

Introducing Ocular Nutrition into the Modern Optometry Practice
COPE # 89337-PH

THE BENEFITS OF SUPPLEMENTATION FOR THE VITREOUS AND RETINA

1

ILLINOIS OPTOMETRIC ASSOCIATION- LIVE CE EVENT


Tim Earley, O.D.
Northeast Ohio Eye Surgeons
drtimearley@gmail.com



2

CAROTENOIDS AND OMEGA-3s: Critical for Ocular Nutrition

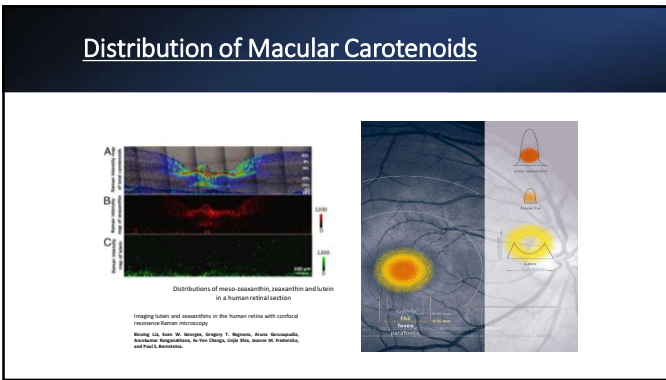
Are you having discussions with your patients around the benefits of a good diet on ocular health?



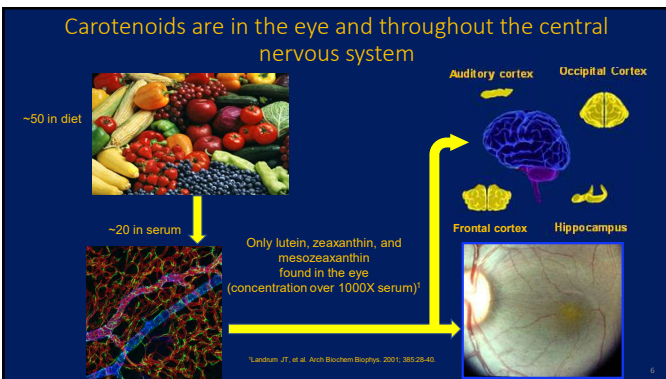
3



4



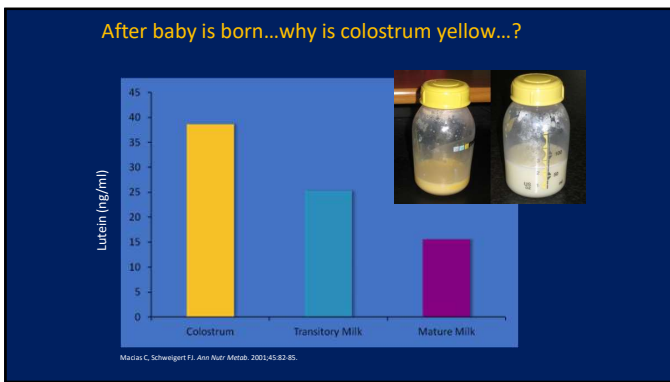
5



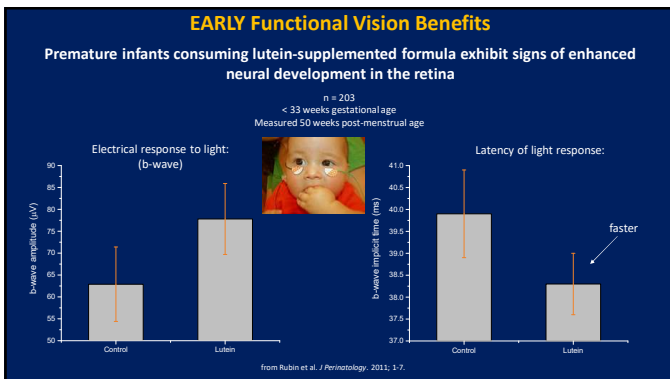
6



7




8



9

HANDHELD fFERG in PEDIATRIC USE



33.3 ms 18.1 μ V
35.4 ms 13.0 μ V
38.0 ms 11.5 μ V

10

CAROTENOIDS IN ADOLESCENCE AND EARLY ADULT LIFE

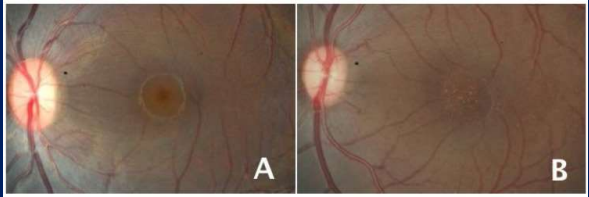
VISUAL PERFORMANCE AND NEURAL FUNCTIONING BENEFITS

- Driving
- Sports/Athletics
- Cognition
- Visual Processing



11

Early Exposure to Macular Carotenoids Matters:



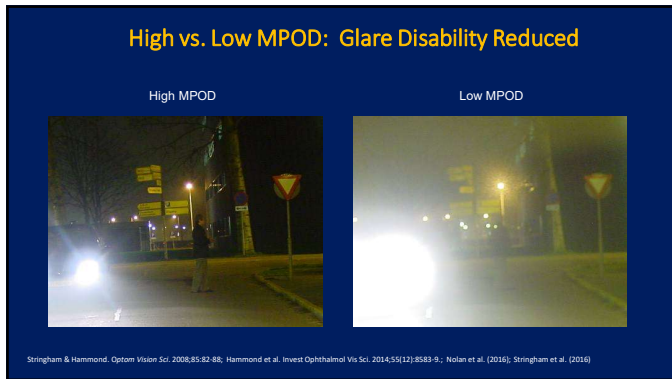
A B

Normal diet (including lutein + zeaxanthin) Early diet devoid of lutein, zeaxanthin, & meso-zeaxanthin

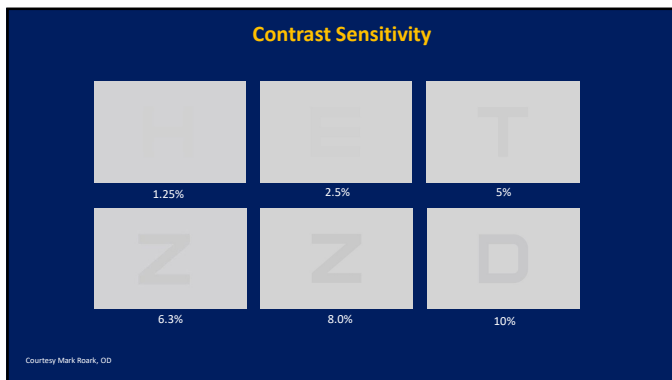
Rhesus monkeys, equivalent age of 25 yo human

From Erdman et al. (2015)

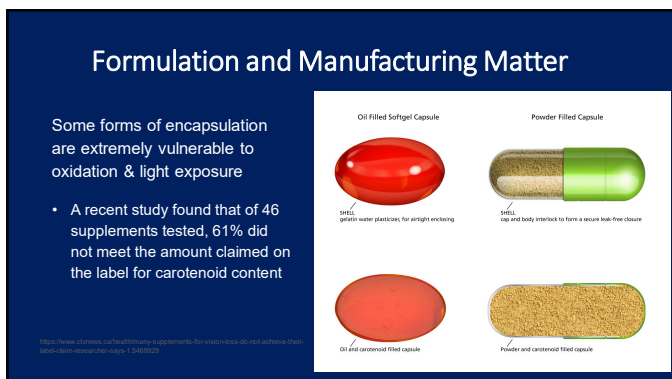
12



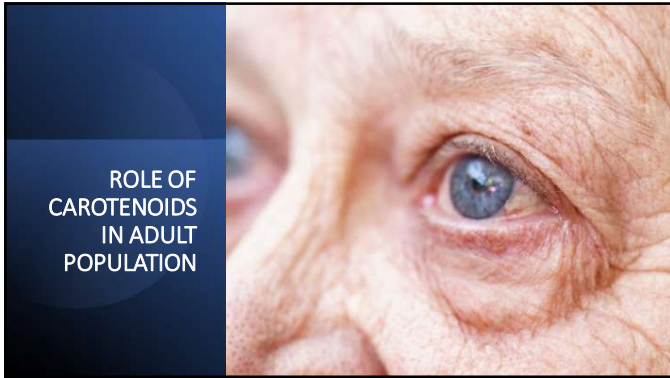
13



14




15



16

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 AMD¹.
- *However...*

90% of patients with AMD were not advised to stop smoking²

<50% of smokers know that smoking may contribute to blindness³


References: 1. Chakraborty D et al. Cigarette smoking and age-related macular degeneration in the EUREYE Study. Ophthalmology. 2007;114(10):1197-1198.
2. Chouaib M et al. Age-related macular degeneration and smoking cessation advice by eye care providers. Prev Chronic Dis. 2011;8(6):A47.
3. Chouaib M et al. Eye-related macular degeneration and smoking cessation advice by eye care providers. Prev Chronic Dis. 2011;8(6):A47.

17

Nutrient devolution


We live in an era of nutrient-deficient food

1953
1 Bowl of Spinach



has the same nutritional content as...

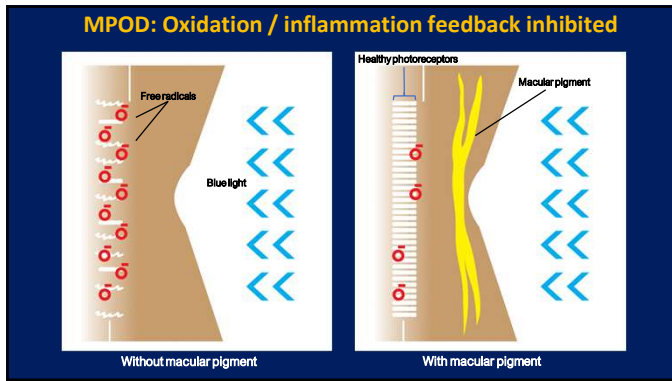
2000
43 Bowls of Spinach



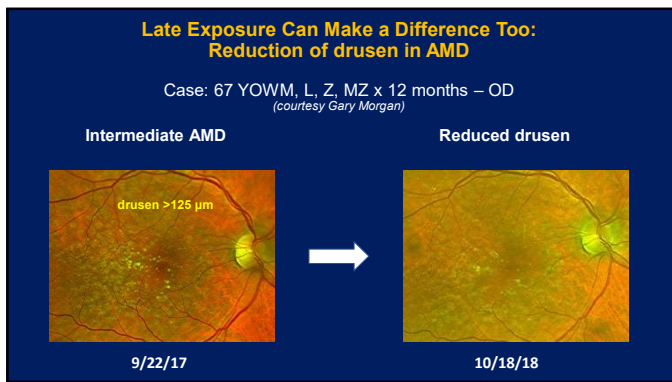
84% less in nutrition according to USDA data

Data from USDA

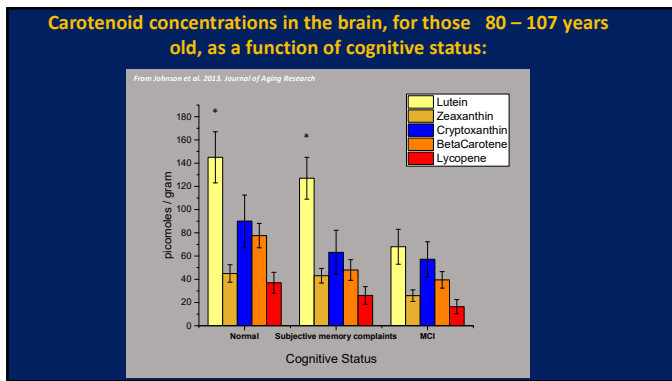
18



19



20



21

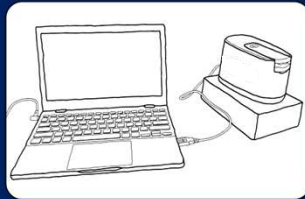
Skin Carotenoid Scanner

- A Skin Carotenoid Scanner is a clinical tool that uses advanced technology to accurately measure a patient's carotenoid concentration in their skin, a key indicator of overall health and visual performance. This non-invasive test can be completed in less than three minutes.
- The assessment empowers you to confidently talk to patients about nutrition. Motivate your patients to make positive changes to improve both visual and systemic health.

22

HOW IT WORKS:

Skin Carotenoid Scanner uses reflection spectroscopy to measure the level of carotenoids in the skin. The patient places a fingertip in the scanner and will get results in less than three minutes.

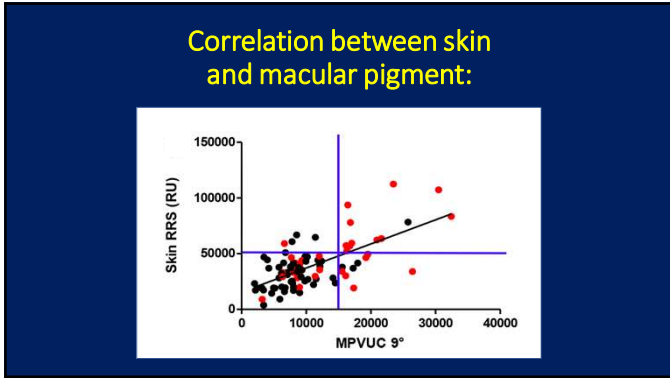


23

QUANTITAVE RESULTS



24



Consistent Carotenoid Intake is Linked To Better Overall Health

- LifeMeter measures all carotenoids in the skin; there are five that are strongly represented there:
 - LUTEIN
 - ZEAXANTHIN
 - MESO-ZEAXANTHIN
 - BETA-CAROTENE
 - BETA-CRYPTOXANTHIN
 - LYCOPENE

26



Question:

- Which two Omega-3 Fatty Acids are essential for retina and brain health?

28

OMEGA-3 FATTY ACIDS IN RETINA/BRAIN

- DHA – Docosahexaenoic Acid
- EPA – Eicosapentaenoic Acid

29

OMEGA 3 FATTY ACIDS:
WHAT ROLE DO THEY PLAY IN RETINAL/NEUROLOGICAL HEALTH?



The diagram on the left illustrates a cross-section of a cell membrane, showing phospholipids with hydrophilic heads and hydrophobic tails. Omega-3 fatty acids are shown as blue chains integrated into the membrane. Labels include 'Cell membranes', 'Molecules (phospholipids)', 'Omega-3 fatty acid', and 'Cell nucleus'. The photograph on the right shows a variety of food sources for Omega-3 fatty acids, including a whole fish, salmon fillets, flaxseed, walnuts, and other oils and seeds. A small chalkboard in the center of the photo has 'OMEGA 3' written on it.

30

Components of neural health and communication:

DHA makes up 30% of the total fat in the brain, and 50% of the neuronal membrane

DHA is a Structural Component in Membranes of Brain and Eye

67% of omega-3 fatty acid in the brain

33% of omega-3 fatty acid in the eyes

Lutein protects DHA from oxidation and inflammation; breaks the oxidation → inflammation feedback loop, improves the health and performance of neural cells

31

SYNERGY!!

The macular carotenoids / omega-3s have several, significant beneficial effects:

- Enhanced visual/cognitive health & performance
- Important role in neurodevelopment; systemic, retina, and brain
 - *Enhanced cognitive performance in pre-adolescents
- Antioxidant & anti-inflammatory effects
 - Enhance neuroplasticity
 - Relieve dry eye
 - Reduce blood cortisol, psychological stress
- THE FUTURE
 - Benefits to cognitive aging
 - May significantly reduce symptoms / pathogenesis of TBI
 - Cardiovascular health
 - Benefits in children / teens
 - Optomety can effectively manage AMD, Cognitive aging
- Effects may be realized within 3-6 months of consistent supplementation

32

SOURCE OF OMEGA-3 FA ALSO IMPORTANT:

<p>LOOK FOR THESE:</p> <ul style="list-style-type: none"> 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 	<p>AVOID THESE:</p> <ul style="list-style-type: none"> 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
---	--

33



34



35



36

The Vitreous & Nutrition



Specific micronutrients are present within the vitreous, which help to maintain optimum health and function.



As with the rest of the body, the vitreous encounters oxidative stress throughout life, which contributes to its structural breakdown.








This oxidative stress, coupled with a natural decline in protective nutrients, contributes to glycation, the clumping of collagen fibers. This results in the loss of transparency & integrity of the vitreous.



Based on the FLIES Study, we know that antioxidant and antiglycation nutrients can be replenished inside the vitreous, improving floater symptoms.

37

Stages of Vitreous Degeneration

In a healthy state, the vitreous is composed of loosely spaced collagen fibers with plenty of space between.

As we age, and exacerbated by some conditions, the fibers begin to clump together, and can cause floaters. This clumping is called glycation.

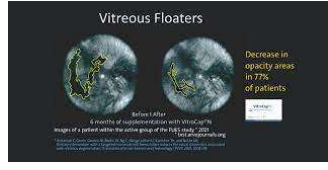
Now these collagen fibers which were spaced out and helped to maintain the structure of the vitreous, are clumping together, and the vitreous begins to lose its shape and shrink, this is called liquefaction.

This liquefaction or shrinking, of the vitreous can ultimately result in PVD – posterior vitreous detachment.

38

FLIES Study Design:

- Enrolled patients age 18 and over with subjective complaints of floaters
- Randomized, single-site, double-blind, placebo-controlled study
- 61 patients were studied over 6 months
- Outcome measure: change in floater disturbance using a subjective questionnaire
- Also compared color fundus photos using a Zeiss VisuCam images at baseline and at 6 months
- Start date 1/2/2017; ended 12/31/2018



Vitreous Floaters
 Before 6 months
 6 months of supplementation with VitaCoQ10
 Images of a patient within the same group of the High-Dose (2000 IU) VitaCoQ10 group
 © 2018 VitaCoQ10, LLC. All rights reserved. VitaCoQ10, LLC. VitaCoQ10.com

39

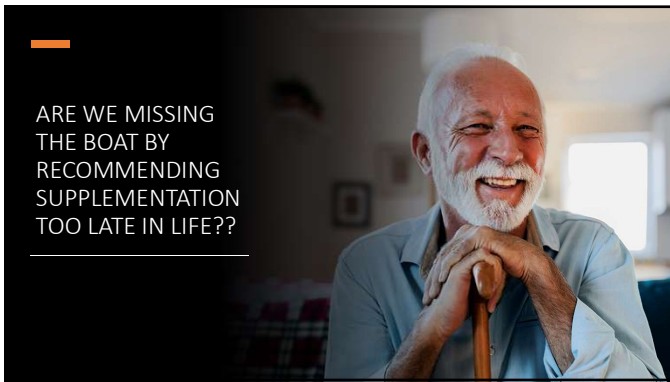
How does it work?

- Functions to counteract the mechanisms of vitreous degeneration, which create floaters.

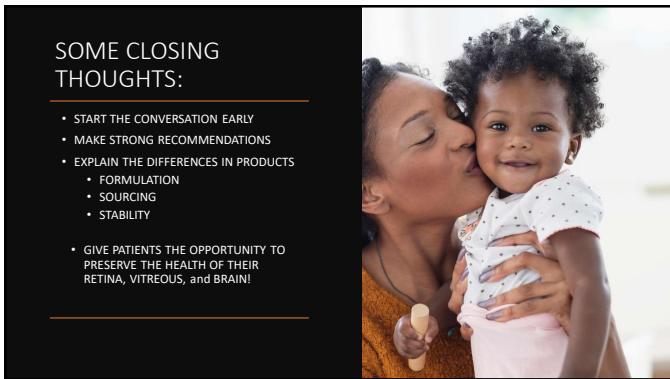
Key Actions are :

- Reduction of collagen glycation
- Reduction of oxidative stress within vitreous
- Increase of antioxidant protection
- Increase in phagocytosis activity in vitreous cavity

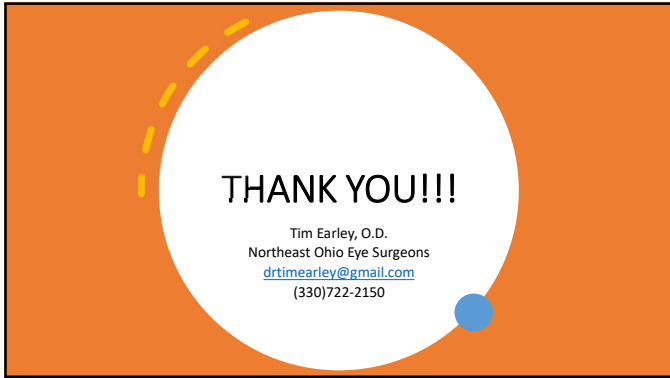
40



41



42



43



44

AMD from A to Z: Innovations in Management and Treatment

COPE# 89609-TD

Timothy W. Earley, O.D.

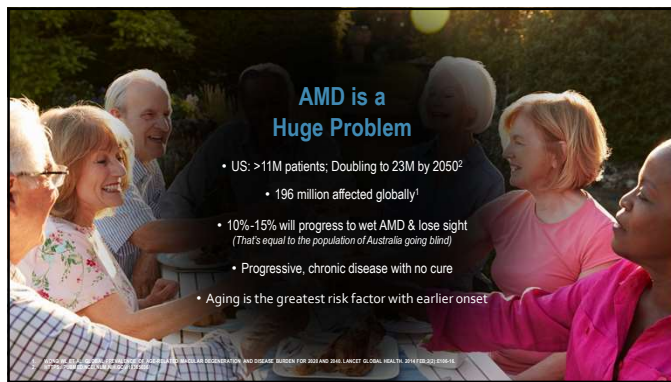
Northeast Ohio Eye Surgeons

Drtimearley@gmail.com

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.

1



2

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)

3

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 clinical trial show promise
- MANY OF THE NEW THERAPIES ARE LIKELY TO BE OPTOMETRY DRIVEN!

4

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

Disease	Millions of People
Open Angle Glaucoma	2.4
Diabetic Retinopathy	6.7
AMD	11.2

5

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

JAMA Ophthalmology | Original Investigation
Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care
 David C. Neely, MD; Kevin J. Bray, MD; Carrie E. Hulsingh, MPH; Mark E. Clark, BS; Gerald McGwin Jr, PhD; Cynthia Owensley, PhD

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

© 2022 JAMA Ophthalmology. All rights reserved.

6




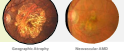
As Clinicians, it is Frustrating That Our Patients are Still Presenting for Anti-VEGF Treatment Having Already Suffered Irreversible Vision Loss

<p>Mean VA at diagnosis of nAMD in the 1st eye:</p>  <p>20/85</p>	<p>Mean VA at diagnosis of nAMD in the 2nd eye:</p>  <p>20/79</p>
---	---

SOURCES: CERVANTES-CARRERA, RA, ET AL. OYE. 2008;20(2):171-175. LO,SEN,TK, ET AL. OPHTHALMOLOGY. 2004;112(2):230-235. HO, ET AL. OPHTHALMIC SURG LASERS IMAGING RETINA. 2003;33:433-439.

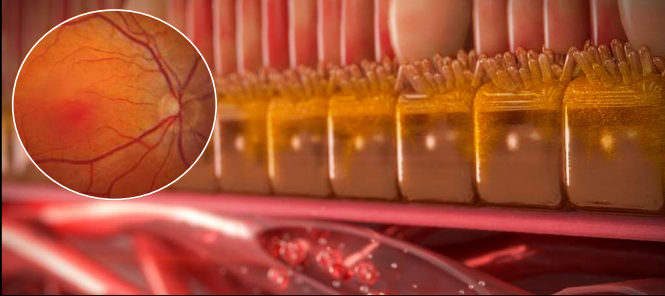
7

The Beckman Classification
4 Stages of AMD

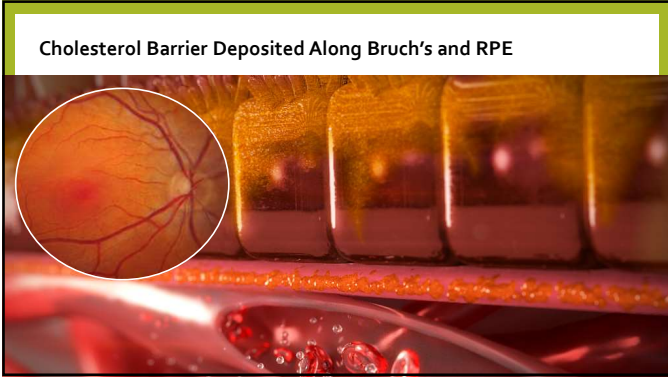
PROGRESSION	No AMD		No drusen or small drusen $\leq 63 \mu\text{m}$ No AMD pigmentary abnormalities
	Early AMD		Medium drusen $> 63 \mu\text{m}$ and $\leq 125 \mu\text{m}$ No AMD pigmentary abnormalities
	Intermediate AMD		1 large druse $> 125 \mu\text{m}$ and/or Any AMD pigmentary abnormalities
	Advanced AMD		≥ 2 forms: Geographic Atrophy and Neovascular AMD

8

Healthy Choriocapillaris, Bruch's, RPE, and Photoreceptors



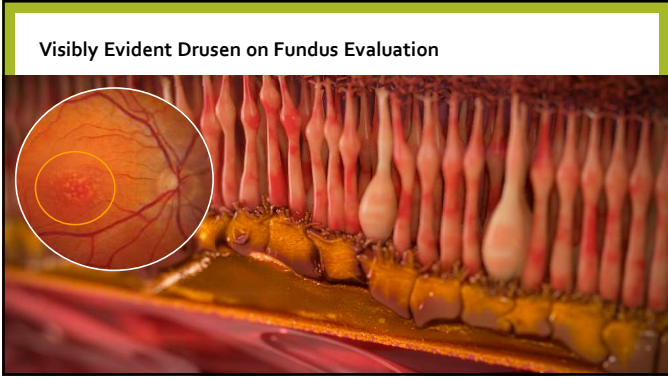
9



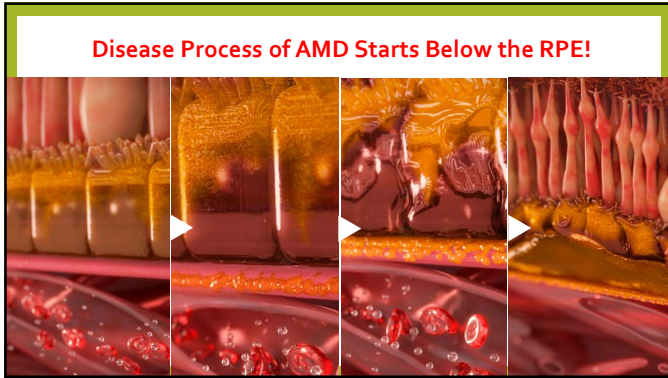
10



11



12



Disease Process of AMD Starts Below the RPE!

13

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.






14

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 reduced macular pigment function; the lack of pigment leads to an outside 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)


15

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		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

16

Dark Adaptometry Validated in Multi-Site Study



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 GP, et al. Invest Ophthalmol Vis Sci. 2014; 55(2):1437-1439

17

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

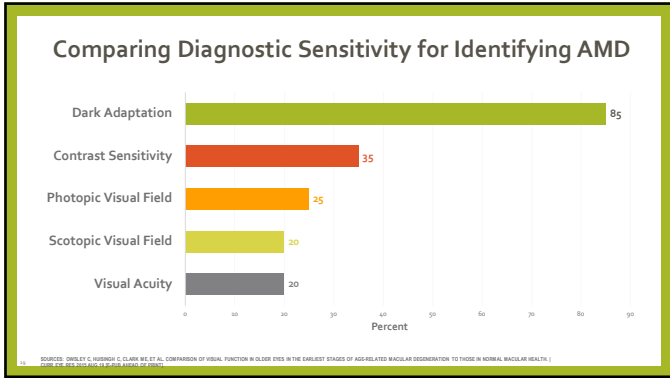
You can find AMD three years earlier with dark adaptation testing.

Impaired dark adaptation is 90% sensitive to the presence of AMD.

Dark adaptation testing can help you monitor progression of AMD.

maculogix

18



19

Goldman-Weekers Dark Adaptometer

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



20


Roland Consult Dark Adaptometer

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



21

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

22

Head-Mounted Dark Adaptometer Now Available for Clinical Use



Handheld Controller
with Rechargeable Battery
and USB-C Cable

Diopter Adjustments

LCD Display

23





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



24

Standard of Care Comparison: Two Multifactorial Diseases

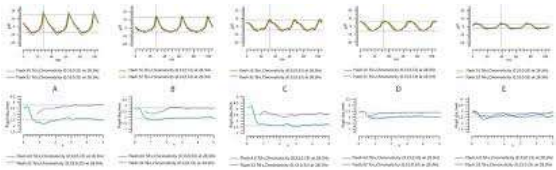
	GLAUCOMA	▶	AMD
Structure	 Cup-to-Disc Ratio		 Drusen
Function	 Visual Field		 Dark Adaptation
Risk	Intraocular Pressure (IOP) Corneal Thickness Demographics and Family History		Macular Pigment Optical Density (MPOD) Contrast Sensitivity Genetic Testing Demographics, Family History, Lifestyle

25



**ANOTHER RECENT
OBJECTIVE,
FUNCTIONAL TEST
OF RETINAL
HEALTH...**

26



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

27


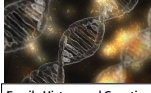



Clinically Useful Objective Measure of Retinal Function:

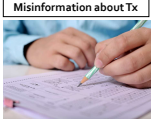
- Hand-held
- Portable
- Tech-driven
- Clinical Utility High; Several disease states can be managed
- Low patient burden; well-tolerated
- Used when subjective testing is not reliable

28



AMD Risk Factors

Environment:
Smoking
Physical Activity
Social Activities
Alcohol consumption
Low MPOD



NUTRITION









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

29

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.

30

**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 AMD¹.

However...

90% of patients with AMD were not advised to stop smoking²

<50% of smokers know that smoking may contribute to blindness³


References: 1. Chakrabarti SK et al. Cigarette smoking and age-related macular degeneration: the ELMG Study. Ophthalmology. 2007;114(6):1152-1163.
2. Cabero-Martinez AJ et al. Age-related macular degeneration and smoking cessation advised by eye care providers. PLoS ONE. 2011;6(4):e18747.
3. Haines JE et al. Awareness of blindness and other consequences of smoking. In: Eye Smoking. PLoS ONE. 2011;6(5):e17164.

31

Devolution


We live in an era of nutrient-deficient foods

1953
1 Bowl of Spinach



has the same nutritional content as...

2000
43 Bowls of Spinach



84% loss in nutrition according to USDA data

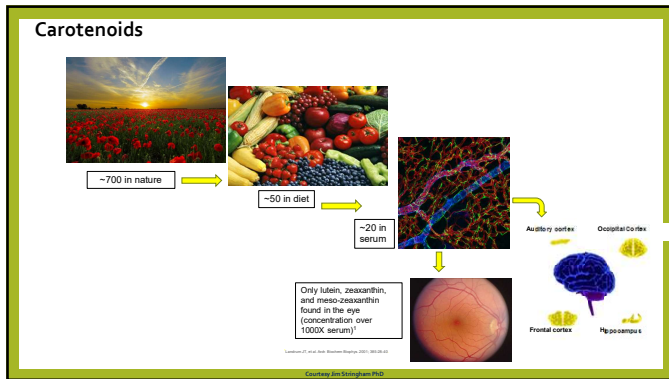
Ref: United States Department of Agriculture

32

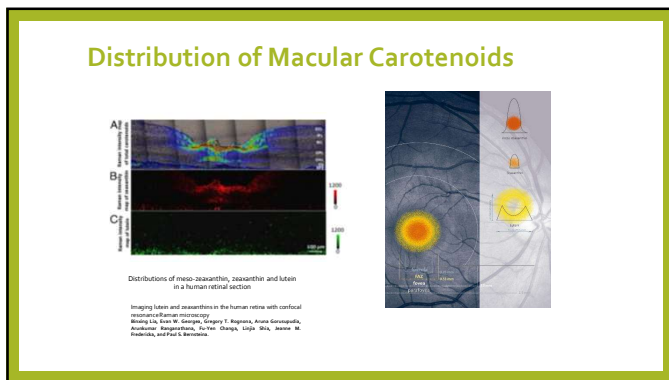


Carotenoids

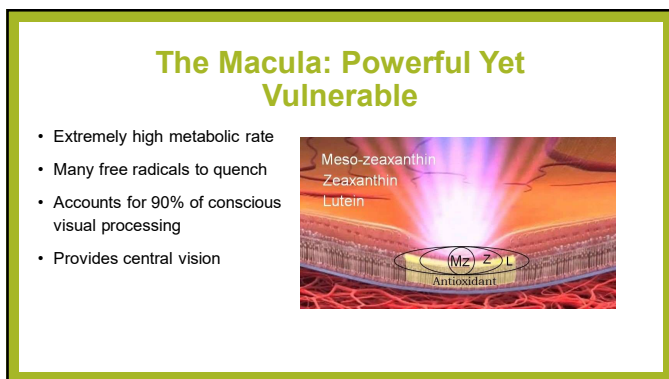
33



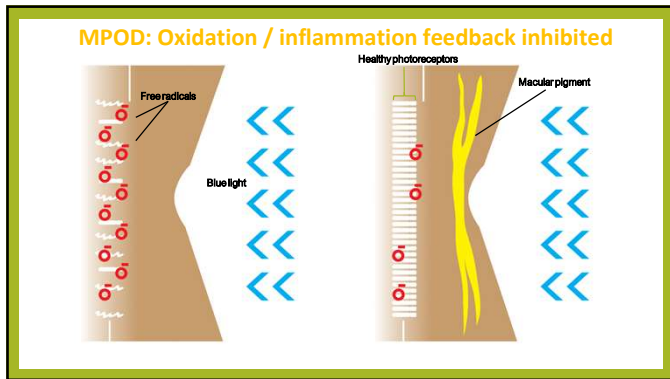
34



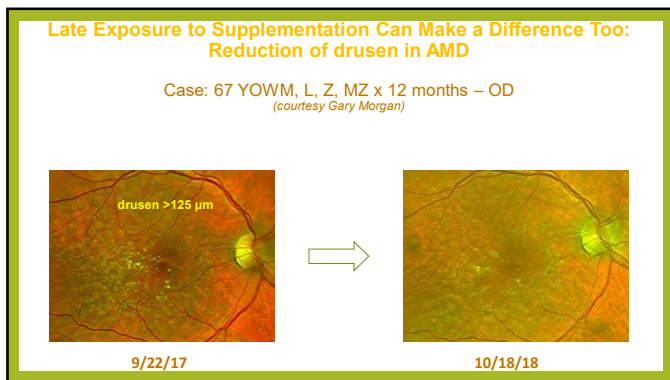
35



36



37



38

Role of Oxidative Stress in Disease

Free Radicals Caused By:

- Cellular Metabolism
- The Environment
- Lifestyle & Choices


The complex block contains a collage of four images: a hand holding a lit cigarette, a woman eating a slice of pizza, a woman in a white dress, and a city skyline.


39

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 IN THE MACULAR PIGMENT: Lutein, Zeaxanthin, Meso-Zeaxanthin

Chemical structure of lutein





40

High vs. Low MPOD: Glare Disability Reduced

High MPOD



Low MPOD

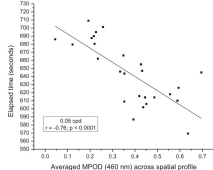



Strigham & Hammond. Optom Vision Sci. 2008;85:82-88; Hammond et al. Invest Ophthalmol Vis Sci. 2014;55(12):8533-8; Nishi et al. (2016); Strigham et al. (2016)

41

Dark Adaptation Speed

Suggests increased visual cycle efficiency promoted by macular carotenoids





Joan Strigham et al. 2015
 *Joan Strigham & Hammond, 2008; Hammond et al. 1998; Patryas et al. 2013; Hammond et al. 2014; Strigham et al. 2016

42

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

Borring L.J, Patel Ahmed, Paul S. Bernstein. Studies on the single oxygen quenching mechanism of normal macular pigment. Arch Biochem Biophys. (2012), doi:10.1016/j.ab.2010.07.024

43

CREST AMD (Trial 2)

Funded by the European Research Council (ERC) €1,462,342 over 5 years; Grant No. 281098

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 100mg lutein, 4mg 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

44

Results

**All data not listed

Variable	Group 1*				Group 2†				Time	Time x Group		
	N	Mean	SD	Mean	N	Mean	SD	Mean			SD	Sig.
Vision												
Best corrected visual acuity, VAR	46	101.22	5.16	100.91	5.80	51	100.78	5.08	101.31	5.20	0.746	0.233
Letter contrast sensitivity, LogCS												
1.2 cpd	46	1.79	0.17	1.89	0.20	51	1.86	0.14	1.91	0.16	<-0.0005	0.038
2.4 cpd	46	1.78	0.22	1.80	0.22	51	1.85	0.16	1.91	0.18	<-0.0005	0.382
6 cpd, POM	46	1.53	0.24	1.57	0.29	51	1.58	0.18	1.61	0.23	0.013	0.801
9.6 cpd	46	1.29	0.28	1.31	0.31	51	1.36	0.21	1.38	0.26	0.134	0.925
15.1 cpd	46	0.92	0.33	0.95	0.34	51	0.96	0.27	1.01	0.33	0.082	0.747
Mesopic contrast sensitivity, LogCS												
1.5 cpd	46	1.55	0.22	1.62	0.24	51	1.63	0.21	1.70	0.23	0.007	0.982
3 cpd	46	1.65	0.24	1.76	0.27	51	1.69	0.18	1.84	0.27	<-0.0005	0.523
6 cpd	46	1.25	0.35	1.48	0.45	51	1.34	0.34	1.49	0.42	<-0.0005	0.228
12 cpd	46	0.81	0.29	0.94	0.36	51	0.87	0.28	0.96	0.35	0.002	0.695
18 cpd	46	0.53	0.13	0.59	0.25	51	0.31	0.08	0.41	0.25	<-0.0005	0.369
Photopic contrast sensitivity, LogCS												
1.5 cpd	46	1.47	0.19	1.60	0.25	51	1.53	0.16	1.64	0.21	<-0.0005	0.862
3 cpd	46	1.75	0.23	1.84	0.25	51	1.82	0.18	1.91	0.21	<-0.0005	0.990
6 cpd	46	1.65	0.28	1.74	0.30	51	1.70	0.20	1.81	0.34	<-0.0005	0.934
12 cpd	46	1.25	0.37	1.34	0.43	51	1.30	0.33	1.34	0.37	0.015	0.468
18 cpd	46	0.56	0.16	0.71	0.44	51	0.65	0.34	0.69	0.36	0.008	0.174

75% (24 of 32) of vision related measures (e.g. contrast sensitivity, glare disability, photo stress recovery) exhibited significant improvements

45

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-Zeaxanthin¹
- Triple Carotenoid formula demonstrated to augment the entire MP spatial profile; a high lutein-only formula was unable to rebuild the central region²
- Analysis of over 700 peer-reviewed journal articles show clinical benefit to including meso-zeaxanthin in a retinal/macular supplement

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

46

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.



47

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. *Focus*, 2017.
2. J. Stringham, et al. Contrast Sensitivity and Lateral Inhibition are Enhanced with Macular Carotenoid Supplementation. *Visual Psychophysics and Physiological Optics*, 2017.
3. Nolen, et al. Enhancement of macular pigment enhances contrast sensitivity in subjects free from retinal disease. *Central Retinal Enrichment Experimentation Trial* - *Optics*, 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*, 2016.

48

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


49

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

Oil Filled Softgel Capsule




Shell, gelatin water plasticizer, for airtight enclosing


Powder Filled Capsule



Shell, cap and body interlock to form a secure leak-free closure



Oil and carotenoid filled capsule



Powder and carotenoid filled capsule

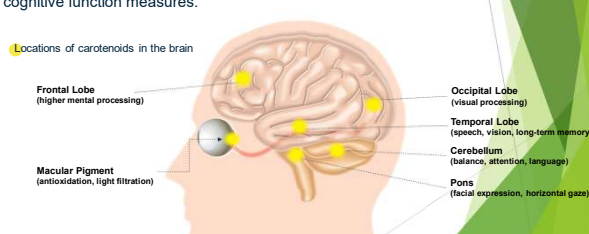
<https://www.chronos.ca/health/many-supplements-for-vision-loss-do-not-achieve-their-label-claim-researcher-says-1-5468929>

50

Support Cognitive Function

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

Locations of carotenoids in the brain



Frontal Lobe
(higher mental processing)

Macular Pigment
(antioxidation, light filtration)

Occipital Lobe
(visual processing)

Temporal Lobe
(speech, vision, long-term memory)

Cerebellum
(balance, attention, language)

Pons
(facial expression, horizontal gaze)

51

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

52

Dark Adaptation Test Results for
DOB: 06-16-1957, Patient ID: 1787

Test Eye: Right
Test Date: 01-04-2019 09:52
Age at Test: 61
Protocol: Enhanced Test
Pupil Size: 5.50 mm
Prescription: +1.50 -1.00 x 97°
Trial Lens: +4.50 -0.50 x 0°

Read threshold is 15.38 minutes.
Fixation Error Ratio is 4%.

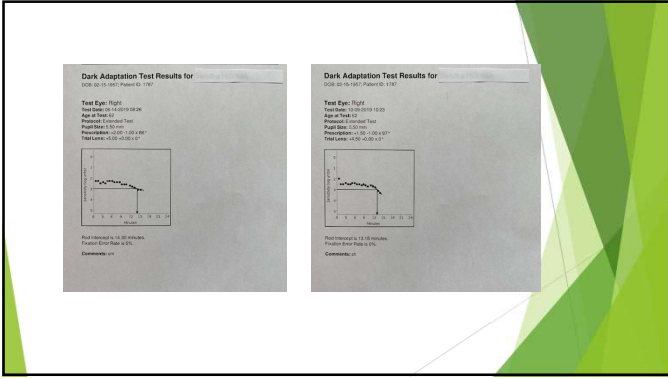
Comments: sm

53

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

54



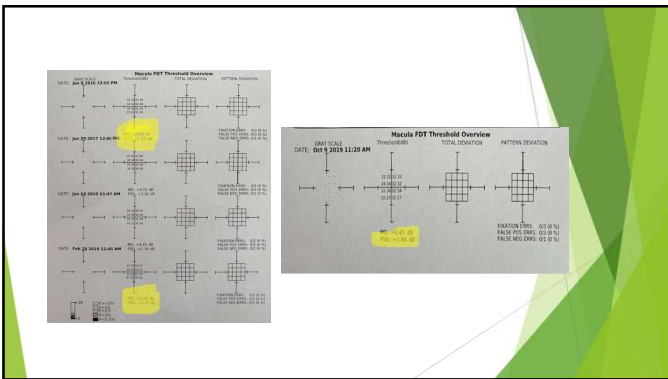
55

► Rod Intercept time improved in same eye (OD):

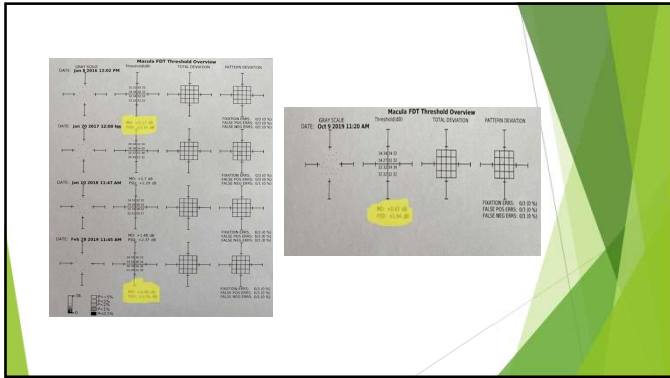
- January 2019: 15.38 minutes (4% fixation error rate)
- June 2019: 14.30 minutes (5% fixation error rate)
- October 2019: 13.15 minutes (0% fixation error rate)

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

56



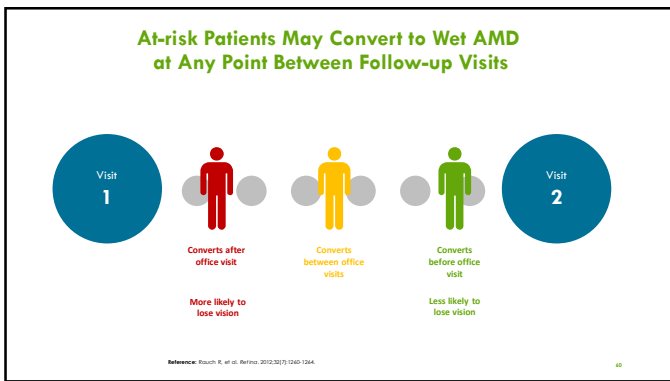
57



58



59



60

Amsler grid alone has limited ability to detect visual changes

- Accurately taking the test^{1,2}
 - Fixation
 - Testing distance
 - Test questions
 - Compliance
- Cortical completion¹
- Low sensitivity; subjectivity exam to exam, patient to patient⁴

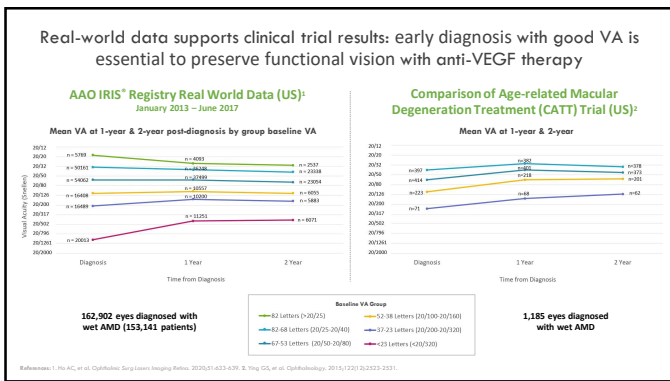
References: 1. Marmor L, Hangerer S. Ophthalmol Rev. 2012;68(1):34-36. 2. Hangerer S, et al. J. Opt. Soc. Am. Opt. Phys. 2007;23(10):1770-1773. 3. Lu Y, et al. J. Opt. Soc. Am. Opt. Phys. 2013;13(12):3325-33. 4. Wang Y, et al. Ophthalmology. 2008;115(10):1741-174.

61

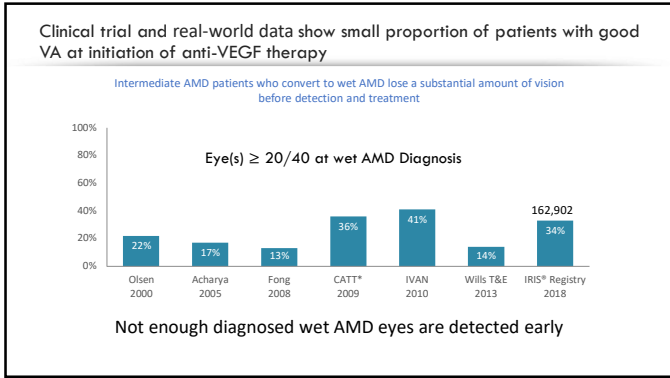
A Perfect Combination for Poor Visual Acuity at Wet AMD Diagnosis

Intermediate AMD may go undiagnosed + Patients progress between visits + Limitations of Amsler grid = Poor VA at wet AMD detection

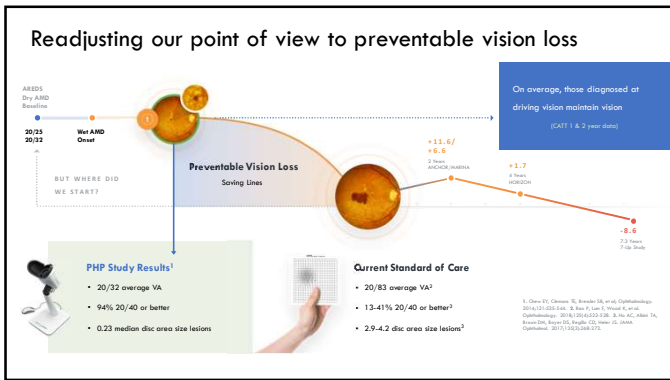
62



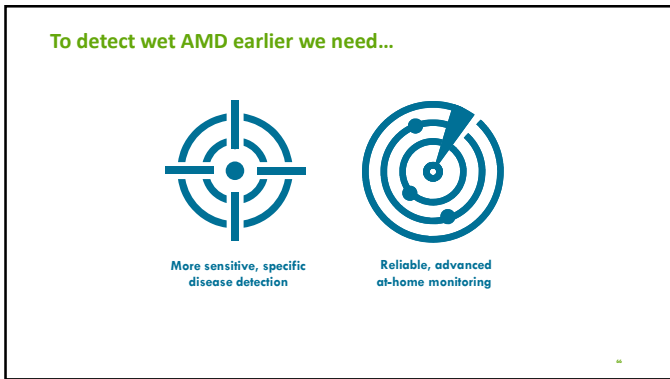
63



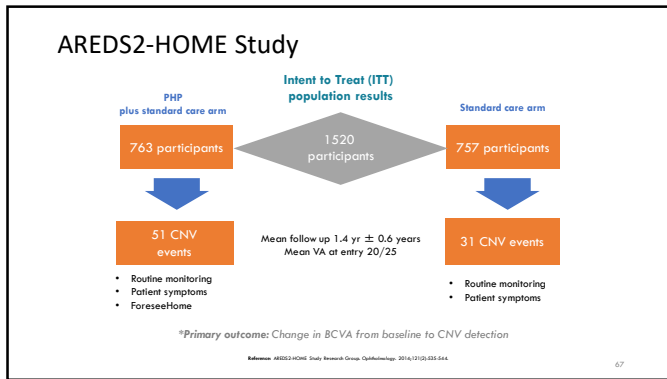
64



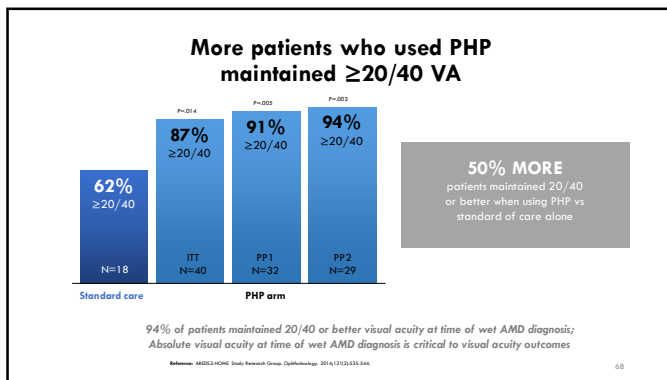
65



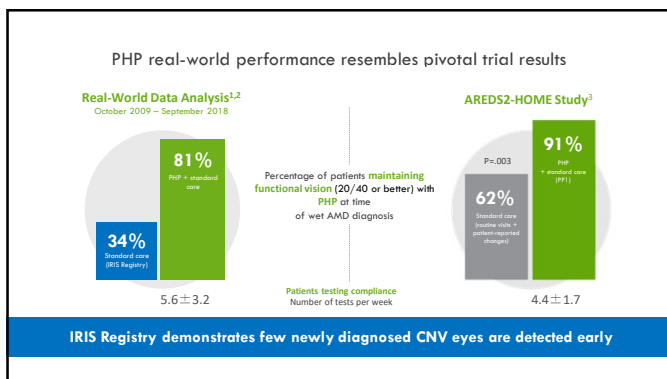
66



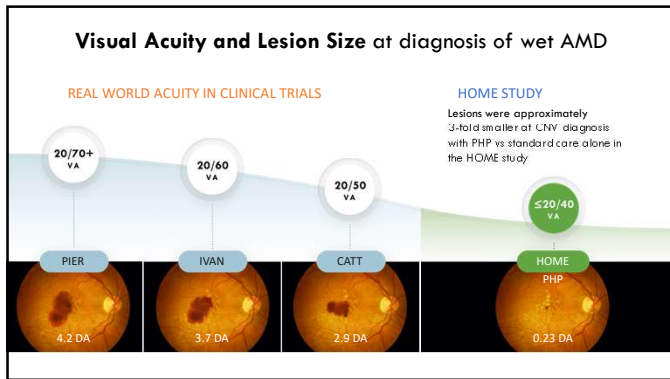
67



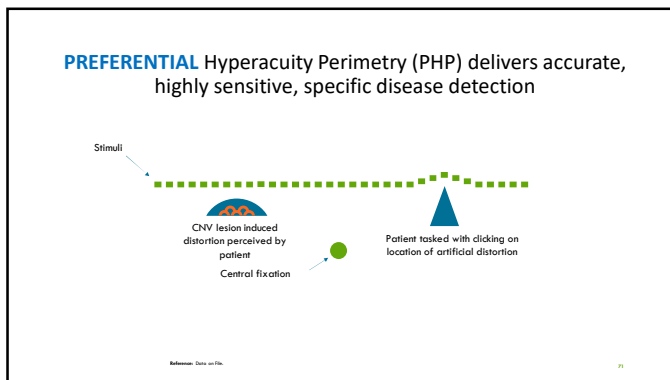
68



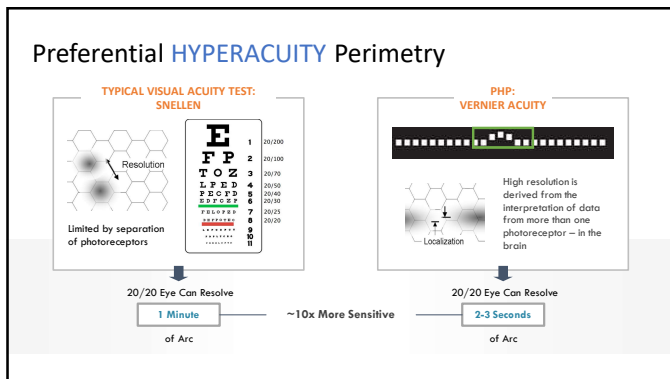
69



70



71



72

PERIMETRY: The Home PHP Test

Total of 500 data points tested 3 to 5 times each
Stimuli are presented on screen for 160 ms

Visual field - central 14° (4200 microns)

Macula

Optic disk

0.75° resolution

73

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

Macula

Optic disk

Pathology

74

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

Baseline

Alert

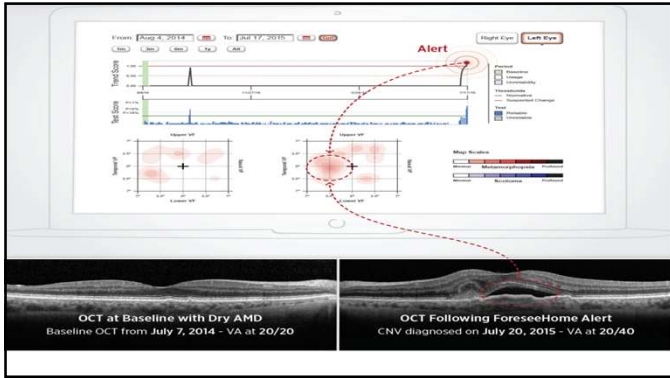
Upper VF

Lower VF

Nasal VF

Temporal VF

75



76

POI 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

77

o)) CASE 1 → Baseline 10/22/18: VA 20/30⁻¹ (OD) prior to alert

BASELINE 10/22/18 STARTED TESTING

9/27/20 ALERTED

78

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

79

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

80

At-home monitoring for conversion to wet AMD

1940s vs 2021

Standard of Care vs Home-based PHP; AMD Monitoring Program

13-41% standard of care alone (based on anti-VEGF trials)

Maintained driving vision at time of diagnosis (20/40 or better)

94% when PHP was added to standard of care (AREDS2-HOME Study PFD)

81

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 Dry Intermediate Right eye	H35-3122 Dry Intermediate Left eye	H35-3132 Dry Intermediate Bilateral
---	--	---

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



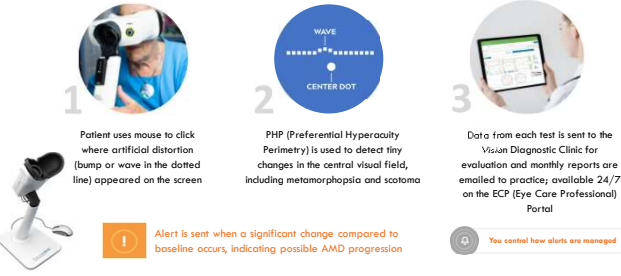
82

Set up and daily tests are quick and easy for patients

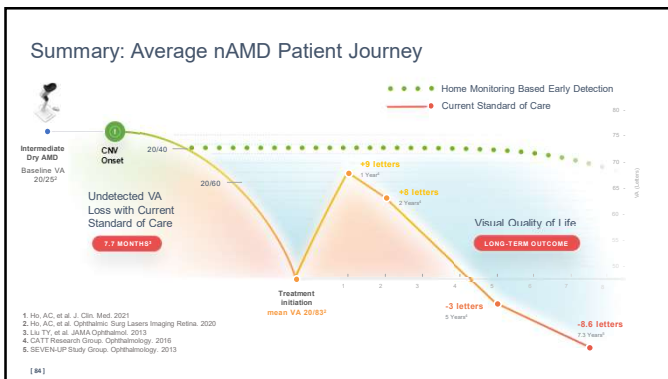
1. Patient uses mouse to click where artificial distortion (bump or wave in the dotted line) appeared on the screen
2. PHP (Preferential Hyperacuity Perimetry) is used to detect tiny changes in the central visual field, including metamorphopsia and scotoma
3. Data from each test is sent to the Vision 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

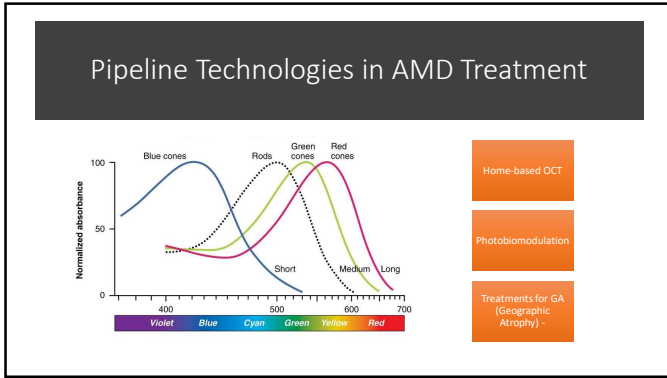
You control how alerts are managed



83



84



85

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)

86

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...

87

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

88

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

89

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%

90

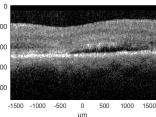
Home OCT for monitoring chronic therapy of neovascular AMD between office visits

- 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

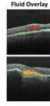
Home Device



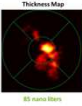
Home OCT Image



Air-based Fluid Overlay

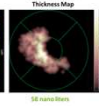


Intraretinal Fluid Thickness Map



85 nano flars

Subretinal Fluid Thickness Map



58 nano flars

91




THANK YOU!!!



92

ALOFT Study Design

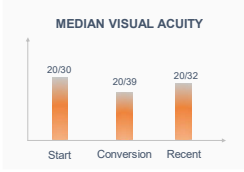
Large retrospective study involving **all referred patients** from 5 clinics over 10 years

 <ol style="list-style-type: none"> 1. Retina Group of Washington 2. Virginia Eye Institute 3. Retina Associates of Kentucky 4. Wagner Macula & Retina Center 5. Elman Retina Group 	 <p>2,123 patients</p>	 <p>3,334 eyes</p>
---	---	---

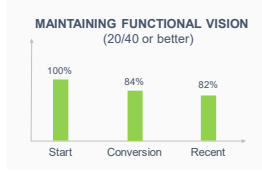
1 million+ tests | 10,000+ monitoring years

93

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

[94]
