

## Optometric Education Consultants

## **Integrative and Functional Medicine**

## New Opportunities for Optometry

Greg Caldwell, OD, FAAO Tracy Offerdahl, PharmD, Bpharm, RPh, FAAO

> CE Sarasota 2023 Optometric Education Consultants

> > Sunday, March 5, 2023



## 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
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••• Has not received any assistance from any commercial interest in the development of this course

# Text me your comments and questions

814-931-2030 Greg Caldwell, OD, FAAO Your favor drink?

# Thank You Dr. Richer

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and coordinator of the optom program, at the Captain Jame Health Care Facility, North C

#### Nutrition Think Zinc:

## **Q&A with Dr. Stuart Richer**

Zinc is necessary for growth,

DNA synthesis, wound healing, reproductive health and night vision.



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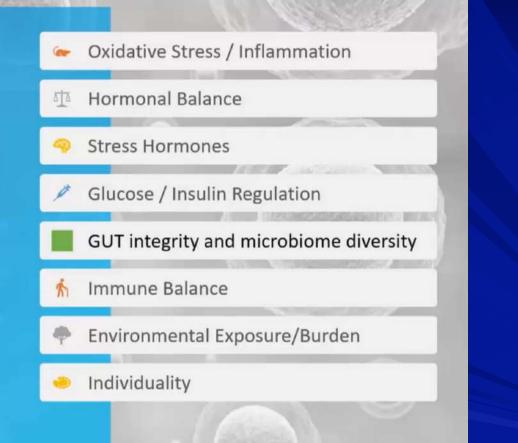
## **FRIDAY** DECEMBER 9<sup>TH</sup> 10:30AM - 6:00PM







# Key Tenants of **Aging**, Performance and Vitality



Credit to: James LaValle, RPh, CCN



# Ocular Disease Career

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







# Patients Are Expecting

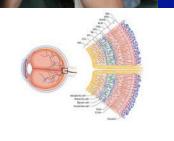
← Early detection
← Wellness
← Prevention

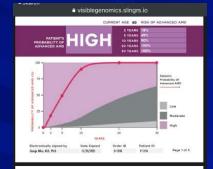
# Early Detection and Allopathic Treatments

## Rabin Cone Contrast Test



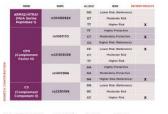
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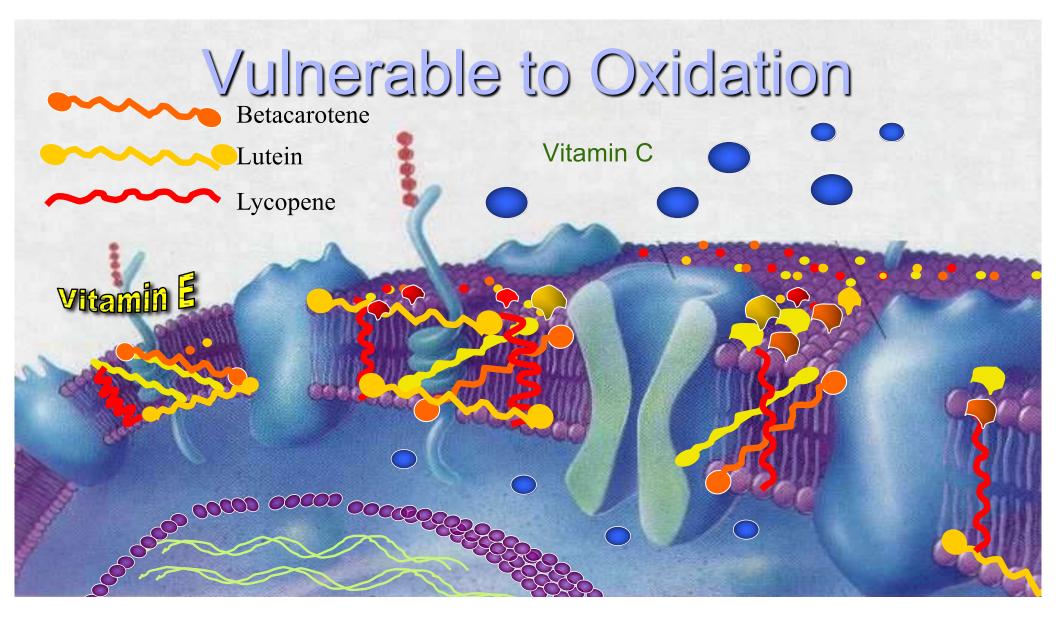


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# **Comprehensive Antioxidant Support**

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

# Question?

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

## Gr Who has done or recommended?

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

# 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

# **Medical Practices**

## Allopathic medicine

- \* Western medicine
- Alternative "homeopathic"
- A Functional
  - \* Medicine of why, treat the cause
- A Integrative medicine
  - \* Complementary medicine Eastern complimenting Western

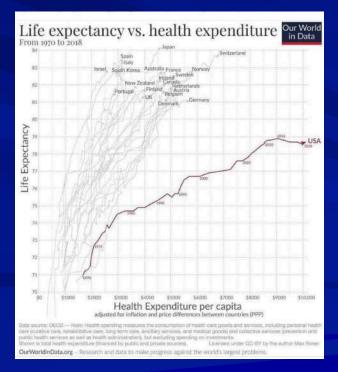
## What is integrative medicine?

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

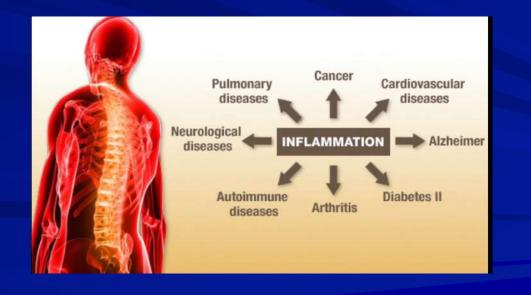
## Chronic and Low-Grade Inflammation

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



## 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)



# "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

# Biomarker

Ar Test that has meaning

- Ger 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
- as Blood pressure, blood work, heart rate, genetic testing, IOP

# Predictive Biomarker

- Ger 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
  - ★ HbAlc
  - \* C-Reactive Protein
  - \* Plasma Homocysteine
  - Vitamin D (25-HydroxyD)
  - \* Omega 3 index
  - \* Carotenoid measure of all antioxidants

# Biohacking

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

## Measure?

Rev. Nutr. 2019 39:95-120. Downloaded from www annualreided by Dartmouth College - Main Library on 01/12/21. For pe

#### ASSESSMENT OF CAROTENOIDS

#### Impact of Carotenoid Assessment

Because carotenoids appear to play a key role in retinal diseases, intensive research has resulted in a variety of innovative carotenoid assessment techniques. The breadth of possibilities for assessing retinal carotenoids is often confusing because methodologies, units of measurement, and the presentation of results vary widely. Accurate readings of carotenoid status are important in order to correctly advise individuals with regards to supplementation. Furthermore, in diseases such as macular telangiectasia type 2 (MacTel), the assessment of carotenoids may be crucial to the diagnosis, as reduced MP levels as well as abnormal distributions are among the first signs of the disease. Therefore, the measurement of carotenoids can impact clinical practice, and the evaluation of MP may eventually become an integral part of comprehensive ophthalmological care. The following sections describe and aim to give an organized overview of different MP assessment techniques.

A large variety of methods are used to assess carotenoid status in humans, most of which are focused on the eye, but carotenoids can also be measured in tissue outside of the eye, such as the <u>skin</u>, <u>blood</u>, and the <u>brain</u>. Measurements of ocular carotenoids can be distinguished between subjective (psychophysical) and objective (optical) methods used to assess the amount of MP. In subjective methods, a direct answer from the patient is required, whereas objective measurement methods typically require just enough cooperation to generate an image (73).

#### Carotenoids in Tissues Other Than the Eye

<u>Carotenoids can be assessed noninvasively in the skin and by high-performance liquid chromatography</u> raphy (HPLC) of blood and tissue samples. It has been shown that RRS measurements of skin carotenoids show strong correlations (r = 0.7 to 0.9) with carotenoids in biopsies of human skin

www.annualreviews.org • Ocular Carotenoid Status in Health and Disease 103

(57, 96). Skin RRS and reflectometry are particularly useful to assess the carotenoid status of children, with <u>skin carotenoid levels strongly associated with fruit and vegetable intake (123)</u>. Using HPLC, the carotenoid status in the plasma can also be assessed (77, 104), and higher L levels in the serum of patients have been associated with higher visual function. Similarly, carotenoid assessment in brain tissue suggests that higher carotenoid levels might be beneficial for overall cognitive performance (65, 74).

## ANNUAL REVIEWS

Annual Review of Nutrition

Ocular Carotenoid Status in Health and Disease

Click on Tools to PDF.

Lydia Sauer, Binxing Li, and Paul S. Bernstein Department of Ophthaluology and Visual Sciences, John A. Moran Fee Conter, University of Utah, Salt Like City, Unit 84152, USA email: Hitzanet@hoc.unit.edu, Brinnigl.J@becum.edu, pnal.bernini@hbc.unit.edu

### ANNUAL CONNECT

The Annual Review of Natrition is online at

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https://doi.org/10.1146/annurcv-nutr-082918-124555

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#### Annue Rev. Nutr. 2019. 39:95–120 First published as a Roview in Advance on May 16 2010

macular pigment, macular carotenoids, carotenoid supplementation, ocular nutrition, retinal imaging

#### Abstract

Keywords

Retinal carotenoids are dictary nutrients that uniquely protect the eye from light damage and various retinal pathologies. Their antioxidative properties protect the cyef from many retinal diseases, such as age-related macular degeneration. As many retinal diseases are accompanied by low carotenoid levels, accurate noninvasive assessment of carotenoid status can help ophthalmologies identify the patients most likely to benefit from carotenoid supplementation. This review focuses on the different methods available to assess carotenoid status and highlights disease-related changes and potential nutritional interventions.

04

# Chronic and Low-Grade Inflammation



# **DNA** Sciences

Genomics = all of our genes

 Epigenetics – the study of how our cells control gene activity without changing the DNA
 \* Internal and external environments

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

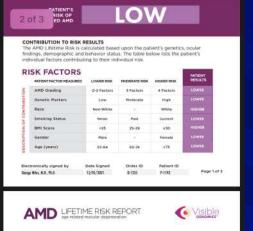
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https://www.cdc.gov > niosh > topics CDC

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

Google Search Definition

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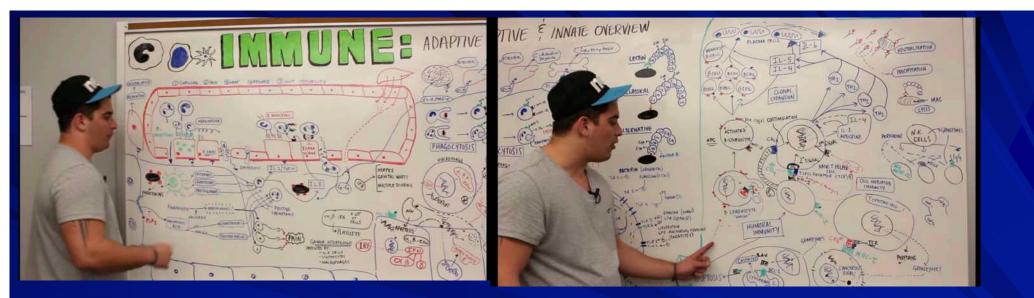
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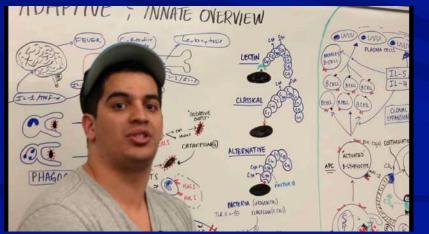
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Ninja Nerd Science YouTube Complement factor H in AMD: Bridging genetic associations and pathobiology

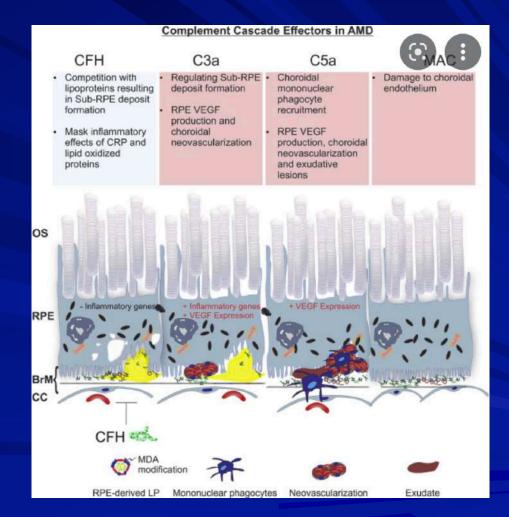
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https://doi.org/10.1016/j.preteyeres.2017.09.001 Get rights and content

### Abstract

Age-Related Macular Degeneration (AMD) is a complex <u>multifactorial disease</u> characterized in its early stages by <u>lipoprotein</u> accumulations in <u>Bruch's Membrane</u> (BrM), seen on fundoscopic exam as <u>drusen</u>, and in its late forms by neovascularization ("wet") or <u>geographic</u> <u>atrophy</u> of the Retinal Pigmented Epithelial (RPE) cell layer ("dry"). Genetic studies have strongly supported a relationship between the alternative complement cascade, in particular the common H402 variant in <u>Complement Factor H</u> (CFH) and development of AMD. However, the functional significance of the CFH Y402H polymorphism remains elusive. In this <u>FEEDBACK</u> **Q** 

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Learn About Eye Health 📀	Grants and Training $ \odot $	Research at NEI $\odot$	About NEI ⊙

Home > Research at NEI > Clinical Trials > Age-Related Eye Disease Studies (AREDS/AREDS2) > AREDS/AREDS2 Frequently Asked Questions

## **AREDS/AREDS2 Frequently Asked Questions**

## What is the basis for the concentration of zinc in the AREDS supplements? What concentration should I take?

In the AREDS trial, the 80 mg zinc dose (alone or in combination with antioxidant vitamins) was found to be effective compared to a placebo. Although zinc was found to be an essential component of the AREDS formulation, some nutritional experts recommended a lower dose. In the AREDS2 trial, there was no placebo control. Instead, participants were given the option to take the original formula or to be randomly assigned to receive a modified version, such as a formula containing 25 mg zinc. The investigators did not find a difference in the effects of 80 mg vs. 25 mg zinc. Because AREDS2 did not include a placebo control, results from AREDS, placebo-controlled trial, are still considered the gold standard.

Zinc is found in vegetables, grains, and meat. Vegetables and grains contain other molecules that can prevent zinc absorption and thus reduce its bioavailability. Supplements contain purified zinc, without these competing molecules. Although the chemical form of zinc affects its rate of absorption in the stomach, it is not clear how this affects bioavailability (i.e., the amount of zinc that reaches the retina). For more on this topic, please see the zinc fact sheet from the NIH Office of Dietary Supplements [7].

## Ingredients

% Daily Value

Other Ingredients: Gelatin, Microcrystalline Cellulose, Stearic Acid, Silicon Dioxide, Magnesium Stearate.



#### Randomized Controlled Trial

## Treatment response to antioxidants and zinc based on CFH and ARMS2 genetic risk allele number in the Age-Related Eye Disease Study

Carl C Awh et al. Ophthalmology. 2015 Jan.



## Abstract

**Objective:** To evaluate the impact of complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) risk alleles on the observed response to components of the Age-Related Eye Disease Study (AREDS) formulation.

**Design:** Genetic and statistical subgroup analysis of a randomized, prospective clinical trial.

**Participants:** White patients from the AREDS with category 3 or 4 age-related macular degeneration (AMD) with available DNA (n = 989).

Results: Patients with 2 CFH risk alleles and no ARMS2 risk alleles progressed more with zinccontaining treatment compared with placebo, with a hazard ratio (HR) of 3.07 (P = 0.0196) for zinc and 2.73 (P = 0.0418) for AREDS formulation (AF). Sevenyear treatment-specific progression rates were: placebo, 17.0%; zinc, 43.2% (P = 0.023); and AF, 40.2% (P = 0.039). Patients with 0 or 1 CFH risk alleles and 1 or 2 ARMS2 risk alleles benefited from zinc-containing treatment compared with placebo, with an HR of 0.514 for zinc (P = 0.012) and 0.569 for AF (P = 0.0254). Seven-year treatment-specific AMD progression rates were as follows: placebo, 43.3%; zinc, 25.2% (P = 0.020); and AF, 27.3% (P = 0.011). Zinc and AF treatment each interacted statistically with these 2 genotype groups under a Cox model, with P values of 0.000999 and 0.00366, respectively. For patients with 0 or 1 CFH risk alleles and no ARMS2 risk alleles, neither zinc-containing treatment altered progression compared with placebo, but treatment with antioxidants decreased progression (HR, 0.380; P = 0.034). Seven-year progression with placebo was 22.6% and with antioxidants was 9.17% (P = 0.033). For patients with 2 CFH risk alleles and 1 or 2 ARMS2 risk alleles, no treatment was better than placebo (48.4%).

**Conclusions:** The benefit of the AREDS formulation seems the result of a favorable response by patients in only 1 genotype group, balanced by neutral or unfavorable responses in 3 genotype groups.

pubmed.ncbi.nlm.nih.gov

*CFH* and *ARMS2* genetic risk determines progression to neovascular agerelated macular degeneration after antioxidant and zinc supplementation

RESEARCH ARTICLE OPEN ACCESS

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Demetrios G. Vavvas, Kent W. Small, Carl C. Awh. -2 , and Rafal Kustra Authors Info & Affiliations

January 8, 2018 115 (4) E696-E704 https://doi.org/10.1073/pnas.1718059115

#### AMARCAN ACHERIN CP CPHYNALHOLOD

#### Genetic Polymorphisms of *CFH* and *ARMS2* Do Not Predict Response to Antioxidants and Zinc in Patients with Age-Related Macular Degeneration

Independent Statistical Evaluations of Data from the Age-Related Eye Disease Study

Mehned, Asael, MS,<sup>1</sup> = Fon LL, MS,<sup>2</sup> = Ying Wong, PHD,<sup>3</sup> = Androne S. Allen, PhD,<sup>21</sup> Kenk A. Bagnery, PhD,<sup>3</sup> Andrew J. Vickers, PhD<sup>3</sup>

Parpose: Considerable controlwesy has mughed in recent years regarding whether georgical advaids to part of standard care for partients with age-related moscilar dependention (WMD) who are being considered to insurrent with influentiation and also. We simed to determine whether genotype predicts response to supple means that with the standard statement of the statement of the standard statement of the statem

Design: Three spacese institutions analyzed data served for the Apri-Eledent Sty Based Soci 2005; Merching data provide for the ARES interactions and analyzed metal server transformation respective Design and the ARES and Providents. The population of thermat sease AREED property with AREO wereas the analyzed is a design and analyzed and analyzed and analyzed and analyzed and analyzed and analyzed and property data analyzed and analyzed and analyzed and analyzed and analyzed and analyzed analyzed and analyzed analyzed and analyzed analyzed and analyzed and analyzed a

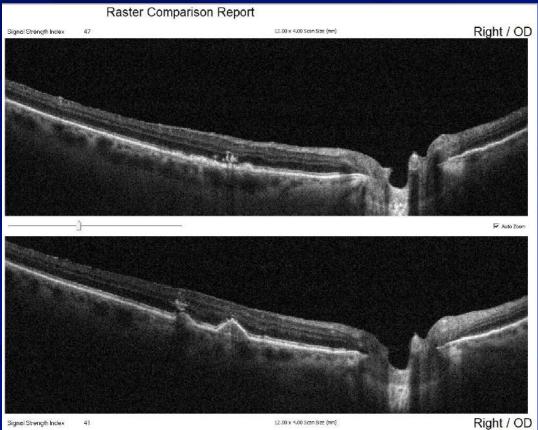
And the control measurement in representation to the metal control of the control

Suppremental material evaluate at mms.acquumat.org

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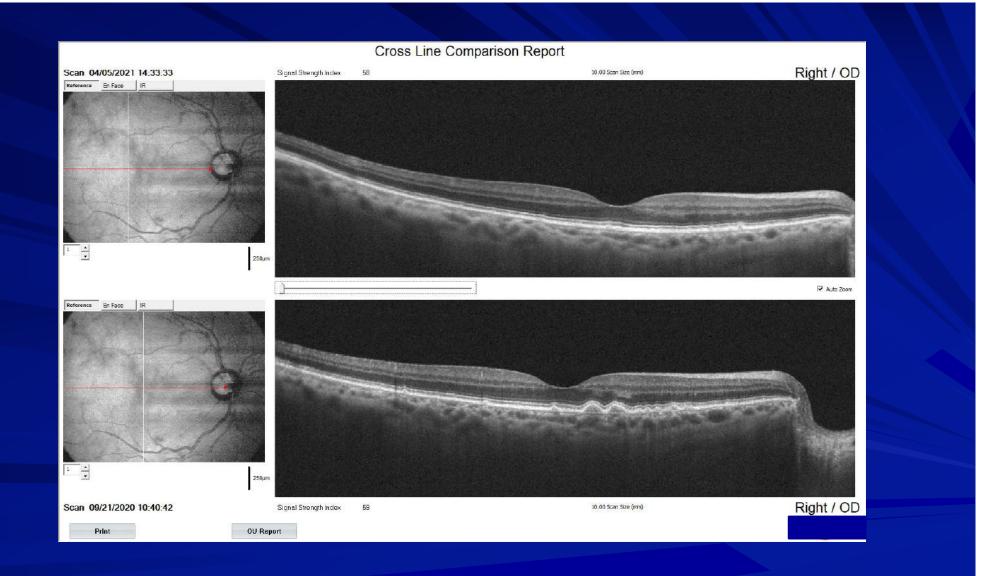
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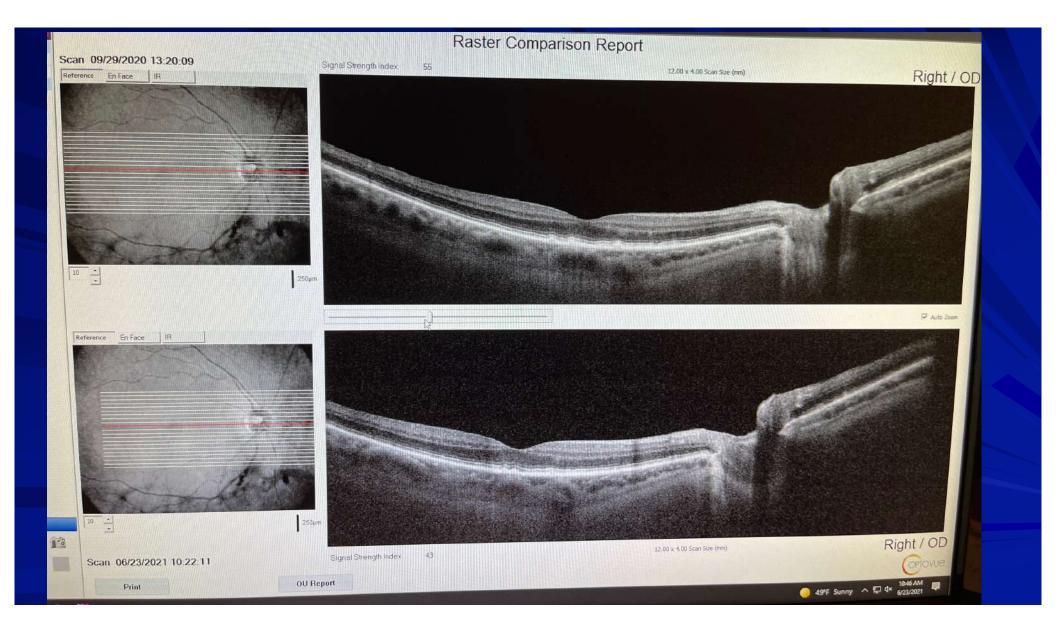
## April 27, 2021 – January 26, 2022 (9 months)





Melonie Clemmons, OD May 20, 2022 AACO Nashville





## Ingredients

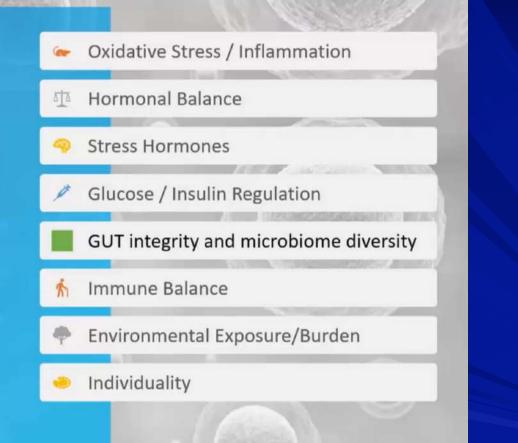
Ingredients	Amount	% Daily Value
Serving Size: 1 Packet		
Vitamin A (83% as Beta Carotene (1875 mcg RAE) from <i>Blakeslea trispora</i> , and Vitamin A palmitate) (375 mcg RAE)	2250 mcg RAE	250%
Vitamin C (as Calcium Ascorbate)	200 mg	222%
Vitamin D (as Cholecalciferol)	5 mcg (200 IU)	25%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha Tocopherol, Tocotrienols)	50.3 mg	335%
Vitamin K (as Phytonadione)	20 mcg	17%
Thiamin (as Thiamine Mononitrate)	3.75 mg	313%
Riboflavin (as Riboflavin)	4.25 mg	327%
Niacin (as Niacinamide)	17.5 mg NE	109%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	294%
Folate	500 mcg DFE (300 mcg folic acid)	125%
Vitamin B12 (as Cyanocobalamin)	15 mcg	625%
Biotin (as Biotin)	75 mcg	250%
Pantothenic Acid (as D-Calcium Pantothenate)	15 mg	300%
Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%

Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%
lodine (as Potassium Iodide)	50 mcg	33%
Magnesium (as Magnesium Glycinate, Magnesium Oxide)	125 mg	30%
Zinc (as Zinc Bisglycinate)	7.5 mg	68%
Selenium (as L-Selenomethionine, Sodium Selenite)	70 mcg	127%
Copper (as Copper Bisglycinate)	0.5 mg	56%
Manganese (as Manganese Bisglycinate)	1 mg	43%
Chromium (as Chromium Nicotinate Glycinate)	100mcg	286%
Molybdenum (as Molybdenum Bisglycinate)	37.5 mcg	83%
Polyphenol and Flavonoid Blend	97.5 mg	*
Catechins (from Camellia sinensis Leaf Extract)	(45 mg)	*
Quercetin	(25 mg)	*
Grape Seed Extract (min. 95% Polyphenols)	(12.5 mg)	*
Citrus Bioflavonoids (from Citrus Fruits)	12.5 mg)	*
Resveratrol (from Polygonum cuspidatum root extract)	(2.5 mg)	*
Mixed Tovopherols (Gamma, Delta & Beta Tocopherols)	53 mg	*
Alpha-Lipoic Acid	15 mg	*
Inositol (as Inositol)	5 mg	*
Carotenoid Blend	3.5 mg	*
Lycopene (as Lycopene)	(2.5 mg)	*
Lutein (from Marigold Flower Extract)	(1 mg)	*
Boron (as Boron Citrate)	1.5 mg	*
Vanadium (as Vanadyl Sulfate)	10 mcg	*

OTHER INGREDIENTS: Gelatin, Microcrystalline Cellulose, Crosmarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

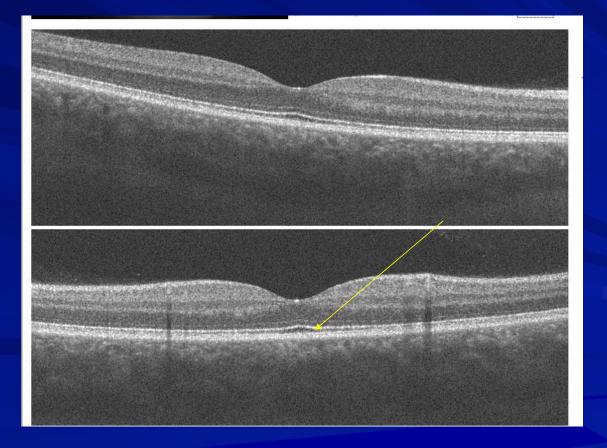
CONTAINS: Fish (Cod, Pollack, Haddock, Hake, Cusk, Redfish, Sole, Flounder).

# Key Tenants of **Aging**, Performance and Vitality

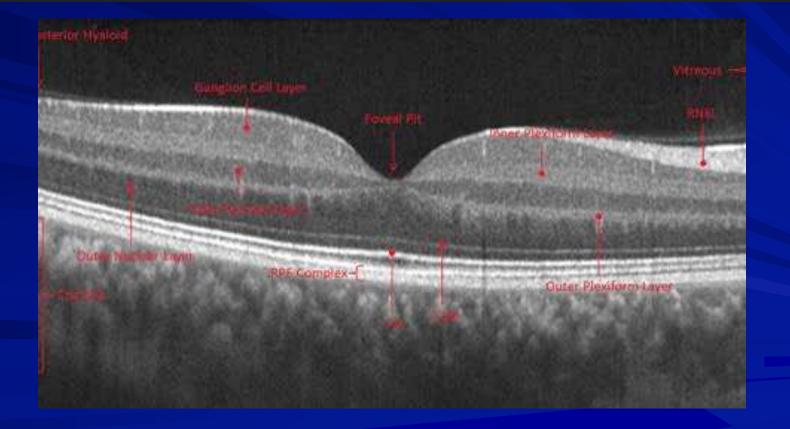


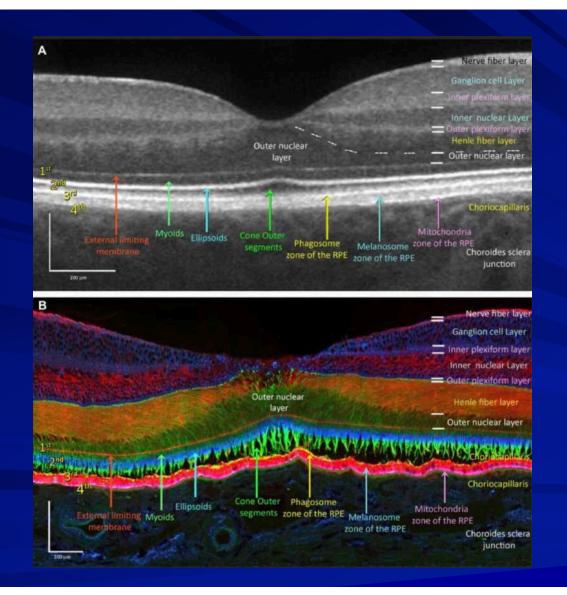
Credit to: James LaValle, RPh, CCN

# What is this layer called?



The ellipsoid zone (EZ)is considered to be formed mainly by mitochondriawithin 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).







## 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 product 90% of the free radicals
- ↔ When they become dysfunction when get many clinical consequences
- Ar Mitochondria are very sensitive to reactive oxygen and need antioxidant support
- Ar 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** 

N<u>Suron</u>, Author manuscript; available in PMC 2018 Nov 1. Published in final edited form as: Neuron. 2017. Nov 1: 9603: 631–686. doi: 10.1016/j.neuron.2017.09.055 PMCID: PMC5687842 NIHMSID: NIHMS909951 PMID: 29096078

Mitostasis in neurons: Maintaining mitochondria in an extended cellular architecture Thomas Misgeld<sup>12,3,4</sup> and Thomas L. Schwarz<sup>5,6</sup>

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#### scientific reports

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Article | Open Access | Publicate: 22 Sectomer 2021 The 3D organisation of mitochondria in primate photoreceptors

Marthew J. Haves 55, Drain Tracey Write, Jaima Hoh Kam, Michael B. Powner & Gen Jeffery Scientific Basers 11, Article number: 18863 (2021) | Che this article 913 Accesses | 21 Abretic | Merica

### Inflamm-aging

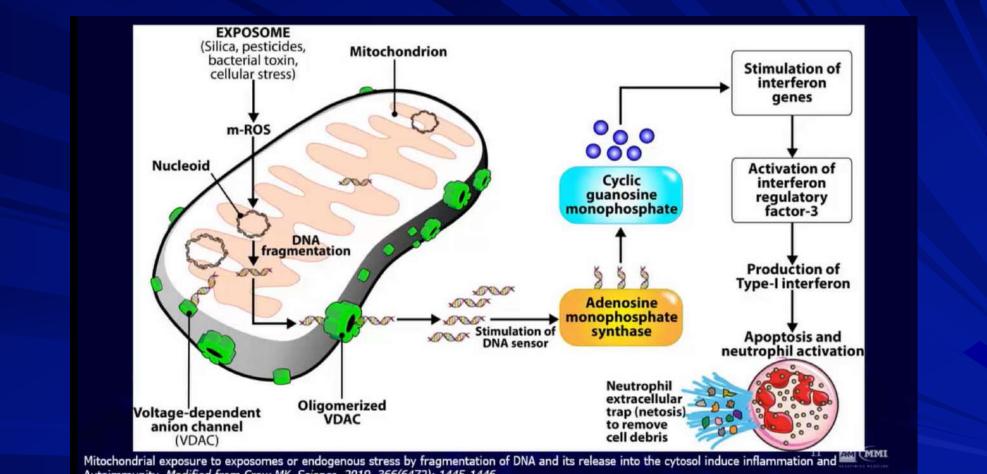
One of the consequences of failing mitochondria due to aging, beyond mtROS, is the release of mtDNA. Plasma levels of mtDNA increase gradually after the fifth decade of life, correlating with elevated levels of pro-inflammatory cytokines (i.e., TNF- $\alpha$ , IL-6, RANTES, and IL-1ra)

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 mtDAMPs, or their cognate receptors (e.g., TLRs or FPR1) may be a viable strategy to approaching IA and its associated conditions.

AM (MMI

Credit to: Elroy Vojdani, MD -

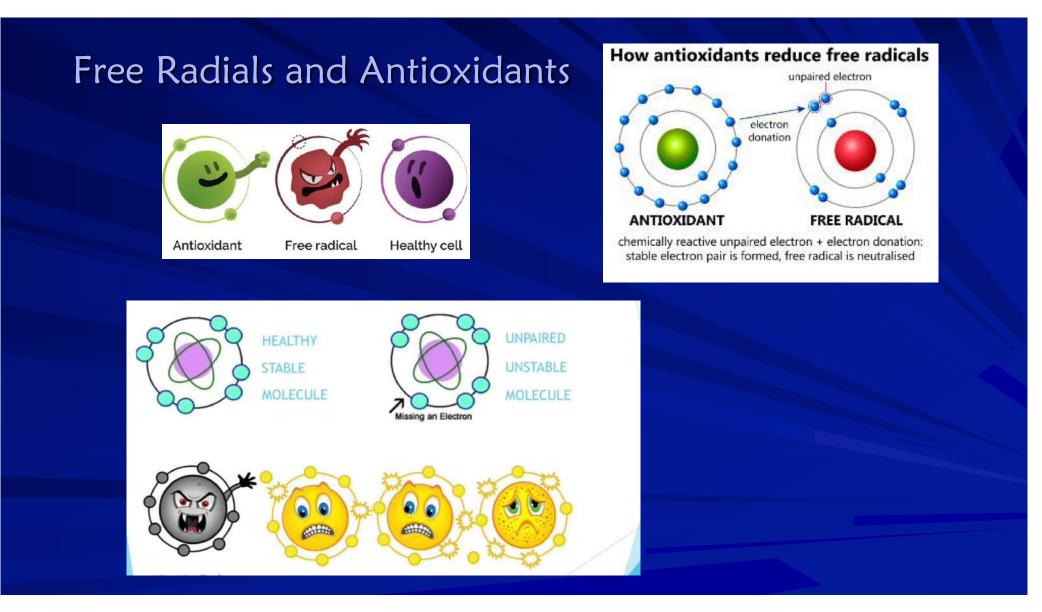
Dead Batteries: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutraceutical Interventions



Autoimmunity. Modified from Crow MK, Science, 2019, 366(6472): 1445-1446

Credit to: Elroy Vojdani, MD -

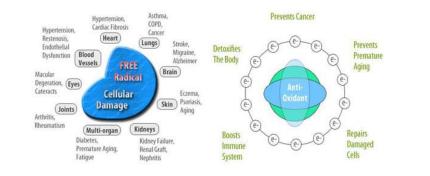
Dead Batteries: The Role of Mitochondrial Dysfunction in Immunological Decline - Emerging Diagnostic Tools and Nutraceutical Interventions



# Oxidative Stress

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





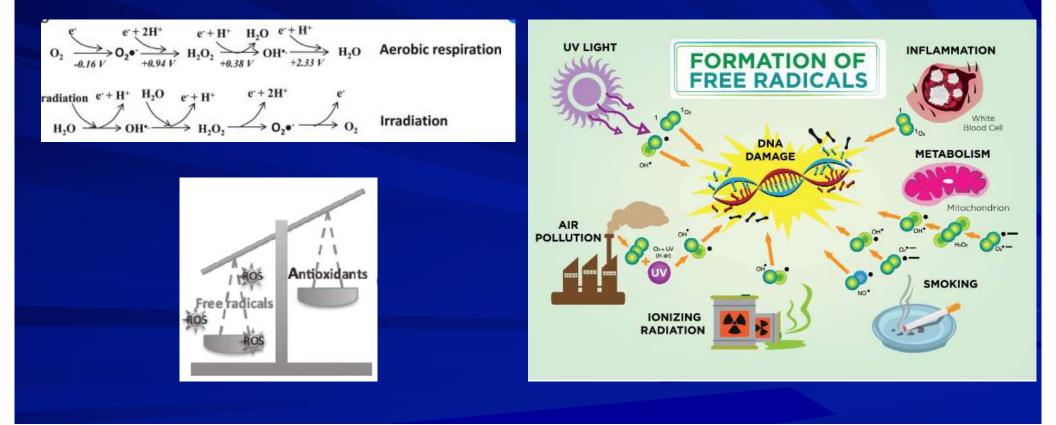
# Free Radicals

### $\Leftrightarrow$ During metabolism the O<sub>2</sub> 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
- Ar These molecules can be proteins, lipids, and DNA
  - Proteins (enzymes) kinases, phosphatases, and transcription factors

Reactive oxygen species ( • unpaired electrons)			
·ö::ö	·ö::ö·	• <b>0</b> : H	: <mark>Ö</mark> :Н
Superoxide anion	Peroxide	Hydroxyl radical	Hydroxyl ion
0 <sub>2</sub> -	02 <sup>-2</sup>	•он	он−
	• O::O Superoxide anion	• O::O Superoxide anion Peroxide	• O::O • O::O • O:H Superoxide anion Peroxide Hydroxyl radical

## Endogenous and Exogenous Free Radial Formation



# Oh no

A Increasing exogenous free radicals A Less antioxidant protection in our diet A 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.

# The Equalizer



# October 23, 2021



# Nutritional Antioxidants

### **Exogenous antioxidants**

\* Tocopherols (E), ascorbic acid (C), carotenoids, ubiquinone, and polyphenols

### a Well know antioxidants

\* Vitamin C, E, Beta-carotene, lutein, zeathanin, selenium, quercetin, and resveratrol

### A Mechanisms of action;

- \* Neutralize free radicals
- \* Repair oxidized membranes
- \* Decrease reactive oxygen species
- \* Neutral reactive oxygen species



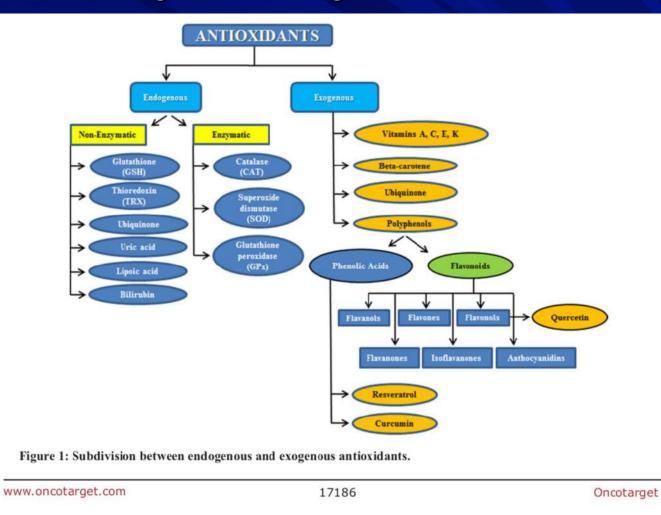
Optometric Education Consultants

### Text me your answer 814-931-2030

Can our body manufacture these antioxidants? Vitamins A, C, and E, carotenoids, flavonoids, resveratrol, and quercetin

- A. Yes
- B. No
- C. Hmmmm I am not sure

### Endogenous and Exogenous Antioxidants



## **Comprehensive Antioxidant Support**

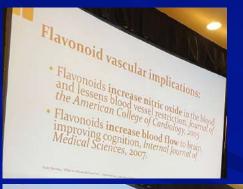
Cell membrane support
Immune support
Support to the oxidative stress to the extracellular matrix
Support to cell signaling

# Carotenoids

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









# Carotenoids

Greanic 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

A 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

## Measure?

Rev. Nutr. 2019 39:95-120. Downloaded from www.annualrev ided by Dartmouth College - Main Library on 0.1/12/21. For per

#### ASSESSMENT OF CAROTENOIDS

#### Impact of Carotenoid Assessment

Because carotenoids appear to play a key role in retinal diseases, intensive research has resulted in a variety of innovative carotenoid assessment techniques. The breadth of possibilities for assessing retinal carotenoids is often confusing because methodologies, units of measurement, and the presentation of results vary widely. Accurate readings of carotenoid status are important in order to correctly advise individuals with regards to supplementation. Furthermore, in diseases such as macular telangiectasia type 2 (MacTel), the assessment of carotenoids may be crucial to the diagnosis, as reduced MP levels as well as abnormal distributions are among the first signs of the disease. Therefore, the measurement of carotenoids can impact clinical practice, and the evaluation of MP may eventually become an integral part of comprehensive ophthalmological care. The following sections describe and aim to give an organized overview of different MP assessment techniques.

A large variety of methods are used to assess carotenoid status in humans, most of which are focused on the eye, but carotenoids can also be measured in tissue outside of the eye, such as the <u>skin, blood, and the brain</u>. Measurements of ocular carotenoids can be distinguished between subjective (psychophysical) and objective (optical) methods used to assess the amount of MP. In subjective methods, a direct answer from the patient is required, whereas objective measurement methods typically require just enough cooperation to generate an image (73).

#### Carotenoids in Tissues Other Than the Eye

<u>Carotenoids can be assessed noninvasively in the skin</u> and by high-performance liquid chromatography (HPLC) of blood and tissue samples. It has been shown that RRS measurements of skin carotenoids show strong correlations (r = 0.7 to 0.9) with carotenoids in biopsies of human skin

www.annualreviews.org • Ocular Carotennid Status in Health and Disease 103

(57, 96). Skin RRS and reflectometry are particularly useful to assess the carotenoid status of children, with <u>skin carotenoid levels strongly associated with fruit and vegetable intake (123)</u>. Using HPLC, the carotenoid status in the plasma can also be assessed (77, 104), and higher L levels in the serum of patients have been associated with higher visual function. Similarly, carotenoid assessment in brain tissue suggests that higher carotenoid levels might be beneficial for overall cognitive performance (65, 74).

### A ANNUAL REVIEWS

#### Annual Review of Nutrition

Ocular Carotenoid Status in Health and Disease

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Lydia Sauer, Binxing Li, and Paul S. Bernstein Department of Ophthalmology and Visual Sciences, John A. Moran Eye Center, University of Utah, Sah Lake City, Utah 84152, USA: email: Fuli.sauer@htscarah.edu, Bming Li@bac.utah.edu, paul bearterini@htscarah.edu

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#### Annu. Rev. Nutr. 2019: 39:95-120

First published as a Review in Advance on May 15, 2019 The dunad Brieve of Natrices is online at

nutrannuabreviews.org https://doi.org/10.1146/antrurev-nutr-082018 124555 Copyright © 2019 by Annual Reviews.

#### Keywords

macular pigment, macular carotenoids, carotenoid supplementation, ocular nutrition, retinal imaging

#### Abstract

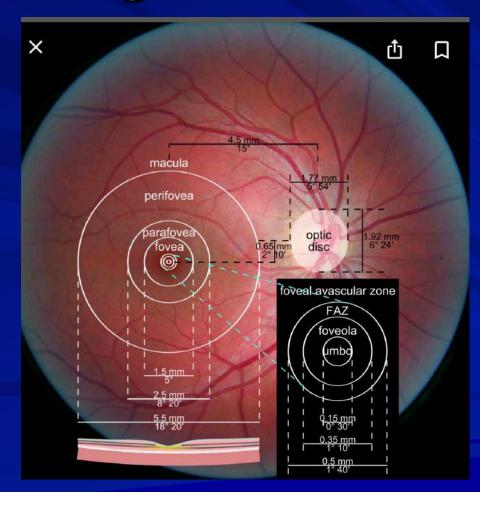
Retinal carotenoids are dietary nutrients that uniquely protect the eye from light damage and various retinal pathologies. Their antioxidative prosperties protect the eye from many retinal diseases, such as age-related macular degeneration. As many retinal diseases are accompanied by low carotenoid levels, accurate noninvasive assessment of carotenoid status can help ophhalmologists identify the patients most likely to benefit from enotenoid supplementation. This review focuses on the different methods available to assess carotenoid status and highlights disease-related changes and potential nutritional interventions.

95

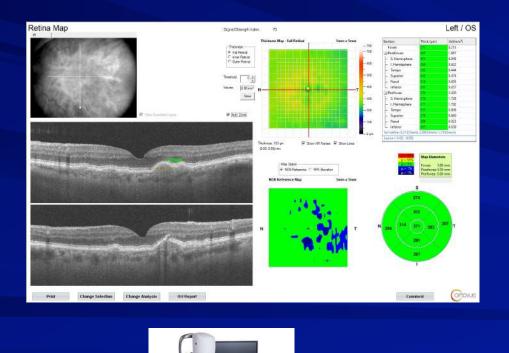
### Significance of Carotenoids



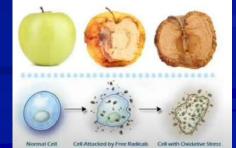
# How large is the macula?



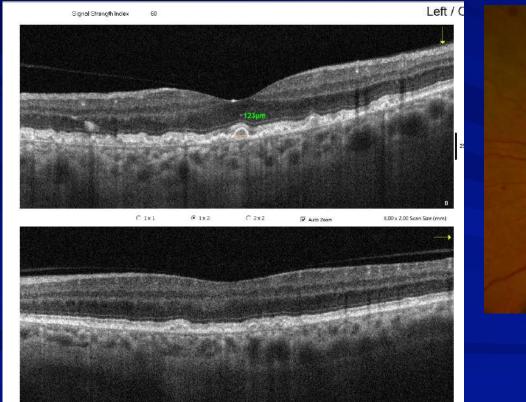
## **Oxidative Stress with Your OCT**







## Oxidative Stress with Your OCT







# Oxidative Stress with Your OCT



### Healthy choriocapillaris, Bruch's, RPE, and Photoreceptors



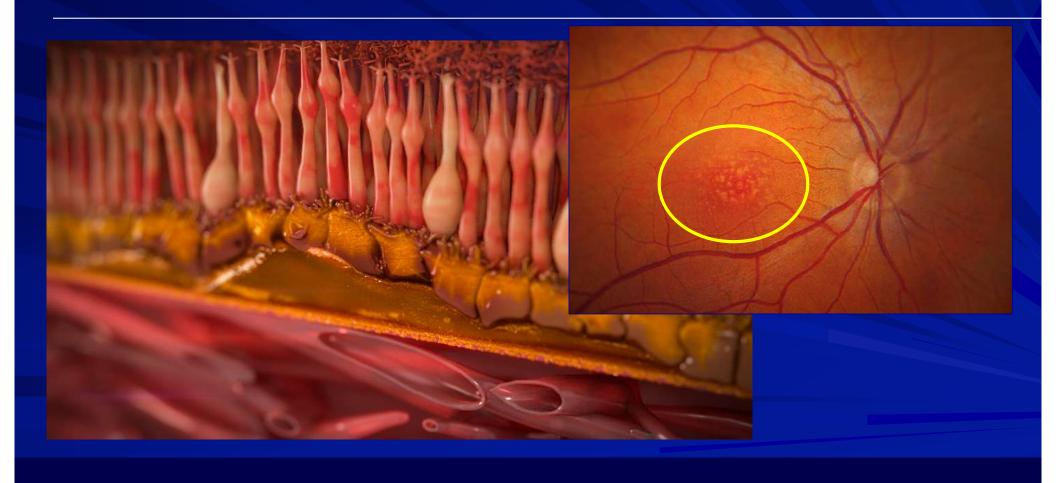
### Cholesterol barrier deposited along Bruch's and RPE



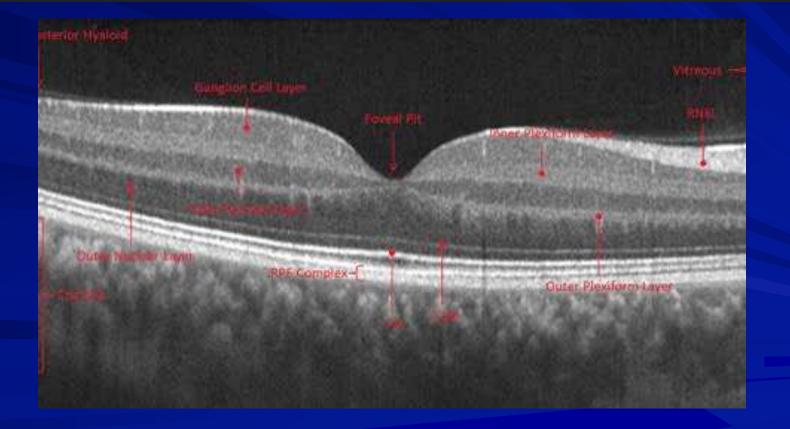
### RPE Secretes even more cholesterol and degenerates

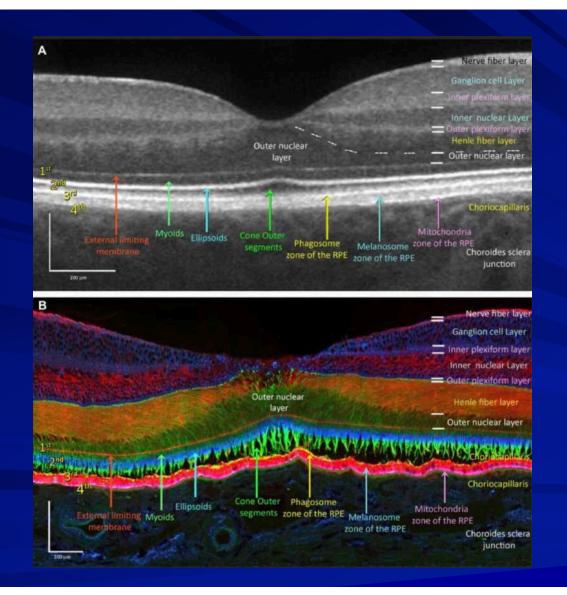


## Finally, visibly evident drusen on fundus evaluation



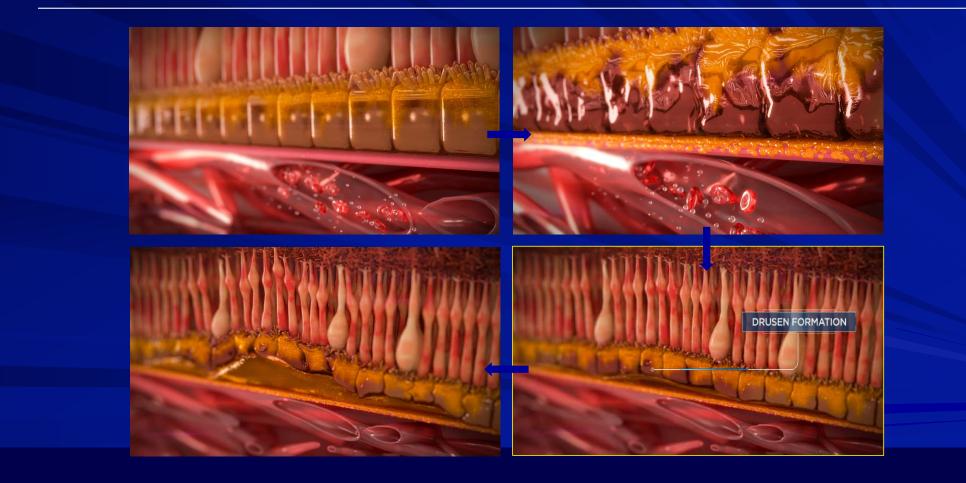
The ellipsoid zone (EZ)is considered to be formed mainly by mitochondriawithin the ellipsoid layer of the outer portion of the inner segments of the photoreceptors.However, it was previously known as the junction between the photoreceptor IS/OS).







### AMD is a Disease Process that Starts Below the Surface



### Beckmann Committee Classification of AMD

# Based on presence of lesions within 2 DD of fovea in either eye

\* No AMD

None or few small drusen, <</p>

No AMD pigmentary abnorr

\* Early AMD

**Medium drusen**, > 63 – <125 mic

No AMD pigmentary change

Intermediate AMD

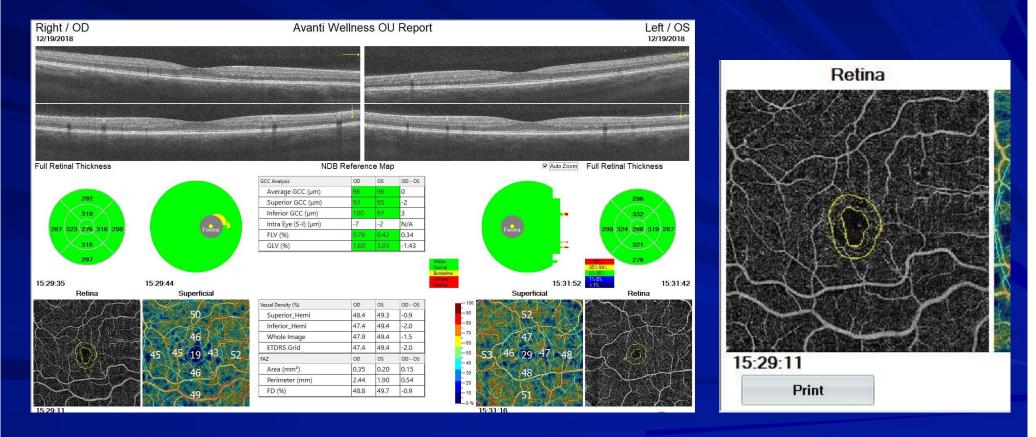
1 large drusen, > 125 microns

Any AMD pigmentary changes

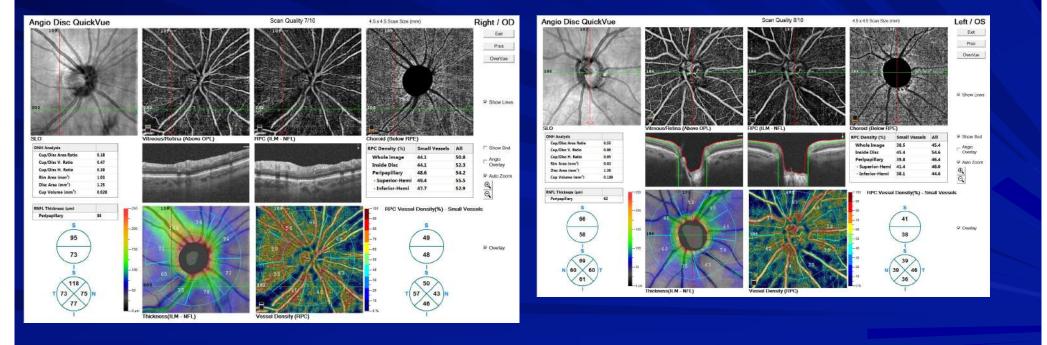


Promlily Dress - Never worn \$50

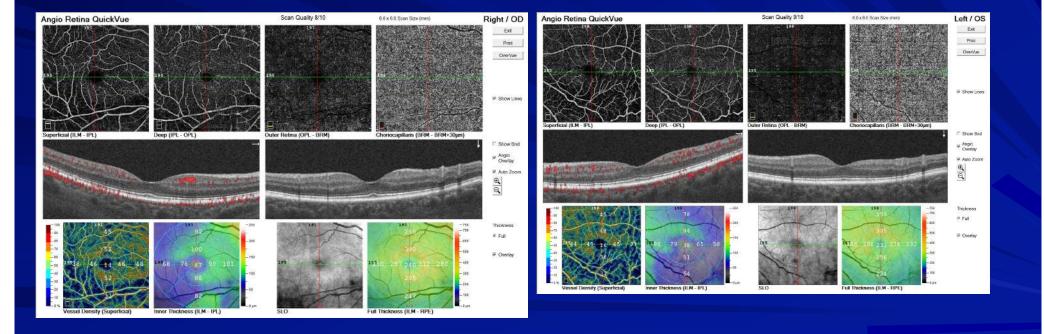
### AngioWellness Report Patient with Diabetes



# Angiography and AngioAnalytics of Disc



## Angiography and AngioAnalytics of Retina



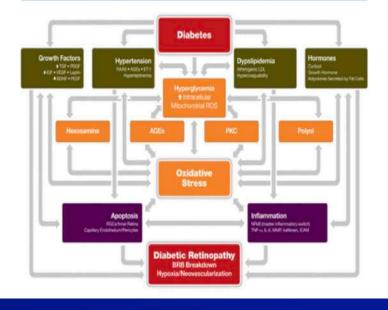
Randomized Controlled Trial > Br J Ophthalmol. 2016 Feb;100(2):227-34. doi: 10.1136/bjophthalmol-2014-306534. Epub 2015 Jun 18.

### The Diabetes Visual Function Supplement Study (DiVFuSS)

A Paul Chous <sup>1</sup>, Stuart P Richer <sup>2</sup>, Jeffry D Gerson <sup>3</sup>, Renu A Kowluru <sup>4</sup>

Affiliations + expand PMID: 26089210 PMCID: PMC4752618 DOI: 10.1136/bjophthalmol-2014-306534 Free PMC article

### PATHWAYS CONTRIBUTING TO DIABETIC RETINOPATHY



DIVFuSS Constituents	Mitigates DR in animal models	Blocks capillary cell apoptosis	Improves retinal capillary fragility	Reduces VEGF		Redu oxida stres	tive .			Reduces Polyol activity	Reduc PKC activity	11.4	Reduces NF-Kß
Alpha-Lipoic Acid	•			1	•		•				_		•
Benfotiamine	•	•						•			•		
Vitamins C/E	•						•			•			0.00
Curcumin	•				•	-	•	•					
Vitamin D3					•				_			_	
DHA/EPA		•				_	•	-	_		-	_	
Grape Seed Extract		•				_	•	•	2		_		
Resveratrol	•	•		-		3	•		_				
Green Tea Extract		-		-	÷	-				_	-		
N-Acetyl Cysteine	•	-		-	•		•	-	-	-	-		-
CoQ10 Zinc		-		-	_		•	-			-	-	
2,000	H-ANDS												
Pycnogenol	•		•	-	_		•						
Lutein/Zeaxanthin	•				٠	1	•						
DIVFuSS Constituents	Improves visual function in humans	Reduces retinal edema in humans	in hums	elial ction ans	on blood flow human		c in Dyslipi-		niain	Reduces blood pressure humans	in	Reduces DPN symptoms in humans	
Alpha-Lipoic Acid			•										
Benfotiamine			•							•			0.03
Vitamins C/E	-	-	•			-		_		•		_	
Curcumin	•	•				_					_		
Vitamin D3		1		-			-		-			_	
DHA/EPA		-	•							•			
Grape Seed Extract		-		_		_				_		-	
Resveratrol		-				-	_	•	_			_	
Green Tea Extract		-	•	_		_		_	-	•	•	-	
N-Acetyl Cysteine			-	-	-		-	_	-		_	-	
Co010				_		_	-	-			-	-	_
Zinc			_	-	-	_			-	•		-	
Pycnogenol	•	•	_	-			_	•	_	•	•	-	
Lutein/Zeaxanthin	•	•	_	_									
Note: Suggeste models, except												/or	cell

Download figure

Review > Nutrients. 2019 Apr 2;11(4):771. doi: 10.3390/nu11040771.

#### Nutraceuticals for the Treatment of Diabetic Retinopathy

Maria Grazia Rossino <sup>1</sup>, Giovanni Casini <sup>2</sup> <sup>3</sup>

Affiliations + expand PMID: 30987058 PMCID: PMC6520779 DOI: 10.3390/nu11040771 Free PMC article

#### Abstract

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus and is characterized by degeneration of retinal neurons and neoangiogenesis, causing a severe threat to vision. Nowadays, the principal treatment options for DR are laser photocoagulation, vitreoretinal surgery, or intravitreal injection of drugs targeting vascular endothelial growth factor. 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 upstream of 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-driven 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.

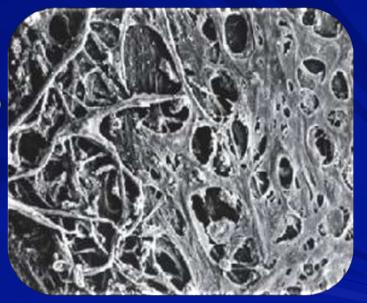
**Keywords:** carotenoids; flavonoids; inflammation; microvascular lesions; neoangiogenesis; oxidative stress; polyphenols; retina; saponins.

## Disease at the TM is responsible for elevated IOP in glaucoma<sup>1,2</sup>

Healthy TM Normal IOP POAG TM Stiffness Elevated IOP



Cellular Damage (eg, Oxidative Stress)



Scanning electron microscopy (2000x) was used to examine human TM under physiological conditions and in patients with POAG.<sup>2</sup> POAG, primary open-angle glaucoma; TM, trabecular meshwork. 1. He et al. *Invest Ophthalmol Vis Sci.* 2008;49:1447. 2. Saccà et al. *J Cell Physiol.* 2015;230:510.

## Glaucoma

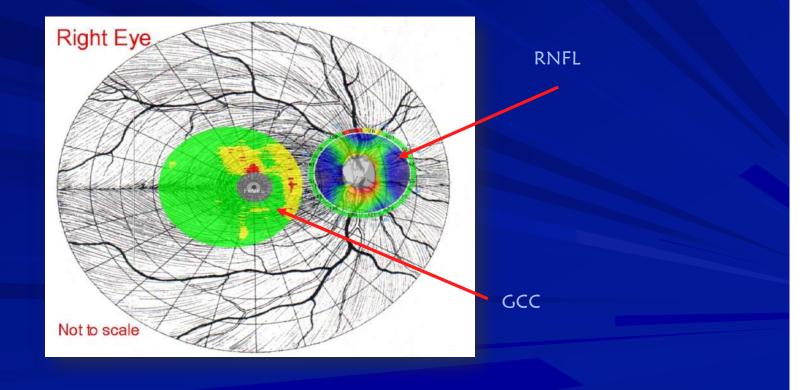
#### PERSPECTIVES ON GLAUCOMA

# Antioxidants enhance ocular perfusion in Open Angle Glaucoma

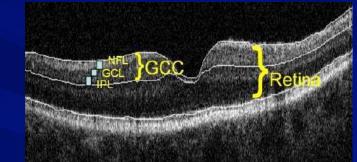
Harris A, et al. Acta Ophthalmol. 2018;doi:10.1111/aos.13530.

"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 <u>oral antioxidant supplementation</u> may decrease vascular resistance over a longer period of time than previous trials investigated."

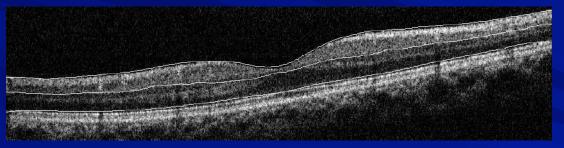
## Overlay of the RNFL and GCC



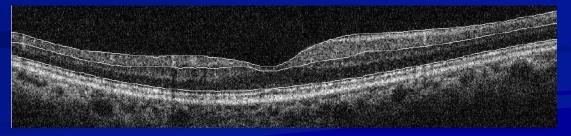
### GCC Thinning in Glaucoma

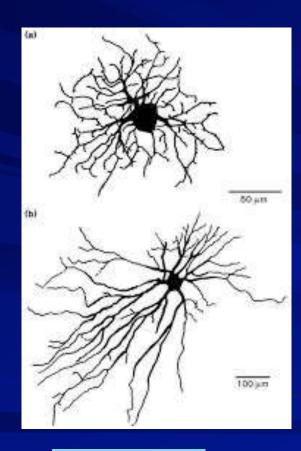


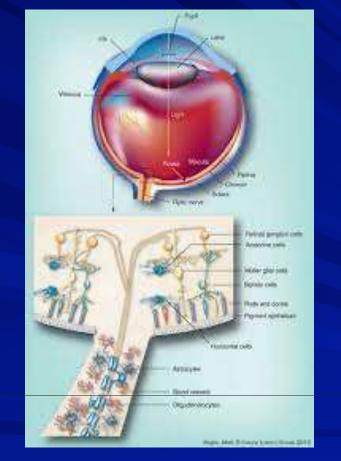
Normal



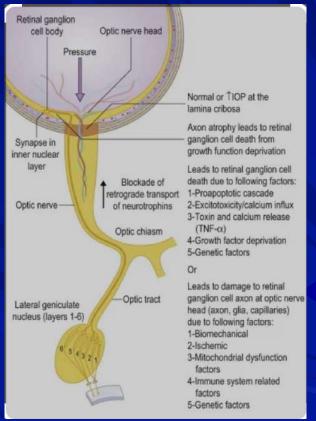
#### Glaucoma with thinner GCC





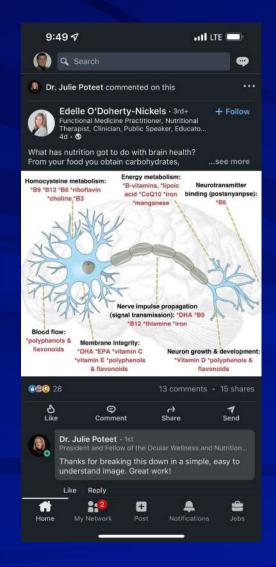


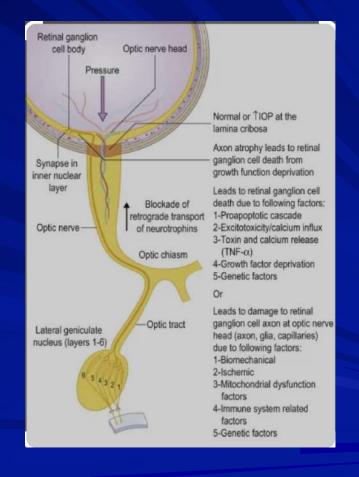
retinal ganglion cell regeneration ...futuremedicine.com



Pu Eble Rino **Retinal Ganglion Cells Optic Nerve** 

alpha and beta retinal ganglion cells ... cell com







Sissy D. Johns · 2nd 1w · ©

The development of atherosclerotic plaque, or atheroma, involves a multistep process:

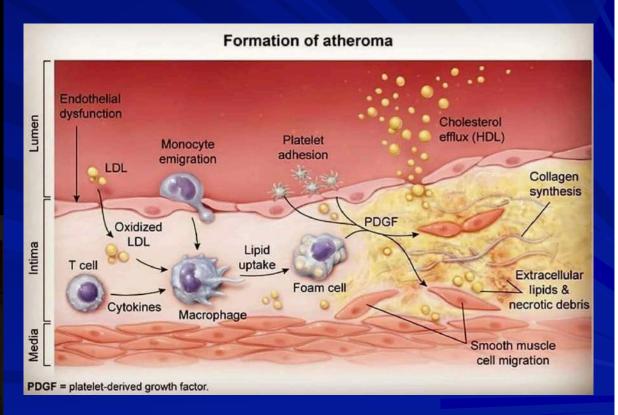
 $\mathbf{F}$ 

Initially, factors including hyperlipidemia, hypertension, hyperglycemia, and smoking trigger endothelial injury and/ or dysfunction. This leads to increased vascular permeability, enhanced leukocyte adhesion, and a higher propensity for thrombosis.

Lipoproteins (ie, LDL and oxidized LDL) enter the arterial wall intima and begin to accumulate. Monocytes adhere to the endothelial wall

and enter into the intima as well; these cells transform into macrophages and engulf lipid particles to become foam cells. Platelets adhere to the abnormal endothelium and become activated.

Growth factors, namely platelet-derived growth factor (PDGF), are released from platelets, activated macrophages, and endothelial cells. This triggers smooth muscle cell (SMC) recruitment from the media and proliferation in the intima.



See less

## Treatments for AMD

- G→ Early detection and meaningful treatments with significant value, do not cure, but have been shown to slow or halt progression. Not limited to early stages but all stages of AMD
  - \* Prescribe smoking cessation programs
    - **Smoking and AMD** 
      - Depletes serum antioxidants
      - Decreases pigmentary density
      - Increases risk to advanced AMD
  - \* Lifestyle changes
    - Diet
    - **Exercise**
  - \* Systemic disease management
    - Cardiovascular disease, DM, obesity, high cholesterol



Learn About Eye Health 📀

50	Español	

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Research at NEI 📀

Home » Research at NEI » Clinical Trials » Age-Related Eye Disease Studies (AREDS/AREDS2) » AREDS/AREDS2 Frequently Asked Questions

Grants and Training 💿

#### **AREDS/AREDS2** Frequently Asked Questions

On this page: <u>AREDS formulas</u> | <u>Formulation components</u> | <u>Risks and side-effects</u> | <u>About the trials</u> | <u>Genetic testing</u> | <u>References</u> | <u>Definitions</u>

#### **Taking the AREDS formulas**

#### Are the AREDS vitamins right for me?

In clinical trials, the AREDS and AREDS2 formulas benefited people with intermediate or late AMD. There was no benefit for people with early AMD or for people who do not have AMD.

Your primary care physician or eye care provider is in the best position to advise you on how treat your AMD. You may wish to discuss AREDS/AREDS2 supplements with your health care providers to decide which, if any, supplements are right for you.

#### Will taking the AREDS or AREDS2 supplements prevent AMD?

Nutritional supplements cannot prevent AMD. However, the AREDS/AREDS2 supplements may delay progression of intermediate to advanced AMD and may help you keep your vision longer. The participants AREDS trial have now been followed for more than 10 years, and the benefits of the AREDS formulation have persisted over this time.

#### Additional Resources

**AREDS and AREDS2 Information** 

Search

About NEI 📀

Age-Related Eye Disease Studies 🔊

AREDS/AREDS2 - Background and Design ()

AREDS/AREDS2 Nutritional Supplements (>)

AREDS/AREDS2 News

Information about AMD

Age-Related Macular Degeneration

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## Can I take a daily multivitamin if I am taking one of the AREDS/AREDS2 formulas?

Yes. The AREDS and AREDS2 formulas do not substitute for multivitamins. In AREDS, two-thirds of the study participants took multivitamins along with the AREDS formulation. In AREDS2, almost nine of ten participants took multivitamins.

#### ↔ Nutritional supplements

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

## Treatment for AMD

## 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 Chronography



### 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.

### An Evening with Dr. Paul Bernstein

Dr. Paul Bernst

MP Line Plot

Distribution

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

- Will addition of L and Z to standard-of-care prenatal vitamins combat 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 macular pigment by Spectralis AFI
  - Infant macular pigment and foveal structure by RetCam and Bioptigen OCT
- Fully enrolled
- NEI funded

### An Evening with Dr. Paul Bernstein

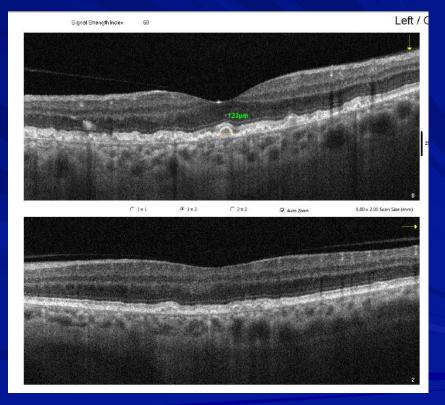
#### The Moran AMD Genetic Testing Assessment Study: The Magenta Study

- 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 deferred disclosure
- 18-64 years-old w/o AMD
- Outcomes
  - Skin carotenoids by RRS and RS
  - Macular pigment by Spectralis AFI
  - · Lifestyle surveys
- · Awaiting NEI funding



# Macular Pigment





# Macular Pigment

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

Binxing Li<sup>a</sup><sup>(a)</sup>, Evan W. George<sup>a</sup>, Gregory T. Rognon<sup>a</sup>, Aruna Gorusupudi<sup>a</sup>, Arunkumar Ranganathan<sup>a</sup><sup>(a)</sup>, Fu-Yen Chang<sup>a</sup>, Linjia Shi<sup>a</sup>, Jeanne M. Frederick<sup>a</sup>, and Paul S. Bernstein<sup>a,1</sup><sup>(a)</sup>

<sup>a</sup>Department of Ophthalmology and Visual Sciences, Moran Eye Center, University of Utah School of Medicine, Salt Lake City, UT 84132

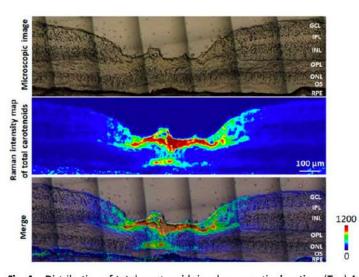
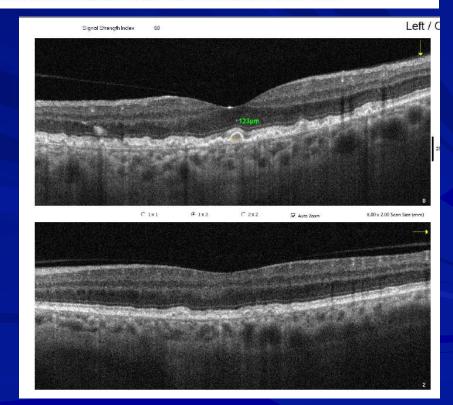
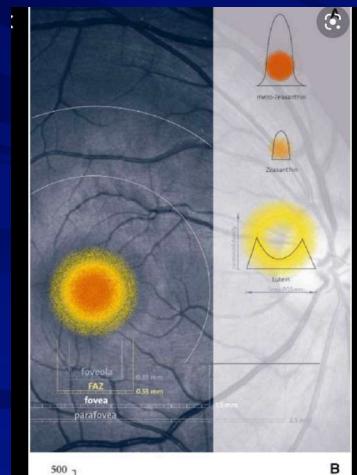
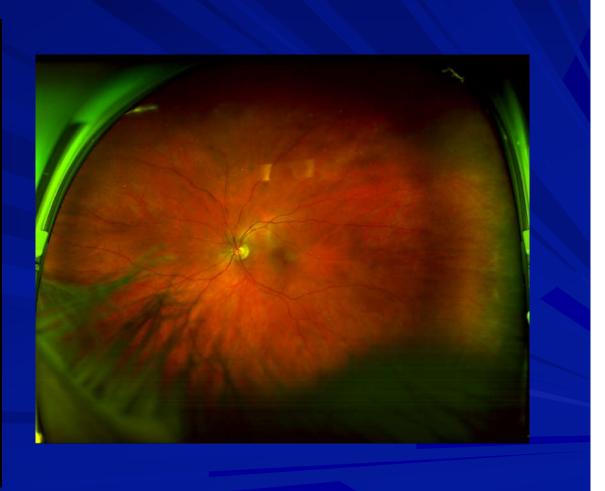


Fig. 4. Distribution of total carotenoids in a human retinal section. (Top) A



lheak for







Do you recommend resveratrol and quercetin antioxidants when treating ocular/retinal conditions?

\* Yes\* No

Oxidative Medicine and Cellular Longevity

<u>Oxid Med Cell Longev</u>. 2019; 2019: 9783429. Published online 2019 Feb 12. doi: <u>10.1155/2019/9783429</u> PMCID: PMC6390265 PMID: <u>30891116</u>

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

Simona Bungau, <sup>1</sup> Mohamed M. Abdel-Daim, <sup>II</sup> <sup>2</sup>, <sup>3</sup> Delia Mirela Tit, <sup>1</sup> Esraa Ghanem, <sup>II</sup> <sup>4</sup> Shimpei Sato, <sup>3</sup> Maiko Maruyama-Inoue, <sup>3</sup> Shin Yamane, <sup>3</sup> and Kazuaki Kadonosono <sup>3</sup>

+ Author information + Article notes + Copyright and License information Disclaimer

This article has been <u>cited by</u> other articles in PMC.

#### Abstract

Oxid Med Cell Lor

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Oxidative stress and inflammation play a critical role in the initiation and progression of age-related ocular abnormalities as cataract, glaucoma, diabetic retinopathy, and macular degeneration. Therefore, phytochemicals with proven antioxidant and anti-inflammatory activities, such as carotenoids and polyphenols, could be of benefit in these diseases. We searched PubMed and Web of Science databases for original studies investigating the benefits of different carotenoids and polyphenols in age-related ophthalmic diseases. Our results showed that several polyphenols (such as anthocyanins, Ginkgo biloba, quercetin, and resveratrol) and carotenoids (such as lutein, zeaxanthin, and mezoxanthin) have shown significant preventive and therapeutic benefits against the aforementioned conditions. The involved mechanisms in these findings include mitigating the production of reactive oxygen species, inhibiting the tumor necrosis factor- $\alpha$  and vascular endothelial growth factor pathways, suppressing p53-dependent apoptosis, and suppressing the production of inflammatory markers, such as interleukin- (IL-) 8, IL-6, IL-1a, and endothelial leucocyte 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 synergistic effects on the prevention and treatment of age-related eye diseases that are induced or augmented by oxidative stress and inflammation.

## Why Are We Only Treating Half the Retina?

## **Carotenoids and Polyphenols**

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Review

#### Oncotarget, 2018, Vol. 9, (No. 24), pp: 17181-17198

#### Oxidative stress: role of physical exercise and antioxidant nutraceuticals in adulthood and aging

#### Carolina Simioni<sup>1</sup>, Giorgio Zauli<sup>1</sup>, Alberto M. Martelli<sup>2</sup>, Marco Vitale<sup>3,4</sup>, Gianni Sacchetti<sup>5</sup>, Arianna Gonelli<sup>1</sup> and Luca M. Neri<sup>1</sup>

Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy
 <sup>3</sup>Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
 <sup>4</sup>CoreLab, Azienda Ospedallero-Universitaria di Parma, Parma, Italy
 <sup>6</sup>Department of Life Sciences and Biotechnology, Pharmaceutical Biology Laboratory, University of Ferrara, Ferrara, Italy
 <sup>6</sup>CoreLab, Azienda Ospedallero-Universitaria di Parma, Parma, Italy
 <sup>6</sup>CoreLab, Azienda Ospedallero-Unive

Resveratrol can be implied in anti-aging actions by influencing the mitochondrial environment and metabolic diseases, by regulating the levels of some inflammatory mediators and cytokines and by modulating lipolysis [125, 152, 153]. Mitochondrial dysfunction has been proved to be associated with aging and disease development [154], and it was seen

39

w.oncotarget.com

Oncotarget

Furthermore, resveratrol maintains the vascular fitness through its antioxidant and anticoagulant activities, and on the other hand is relevant in blocking the formation of new blood vessels, in inhibiting the VEGF release and attenuating Hypoxia-Inducible Factor (HIF-1 $\alpha$ ) in different tumor cells [163].

#### ASSESSMENT OF CAROTENOIDS

#### Impact of Carotenoid Assessment

Because carotenoids appear to play a key role in retinal diseases, intensive research has resulted in a variety of innovative carotenoid assessment techniques. The breadth of possibilities for assessing retinal carotenoids is often confusing because methodologies, units of measurement, and the presentation of results vary widely. Accurate readings of carotenoid status are important in order to correctly advise individuals with regards to supplementation. Furthermore, in diseases such as macular telangiectasia type 2 (MacTel), the assessment of carotenoids may be crucial to the diagnosis, as reduced MP levels as well as abnormal distributions are among the first signs of the disease. Therefore, the measurement of carotenoids can impact clinical practice, and the evaluation of MP may eventually become an integral part of comprehensive ophthalmological care. The following sections describe and aim to give an organized overview of different MP assessment techniques.

A large variety of methods are used to assess carotenoid status in humans, most of which are focused on the eye, but carotenoids can also be measured in tissue outside of the eye, such as the <u>skin, blood, and the brain</u>. Measurements of ocular carotenoids can be distinguished between subjective (psychophysical) and objective (optical) methods used to assess the amount of MP. In subjective methods, a direct answer from the patient is required, whereas objective measurement methods typically require just enough cooperation to generate an image (73).

### 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



## Carotenoid Levels

Scanner correlates to blood and macular pigment

ØΛR

read stud

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



#### Clinical and Epidemiologic Research

Correlations Between Macular, Skin, and Serum Carotenoids

Christopher D. Conrady,<sup>1</sup> James P. Bell,<sup>1</sup> Brian M. Besch,<sup>1</sup> Aruna Gorusupudi,<sup>1</sup> Kelliann Farnsworth,<sup>1</sup> Igor Ermakov,<sup>2</sup> Mohsen Sharifzadeh,<sup>2</sup> Maia Ermakova,<sup>2</sup> Werner Gellermann,<sup>1,2</sup> and Paul S. Bernstein<sup>1</sup>

<sup>1</sup>Department of Ophthalmology and Visual Sciences, Moran Eye Center, Salt Lake City, Utah, United States
<sup>2</sup>Image Technologies Corporation, Salt Lake City, Utah, United States

Correspondence: Paul S. Bernstein, Moran Eye Center, University of Utah School of Medicine, 65 Mario Capecchi Drive, Salt Lake Gity, UT 84132, USA; paul.bernstein@hsc.utah.edu. Submitted: March 7, 2017 Accepted: June 18, 2017 Citation: Conrady CD. Bell JP. Besch BM, et al. Correlations between macular skin, and serum carotenoids. *Invest Ophtbalmol Vis Sci.* 2017;58:5616–5627. DOI:10.1167/

iovs.17-21818

Pursors, Ocular and systemic measurement and imaging of the macular carotenoids lutein and zeaxanthin have been employed extensively as potential biomarkers of AMD risk. In this study, we systematically compare dual wavelength retinal autofluorescence imaging (AFD) of macular pigment with skin resonance Raman spectroscopy (RRS) and serum carotenoid levels in a clinic-based population.

Mernons. Eighly-eight patients were recruited from retina and general ophthalmology practices from a tertiary referral center and excluded only if they did not have all three modalities tested, had a diagnosis of macular telangicetasia (MacTel) or Stargardt disease, or had poor AFI image quality. Skin, macular, and serum carotenoid levels were measured by RRS, AFI, and HPLC, respectively.

RESULTS. Skin RRS measurements and serum zeaxanthin concentrations correlated most strongly with AFI macular pigment volume under the curve (MPVUC) measurements up to 9° eccentricity relative to MPVUC or rotationally averaged macular pigment optical density (MPOD) measurements at smaller eccentricities. These measurements were reproducible and not significantly affected by cataracts. We also found that these techniques could readily identify subjects taking oral carotenoid-containing supplements.

Concussions. Larger macular pigment volume AFI and skin RRS measurements are noninvasive, objective, and reliable methods to assess ocular and systemic carotenoid levels. They are an attractive alternative to psychophysical and optical methods that measure MPOD at a limited number of eccentricities. Consequently, skin RRS and MPVUC at 9° are both reasonable biomarkers of macular carotenoid status that could be readily adapted to research and clinical settings.

Keywords: macular pigment, carotenoids, macula

## The New Standard



National Institutes of Health



Quick Test (approx. 30 sec)

Portable

**Cost Effective** 

Remeasure in 60 days

Reassurance to you and patient

## Raman Spectroscopy



478nm PHOTONS ARE EMITTED FROM THE SCANNER AS 478nm PHOTONS STRIKE CAROTENOIDS IN THE SKIN, THEY ARE REFLECTED BACK AS 518nm PHOTONS

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

Susan T. Mayne <sup>a,\*</sup>, Brenda Cartmel <sup>a</sup>, Stephanie Scarmo <sup>a,b</sup>, Lisa Jahns <sup>c</sup>, Igor V. Ermakov <sup>d</sup>, Werner Gellermann <sup>d</sup>



<sup>4</sup> Yale School of Public Health and Yale Cancer Center, 60 College St., P.O. Box 208034, New Haven, CT 06520, USA <sup>b</sup> Center for Science in the Public Interest, 1220 L Street, N.W., Suite 300, Washington, DC 20005, USA <sup>c</sup> USDA/ARS Grand Forks Human Nutrition Research Center, 2420 2nd Avenue North, Grand Forks, 58203, A <sup>d</sup> Department of Physics and Astronomy, University of Utah, Salt Lake City, UT 8400, 100

#### ARTICLE INFO

Article history: Available online xxxx

Keywords: Carotenoids Skin Resonance Raman spectroscopy Beta-carotene Biomarker

#### ВАСТ

RS) is a ... invasive method that has been developed to assess carot-Resonance man sp oscopy enoid statu human uding human skin in vivo. Skin carotenoid status has been suggested as marker for numan studies. This endue tript describes research done relevant to the devela promising biomarker, including its report cibility, lidity, feasibility for use in field settings, and opment of th mok factors that affect the biomark ch a and adiposity. Recent studies have evaluated otenoid interventions, both supplement-based and dietary the response of the uari r to olle [e.g., provision of a hith-capter id wat and vegetable (F/V)-enriched diet], demonstrating consistent response to intervation. The totality of evidence supports the use of skin carotenoid status as an objective biomarker V intake, although in the cross-sectional setting, diet explains only some of the variation in this biomarker. However, this limitation is also a strength in that skin carotenoids may effectively serve as an integrated biomarker of health, with higher status reflecting greater F/V intake, lack of smoking, and lack of adiposity. Thus, this biomarker holds promise as both a health biomarker and an objective indicator of F/V intake, supporting its further development and utilization for medical and public health purposes.

\*Arch Biochem Biophys. PMC 2014 Nov 15.

### **ARVO STUDY**

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

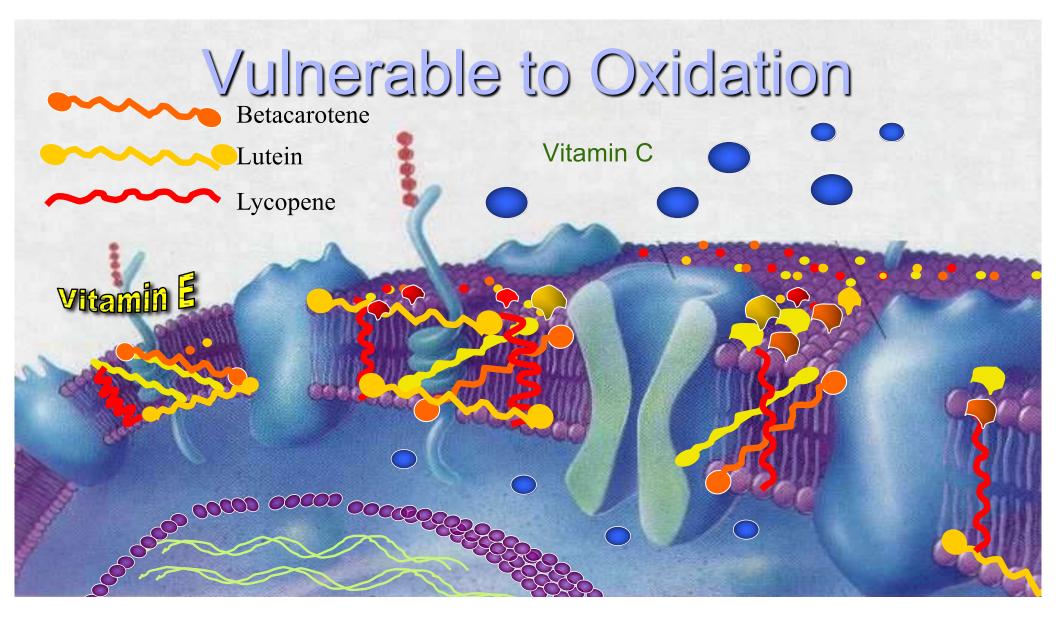
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# Are you taking a supplement?

## 53-year-old man

A Family history of AMD

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

#### CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Dear

Recently, on 12/15/2020, you met with me and I scanned the palm of your hand with the BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 26000.

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



26000

#### Ingredients

Ingredients	Amount	% Daily Value
Serving Size: 1 Packet		
Vitamin A (83% as Beta Carotene (1875 mcg RAE) from <i>Blakeslea trispora</i> , and Vitamin A palmitate) (375 mcg RAE)	2250 mcg RAE	250%
Vitamin C (as Calcium Ascorbate)	200 mg	222%
Vitamin D (as Cholecalciferol)	5 mcg (200 IU)	25%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha Tocopherol, Tocotrienols)	50.3 mg	335%
Vitamin K (as Phytonadione)	20 mcg	17%
Thiamin (as Thiamine Mononitrate)	3.75 mg	313%
Riboflavin (as Riboflavin)	4.25 mg	327%
Niacin (as Niacinamide)	17.5 mg NE	109%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	294%
Folate	500 mcg DFE (300 mcg folic acid)	125%
Vitamin B12 (as Cyanocobalamin)	15 mcg	625%
Biotin (as Biotin)	75 mcg	250%
Pantothenic Acid (as D-Calcium Pantothenate)	15 mg	300%
Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%

Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%
lodine (as Potassium Iodide)	50 mcg	33%
Magnesium (as Magnesium Glycinate, Magnesium Oxide)	125 mg	30%
Zinc (as Zinc Bisglycinate)	7.5 mg	68%
Selenium (as L-Selenomethionine, Sodium Selenite)	70 mcg	127%
Copper (as Copper Bisglycinate)	0.5 mg	56%
Manganese (as Manganese Bisglycinate)	1 mg	43%
Chromium (as Chromium Nicotinate Glycinate)	100mcg	286%
Molybdenum (as Molybdenum Bisglycinate)	37.5 mcg	83%
Polyphenol and Flavonoid Blend	97.5 mg	*
Catechins (from Camellia sinensis Leaf Extract)	(45 mg)	*
Quercetin	(25 mg)	*
Grape Seed Extract (min. 95% Polyphenols)	(12.5 mg)	*
Citrus Bioflavonoids (from Citrus Fruits)	12.5 mg)	*
Resveratrol (from Polygonum cuspidatum root extract)	(2.5 mg)	*
Mixed Tovopherols (Gamma, Delta & Beta Tocopherols)	53 mg	*
Alpha-Lipoic Acid	15 mg	*
Inositol (as Inositol)	5 mg	*
Carotenoid Blend	3.5 mg	*
Lycopene (as Lycopene)	(2.5 mg)	*
Lutein (from Marigold Flower Extract)	(1 mg)	*
Boron (as Boron Citrate)	1.5 mg	*
Vanadium (as Vanadyl Sulfate)	10 mcg	*

OTHER INGREDIENTS: Gelatin, Microcrystalline Cellulose, Crosmarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

CONTAINS: Fish (Cod, Pollack, Haddock, Hake, Cusk, Redfish, Sole, Flounder).

#### SUPPLEMENT FACTS

### **Supplement Facts**

Serving Size 2 Softgels	Servings Per Conta	ainer 60
Amount Per Serving		% DV
Total Calories Total Fat Saturated Fat Trans Fat	15 1 g 0 g 0 g	196* 096*
Vitamin Dg (as cholecalciferol) Vitamin Kg (as menaquinone-7)	12.5 mcg (500 IU) 20 mcg	63% 17%
Ultra-pure fish oil concentrate:	1055 mg	
EPA (Eicosapentaenoic acid)	300 mg	
DHA (Docosahexaenoic acid)	200 mg	**
Citrus Bioflavonoids (including hesperidin and naringin)	100 mg	**
Purple corn (Zea mays L) cob extract including anthocyanins	66.67 mg	•
Alpha Lippic Acid	50 ma	**
Quercetin (from Dimorphandra moli/s fruit extract)	37.5 mg	
D-Limonene (from Citrus sinensis peel)	25 mg	
Rosemary (Rosmarinus officinalis L) leaf extract including carnosic acid	18.75 mg	
Resveratrol (from Polygonum cuspidatum root)	15 mg	
Coenzyme Q10	15 mg	**
Lycopene	2.5 mg	-
Lutein (from marigold flower (Targetes erectal)	2 mg	**
Astaxanthin (from Haematococcus pluvialis algae		
Personal Daily Values are based as a 2,000 Cales	a milat	- C.

\* Percent Daily Values are based on a 2,000 Calorie Diet. \*\* Daily Value (DV) not established.

OTHER INGREDIENTS: Gelatin, Glycerin, Beeswax, Sunflower Lecithin,

Vanillin.

CONTAINS: Fish (anchovies, sardines, mackerel).

## 53-year-old man

#### CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Dear

Recently, on 12/27/2020, you met with me and I scanned the palm of your hand with the BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 33000.

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



33000

#### CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Dear

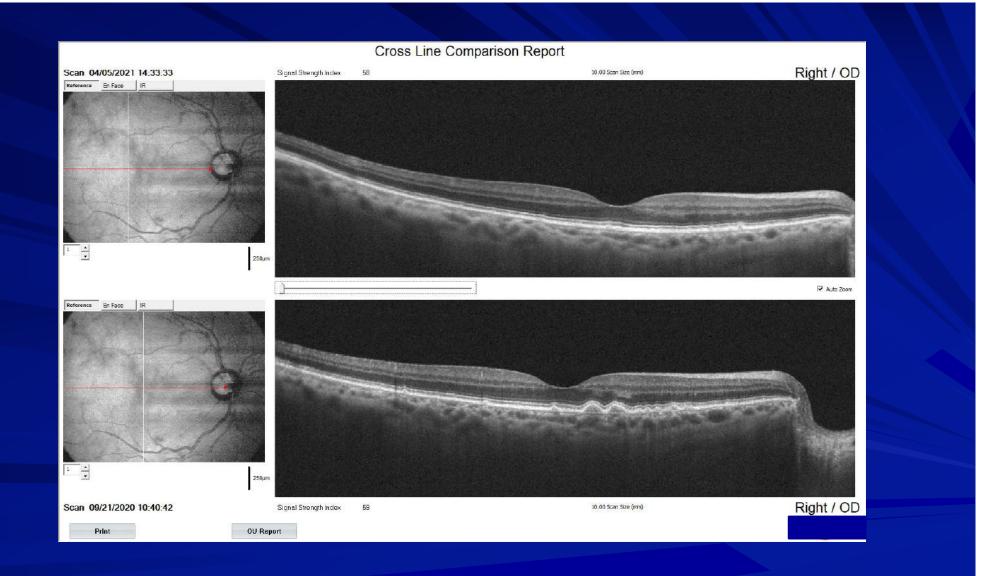
Recently, on 01/23/2021, you met with me and I scanned the palm of your hand with the BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 47000.

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



47000

#### Raster Comparison Report Scan 09/29/2020 13:20:09 Signal Strength Index 55 12.00 x 4.00 Scan Size (mm) Reference En Face IR Right / OD N of 3 So Far 10 -250µm Auto Zoom Reference En Face IR 250µm 173 Right / OD 12.00 x 4.00 Scan Size (mm) Signal Strength Index 43 Scan 06/23/2021 10:22:11 OU Report Print 🥥 49"F Sunny \land 🔛 🗛



#### Ingredients

Ingredients	Amount	% Daily Value
Serving Size: 1 Packet		
Vitamin A (83% as Beta Carotene (1875 mcg RAE) from <i>Blakeslea trispora</i> , and Vitamin A palmitate) (375 mcg RAE)	2250 mcg RAE	250%
Vitamin C (as Calcium Ascorbate)	200 mg	222%
Vitamin D (as Cholecalciferol)	5 mcg (200 IU)	25%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha Tocopherol, Tocotrienols)	50.3 mg	335%
Vitamin K (as Phytonadione)	20 mcg	17%
Thiamin (as Thiamine Mononitrate)	3.75 mg	313%
Riboflavin (as Riboflavin)	4.25 mg	327%
Niacin (as Niacinamide)	17.5 mg NE	109%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	294%
Folate	500 mcg DFE (300 mcg folic acid)	125%
Vitamin B12 (as Cyanocobalamin)	15 mcg	625%
Biotin (as Biotin)	75 mcg	250%
Pantothenic Acid (as D-Calcium Pantothenate)	15 mg	300%
Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%

Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%
lodine (as Potassium Iodide)	50 mcg	33%
Magnesium (as Magnesium Glycinate, Magnesium Oxide)	125 mg	30%
Zinc (as Zinc Bisglycinate)	7.5 mg	68%
Selenium (as L-Selenomethionine, Sodium Selenite)	70 mcg	127%
Copper (as Copper Bisglycinate)	0.5 mg	56%
Manganese (as Manganese Bisglycinate)	1 mg	43%
Chromium (as Chromium Nicotinate Glycinate)	100mcg	286%
Molybdenum (as Molybdenum Bisglycinate)	37.5 mcg	83%
Polyphenol and Flavonoid Blend	97.5 mg	*
Catechins (from Camellia sinensis Leaf Extract)	(45 mg)	*
Quercetin	(25 mg)	*
Grape Seed Extract (min. 95% Polyphenols)	(12.5 mg)	*
Citrus Bioflavonoids (from Citrus Fruits)	12.5 mg)	*
Resveratrol (from Polygonum cuspidatum root extract)	(2.5 mg)	*
Mixed Tovopherols (Gamma, Delta & Beta Tocopherols)	53 mg	*
Alpha-Lipoic Acid	15 mg	*
Inositol (as Inositol)	5 mg	*
Carotenoid Blend	3.5 mg	*
Lycopene (as Lycopene)	(2.5 mg)	*
Lutein (from Marigold Flower Extract)	(1 mg)	*
Boron (as Boron Citrate)	1.5 mg	*
Vanadium (as Vanadyl Sulfate)	10 mcg	*

OTHER INGREDIENTS: Gelatin, Microcrystalline Cellulose, Crosmarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

CONTAINS: Fish (Cod, Pollack, Haddock, Hake, Cusk, Redfish, Sole, Flounder).

## Treat and Extend!

#### Comment:

Mr. Barket has exudative AMD in each eye. He is doing well in each eye today with no recurrent CNVM activity. I recommend we treat each eye with Eylea again today and increase our follow-up interval.

The patient has a stable operculated break in the right eye which we will continue to monitor moving forward as well.

We'll see him again in about 11 or 12 weeks and keep you apprised as to his progress. Since this is longer than we have gone before, especially in his left eye, I asked him to keep a close watch on his vision and contact us right away if there is any worsening prior to his next visit.

Sincerely,

Deepam Rusia, M.D., M.B.A.

PITTSBURGH

Suite 300

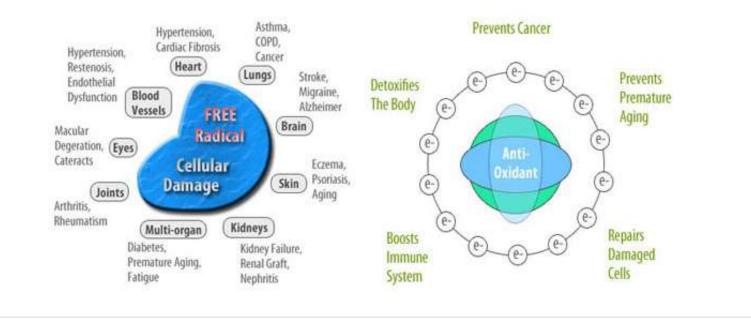
300 Oxford Drive

CC: Julie Lesneski CRNP

Phone: 412-683-5300

2000 Oxford Drive Suite 670 Cloverleat Commons 51 Dutilh Road Suite 200

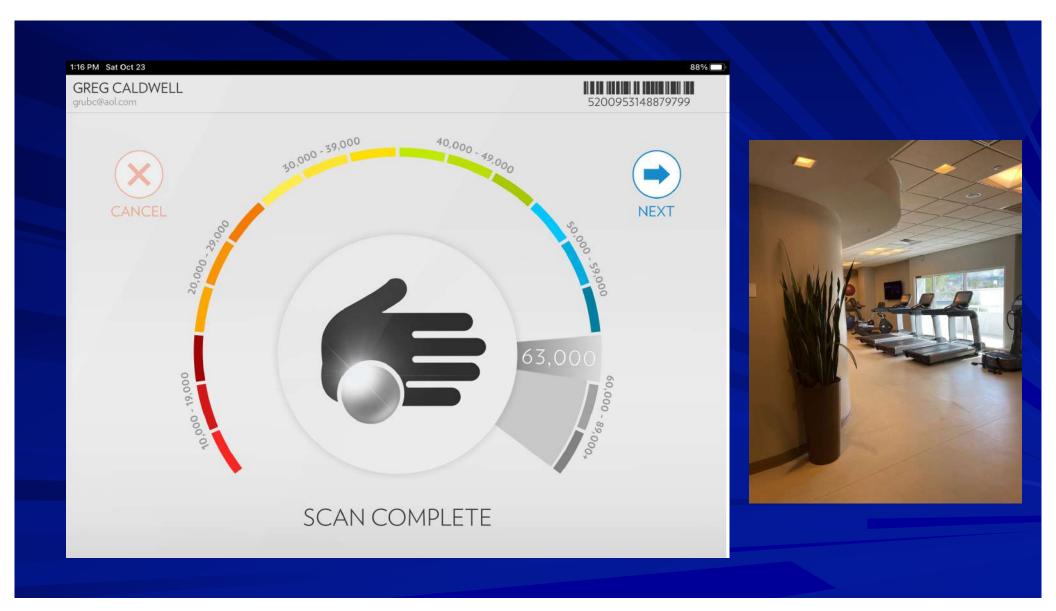
## Screen Everyone



### Carotenoid and Antioxidant Levels in Ocular Disease and Systemic Health

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







### Optometric Education Consultants

Questions? Thank You! Integrative and Functional Medicine

New Opportunities for Optometry

Greg Caldwell, OD, FAAO Tracy Offerdahl, PharmD, Bpharm, RPh, FAAO

> CE Sarasota 2023 Optometric Education Consultants

> > Sunday, March 5, 2023

