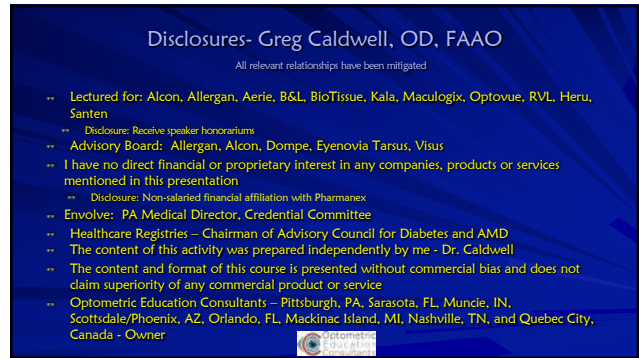


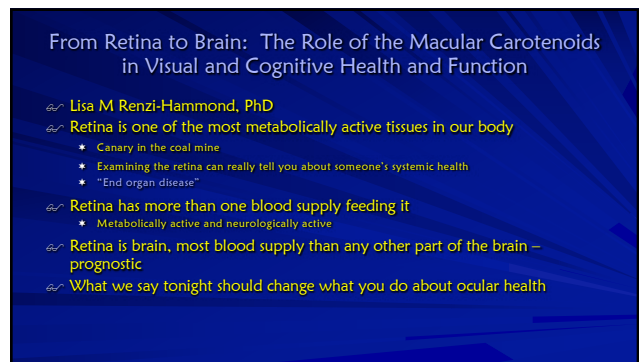
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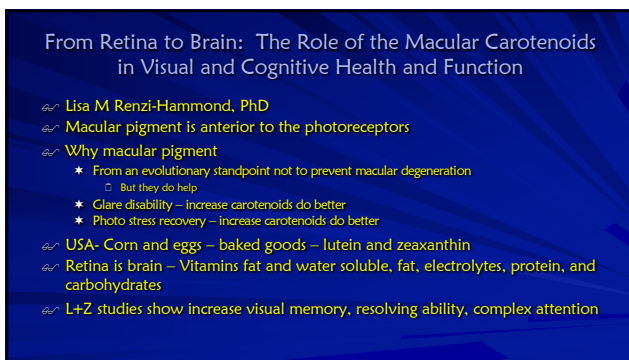
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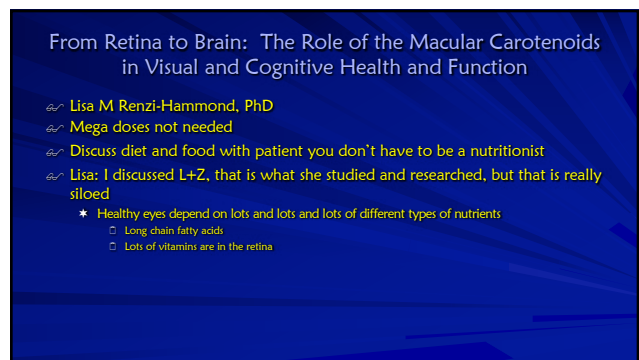
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7



8

An Evening with Dr. Paul Bernstein

- ~ Ocular nutrition research is important as a lot of eye disease points to nutritional interventions
- ~ Many nutrients are very important to the eye
 - * Original research vitamin A then lutein and zeaxanthin
- ~ Nutritional intervention have less pharmaceutical side effects
 - * Compliance can be high and motivating
 - * Patient and practitioner interest is high
 - * Can be lower cost compared to pharmaceuticals and/or surgery for treatment of disease
- ~ Research of Ocular Nutrition
 - * Clinical observation and epidemiologic
 - * Biochemistry and physiological
 - * Animal studies
 - * Human trials

9

An Evening with Dr. Paul Bernstein

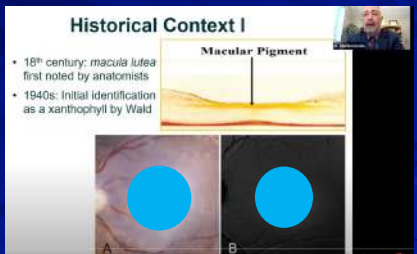
- ~ Macular pigment is "very focal" and found in a small spot
 - * Binding proteins are needed to hold the lutein and zeaxanthin in this part of the eye
 - GSTP1 - zeaxanthin
 - STARD3 - lutein
 - * Embed into cell membrane
- ~ Eye is designed to take on light
 - * Under a lot of oxidative stress
 - * L&Z strong blue light absorber – peak 450 nm
- ~ L&Z are found only in the retina
 - * Does not mean that they are the only carotenoids and nutrients form in the retina
- ~ Z and Zm – are mainly foveal and lutein are spread through the macula

10

An Evening with Dr. Paul Bernstein

Historical Context I

- 18th century: macula lutea first noted by anatomists
- 1940s: Initial identification as a xanthophyll by Wald



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An Evening with Dr. Paul Bernstein

Measurement of Macular Pigment

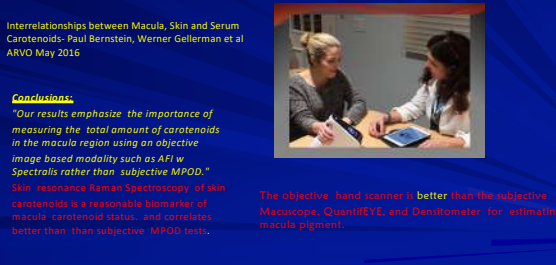


- HPLC
- Psychophysical
 - Heterochromatic flicker photometry (HFP)
 - Minimum motion photometry
- Image Based
 - Autofluorescence attenuation
 - Reflectometry
 - Resonance Raman spectroscopy (skin and eye)

12

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 MPD."

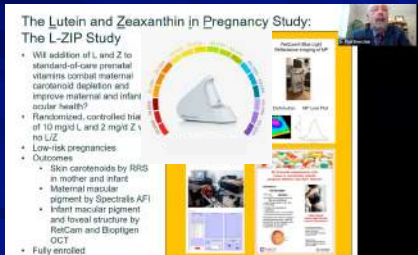
Skin resonance Raman Spectroscopy of skin carotenoids is a sensitive estimator of macula carotenoid status, and correlates better than than subjective MPD test.

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

13

An Evening with Dr. Paul Bernstein

The Lutein and Zeaxanthin in Pregnancy Study: The L-ZIP Study



- Will addition of L and Z to standard-of-care prenatal vitamins correct maternal carotenoid depletion and improve maternal and infant ocular health?
- Randomized, controlled trial of 10 mg/d L and 2 mg/d Z v no L&Z
- Low-risk pregnancies
- Outcomes
 - Skin carotenoids by RRS in mother and infant
 - Maternal macula pigment by Spectralis AFI
 - Infant macula pigment and foveal structure by ResCam and Eboptigen OCT
- Fully enrolled
- NEI funded

14

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 presymptomatic genetic risk testing and counseling
 - Immediate versus deferred disclosure
- 18-64 year-old with AMD
- Outcomes
 - Diet carbohydrate by RRS and RS
 - Macular pigment by Spectral-PI
 - Lifestyle surveys
 - Awaiting NEI funding

15

Use the Chat Box

What nutrient do you think should be included in the AREDS 3 formula?

AREDS 3 Formulation

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

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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 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

17

Greg Comment's

- ~ Short wavelength filter embedded at a pre-receptor position (Layer of Henle)
 - * Blue-blocker absorbing high energy visible light before it strikes the photoreceptor
- ~ What about the the RPE – where the disease is taking place?
 - * L/Z is found in the RPE at negligible levels
 - * They are detectable through HPLC - High Performance Liquid Chromatography
 - * Supports the supplementation synergy of curcumin, quercetin, anthocyanins, and resveratrol

18

Patients Are Expecting

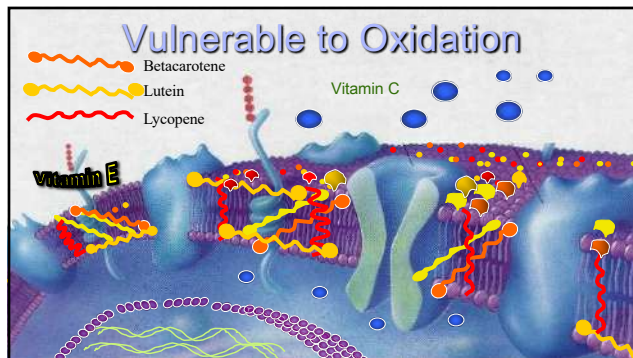
- ~ Early detection
- ~ Wellness
- ~ Prevention

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Early Detection and Allopathic Treatments

Rabin Cone Contrast Test **ERG and VEP**

20



21

Comprehensive Antioxidant Support

- ⌘ Cell membrane support
- ⌘ Immune support
- ⌘ Support to the oxidative stress to the extracellular matrix
- ⌘ Support to cell signaling

22

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

24

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

25

Medical Practices

- ⌘ Allopathic medicine
 - * Western medicine
- ⌘ Alternative "homeopathic"
- ⌘ Functional
 - * Medicine of why, treat the cause
- ⌘ Integrative medicine
 - * Complementary medicine - Eastern complimenting 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.

26

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

27

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)

28

“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

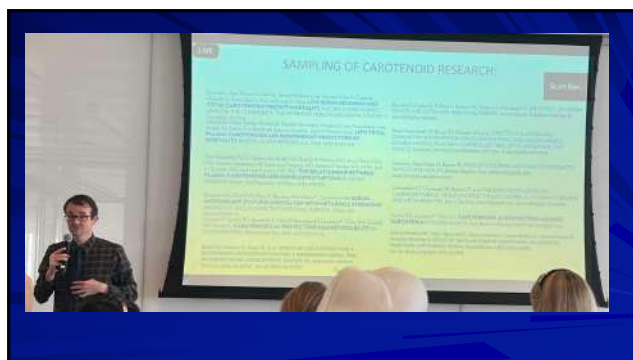
- ☞ Test that has meaning
- ☞ Biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.
- ☞ A biomarker may be used to see how well the body responds to a treatment for a disease or condition
- ☞ Blood pressure, blood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

32



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Bio Hacking

- ☞ The Art and Science of changing the environment around you and inside you so you have more control over your own biology.
- ☞ Somebody who uses science and technology to make his or her body function better and more efficiently – Dave Asprey
- ☞ XXXXXX with 75 scientists allow me to be a biohacker with science, quality, and safety

35

Measure?

ANNUAL REVIEWS
Annual Review of Ocular Care
Ocular Care and Status in Health and Disease
Lyle A. Hwang, MD, and Paul S. Bernstein, MD

CONNECT

ASSESSMENT OF CAROTENOID
Report of Carotenoid Assessment
Recent research investigating the role of carotenoids in vision research has resulted in a number of interesting and important findings. The health of photoreceptors for visual function depends on their ability to absorb light energy, and the preservation of this ability requires a steady supply of carotenoids. In addition, the ability to absorb light energy is dependent on the presence of a steady supply of carotenoids. In addition, the ability to absorb light energy is dependent on the presence of a steady supply of carotenoids.

Carotenoids in Vision: Other Than the Eye
Carotenoids are known to be important for the eye and for high-resolution visual function. However, they are also known to be important for other parts of the body, including the immune system, the cardiovascular system, and the brain.

36

Chronic and Low-Grade Inflammation

19,000 26,000 64,000

Inflammation

Immune System Cytokines Chemokines Growth Factors Hormones Neurotransmitters

Photo of two people talking.

37

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

38

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 results from environmental and occupational sources. Understanding how exposures from our environment, diet, lifestyle, etc.

<https://www.cdc.gov/niosh/topics/exposome/>

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

39

LOW **HIGH** **MODERATE**

AMD RISK FACTORS

40

IMMUNE: ADAPTION **HOW? IMMUNE: GROWTH**

IMMUNE: ADAPTION

IMMUNE: GROWTH

Ninja Nerd Science YouTube

41

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 LaValle, RPh, CCN

49

What is this layer called?

50

The ellipsoid zone (EZ) is considered to be formed mainly by mitochondria within the ellipsoid layer of the outer portion of the inner segments of the photoreceptors. However, it was previously known as the junction between the photoreceptor (IS/OS).

51

Interpretation of OCT and OCTA images from a histological approach: Clinical and experimental implications

52

A+M FEST 2022
FRIDAY DECEMBER 9TH 10:30AM - 6:00PM

The Importance of Power Density

Mitochondrial health is key to healthy aging

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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 dysfunction 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**

54

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- α , IL-6, RANTES, and IL-1ra)

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

Credit to: Eroy Vojdani, MD - Dead Batteries: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutritional Interventions

55

The diagram shows a mitochondrion with DNA fragmentation. Key components include:

- ESPOSOME** (SICA, pesticides, bacterial toxin, cellular stress) leading to **m-ROS**.
- Nucleoid** containing **DNA fragmentation**.
- Voltage-dependent anion channel (VDAC)** and **Oligomerized VDAC**.
- Released DNA fragments lead to **Stimulation of DNA sensor**.
- This triggers **Cyclic guanosine monophosphate synthase** and **Adenosine triphosphatase synthase**.
- These enzymes lead to **Stimulation of interferon genes**, **Activation of interferon regulatory factor-3**, and **Production of Type I interferon**.
- The final outcome is **Apoptosis and neutrophil activation**, leading to **Neutrophil extracellular trap (NETs) to remove cell debris**.

Credit to: Eroy Vojdani, MD - Dead Batteries: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutritional Interventions

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Free Radicals and Antioxidants

How antioxidants reduce free radicals

Antioxidant + Free radical + Healthy cell

ANTIOXIDANT: chemically reactive unpaired electron + electron dotant stable electron pair is gained, free radical is neutralized

FREE RADICAL: chemically reactive unpaired electron + electron dotant stable electron pair is gained, free radical is neutralized

HEALTHY MOLECULE (Stable) vs. UNSTABLE 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 O₂ 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 ^{•-}	Peroxide O ₂ ⁻²	Hydroxyl radical •OH	Hydroxyl ion OH ⁻

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Endogenous and Exogenous Free Radical Formation

Aerobic respiration: O₂ → O₂^{•-} → H₂O₂ → H₂O

Irradiation: H₂O → •OH

Exogenous sources: UV LIGHT, AIR POLLUTION, IONIZING RADIATION, METABOLISM, CHOKING, INFLAMMATION.

Effects: DNA DAMAGE, METABOLISM.

60

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




62

October 23, 2021



63

M Lounge

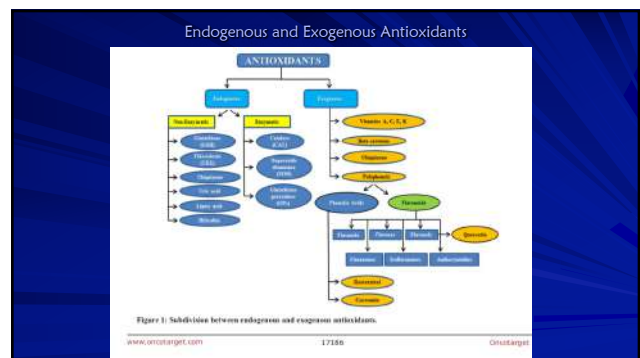


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Nutritional Antioxidants

- 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

65



67

Comprehensive Antioxidant Support

- ~ Cell membrane support
- ~ Immune support
- ~ Support to the oxidative stress to the extracellular matrix
- ~ Support to cell signaling

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Carotenoids

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




69

Carotenoids

- ~ Organic pigments produced by plants, algae, and bacteria
- ~ Cannot be synthesized by the human body
 - * Hydrophobic compounds
 - Important for the phospholipid bilayer
- ~ 600 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

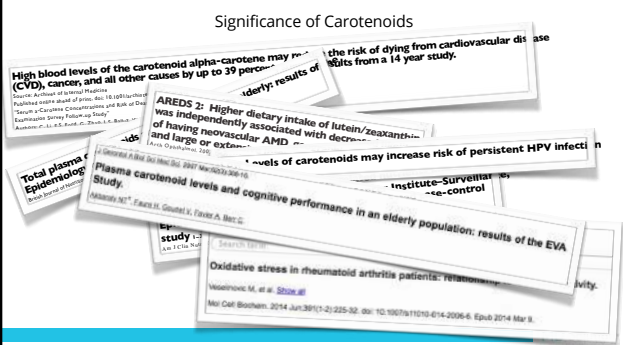
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Measure?



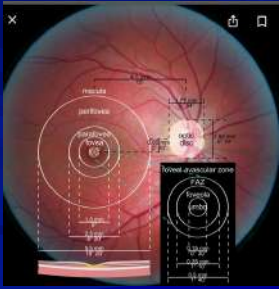
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Significance of Carotenoids

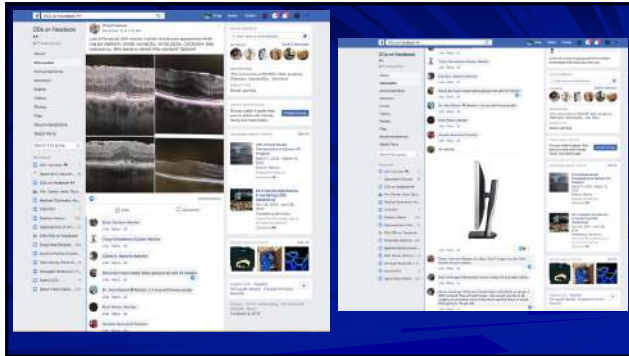


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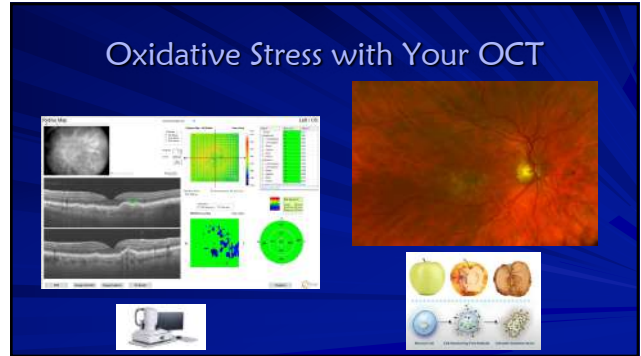
How large is the macula?



74



75



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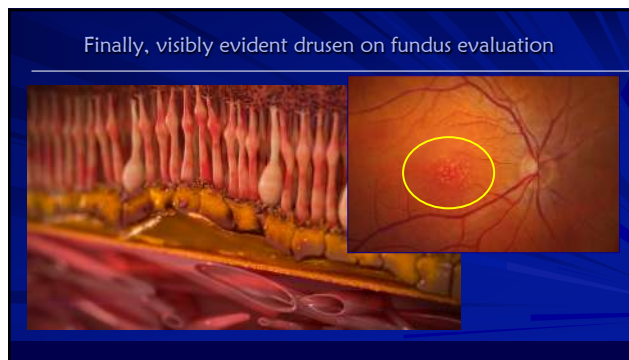
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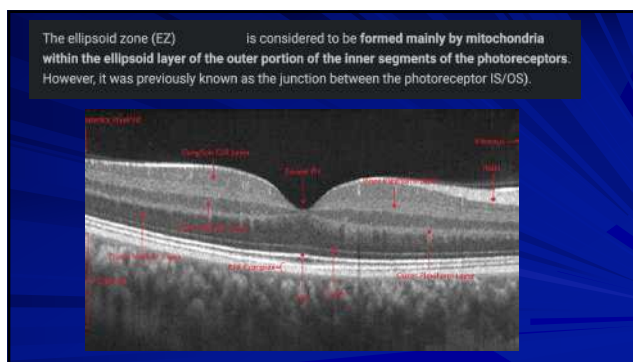
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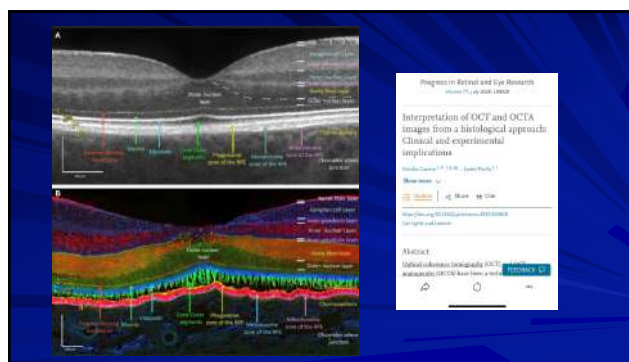
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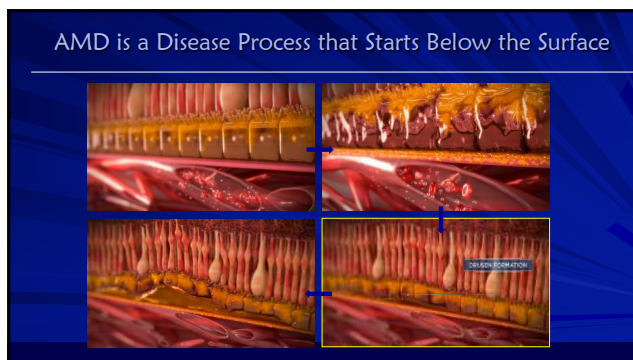
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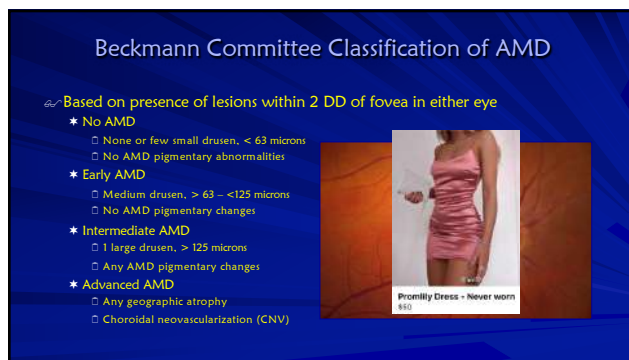
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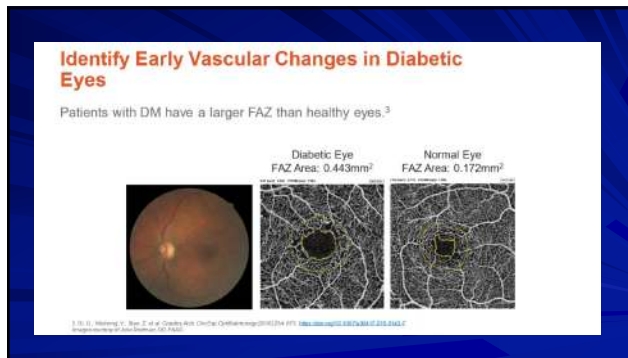
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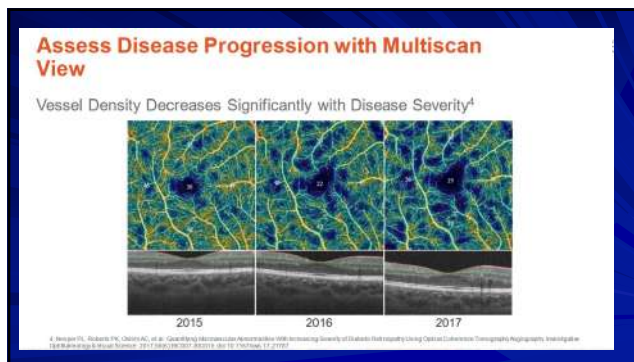
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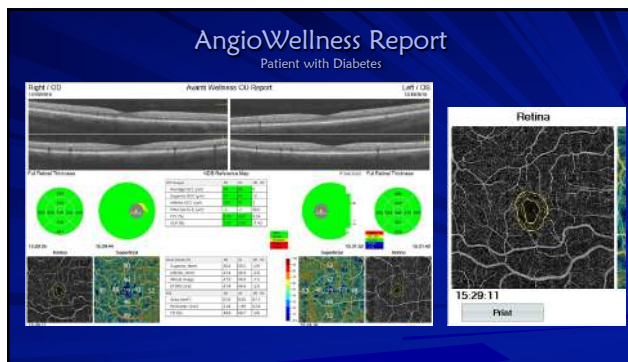
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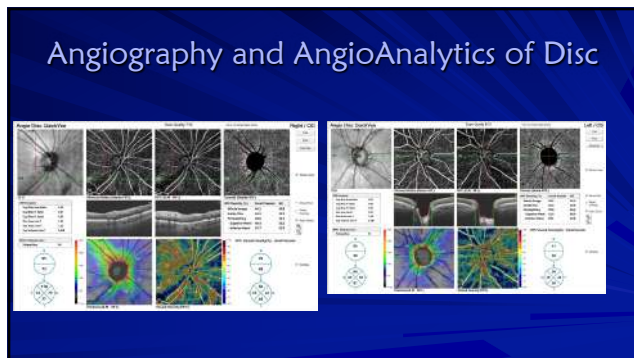
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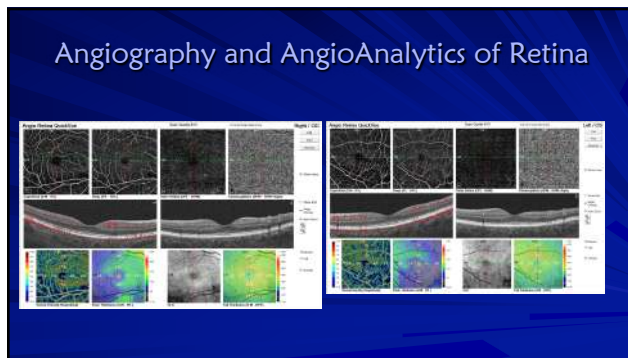
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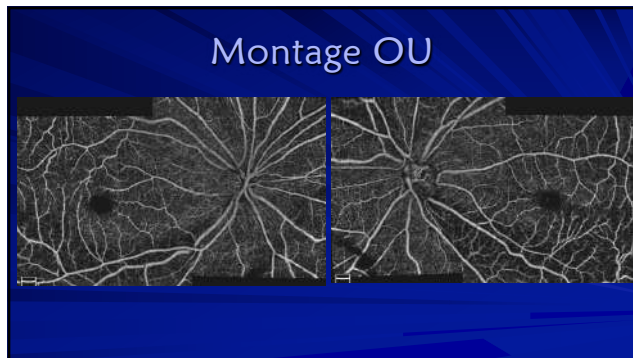
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The Diabetes Visual Function Supplement Study (DVFuSS)

PATHWAYS CONTRIBUTING TO DIABETIC RETINOPATHY

Study	Year	Design	Population	Intervention	Outcome
1	2015	Retrospective	1000
2	2016	Prospective	500
3	2017	Cross-sectional	2000
4	2018	Interventional	1500
5	2019	Case-control	300
6	2020	Longitudinal	800
7	2021	Systematic Review	10000
8	2022	Meta-analysis	15000

Downloaded figure

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Nutraceuticals for the Treatment of Diabetic Retinopathy

Maria Gracia Rosales¹, Daniela Casas²

Abstract

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus and is characterized by degeneration of retinal neurons and neuroangiogenesis, causing a severe threat to vision. Nowadays, the principal treatment options for DR are laser photocoagulation, vitreoretinal surgery, or intravitreal injection of drug-injecting vascular endothelial growth factors. However, these treatments only act at advanced stages of DR, have short term efficacy, and cause side effects. Treatment with nutraceuticals (foods providing medical or health benefits) at early stages of DR may represent a reasonable alternative to act against the disease, preventing its progression. In particular, in vitro and in vivo studies have revealed that a variety of nutraceuticals have significant antioxidant and anti-inflammatory properties that may inhibit the early diabetes-related molecular mechanisms that induce DR, reducing both the neural and vascular damage typical of DR. Although most studies are limited to animal models and there is the problem of low bioavailability for many nutraceuticals, the use of these compounds may represent a natural alternative method to standard DR treatments.

Keywords: carotenoids; flavonoids; inflammation; microvascular lesions; neuroangiogenesis; oxidative stress; polyphenols; retina; xanthones.

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Disease at the TM is responsible for elevated IOP in glaucoma^{1,2}

Healthy TM Normal IOP

POAG TM Stiffness Elevated IOP

Cellular Damage (eg, Oxidative Stress)

Scanning electron microscopy (SEM) was used to examine human TM under physiological conditions and in patients with POAG.¹ POAG primarily pathologic processes: TM molecular framework. J. Biol. Chem. 2005;280:16147-16157.

96

Glaucoma

PERSPECTIVES ON GLAUCOMA

Antioxidants enhance ocular perfusion in Open Angle Glaucoma

Harris A, et al. Acta Ophthalmol. 2018;doi:10.1111/aos.13530.

"In agreement with previous findings, our results indicate that the supplementation of certain antioxidants may increase blood supply to the orbit and within retinal capillary beds following 4 weeks administration," the authors wrote. "Our data suggest oral antioxidant supplementation may decrease vascular resistance over a longer period of time than previous trials investigated."

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Overlay of the RNFL and GCC

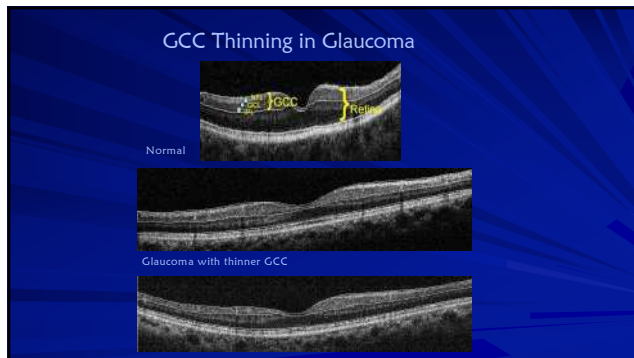
Right Eye

RNFL

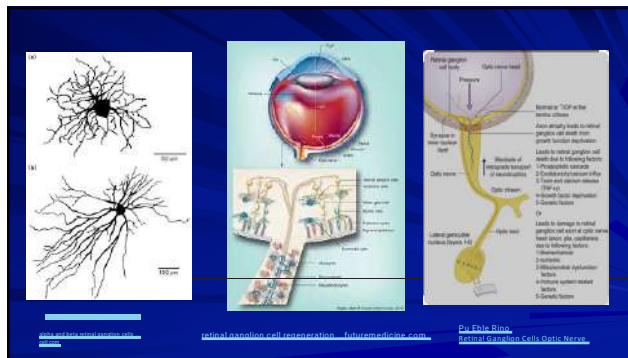
GCC

Not to scale

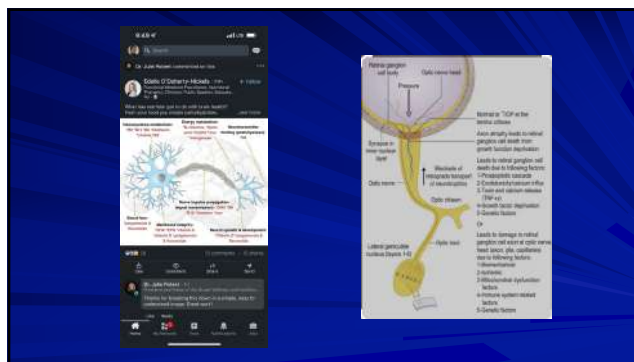
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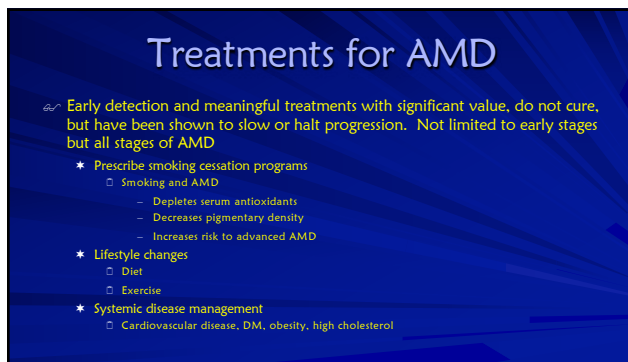
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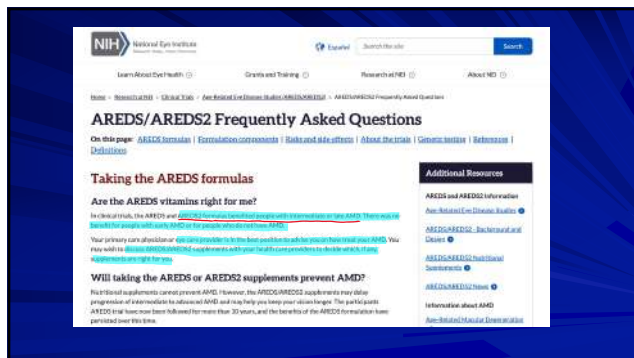
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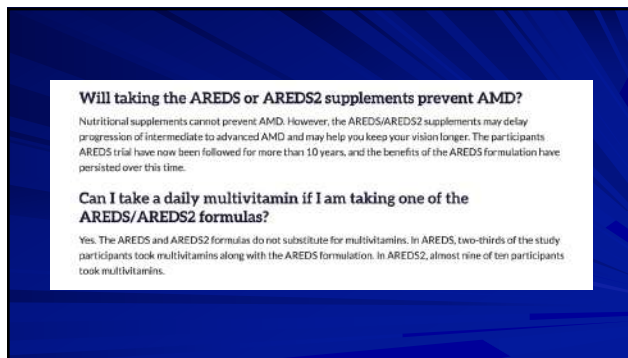
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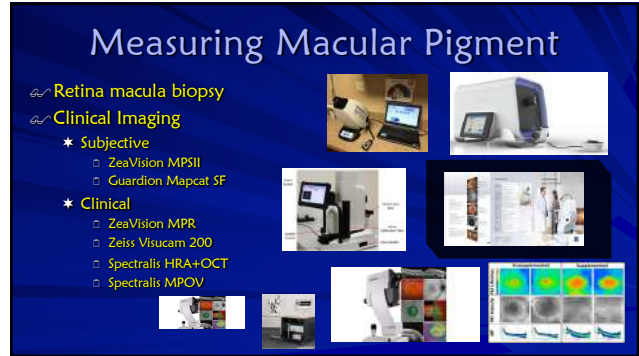
Treatment for AMD

- ~ Nutritional supplements
 - * Sub-clinical/sub-structural or early disease
 - o Controversy flourishes
 - No definitive guideline exists
 - Despite consensus evidence suggests using supplements
 - * Intermediate - advance disease
 - o No controversy on advocating for supplements
 - * AREDS 1
 - o Contains Beta-carotene and no lutein or zeaxanthin, no longer recommended
 - o Investigated early AMD, no statistically significant benefit
 - * AREDS 2
 - o Recommended for intermediate and advanced AMD, study protocol
 - * The Practical Guide for the Treatment of AMD - 3 primary options
 - o Macular pigment supplement
 - Carotenoids: lutein, zeaxanthin, meso-zeaxanthin
 - o Carotenoids, antioxidants, zinc, and vitamins C & E
 - AREDS 2
 - o Carotenoid macular supplement in subclinical and early AMD. Carotenoid and antioxidant is intermediate and AMD that is progressing

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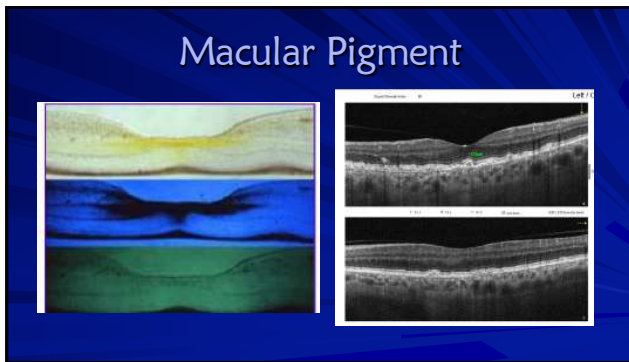
Measuring Macular Pigment

- ~ Retina macula biopsy
- ~ Clinical Imaging
 - * Subjective
 - o ZeaVision MPSII
 - o Guardian Mapcat SF
 - * Clinical
 - o ZeaVision MPR
 - o Zeiss Visucam 200
 - o Spectralis HRA+OCT
 - o Spectralis MPOV



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Macular Pigment



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Macular Pigment

Imaging lutein and zeaxanthin in the human retina with confocal resonance Raman microscopy

Wang J^{1,2}, Park W, George J, Gregory T, Dagnone C, Arora S, Srinivasan M, Ananthakrishnan R, Fu Y, Chen Y, Lin J, Li J, Moore W, Fradette J, and Paul S, Barak O^{1,2}

¹Department of Ophthalmology and Visual Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA; ²NIH

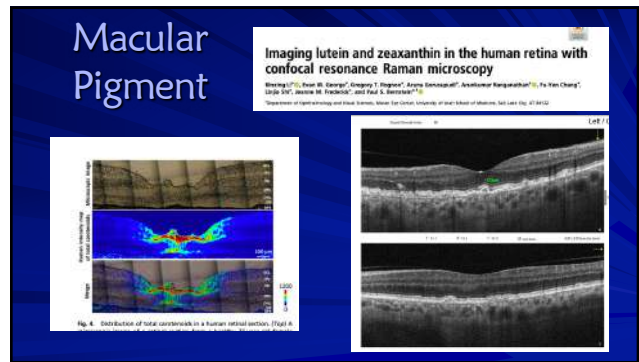
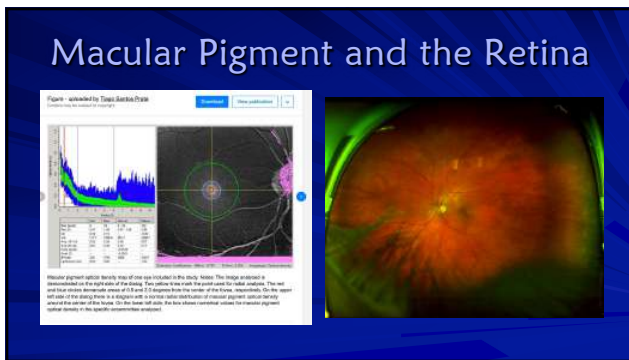


Fig. 4. Distribution of total carotenoids in a human retinal section. (Fig) A

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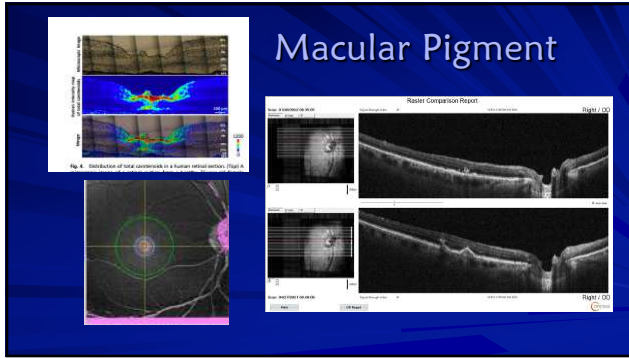
Macular Pigment and the Retina



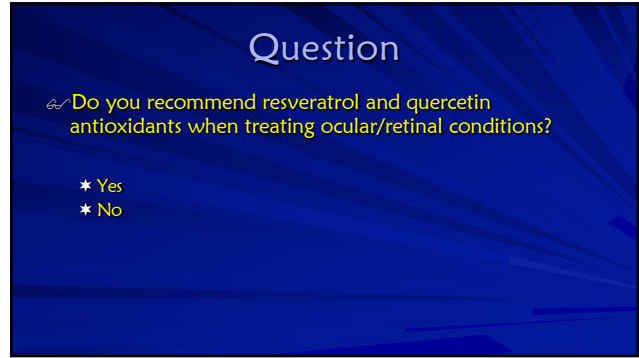
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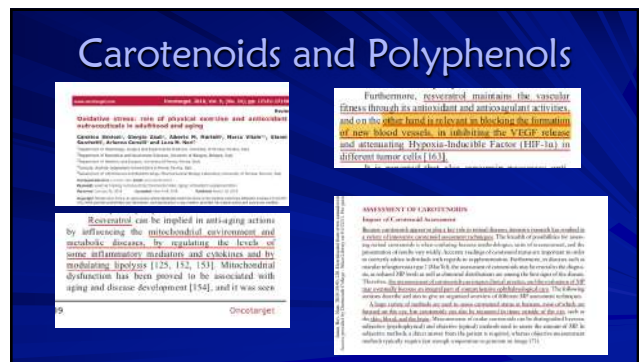
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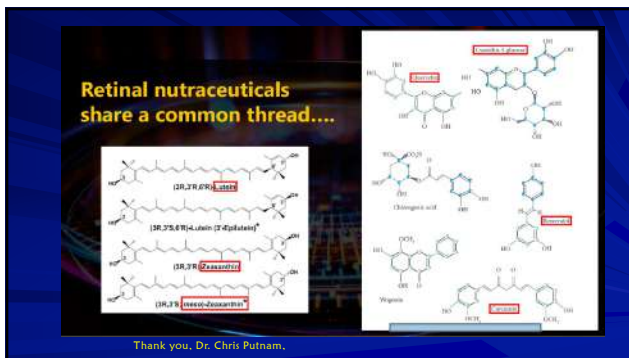
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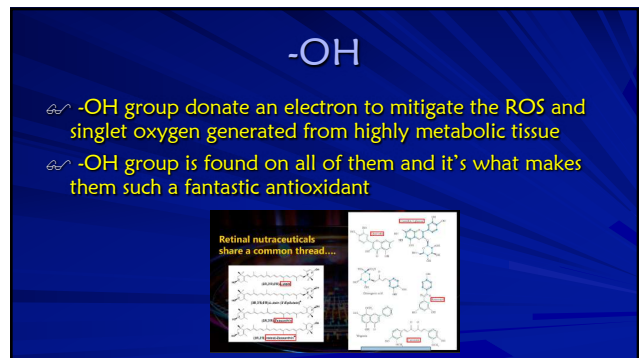
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Polyphenols
Flavonoids
Quercetin

Thank you, Dr. Chris Putnam.

Quercetin inhibits chorioidal and retinal angiogenesis *in vitro*.
Graefes Arch Clin Exp Ophthalmol (2008) 246:3:373-378.

Singlet oxygen quenching-and chain-breaking antioxidant-properties of a quercetin dimer able to prevent AMD.
Biophysical chemistry 243 (2018): 17-23.

Quercetin and cyanidin-3-glucoside protect against photooxidation and photodegradation of A2E in RPE cells.
Experimental eye research 160 (2017): 45-55.

Neuroprotective effects of quercetin in diabetic rat retina.
J Bio Sciences (2017) 24.6:1186-1194.

Protective effect of quercetin and chlorogenic acid, two polyphenols widely present in edible plant varieties, on visible light-induced retinal degeneration *in vivo*.
J Func Foods (2017) 33, 103-111.

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Polyphenols
Flavonoids
Anthocyanins

Thank you, Dr. Chris Putnam.

Antioxidant and anti-inflammatory effects of blueberry anthocyanins on high glucose-induced human retinal capillary endothelial cells.
Oxidative medicine and cellular longevity, (2018)

Protective effects of blueberry anthocyanins against H₂O₂-induced oxidative injuries in human retinal pigment epithelial cells.
J Agricultural Food Chem. (2018) 66(7):1638-1648.

Protective effect of anthocyanins and xanthophylls on UVB-induced damage in retinal pigment epithelial cells.
Food and Function (2016) 7(2):1067-1076.

Effects of blueberry anthocyanins on retinal oxidative stress and inflammation in diabetes through Nrf2/HO-1 signaling.
J Neuroimmunology (2016) 301:1-6.

Identification of anthocyanins in the liver, eye and brain of blueberry-fed pigs
J Agric Food Chem (2008) 56:3:705-712

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Polyphenols
Non-Flavonoids
Curcumin

Thank you, Dr. Chris Putnam.

Therapeutic potential of curcumin in major retinal pathologies.
Int ophthalm (2019) 39:3:725-734.

Vascular endothelial growth factor: An important molecular target of curcumin.
Crit Review Food Sci Nutrition (2019) 59:2:299-312.

Retinal protection and distribution of curcumin *in vitro* and *in vivo*.
Frontiers in pharmacology 9 (2018) 670.

Curcumin acts to regress macular drusen volume in dry AMD.
Invest Ophthalm Vis Sci (2020) 61.7:1036-1038.

Curcumin-Based Treatment for Macular Edema from Uncommon Etiologies: Efficacy and Safety Assessment.
Journal of Medicinal Food (2020) 23:8

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Polyphenols
Non-Flavonoids
Resveratrol

Thank you, Dr. Chris Putnam.

Resveratrol based oral nutritional supplement produces long-term beneficial effects on structure and visual function in human patients.
Nutrients. (2014), 6:10:4404-4420.

Resveratrol suppresses expression of VEGF by human retinal pigment epithelial cells: potential nutraceutical for age-related macular degeneration.
Aging and disease (2014) 5:2:88.

SIRT1 mediated inhibition of VEGF/VEGFR2 signaling by Resveratrol and its relevance to chorioidal neovascularization.
Cytokine 76.2 (2015):549-552.

Anti-oxidant, anti-inflammatory and anti-angiogenic properties of resveratrol in ocular diseases.
Molecules 21.3 (2016)304.


Toxic effects of A2E in human ARPE-19 cells were prevented by resveratrol: A potential nutritional bioactive for age-related macular degeneration treatment.
Archives of Toxicology 94.2 (2020): 553-572.

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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)
 - o Used for many years in research laboratories
- * Skin RRS measurements
 - o Noninvasive
 - o Objective
 - o 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

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

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Raman Spectroscopy

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

Susan T. Mayne^{1,2*}, Brenda Cartmel³, Stephanie Scarmo^{4,5}, Lisa Jahns⁵, Igor V. Ermakov⁶, Werner Gellermann⁶

100 STUDIES

**Arch Biochem Biophys. PMC 2014 Nov 15.*

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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 Macuscope, QuantifEye, and Densitometer for estimating macula pigment.

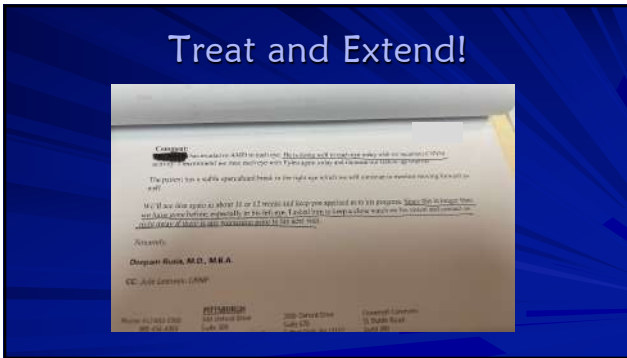
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Vulnerable to Oxidation

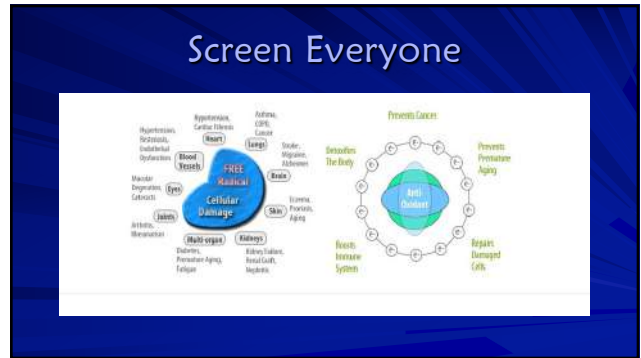
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Are you taking a supplement?

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Carotenoid and Antioxidant Levels in Ocular Disease and Systemic Health

- Plenty of evidence that carotenoids are beneficial in ocular and systemic prevention
- Patients are looking for guidance
 - Many are on supplements
 - Surprised what they are doing is minimally helping
- Measuring ensures the patient
- Antioxidants in the eye and body go beyond lutein and zeaxanthin
- Dr. Oz "Ultimate nutritional lie detector"
- Best benefit of all...

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Thank You for This Opportunity

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

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Questions and Thank You!

Ocular Nutrition

Tying Function, Structure, and Molecular All Together

Greg Caldwell OD, FAAO
 The Saratoga Springs
 Primary Eye Care Symposium
 Saturday, March 25, 2023

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