



Optometric  
Education  
Consultants



## Nutrition Carotenoids in Ocular Disease and Systemic Health

Greg Caldwell, OD, FAAO  
Phoenix, AZ  
Saturday, April 16, 2023




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### Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated




- Lectured for: Alcon, Allergan, Aerie, B&L, BioTissue, Kala, Maculogix, Optovue, RVL, Heru, Santen
- Disclosure: Receive speaker honorariums
- Advisory Board: Allergan, Alcon, Dompe, Eyenovia Tarsus, Visus
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
- Disclosure: Non-salaried financial affiliation with Pharmanex
- Envolve: PA Medical Director, Credential Committee
- Healthcare Registries - Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
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## Ocular Disease Career


- 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


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## Early Detection and Allopathic Treatments


### Rabin Cone Contrast Test



### ERG and VEP






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## Patients Are Expecting

- Early detection
- Wellness
- Prevention

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## 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

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## 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 "opposite"
  - \* 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
  - \* Homeopathy, 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

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## 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.

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## 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



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## 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)



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## "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

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## 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

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## 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

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## Measure?



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## Chronic and Low-Grade Inflammation



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## 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

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## Exposome



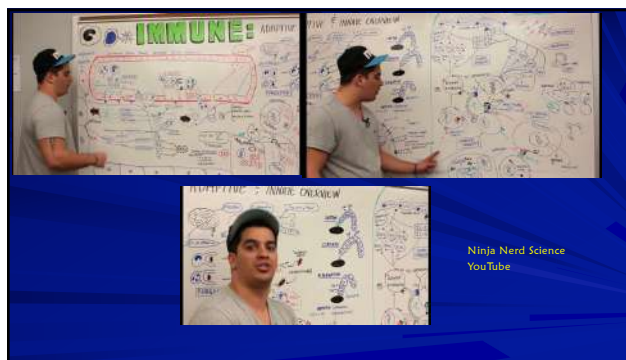
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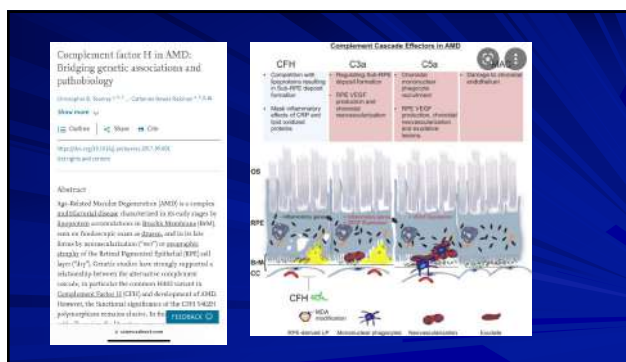
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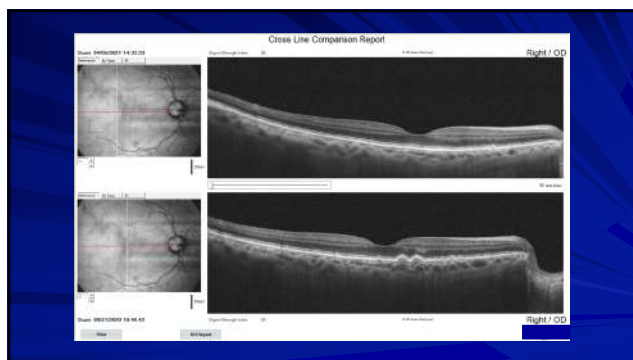
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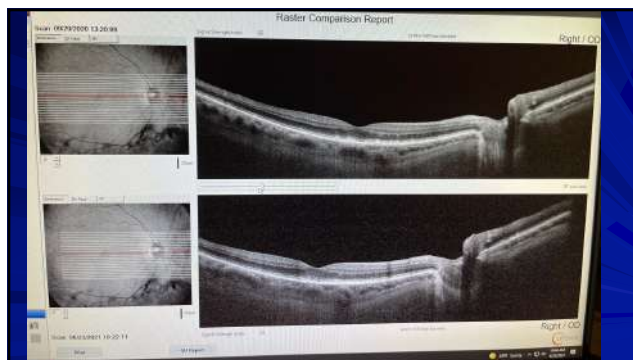
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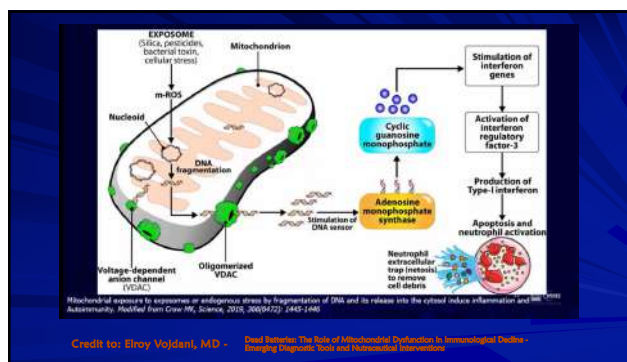
### Inflamm-aging

One of the consequences of failing mitochondria due to aging, beyond mtROS, 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- $\alpha$ , IL-6, RANTES, and IL-1 $\alpha$ ).

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 mtDAMPs, or their cognate receptors (e.g., TLRs or FFR1) may be a viable strategy to approaching IA and its associated conditions.

Credit to: Elroy Vojdani, MD - David Reardon: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutritional Interventions

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### 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 when 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 broadly parallel to the long axis of the photoreceptor. The cell contained **498 individual mitochondria**.

Credit to: Elroy Vojdani, MD - David Reardon: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutritional Interventions

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### Question

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

- \* Yes
- \* No

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### Free Radicals and Antioxidants

**How antioxidants reduce free radicals**

ANTIOXIDANT: chemically reactive unpaired electron + electron donation: stable electron pair is formed, free radical is neutralized

FREE RADICAL: chemically reactive unpaired electron + electron donation: stable electron pair is formed, free radical is neutralized

HEALTHY STABLE MOLECULE vs. UNPAIRED MOLECULE (Missing an Electron)

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### 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 medicines

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### 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

Reactive oxygen species (• = unpaired electrons)				
Oxygen $O_2$	Superoxide anion $O_2^{\bullet -}$	Peroxide $O_2^{\bullet - 2}$	Hydroxyl radical $\bullet OH$	Hydroxyl ion $OH^-$

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### Endogenous and Exogenous Free Radical Formation

**FORMATION OF FREE RADICALS**

Endogenous: Aerobic respiration, Radiation

Exogenous: UV LIGHT, AIR POLLUTION, INFLAMMATION, METABOLISM, SMOKING, IONIZING RADIATION

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### 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 amounts 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 yesteryear, you would have to eat 100 today.

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### The Equalizer

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October 23, 2021



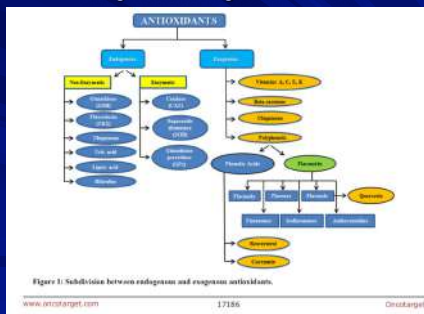
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## Nutritional Antioxidants

- ~ 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

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## Endogenous and Exogenous Antioxidants



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## Carotenoids

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



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## Carotenoids

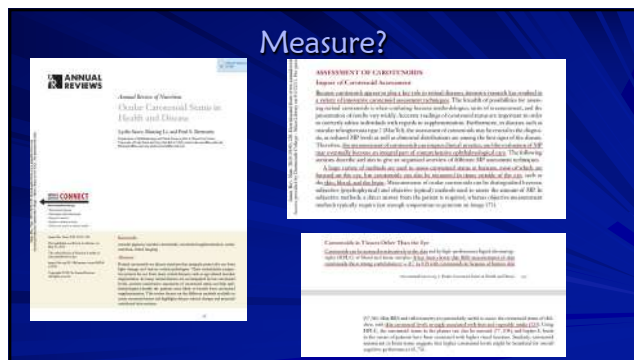
- ~ Organic pigments produced by plants, algae, and bacteria
- ~ Cannot be synthesized by the human body
  - \* Hydrophobic compounds
    - o Important for the phospholipid bilayer
- ~ 700 in nature – 50 human food chain – 15-20 human blood stream
- ~ Macular carotenoids (L and Z) – highest concentration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

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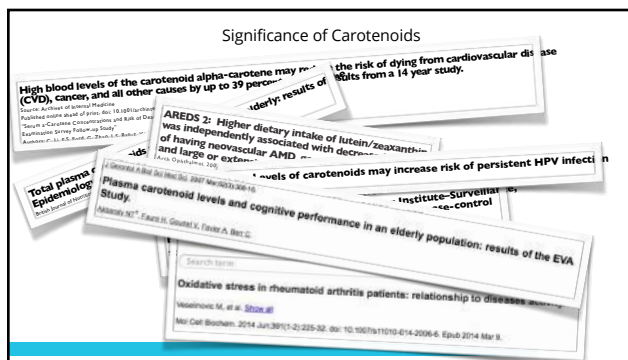
## Question

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

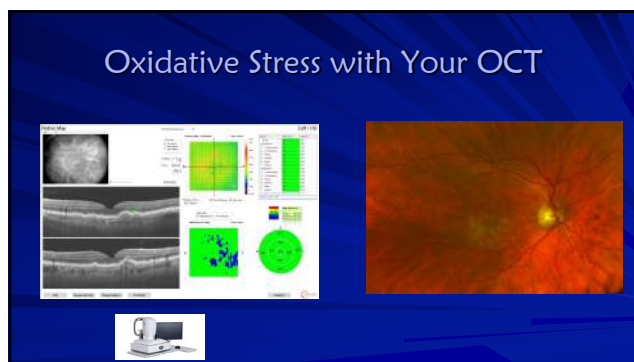
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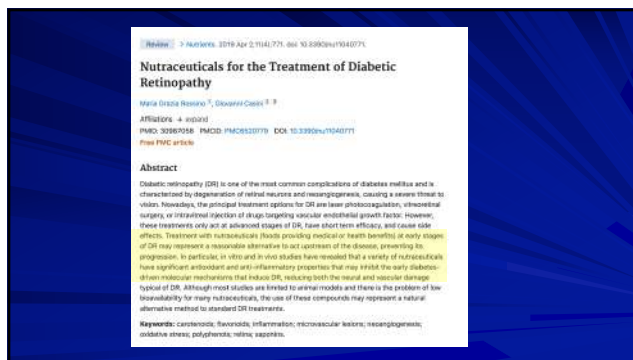


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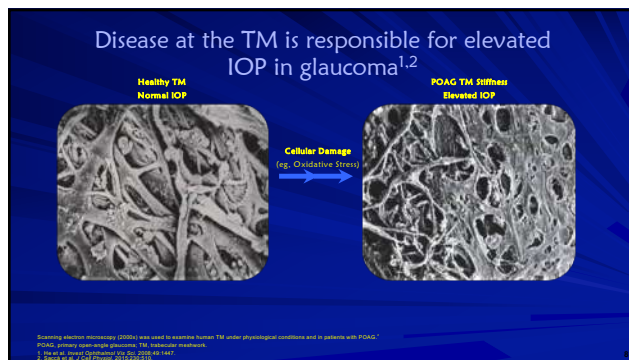




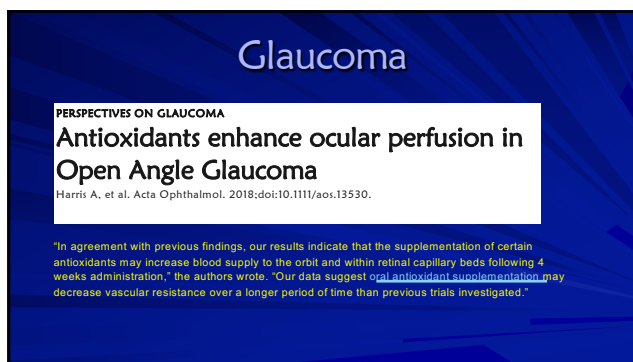




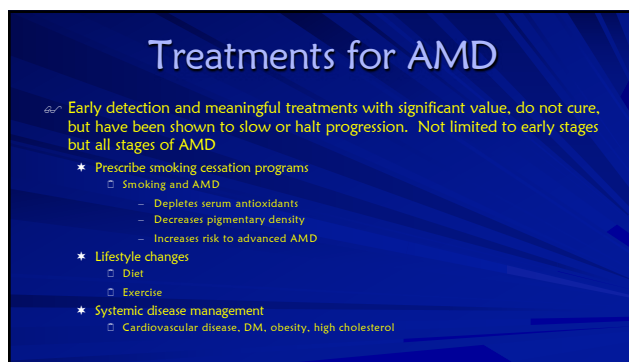
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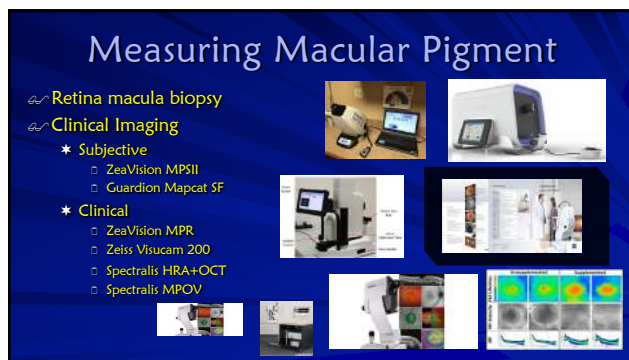
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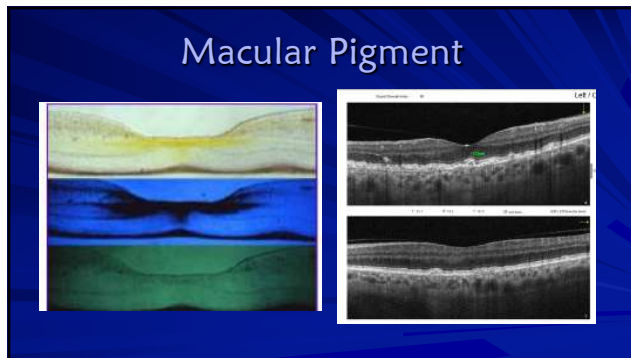


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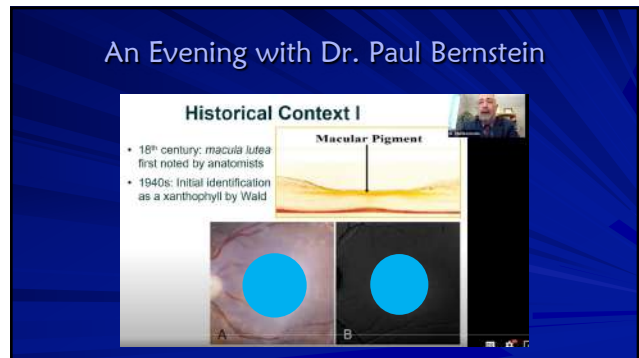


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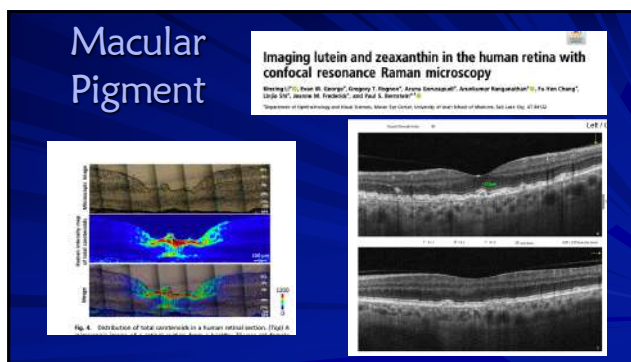




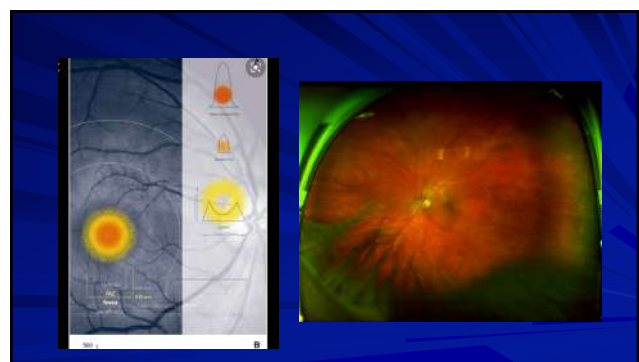
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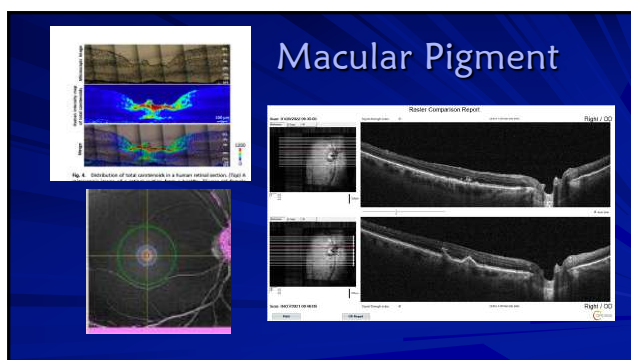
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## An Evening with Dr. Paul Bernstein

### Measurement of Macular Pigment



- HPLC
- Psychophysical
  - Heterochromatic flicker photometry (HFP)
  - Minimum motion photometry
- Image Based
  - Autofluorescence attenuation
  - Reflectometry
  - Resonance Raman spectroscopy (skin and eye)

### High Performance Liquid Chromatography




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## An Evening with Dr. Paul Bernstein

### The Moran AMD Genetic Testing Assessment Study: The Magenta Study

- Will knowledge of AMD genetic risk lead to quantifiable, sustained healthy changes in lifestyle?
- Randomized, controlled trial of pre-symptomatic genetic risk testing and counseling
  - Immediate versus delayed disclosure
- 18-64 year-old w/o AMD
- Outcomes
  - Skin carotenoids by RRS and RS
  - Macular pigment by Spectralis AFI
  - Lifestyle surveys
  - Awaiting NEI funding



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## ARVO STUDY

Interrelationships between Macula, Skin and Serum Carotenoids- Paul Bernstein, Werner Gellerman et al ARVO May 2016

### Conclusions:

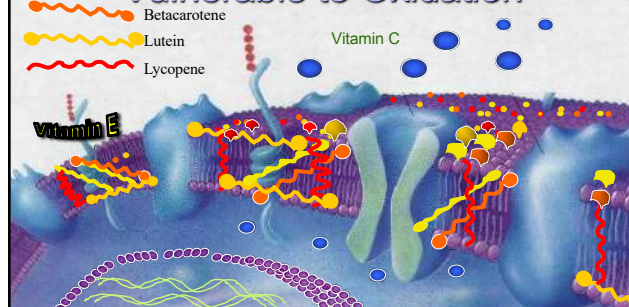
"Our results emphasize the importance of measuring the total amount of carotenoids in the macula region using an objective image based modality such as AFI w Spectralis rather than subjective MPOD." Skin resonance Raman Spectroscopy of skin carotenoids is a reasonable biomarker of macula carotenoid status, and correlates better than than subjective MPOD tests.



The objective hand scanner is better than the subjective Macroscope, QuantREYE, and Densitometer for estimating macula pigment.

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## Vulnerable to Oxidation



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Are you taking a supplement?

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## 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.

Dear [Name],

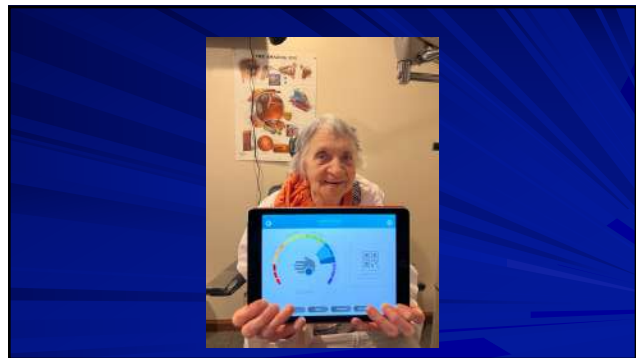
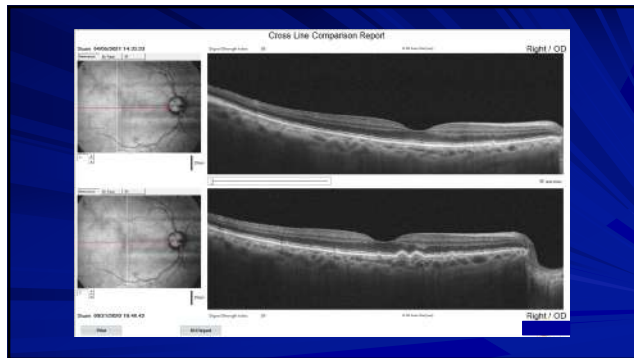
Reporting on 12/17/2022, you met with me and scanned the path of your food with the BioPhotonic Scanner. Your score reflected a Skin Carotenoid Score (SCS) of 23000.

This score represents the current measured level of your skin. The higher the score, the more carotenoids your body is storing.

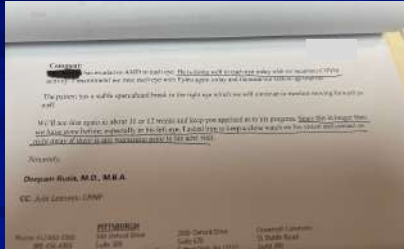


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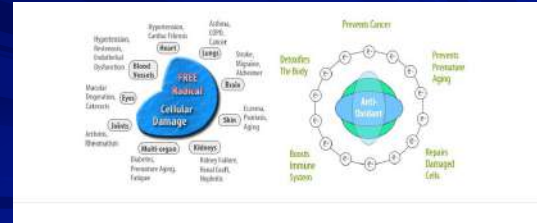
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## Treat and Extend!



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## Screen Everyone

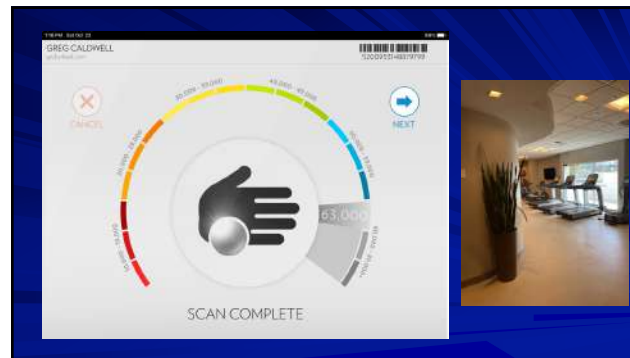


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## Greg's Comments

- ✓ I think macular pigment is miss named and should be called fovea pigment
- ✓ Binding proteins need coenzymes and cofactors
- ✓ The macula/fovea is 3<sup>rd</sup> 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

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## Thank You for This Opportunity

- ✓ Do it for:
  - ★ Yourself
  - ★ Your family
  - ★ Your staff
  - ★ Your patients



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## Questions Thank You!

## Nutrition in Ocular Disease and Systemic Health

Greg Caldwell, OD, FAAO  
PSS Eyecare – Niagara Falls  
Saturday, April 1, 2023



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### Why Are We Only Treating Half the Retina?

**Health Benefits of Polyphenols and Carotenoids in Age-Related Eye Diseases**

**Abstract**

Oxidative stress and inflammation play a critical role in the initiation and progression of age-related ocular abnormalities including cataracts, glaucoma, diabetic retinopathy, and macular degeneration. Therefore, phytochemicals with potent antioxidant and anti-inflammatory activities, such as carotenoids and polyphenols, available to benefit from these diseases. We searched PubMed and Web of Science databases for the English literature investigating the benefits of different approaches and polyphenols in age-related eye diseases. Our results showed that several polyphenols (such as resveratrol, quercetin, genistein, and epigallocatechin gallate) have been shown to have antioxidant, anti-inflammatory, and neuroprotective effects. These findings include mitigating the production of reactive oxygen species, inhibiting the tumor necrosis factor- $\alpha$  and vascular endothelial growth factor pathways, suppressing p21-dependent apoptosis, and suppressing the production of inflammatory cytokines, such as interleukin-1 $\beta$ , IL-6, IL-8, IL-1 $\alpha$ , and intercellular adhesion molecule-1. Consumption of products containing these phytochemicals may be protective against these diseases; however, adequate human data are lacking. This review discusses the role and mechanisms of polyphenols and carotenoids and their possible protective effects on the prevention and treatment of age-related eye diseases from an integrative perspective from oxidative stress and inflammation.

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### Carotenoids and Polyphenols

**Oxidative stress: role of physical exercise and antioxidant interventions in age-related eye diseases**

**Abstract**

Oxidative stress is a key factor in the pathogenesis of age-related eye diseases. Physical exercise and antioxidant interventions have been shown to have beneficial effects on oxidative stress and eye health. This review discusses the role and mechanisms of carotenoids and polyphenols in oxidative stress and eye health.

**Carotenoids and Polyphenols**

Carotenoids and polyphenols are phytochemicals with potent antioxidant and anti-inflammatory activities. They have been shown to have beneficial effects on oxidative stress and eye health. This review discusses the role and mechanisms of carotenoids and polyphenols in oxidative stress and eye health.

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### Measuring Carotenoids and the Macular Pigment

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

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### Carotenoid Levels

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

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### The New Standard

NIH National Institutes of Health  
Turning Discovery Into Health

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

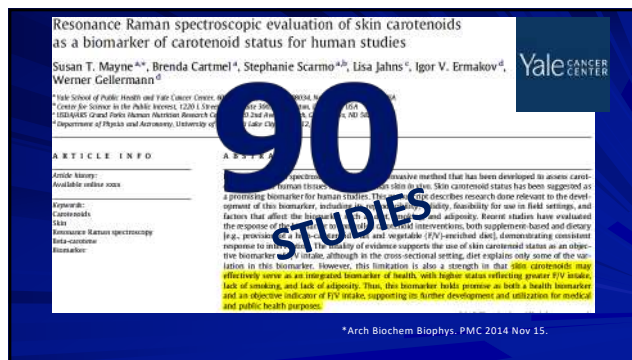
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### Raman Spectroscopy

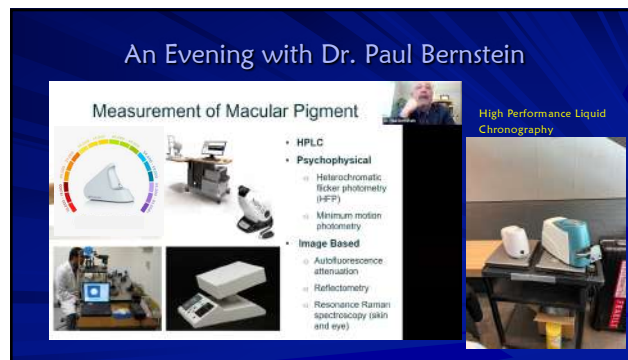
476nm PHOTONS ARE EMITTED FROM THE SCANNER

AS PHOTONS PENETRATE DEEPER CAROTENOIDS IN THE SKIN, THEY ARE REFLECTED BACK AS SYSTEM PHOTONS

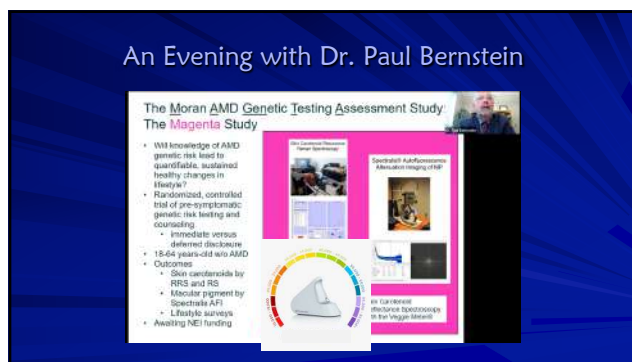
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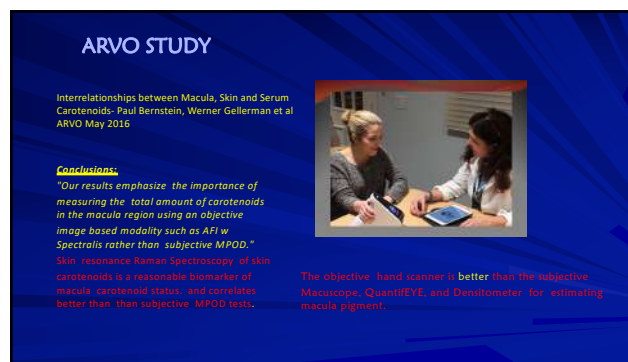
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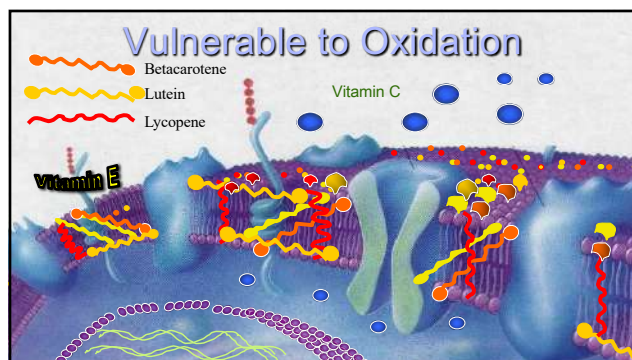
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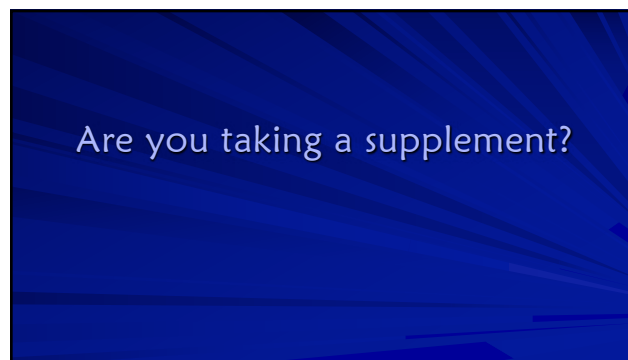
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## 53-year-old man

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## SUPPLEMENT FACTS

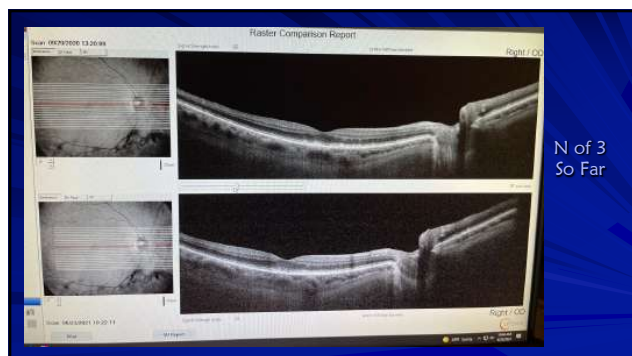
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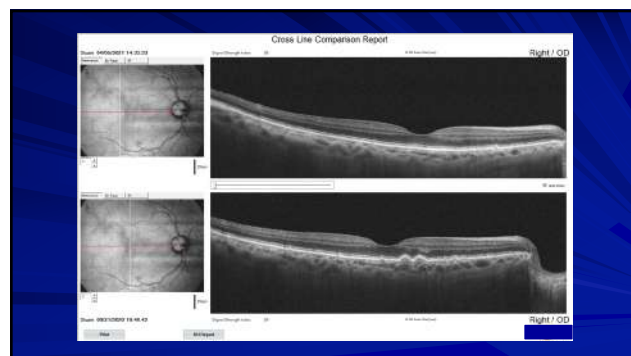
## 53-year-old man



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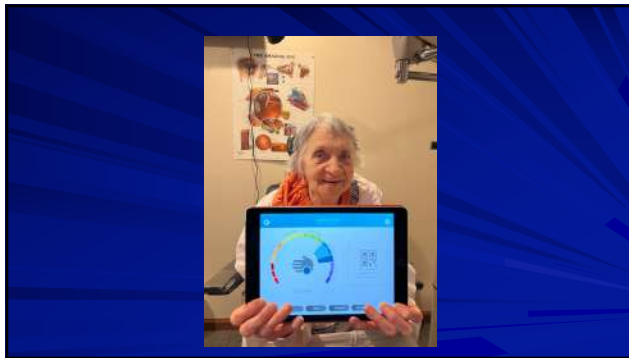


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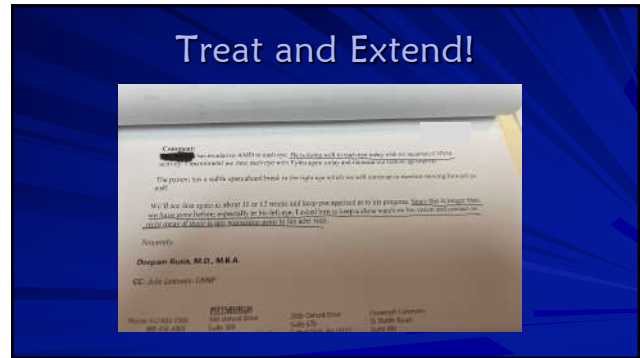


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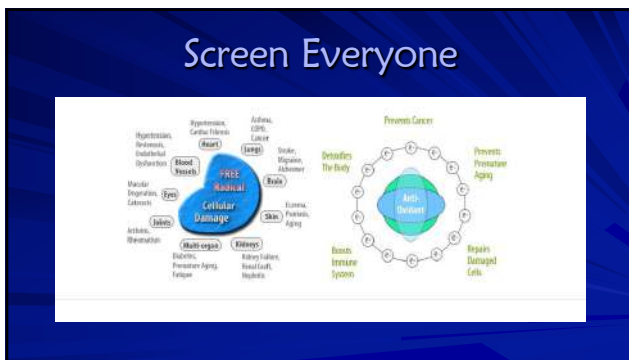




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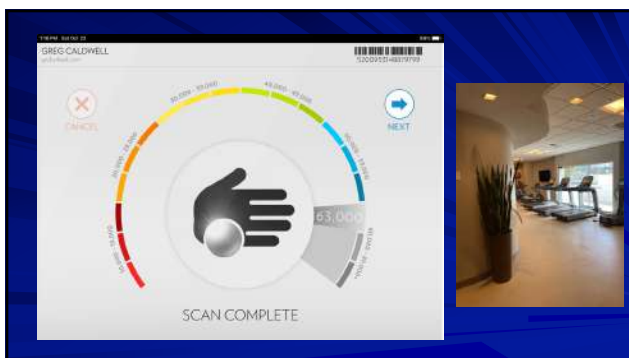


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### Thank You for This Opportunity

- Do it for:
  - Yourself
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  - Your patients

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 <p>Optometric Education Consultants</p> 	<p>Question and Thank You!</p> <p><b>Nutrition Carotenoids in Ocular Disease and Systemic Health</b></p> <p>Greg Caldwell, OD, FAAO Phoenix, AZ Saturday, April 16, 2023</p> 
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