No AMD	No drusen or small drusen ≤ 63 µm No AMD pigmentary abnormalities
Early AMD	Medium drusen > 63 µm and ≤ 125 µm No AMD pigmentary abnormalities
Intermediate AMD	1 large druse > 125 µm and/or Any AMD pigmentary abnormalities
Advanced AMD	**2 forms:** Geographic Atrophy and Neovascular AMD

Geographic Atrophy Neovascular AMD

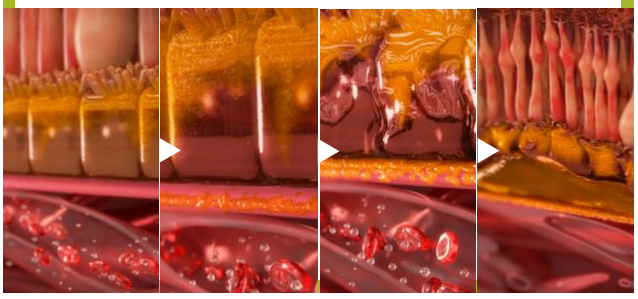
Healthy Choriocapillaris, Bruch's, RPE, and Photoreceptors

Cholesterol Barrier Deposited Along Bruch's and RPE

RPE Secretes Even More Cholesterol and Degenerates

Visibly Evident Drusen on Fundus Evaluation

Disease Process of AMD Starts Below the RPE!



Impaired Dark Adaptation is Earliest Biomarker of AMD

RESEARCH SHOWS:
Impaired dark adaptation identifies subclinical AMD
at least three years before
it can be seen with imaging, OCT or clinical exam.

UAB ALSTAR Study

Prospective Study of Subclinical AMD

- Sample consisted of 325 adult's w/o clinically detectable AMD
- At baseline, 24% of the subjects exhibited impaired dark adaptation
- AMD status determined at 3-year follow-up visit

sources: Owsley, C et al. Ophthalmology. 2016;123(2):344-351.

What IS Dark Adaptometry?

- Dark Adaptometry is the time it takes for the macular ROD photoreceptors to recover from a bleaching event.
- The photoreceptors that are bleached are slightly superior to the fovea centralis (this allows for normal fixation during testing)
- **A normal adult macula will recover from a bleaching event in 6.5 minutes or less!**
- If the adaptation time is greater than 6.5 minutes, this indicates a reduces macular pigment function; the lack of pigment leads to an outsize dose of light hitting the photoreceptors causing a delayed adaptation time
- The RODS are tested (not the cones) because they outnumber the cones and are active in scotopic conditions (patients with poor macular pigment will describe difficulty driving at night)

This Leads to a More Comprehensive AMD Classification System: Structure + FUNCTION!

PROGRESSION

No AMD		No drusen or small drusen ≤ 63 µm No AMD pigmentary abnormalities **Normal dark adaptation**
Subclinical AMD	RI	No drusen or small drusen ≤ 63 µm No AMD pigmentary abnormalities **Impaired dark adaptation**
Early AMD		Medium drusen > 63 µm and ≤ 125 µm No AMD pigmentary abnormalities **Impaired dark adaptation**
Intermediate AMD		1 large druse > 125 µm and/or Any AMD pigmentary abnormalities **Impaired dark adaptation**
Advanced AMD		**2 forms:** Geographic Atrophy and Neovascular AMD

Dark Adaptometry Validated in Multi-Site Study

JOHNS HOPKINS UNIVERSITY

HARVARD

PENNSTATE HERSHEY College of Medicine

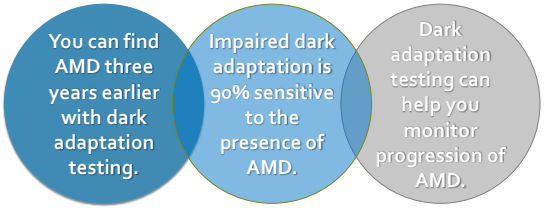
High Sensitivity
Correctly identified
90.6%
of confirmed AMD cases

High Specificity
Correctly identified
90.5%
of confirmed normal cases

High Accuracy
90.6%
overall

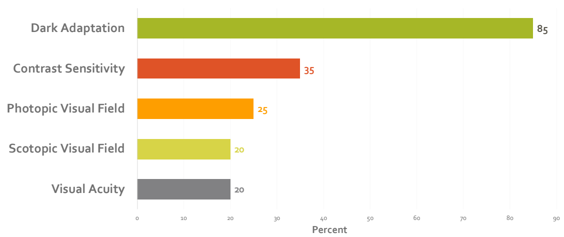
sources: Jackson GR, et al. Invest Ophthalmol Vis Sci. 2014;55(3):1427-1431.

Using Dark Adaptometry in Clinical Practice Allows for Enhanced Confidence When Managing All Stages of AMD



maculogix

Comparing Diagnostic Sensitivity for Identifying AMD



SOURCES: OWSLEY C, HUISINGH C, CLARK ME, ET AL. COMPARISON OF VISUAL FUNCTION IN OLDER EYES IN THE EARLIEST STAGES OF AGE-RELATED MACULAR DEGENERATION TO THOSE IN NORMAL MACULAR HEALTH. | CURR EYE RES 2015 AUG 19 [E-PUB AHEAD OF PRINT].

19

Goldman-Weekers Dark Adaptometer

- Manual dark adaptometer
- High patient burden
- Expert technician required
- Used in academic clinics for research and retinal degeneration diagnosis

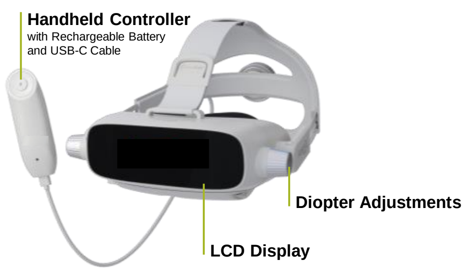
Roland Consult Dark Adaptometer

- Automated dark adaptometer
- Interfaces with external computer
- No automated analysis

First Automated Dark Adaptometer Available for Clinical Use

- ✓ Easy to administer
- ✓ Low patient burden
- ✓ Reimbursable (CPT 92284)
- ✓ Objective output (Rod Intercept)
- ✓ Rapid & Extended Tests
- ✓ FDA 510(k) Cleared & CE Mark

Head-Mounted Dark Adaptometer Now Available for Clinical Use



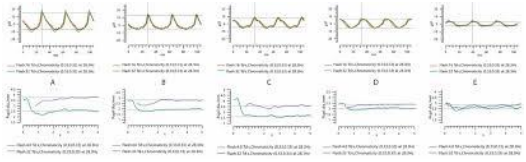
Wearable Diagnostic Testing: Here to Stay!!

- Head-Mounted VR-style Diagnostic Testing Offers Advantages Over Traditional Larger-Footprint Devices
  - Frees Up Our Technicians
  - Does Not Confine Testing to a Pretest Room
  - Easy to Adjust/Customize for a Comfortable Experience
  - Consistency of Testing with AI

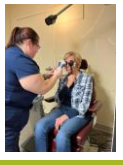
Standard of Care Comparison: Two Multifactorial Diseases

	GLAUCOMA		AMD
Structure	 Cup-to-Disc Ratio	▶	 Drusen
Function	 Visual Field	▶	 Dark Adaptation
Risk	Intraocular Pressure (IOP) Corneal Thickness Demographics and Family History	▶	Macular Pigment Optical Density (MPOD) Contrast Sensitivity Genetic Testing Demographics, Family History, Lifestyle

ANOTHER RECENT OBJECTIVE, FUNCTIONAL TEST OF MACULAR/RETINAL HEALTH…



IN CHRONIC RETINAL/MACULAR/ONH DISEASE, THE SPEED OF THE LIGHT SIGNAL AND THE STRENGTH OF THE SIGNAL ARE REDUCED BY DEAD/DYING CELLS



Clinically Useful Objective Measure of Retinal Function:

- Hand-held
- Portable
- Tech-driven
- Clinical Utility High; Several disease states can be managed
- Low patient burden; well-tolerated
- Used when subjective testing is not reliable

AMD Risk Factors

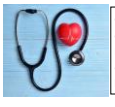
Aging

Family History and Genetics

Environment:
Smoking
Physical Activity
Social Activities
Alcohol consumption
Low MPOD

Misinformation about Tx

NUTRITION



Cardiovascular disease:
Hypertension, high cholesterol, stroke, heart disease

Practical AMD Treatments

Once detected, early treatment and lifestyle modifications can slow disease progression

Proven Treatments/Preventive Options

Smoking Cessation

Nutritional Supplementation

Diet & Exercise

Systemic Disease Management

Retinal Light Protection

Leading optometrists agree: Practical treatments should be used for ALL STAGES OF AMD to slow progression and improve outcomes.

Once Detected, Early Treatment Can Slow Disease Progression
Smoking Cessation is the First Step

SMOKING IS THE LARGEST MODIFIABLE RISK FACTOR FOR AMD.

Current smokers carry a **2.5 to 4.8 times** higher risk than non-smokers for late AMD[1].

However…

90% of patients with AMD were not advised to stop smoking[2]

<50% of smokers know that smoking may contribute to blindness[3]

References: 1. Chakravarthy U.et al. Cigarette smoking and age-related macular degeneration in the EUREYE Study. Ophthalmology 2007;114(8):1157-1163.
2. Caban-Martinez AJ et al. Age-related macular degeneration and smoking cessation advice by eye care providers. Prev Chronic Dis. 2011;8(6):A147
3. Handa S et al. Awareness of blindness and other smoking-related diseases ... in eye patients. Eye. 2011;25(9):1170-1176.

Devolution

We live in an era of nutrient-deficient foods

1953
1 Bowl of Spinach

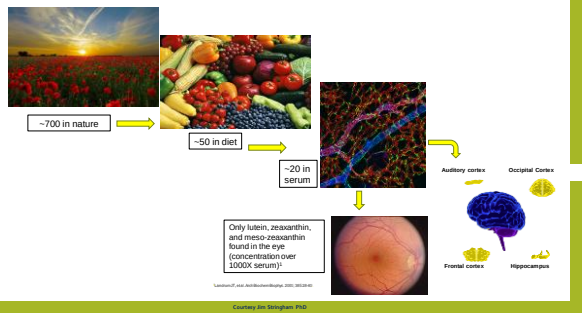
has the same nutrional content as..

2000
43 Bowls of Spinach
84% less in nutrition according to USDA data

Ref: United States Department of Agriculture

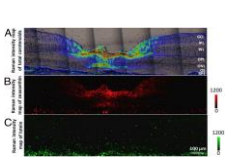
Carotenoids

Carotenoids

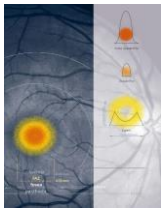


Courtesy Jim Stringham PhD

Distribution of Macular Carotenoids



Distributions of meso-zeaxanthin, zeaxanthin and lutein in a human retinal section

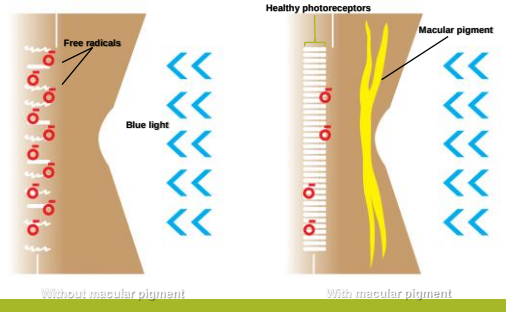


Imaging lutein and zeaxanthins in the human retina with confocal resonance Raman microscopy
Binxing Liu, Evan W. Georges, Gregory T. Rognon, Anura Gorucupalia, Arunkumar Rangarathnam, Fu-Yen Chang, Linjie Shi, Joanne M. Fredericks, and Paul S. Bernstein.

The Macula: Powerful Yet Vulnerable

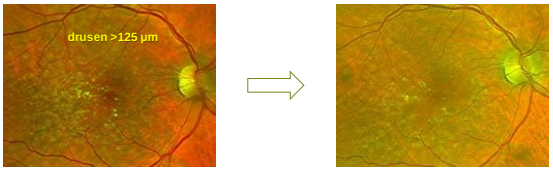
- Extremely high metabolic rate
- Many free radicals to quench
- Accounts for 90% of conscious visual processing
- Provides central vision

MPOD: Oxidation / inflammation feedback



Late Exposure to Supplementation Can Make a Difference Too: Reduction of drusen in AMD

Case: 67 YOWM, L, Z, MZ x 12 months – OD
(courtesy Gary Morgan)



9/22/17 10/18/18

Role of Oxidative Stress in Disease

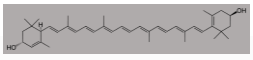
Free Radicals Caused By:

- Cellular Metabolism
- The Environment
- Lifestyle & Choices

Reduced by Antioxidants

- There are many antioxidants in our diet Vitamins C, E, Zinc, Lutein, Zeaxanthin and Meso-Zeaxanthin to name a few…
- Antioxidants donate / accept electrons to stabilize singlet oxygen
- Only 3 antioxidants present at the macula: Lutein, Zeaxanthin, Meso-Zeaxanthin

Chemical structure of lutein

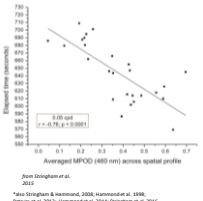


High vs. Low MPOD: Glare Disability Reduced

Stringham & Hammond. Optom Vision Sci. 2008;85:82-88; Hammond et al. Invest Ophthalmol Vis Sci. 2014;55(12):8583-9.; Nolan et al. (2016); Stringham et al. (2016)

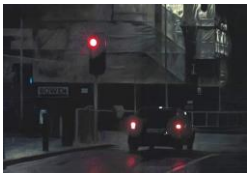
Dark Adaptation Speed

Suggests increased visual cycle efficiency promoted by macular carotenoids



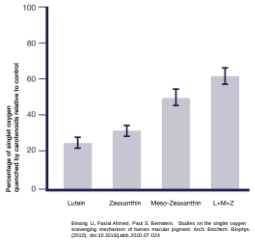
from Stringham et al. 2015

*also Stringham & Hammond, 2008; Hammond et al. 1998; Patryas et al. 2013; Hammond et al. 2014; Stringham et al. 2016



The Triple Carotenoid Formula

- The macular carotenoids are all exceptional antioxidants
- MZ has the highest antioxidant capacity, followed by Z, and L
- Synergistic effect of the 3 carotenoids together



Bhosale, U.; Fazial Ahmed, Paul S. Bernstein. Studies on the singlet oxygen scavenging mechanism of human macular pigment. Arch. Biochem. Biophys. (2010), doi:10.1016/j.abb.2010.07.024

CREST AMD (Trial 2)

Funded by the European Research Council (ERC) €1,492,342 over 5 years; Grant No. 281096

Objective

To study the effects of nutritional supplementation with the macular carotenoids on visual performance in normal subjects with early age-related macular degeneration

Design

24-month, double-blind, head to head randomized clinical.

Subjects were randomly assigned to consume 10mg lutein, **10mg *meso*-zeaxanthin,** 2mg zeaxanthin, 500mg vitamin C, 400 IU vitamin E, **25mg zinc**, 2mg copper (i.e. **Group 1**; n = 75) or 10mg lutein, 2mg zeaxanthin, 500mg vitamin C, 400 IU vitamin E, **25mg zinc**, 2mg copper (i.e. Group 2; n = 75).

Study visits were performed at baseline, 6- and 12-, 18- and 24-months.

Primary outcome measure (POM)

Change in contrast sensitivity at 6cpd

The Importance of Meso-Zeaxanthin

Of the 3 macular carotenoids, **MZ is the most powerful antioxidant**, found in the center of the fovea - where oxidative stress is highest

Estimated that 15 - 20% of population has impaired conversion of Lutein into Meso-Zeaxanthin[1]

Triple Carotenoid formula demonstrated to augment the entire MP spatial profile; a high lutein-only formula was unable to rebuild the central region[2]

Analysis of over 700 peer-reviewed journal artiicls show clinical benefit to including meso-zeaxanthin in a retinal/macular supplement

References: 1. MOST. **2.** Nolan et al. 2012 (Atypical Dip Study)

Conclusion

Sustained supplementation with all three macular carotenoids (lutein, zeaxanthin and meso-zeaxanthin) is recommended.

Formulations containing meso-zeaxanthin offer advantages over formulations lacking meso-zeaxanthin.

Supplementation with meso-zeaxanthin ensures 100% response in patients.

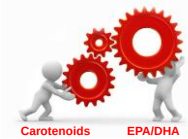
Supplementation with a formulation containing meso-zeaxanthin improves visual function in patients with early (non-advanced) AMD.

Standard of care for AMD = supplementation with lutein, zeaxanthin and meso-zeaxanthin.

The Impact of Supplemental Antioxidants on Visual Function in Nonadvanced Age-Related Macular Degeneration: A Head-to-Head Randomized Clinical Trial

Carotenoids + Omega-3s = Synergy

- L, Z, MZ and Omega 3s accumulate in SAME areas of the body: the retina, the brain and vascular tissues
- L, Z, and MZ protect DHA from oxidation and promote optimal function
- Speed of visual/cognitive processing is enhanced[1,2]
- Cleaner neural processing realized (enhanced signal-to-noise ratio)[3,4]



1. J Stringham, et al. Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure, *Foods*, 2017.
2. J Stringham et al Contrast Sensitivity and Lateral Inhibition are enhanced with macular carotenoid supplementation, *Visual Psychophysics and Physiological Optics*, 2012.
3. Nolan, et al. Enrichment of macular pigment enhances contrast sensitivity in subjects free from retinal disease: Central Retinal Enrichment Supplementation Trials – Report 1. *Retina*, 2016.
4. N Stringham, et al. Effects of macular xanthophyll supplementation on brain-derived neurotrophic factor, pro-inflammatory cytokines, and cognitive performance. *Physiology & Behavior*, 2019.

SOURCE OF OMEGA-3 FA ALSO IMPORTANT:

LOOK FOR THESE:

- Open sea/Wild caught fish
- Smaller Fish (fewer toxins)
- Re-esterified triglyceride supplements
- The purer, the better (more distillations/less "fish burp")
- 75% DHA/EPA in equal concentrations is ideal

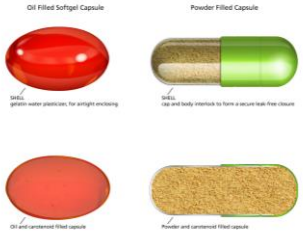
AVOID THESE:

- Farm-raised fish
- Larger fish (tend to accumulate more toxins/heavy metals)
- Ethyl Ester-based supplements
- Read the labels and do the math - some supplements have very little DHA/EPA

Formulation and Manufacturing Matter

Some forms of encapsulation are extremely vulnerable to oxidation & light exposure

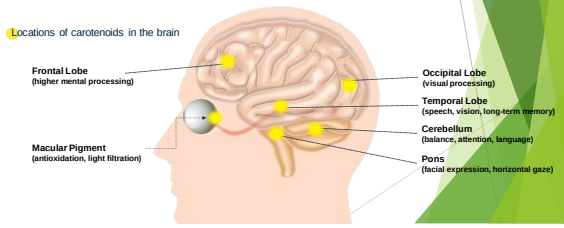
- A recent study found that of 46 supplements tested, 61% did not meet the amount claimed on the label for carotenoid content



https://www.ctvnews.ca/health/many-supplements-for-vision-loss-do-not-achieve-their-label-claim-researcher-says-1.5488929

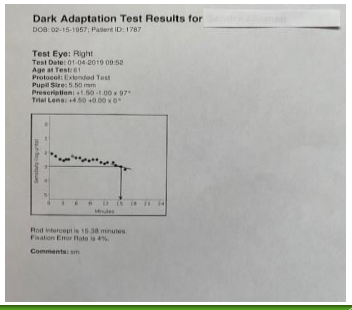
Support Cognitive Function

Carotenoid deposition in the brain improves visual processing and overall cognitive function measures.



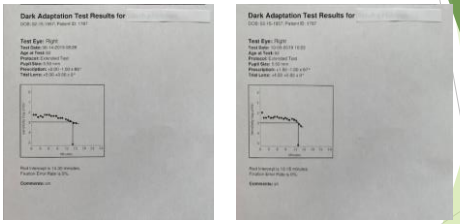
Case Study

- 63 year-old female with history of Rheumatoid Arthritis
- On Plaquenil 200mg PO 3-4x/week
- Family Hx of AMD; pt. never a smoker
- BCVA 20/20, OU but patient reports "I try not to drive at night; I feel very light sensitive and it's getting worse"
- SLE/fundus photography of macula shows no foveal reflex with subtle areas of RPE changes but no drusen or focal atrophy



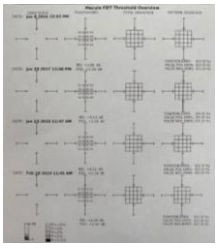
Prescribed Carotenoid Supplementation

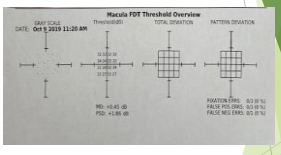
- Discussed with patient the potential for RPE damage from her high-risk medication as well as her risk for AMD (reduced night vision and family history)
- Prescribed triple-carotenoid supplement containing
  - Zeaxanthin
  - Lutein
  - Meso-Zeaxanthin

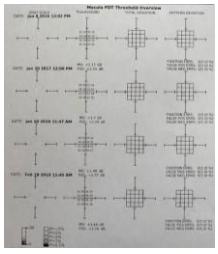


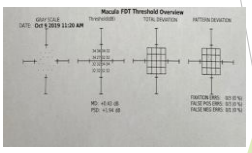
- **Rod Intercept time improved in same eye (OD):**
  - January 2019: 15.38 minutes (4% fixation error rate)
  - June 2019: 14.30 minutes (5% fixation error rate)
  - October 2019: 13.15 minutes (0% fixation error rate)

In this case, RI was not the only improvement we have found……









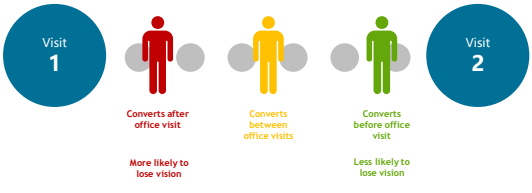
A MODERN APPROACH TO AMD DIAGNOSIS AND MANAGEMENT

- AMD is a disease that we see in our practices every day
- Optometry has a role to play in the early diagnosis, education and treatment of this potentially blinding disease
- We NEED to be having conversations with our patients about AMD!

Optometry is Positioned to Lead the Charge!!

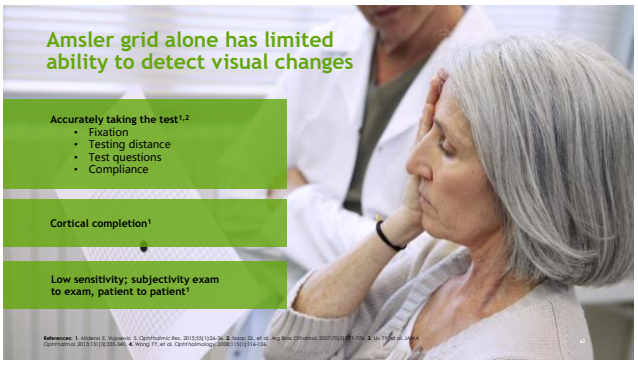
SWITCHING GEARS… HOW DO WE MANAGE HIGH-RISK DRY AMD??

At-risk Patients May Convert to Wet AMD at Any Point Between Follow-up Visits



Reference: Rosch R, et al. *Retina*. 2012;32(7):1240-1264.

Amsler grid alone has limited ability to detect visual changes



Accurately taking the test[1,2]
- Fixation
- Testing distance
- Test questions
- Compliance

Cortical completion[1]

Low sensitivity; subjectivity exam to exam, patient to patient[1]

References: 1. Midena E, Vujosevic S. Ophthalmic Res. 2015;55(1):24-36. 2. Isozaki DL, et al. Arq Bras Oftalmol. 2007;70(5):771-774. 3. Liu T, Hall G, JAMA Ophthalmol. 2013;131(3):335-340. 4. Wong TY, et al. Ophthalmology. 2008;115(11):1-24.

A Perfect Combination for Poor Visual Acuity at Wet AMD Diagnosis

Intermediate AMD may go undiagnosed

Patients progress between visits

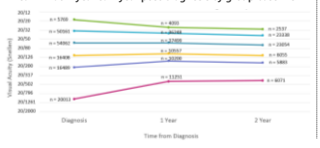
Limitations of Amsler grid

Poor VA at wet AMD detection

Real-world data supports clinical trial results: early diagnosis with good VA is essential to preserve functional vision with anti-VEGF therapy

AAO IRIS® Registry Real World Data (US)[1]
January 2013 - June 2017

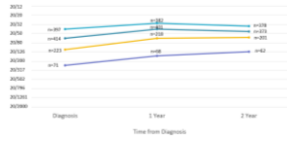
Mean VA at 1-year & 2-year post-diagnosis by group baseline VA



162,902 eyes diagnosed with wet AMD (153,141 patients)

Comparison of Age-related Macular Degeneration Treatment (CATT) Trial (US)[2]

Mean VA at 1-year & 2-year

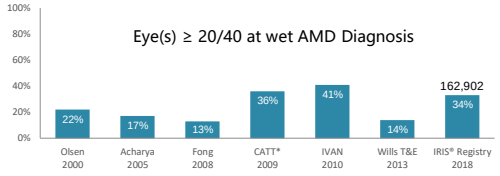


1,185 eyes diagnosed with wet AMD

References: 1. Ho AC, et al. *Ophthalmic Surg Lasers Imaging Retina* 2020;51:633-639. 2. Ying GS, et al. *Ophthalmology*. 2015;122(12):2523-2531.

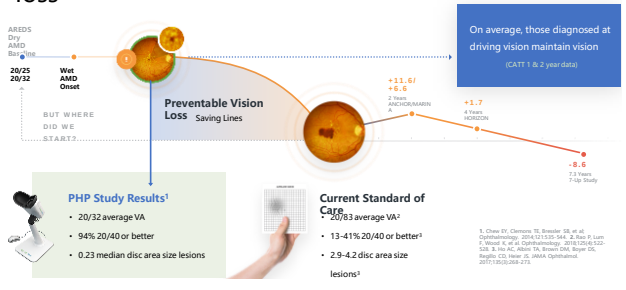
Clinical trial and real-world data show small proportion of patients with good VA at initiation of anti-VEGF therapy

Intermediate AMD patients who convert to wet AMD lose a substantial amount of vision before detection and treatment



Not enough diagnosed wet AMD eyes are detected early

Readjusting our point of view to preventable vision loss

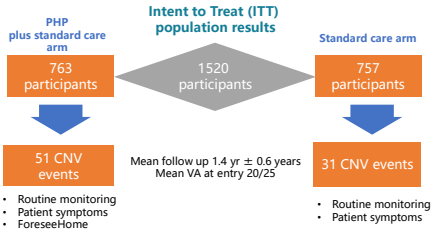


To detect wet AMD earlier we need...

More sensitive, specific disease detection

Reliable, advanced at-home monitoring

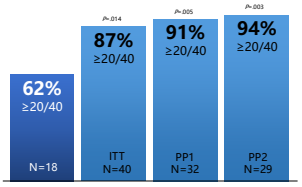
AREDS2-HOME Study



**Primary outcome:* *Change in BCVA from baseline to CNV detection*

Reference: AREDS2-HOME Study Research Group. *Ophthalmology.* 2014;121(2):535-544.

More patients who used PHP maintained ≥20/40 VA

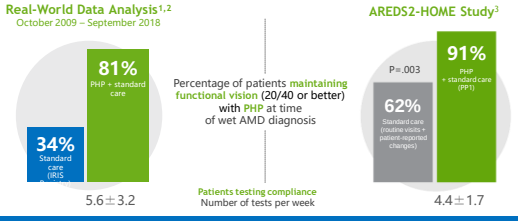


50% MORE
patients maintained 20/40 or better when using PHP vs standard of care alone

94% of patients maintained 20/40 or better visual acuity at time of wet AMD diagnosis;
Absolute visual acuity at time of wet AMD diagnosis is critical to visual acuity outcomes

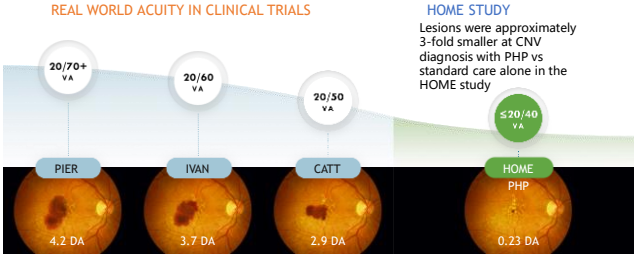
Reference: AREDS2-HOME Study Research Group. *Ophthalmology.* 2014;121(2):535-544.

PHP real-world performance resembles pivotal trial results

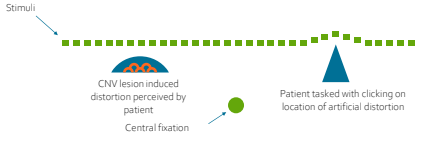


IRIS Registry demonstrates few newly diagnosed CNV eyes are detected early

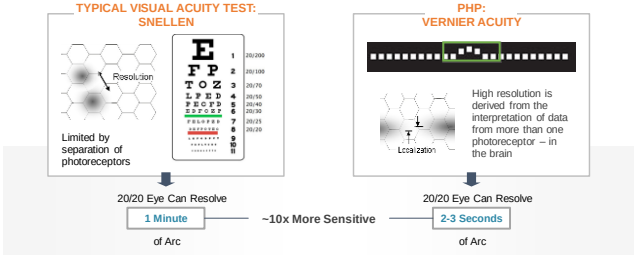
Visual Acuity and Lesion Size at diagnosis of wet AMD



PREFERENTIAL Hyperacuity Perimetry (PHP) delivers accurate, highly sensitive, specific disease detection



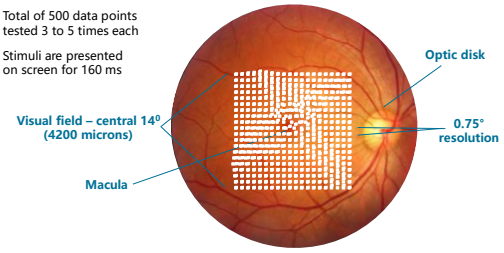
Preferential HYPERACUITY Perimetry



PERIMETRY: The Home PHP Test

Total of 500 data points tested 3 to 5 times each

Stimuli are presented on screen for 160 ms



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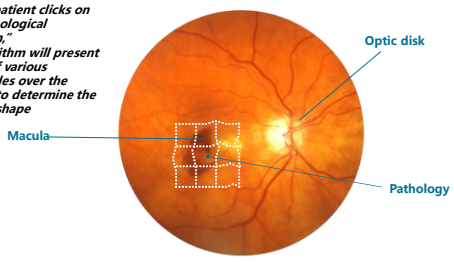
Once pathology is suspected, the area is bracketed to localize and quantify pathology

When a patient clicks on the "pathological distortion," the algorithm will present stimuli of various magnitudes over the location to determine the size and shape



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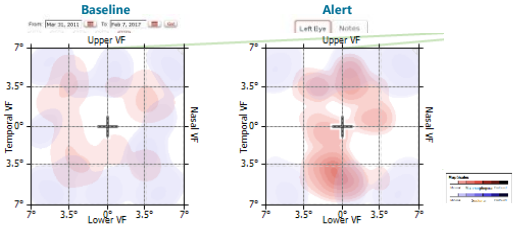
After pathology is quantified and localized, an Alert Metamorphopsia Map is generated



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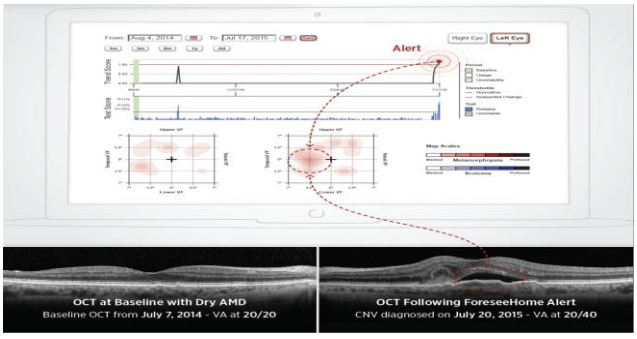
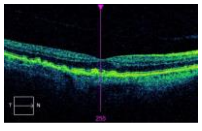


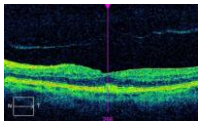
CASE 1 → Initial Exam (OU): 10/5/18

October 5, 2018:

- Patient referred for evaluation of possible age-related macular degeneration (AMD)
- VA CC 20/30^{-1} OU
- Found to have intermediate dry AMD OU
- Referred to Vision Diagnostic Clinic for Home-based PHP program OU and prescribed high-quality carotenoid supplement

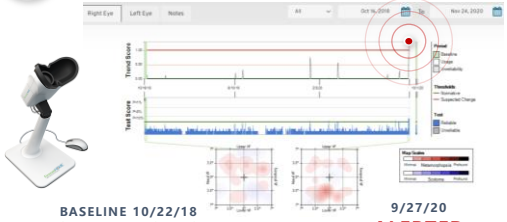


OCT OD



OCT OS

CASE 1 → Baseline 10/22/18: VA 20/30^{-1} (OD) prior to alert



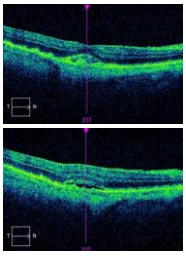
BASELINE 10/22/18
STARTED TESTING

9/27/20
ALERTED

CASE 1 → Exam Post-Alert (OD): 10/1/20

October 1, 2020:

- Patient returned to clinic following PHP Alert on 9/27/20 OD
- VA CC 20/40^{-1} OD, 20/30^{-2} OS
- New SRF noted on OCT OD (images highlight the area of prominent fluid)
- Patient received an injection of ranibizumab 0.5 mg OD
- No prior alerts while using home-based PHP

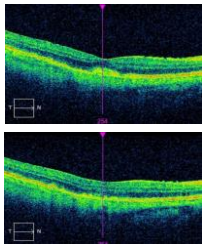


OCT OD

CASE 1 → Exam Post-Injection (OD): 11/3/20

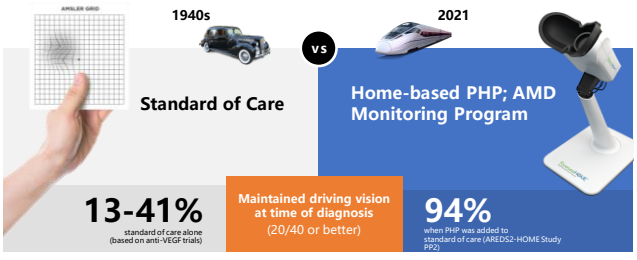
November 3, 2020:

- Patient returned for follow-up after first injection OD
- VA CC 20/20^{-2} OD, 20/25^{-2} OS
- SRF resolved OD (images of the highlighted area again)
- Patient received second injection out of the planned three



OCT OD

At-home monitoring for conversion to wet AMD



Home-based PHP is appropriate for the type of patients you see every day

Unilateral or bilateral dry intermediate AMD OR **Wet AMD in one eye and dry intermediate AMD in fellow eye**

BCVA 20/60 or better

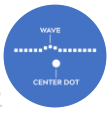
PATIENTS MUST HAVE

H35.3112	H35.3122	H35.3132
Dry intermediate Right eye	Dry intermediate Left eye	Dry intermediate Bilateral

Patients taking high-quality macular vitamins are often good candidates for Home-based PHP

Set up and daily tests are quick and easy for patients

1. Patient uses mouse to click where artificial distortion (bump or wave in the dotted line) appeared on the screen



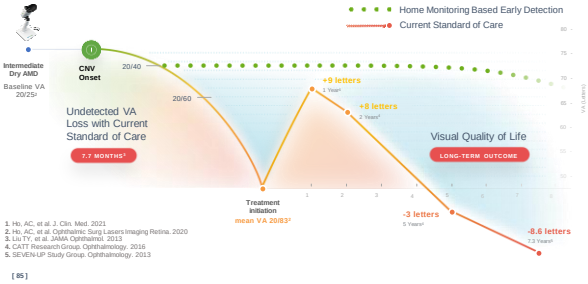
2. PHP (Preferential Hyperacuity Perimetry) is used to detect tiny changes in the central visual field, including metamorphopsia and scotoma

3. Data from each test is sent to the Vision Diagnostic Clinic for evaluation and monthly reports are emailed to practice; available 24/7 on the ECP (Eye Care Professional) Portal

Alert is sent when a significant change compared to baseline occurs, indicating possible AMD progression

You control how alerts are managed

Summary: Average nAMD Patient Journey



1. Ho, AC, et al. J. Clin. Med. 2021
2. Ho, AC, et al. Ophthalmic Surg Lasers Imaging Retina. 2020
3. Liu TY, et al. JAMA Ophthalmol. 2013
4. CATT Research Group. Ophthalmology. 2016
5. SEVEN-UP Study Group. Ophthalmology. 2013

[85]

ALOFT Study Design

Large retrospective study involving **all referred patients** from 5 clinics over 10 years

1. Retina Group of Washington
2. Virginia Eye Institute
3. Retina Associates of Kentucky
4. Wagner Macula & Retina Center
5. Elman Retina Group

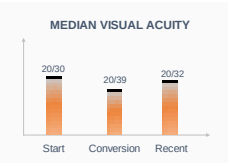
2,123 patients

3,334 eyes

1 million+ tests | 10,000+ monitoring years

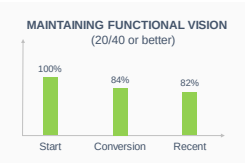
[86]

ALOFT Study: Visual Acuity Results



Median VA

- Start of program – 20/30
- nAMD conversion detected – 20/39
- Most recent visit – 20/32

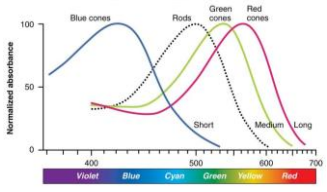


Patients at start with ≥20/40

- Maintaining 20/40 at conversion – 84%
- Maintaining 20/40 at recent visit – 82%

[87]

Pipeline Technologies in AMD Treatment



- Home-based OCT
- Photobiomodulation
- Treatments for GA (Geographic Atrophy) -

Medications for Geographic Atrophy (GA)

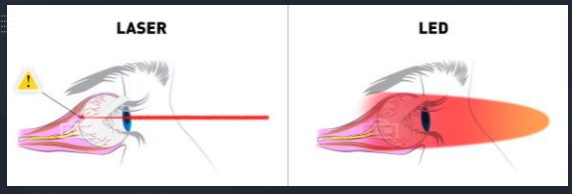
- **Pegcetacoplan (Syfovre)**
  - Slows the progression of lesion growth in GA
  - Complement C3 inhibitor
  - Monthly injection reduced lesion growth by 22% (Oaks Phase 3 trial)
- **Avacincaptad pegol (Izervay)**
  - Also slows progression
  - Targets excessive activation of the complement system; blocks C5 protein
  - Reduced lesion growth rate by 35% (Gather1 and Gather2 trials)

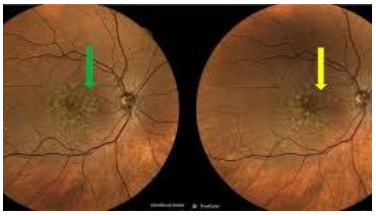
What's Next?

- It is likely that the next intravitreal medications will combine the C3 and C5 protein-inhibitors and affect the complement cascade in more than one area…

LASER vs. Photobiomodulation – not the same!

- Focused Laser can be harmful
- Diffuse Red and other wavelengths act on Mitochondria
- Wavelengths used are critical
- Studies: – LightSite III 24-month data recently published





Small Footpring Device – Uses LED light; not lasers

- Valeda Light Delivery System currently before the FDA for consideration as a "Class II device" - will likely be available for use in U.S. as early as Summer 2024

Uses of Photobiomodulation in Eyecare:

- Treatment is performed without optical correction
- Total treatment time for both eyes is <10 minutes/treatment
- Treatment 3x/week for 3-4 weeks
- LightSite III used three wavelengths of light; all shown to reduce inflammation and improve retinal mitochondrial function

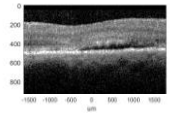
- Fewer PBM eyes were found to progress to GA compared to the sham group:
  - 6.8% vs. 24%

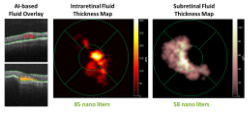
Home OCT for monitoring chronic therapy of neovascular AMD between office visits

- Monitoring of intra- and subretinal fluid based on daily patient self-imaging
- Easy-to-use, patient-operated device
- Takes less than one minute per eye
- AI algorithm analyzes images on cloud
- Remote diagnostic clinic, provider of monitoring program, reports changes meeting physician-selected fluid volume thresholds to referring physician
- 24/7 physician access to all data

Home Device

Home OCT Image





THANK YOU!!!