


Nutrition Carotenoids in Ocular Disease and Systemic Disease


Greg Caldwell, OD, FAAO
Mid-Winter Getaway
Optometric Education Consultants
Sunday, January 28, 2024



3

Disclosures- Greg Caldwell, OD, FAAO
All relevant relationships have been mitigated

- Lectured for: Alcon, B&L, BioTissue, Dompé
- Disclosure: Receive speaker honorarium
- Advisory Board: Dompé, ImmunoGen, Iveric
- Disclosure: Receive participant honorarium
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
- Disclosure: Non-salaried financial affiliation with Pharmacia
- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
- Optometric Education Consultants – Scottsdale, AZ, Pittsburgh, PA, Sarasota, FL, Barcelona, Spain, Orlando, FL, Mackinac Island, MI, Quebec City, Canada, and Nashville, TN- Owner



4

Financial Obligations



5

My Practice

I am a clinician first then a scientist

- Some are scientists first then clinician
- I need to simplify for patient and patient care.
- Science is great, but not good if there isn't a clinical application.
- Some lectures are science based without clinical application.
- My lecture will be a hybrid. Showing clinical applications of the science




It is wonderful to have someone who's bringing so many aspects of optometry (scientific, clinical experience, teacher & lecturer). It is refreshing and very informative. -Sarah

6

Ocular Disease Career
Allopathic

- OCT - Spectral domain
- OCT Angiography
- Visual Fields
- AMD, glaucoma, retinal degenerations, diabetic retinopathy
- Dark Adaptation
- Focusing on structure and function loss or damage
- Patients asking what about supplements
 - Reading about it on internet
 - Promised I would do my due diligence
- Ocular disease optometrist to an Integrative Optometrist




7

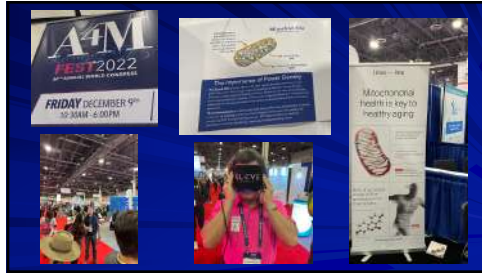
Early Detection and Allopathic Treatments

Rubin Cone Contrast Test

ERG and VEP



8



9

Patients Are Expecting

- ~ Early detection
- ~ Wellness
- ~ Prevention

10

Nutraceuticals

~ Do not claim that a product will treat, cure, or prevent any disease or health condition (including COVID-19 or viruses) or that the product cured your own ailment

11

Who?

~ Recommends a lutein and zeaxanthin supplement?

12

Thoughts?

13

Question?

~ Who in here would consider themselves as an integrative optometrist?

~ Who has done or recommended?

- * Supplements, vitamins, AREDS2
- * Omegas, EPA, DHA
- * Vital tears – ASED
- * Regener-Eyes
- * Amniotic membranes
- * CBD
- * Probiotics

14

Allopathic vs Integrative Medicine

- Allopathic medicine is a term used for modern or mainstream medicine
 - Conventional medicine, mainstream medicine, Western medicine, biomedicine
 - Treating conditions and symptoms with its "opposites"
 - Health system in which medical doctors, nurses, pharmacists, and other healthcare professionals are licensed to practice and treat symptoms and diseases
 - Using medication, surgery, radiation, therapies, and procedures
- Complementary and integrative medicine are commonly used along with mainstream medicine
 - Herbalism, naturopathy, chiropractic care, Chinese medicine
- Allopathic or modern medical schools have recently added more study and information on how food and nutrition can help prevent and treat disease
 - More education is being offered on integrative approaches and potential interactions with mainstream medicine

15

Medical Practices

- Allopathic medicine
 - Western medicine
- Alternative "homeopathic"
 - Functional
 - Medicine of why, treat the cause
- Integrative medicine
 - Complementary medicine - Eastern complementing Western


What is integrative medicine?

The practice of integrative medicine refers to the blending of conventional and evidence-based natural and complementary medicines and/or therapies with lifestyle interventions to deliver holistic, patient-centred care.

16

Chronic and Low-Grade Inflammation


Science has proven that chronic, low-grade inflammation can turn into a silent killer that contributes to cardiovascular disease, cancer, type 2 diabetes, diabetic retinopathy, cataracts, macular degeneration, and many other conditions.



17

Chronic and Low-Grade Inflammation

Like cancers and other slow-burn diseases, identifying these conditions early can make the difference between full recovery or a dramatically reduced quality of life or even death (vision loss or blindness)



18

"Choose Your Parents Wisely"

- This just isn't as true as it's used to be
- Lifetime health
 - 8% genetics "Picking your parents wisely"
 - DNA in our nucleus
 - Can't be influenced
 - 92% epigenetics
 - Lifestyle choices = we can influence
 - Turn on/off gene expression

19

Biomarker

- Test that has meaning
- Biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.
- A biomarker may be used to see how well the body responds to a treatment for a disease or condition
- Blood pressure, blood work, heart rate, genetic testing, IOP

20

Predictive Biomarker

- Used to identify individuals who are more likely to respond to exposure to a particular medical product or environmental agent
- The response could be a symptomatic benefit, improved survival, or an adverse effect
- A value that we can guide therapy around
 - HbA1c
 - C-Reactive Protein
 - Plasma Homocysteine
 - Vitamin D (25-HydroxyD)
 - Omega 3 index
 - Carotenoid

21

Measure?

22

Chronic and Low-Grade Inflammation

23

DNA Sciences

- Genomics = all of our genes
- Genetics = individual genes
- Epigenetics – the study of how our cells control gene activity without changing the DNA
 - Internal and external environments

24

Exposome

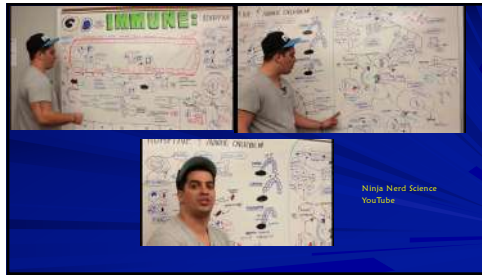
The exposome can be defined as the measure of all the exposures of an individual in a lifetime and how those exposures relate to health. An individual's exposure begins before birth and includes inputs from environmental and occupational sources. Understanding how exposures from air, electronics, diet, lifestyle, etc.,

<https://www.nsk.gov/health-topics>

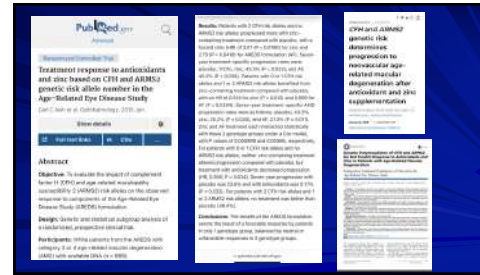
Exposome and Exposomics - NIOSH Workplace Safety and Health Topic - CDC

25

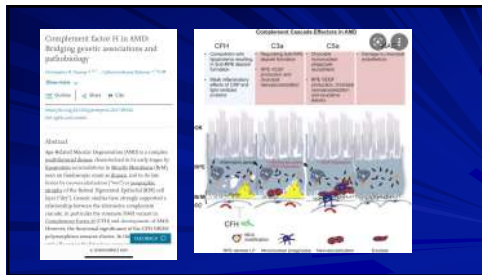
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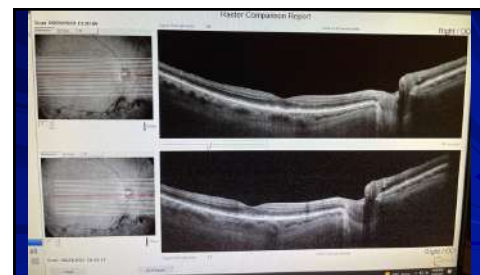
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30



31



32

Key Tenants of Aging, Performance and Vitality

- Oxidative Stress / Inflammation
- Hormonal Balance
- Stress Hormones
- Glucose / Insulin Regulation
- GUT Integrity and microbiome diversity
- Immune Balance
- Environmental Exposure/Burden
- Individuality

Credit to: James LaVita, RPH, CDR

33

Inflamm-aging

One of the consequences of falling mitochondria due to aging, beyond mROS, is the release of mtDNA. Plasma levels of mtDNA increase gradually after the fifth decade of life, correlating with elevated levels of pro-inflammatory cytokines (i.e., TNF-α, IL-6, IL-1, and IL-18).

These data indicate that mtDNA may promote the production of pro-inflammatory cytokines in aging. Because cell stress, senescence and death are a part of the pathophysiology of aging designing new therapeutic strategies against circulating mtDNA, or other mtDNA, or their cognate receptors (e.g., TLRs or PRRs) may be a viable strategy to approaching IA and its associated conditions.

Credit to: Elnoy Veldan, MD - Head Research, The Role of Mitochondrial Dysfunction in Neurodegenerative Diseases: Emerging Insights from and Translational Implications

34

Mitochondrial Dysfunction Pathway

EXPOSURE (e.g., oxidative stress, chemical stress) → Mitochondrial dysfunction → mROS → DNA fragmentation → Cell cycle arrest, oxidative stress, and apoptosis.

EXPOSURE → Mitochondrial dysfunction → mROS → Activation of cellular regulatory factors → Production of Type I interferon → Apoptosis and neuronal cell death.

Credit to: Elnoy Veldan, MD - Head Research, The Role of Mitochondrial Dysfunction in Neurodegenerative Diseases: Emerging Insights from and Translational Implications

35

Fun Facts I Have Learned About the Mitochondria

- Mitochondria produce energy from organic matter
- Live about 100 days
- They produce 90% of energy in the body
- In return they produce 90% of the free radicals
- When they become dysfunctional they get many clinical consequences
- Mitochondria are very sensitive to reactive oxygen and need antioxidant support
- Mitochondria are one of cellular organelles
 - Electron transport chain - uses co-enzyme 10, and many other micronutrients
- Brain cell has 1.2 million/single neuron
- Heart cell has 5,000/cell
- Liver cell has 1000-2000/cell
- Photoreceptors 498/cell
- RPE cells = 700/cell

The ellipsoid contains a densely-packed array of mostly elongated mitochondria arranged linearly parallel to the long axis of the photoreceptor. The cell contains **498 individual mitochondria**.

36

Question

Do you agree that free radical formation is a progressive process that leads to cell damage or death?

- Yes
- No

37

Free Radicals and Antioxidants

How antioxidants reduce free radicals

Antioxidant + Free radical → Stable molecule + Neutralized radical

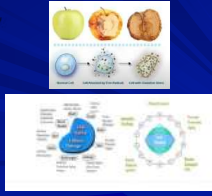
FREE RADICAL
 (An unstable molecule with an unpaired electron + electron donation leads to a more stable state.)

ANTIOXIDANT
 (An electron donor that can donate an electron to a free radical.)

38

Oxidative Stress


- Small percentage of oxygen is not completely reduced
- Accumulation of free radicals
- Oxidative damage
- Oxidative stress
- Considered the starting of several diseases
- Responsible for epigenetic alterations
- Mitochondria - vulnerable
- Not going to make this apple new again
 - Prevention is the one of the best medicine



39

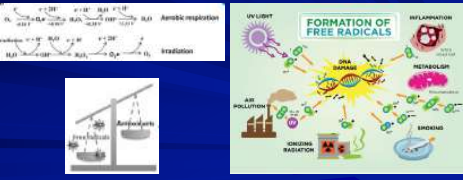
Free Radicals

- During metabolism the O_2 molecule splits and energy is released
 - Endogenous free radical formation
- Regain stability the free single oxygen atom (oxygen free radical) seeks and steals electrons from other molecules
 - Superoxide anion - will accept one electron
 - Peroxide - will accept two electrons
- These molecules can be proteins, lipids, and DNA
 - Proteins (enzymes) - kinases, phosphatases, and transcription factors



40

Endogenous and Exogenous Free Radical Formation



41

Oh no

- Increasing exogenous free radicals
- Less antioxidant protection in our diet
- More bad and less good




Is an orange of the 1950's equivalent to 21 of today's oranges?

An orange from the 1950's was full of vitamin A, precious for our sight and our immune defenses. To attain the same amount today, you would have to consume 21 of them. Onions and potatoes no longer contain any trace of it. The iron content, in meat? Divided by 2. Calcium in broccoli? Divided by 4. To ingest the vitamin C contained in an apple from yesterday, you would have to eat 100 today.

42

The Equalizer



43

October 23, 2021

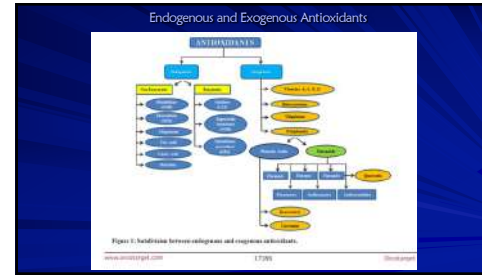


44

Nutritional Antioxidants

- ~ Exogenous antioxidants
 - * Tocopherols (E), ascorbic acid (C), carotenoids, ubiquinone, and polyphenols
- ~ Well know antioxidants
 - * Vitamin C, E, Beta-carotene, lutein, zeaxanthin, selenium, quercetin, and resveratrol
- ~ Mechanisms of action:
 - * Neutralize free radicals
 - * Repair oxidized membranes
 - * Decrease reactive oxygen species
 - * Neutral reactive oxygen species

45



46

Carotenoids

- ~ Why do hear so much about carotenoids
- ~ Melonie Clemmons, OD May 20, 2022 AACO Nashville

47

Carotenoids

- ~ Organic pigments produced by plants, algae, and bacteria
- ~ Cannot be synthesized by the human body
 - * Hydrophobic compounds
 - Important for the phospholipid bilayer
- ~ 700 in nature – 50 human food chain – 15-20 human blood stream
- ~ Macular carotenoids (L and Z) – highest concentration found in the human body
 - * Diet derived
 - * Henle fibers – between the inner and outer plexiform layers
 - * Sequester or absorb blue light

48

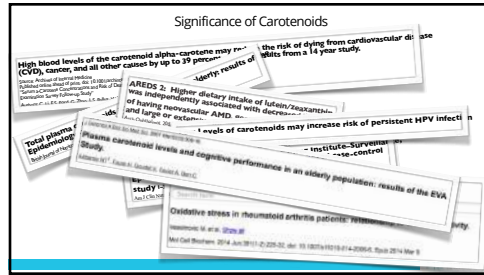
Question

- ~ Do you measure carotenoid levels in your office?
- * Yes
- * No

49

Measure?

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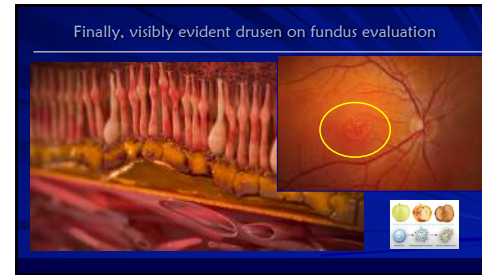
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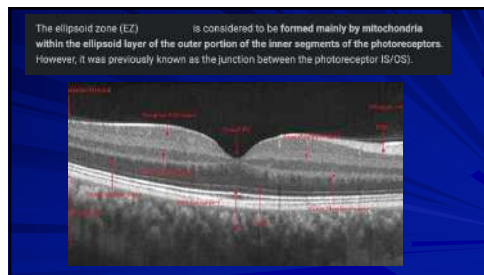
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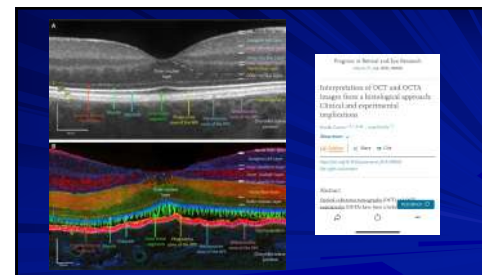
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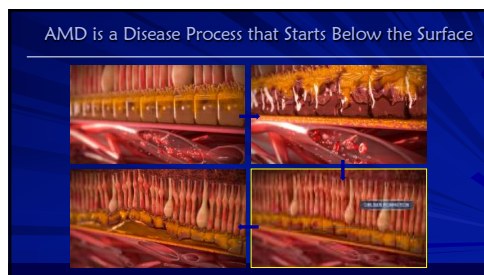
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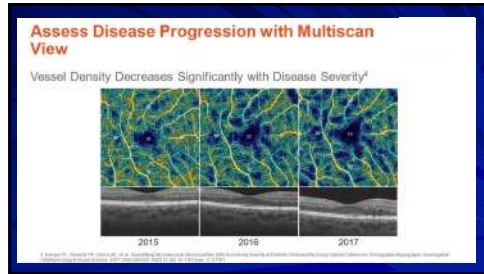
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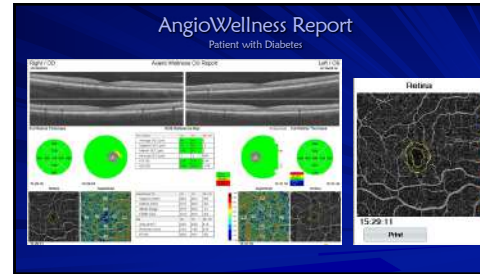
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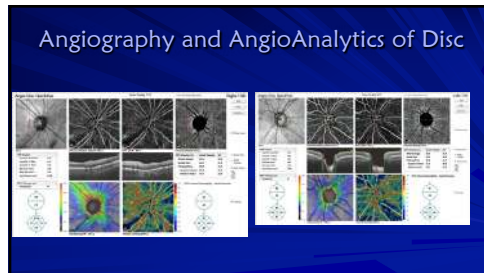
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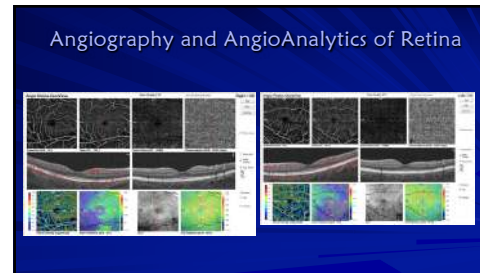
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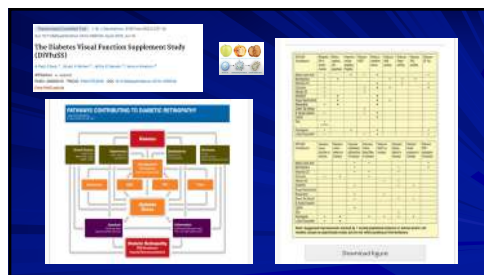
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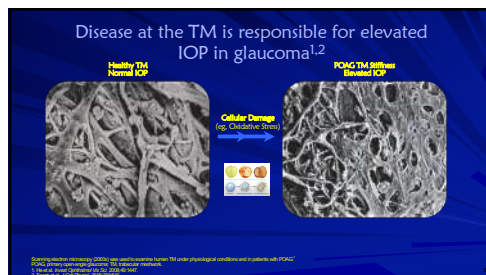
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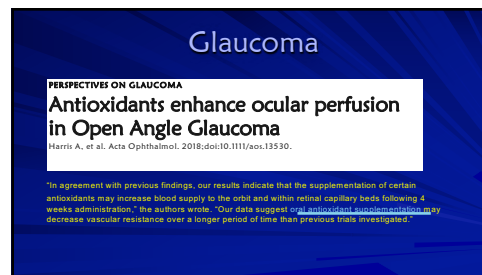
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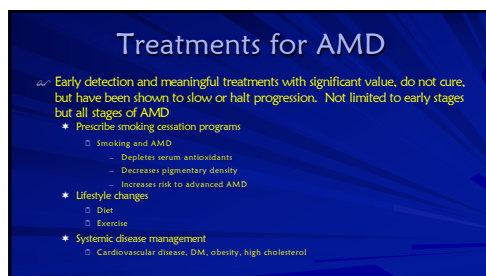
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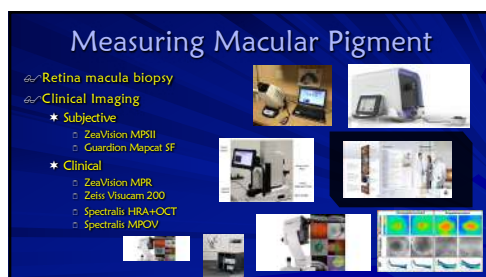
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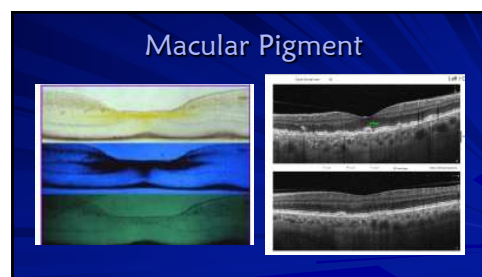
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72




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74

Measuring Carotenoids and the Macular Pigment

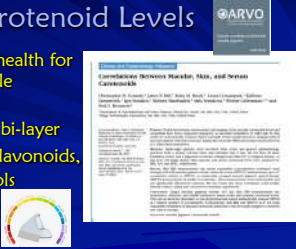
- Biophotonic Scanner
 - Measures carotenoids
 - Based on an optical method known as Resonant Raman Spectroscopy (RRS)
 - Used for many years in research laboratories
 - Skin RRS measurements
 - Noninvasive
 - Objective
 - Reliable methods to assess carotenoid levels
 - Ocular
 - Systemic



81

Carotenoid Levels

- Biomarker of health for diet and lifestyle
- Yale University
- Phospholipid bi-layer
- Carotenoids, flavonoids, and polyphenols



82


The New Standard




- Quick Test (approx. 30 sec)
- Portable
- Cost Effective
- Remeasure in 60 days
- Reassurance to you and patient

83

Raman Spectroscopy



84

Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies

Susan T. Mayne^{1,2}, Brenda Cartmel¹, Stephanie Scarmo^{1,3}, Lisa Johns¹, Igor V. Ermakov¹, Werner Gellermann⁴

90 STUDIES

*Arch Biochem Biophys. PMC 2014 Nov 15.


85

An Evening with Dr. Paul Bernstein

Measurement of Macular Pigment

- HPLC
- Psychophysical
 - Macular color vision (MCV) test
 - Macular media opacity (MPO)
- Image Based
 - Automated densitometry
 - Fluorimetry
 - Resonance Raman spectroscopy (skin and eye)

High Performance Liquid Chromatography



86

An Evening with Dr. Paul Bernstein

The Moran AMD Genetic Testing Assessment Study: The Magenta Study

- With knowledge of AMD genetic risk factors, can lifestyle, diet, and/or healthy changes in lifestyle?
- Epidemiologic, controlled trial of gene-sympomatic genetic risk testing and counseling
- Interventional genetic counseling
- Up-to-date on new AMD diagnosis
- Risk stratification by APOE and RFL
- Molecular epidemiology of AMD
- Lifestyle counseling
- Awaiting FDA funding

87

ARVO STUDY

Interrelationships between Macular, BDNF and Serum Carotenoids- Paul Bernstein, Werner Gellman et al ARVO May 2018

Conclusions:
 "Our results emphasize the importance of measuring the total amount of carotenoids in the macula region using an objective image based modality such as AFw SpectraScan rather than subjective MPD."

with increased serum concentrations of total carotenoids is a reasonable biomarker of macula carotenoid status, and correlates better than than subjective MPD tests.

The objective fundus scanner is better than the subjective Macular, QuantEX, and Densimeter for estimating macula pigment.

88

Vulnerable to Oxidation

89

90

Are you taking a supplement?

91

53-year-old man

- ✓ Family history of AMD
 - Dad with 43 injections for AMD
- ✓ Pre-diabetic with borderline HbA1c
- ✓ Vision 20/20 OU
- ✓ DFE- retina clear
- ✓ OCT normal
- ✓ Passes dark adaptation

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS.

92

Ingredients:		Amount		Daily Value	
Ascorbic Acid (Vitamin C)	100 mg	20%	100%	100%	100%
...

93

SUPPLEMENT FACTS		Amount per Serving		% Daily Value	
...

94

53-year-old man

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCE

95

Master Comparison Report

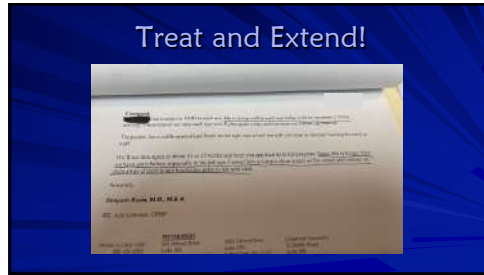
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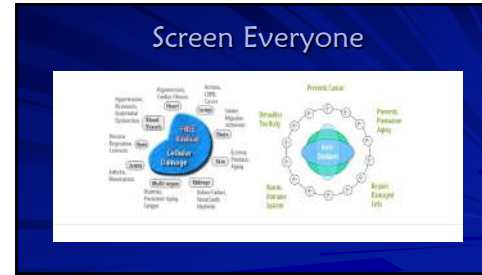
Cross Line Comparison Report

97

98



99



100

Greg's Comments

- ~ I think macular pigment is miss named and should be called fovea pigment
- ~ Binding proteins need coenzymes and cofactors
- ~ The macula/fovea is 3rd lens of the eyes – L&Z are important for vision, focus, glare, and contrast
- ~ Many people talk nutrition, very few are measuring it
- ~ If doctors don't become more like nutritionist, nutritionists will become more like doctors
- ~ "Can't supplement out of a poor diet, needs to be done with food"
 - I bet I have changed more diets by scanning and recommending supplements

101




102

Thank You for This Opportunity

- ~ Do it for:
 - * Yourself
 - * Your family
 - * Your staff
 - * Your patients




103



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Greg Caldwell, OD, FAAO
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Sunday, January 28, 2024



104