

Optometric  
Education  
Consultants

# Integrative and Functional Medicine

New Opportunities for Optometry

Greg Caldwell, OD, FAAO

Sunshine State Summer Conference  
Optometric Education Consultants

Friday, June 16, 2023



# Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

- Lectured for: Alcon, Allergan, Aerie, B&L, BioTissue, Kala, Optovue, RVL, Heru, Santen
  - Received honorarium
- Advisory Board: Allergan, Alcon, Dompe, Eyenovia Tarsus, Visus
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
  - Disclosure: Non-salaried financial affiliation with Pharmanex
- Envolve: PA Medical Director, Credential Committee
- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
- Optometric Education Consultants – Pittsburgh, PA, Sarasota, FL, Muncie, IN, Scottsdale/Phoenix, AZ, Orlando, FL, Mackinac Island, MI, Nashville, TN, and Quebec City, Canada - Owner



# Thank You Dr. Richer

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*In addition to his work with the Board of Medical Education, Dr. Richey is also a member of the Ocular Wellness Committee of the American Academy of Nutrition and Dietetics. He is also a member of the American Academy of Ocular Nutrition and the American Academy of Ocular Health.*



and coordinator of the optometry program, at the Captain James Health Care Facility, North C

**C**orporate Ophthalmology asked Dr. Stuart Richter, OD, PhD, FAAC and executive president of the Ocular Wellness and Nutrition Society, to explain the benefits of stress to eye health, as well as the immune system, as (1) medical and general public look to improve their immune systems during the COVID-19 crisis.

**CO:** How does zinc help the immune system and why is it especially important in the fight against COVID-19?

**Dr. Richiari:** According to the Institute of Functional Medicine (www.ifm.org), zinc has a strong body of clinical trials to support its use with outcomes data that support its mitigating effects on illness on other viral strains with only mild effects on them. These peer-reviewed clinical research findings include reduced severity of symptoms, reduced duration of illness (by 50%) and prevention of lower respiratory infections. Zinc strongly activates both the innate and adaptive immune systems. It does this by increasing RNA polymerase, thereby speeding viral replication or the number of copies while at the same time slowing the thyroid gland for enhanced immunity.

**“Zinc is necessary for growth, DNA synthesis, wound healing, reproductive health and night vision.**

One third of the population is *vitE* deficient. This deficiency increases susceptibility to infection. The function of the thymus gland to produce naive T white blood cells that will become cytotoxic T lymphocytes (CTL) is impaired in *vitE* deficiency (immunopathology) against invading microbes. The thymus gland secretes thymosin  $\alpha$ 1. Depleted thymosin  $\alpha$ 1 levels are associated with aging and immunosenescence, leading to impaired humoral, cellular and humoral responses, including decreased production of lymphocytes, decreased (sterile) inflammation, decreased antibody and weakened immunity to fight off disease via phagocytosis and oxidative killing.

Deficient thymosin  $\alpha$ 1 levels played a role in COVID-19 susceptibility and were common with age, as this hormone is secreted by the thymus gland. Decreased thymosin  $\alpha$ 1 levels suggest the age related decline in thymic function be due in part to *vitE* deficiency. This condition may be partially of the hand connected by zinc supplementation. Only a fraction of dietary or supplemental zinc is absorbed, rising as little as 17% for older men. Zinc absorption declines with advancing age. Zinc deficiency is associated with decreased secretion of thymosin  $\alpha$ 1 which is dependent upon zinc.

**CO:** How much zinc should a person take? How much is too much and are there any negative side effects of zinc consumption that should be aware of?

**Dr. Richetti:** That is a complex question. Zinc deficiency can result from poor absorption from age-related stomach acid decline as mentioned, be exacerbated by chronic and blocker use, from chronic H. Pylori infection, by low selenium or by excess copper from unfiltered tap water in houses with copper plumbing. There are also several zinc-depleting medications besides acid blockers. These include diuretics, ACE inhibitors, vasodilators, oral contraceptives, estrogen replacement and antibiotics.



Unfortunately, the RDA for zinc for people older than 19 years is 11 mg/day per day for men and 8 milligrams/day for women with no special recommendations for pregnancy. Zinc deficiency is rare, but the zinc found in AREDS supplements is the most absorbed. Nonetheless, the AREDS study reported lower rates of blindness in the supplemented group. Zinc glycinates or zinc picolinate are the best forms. Zinc malate is best for fibromyalgia patients. While zinc threonate is best for the brain, zinc methionine (OptiZinc) at 30 mg per day is considered the best form for eyes by several multivitamin manufacturers. Zinc deficiency is rare, but zinc is only about 10 mg of zinc in divided doses.

Excess zinc can cause nausea and vomiting, stomach pain and diarrhea. Flu-like symptoms, lower HDL cholesterol, high-density lipoprotein, or the "good" cholesterol, copper deficiency, loss of taste (hypogeusia), and decreased immune response are also possible. Typically, it is patients who overdo zinc supplements that make much higher doses than that described above. The TEFM recommends 30-60 mg per day in divided doses.

First Name \_\_\_\_\_ Last Name \_\_\_\_\_  
Practice Name \_\_\_\_\_ Retail Brand (s): \_\_\_\_\_  
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# Ocular Disease Career

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





**Mitochondria**  
(cellular powerhouses)

Chromophores on the Mitochondrial Membrane Absorb the 980 nm Infrared Light - Stimulating the Production of ATP and NO

**The Importance of Power Density**

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Photobiomodulation is defined as light being effectively absorbed at a cellular level and stimulating a chemical chain reaction freeing up nitric oxide and producing ATP, the cell's energy source. ATP fuels numerous metabolic processes including rebuilding, repairing and regenerating tissue.

time—line

**Mitochondrial health is key to healthy aging**

- < Trillions of mitochondria in your body produce the energy critical to life
- < The decline of these powerhouses is a hallmark of aging
- < **recharge** repairs and renews your mitochondria to promote healthy aging

90% of our cellular energy (ATP) is generated by our mitochondria >

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Rod Stewart



Cone Stewart



# 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



# Patients Are Expecting

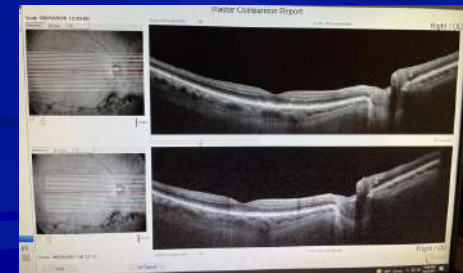
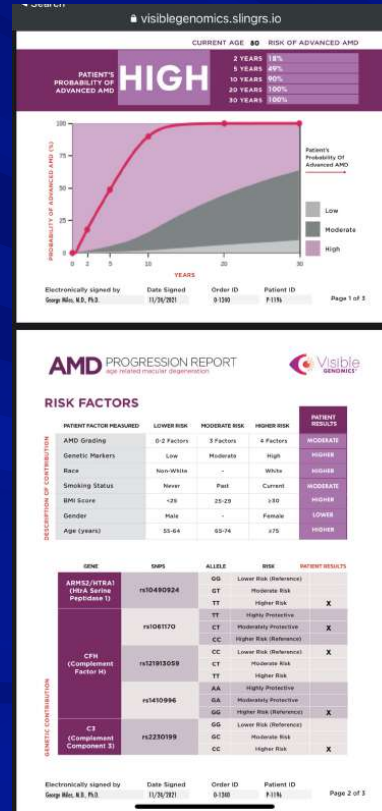
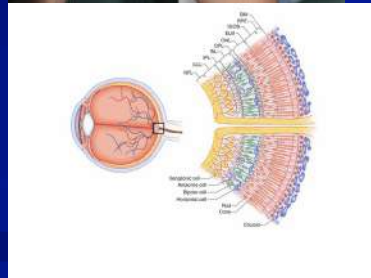
🔗 Early detection

🔗 Wellness

🔗 Prevention

# Early Detection and Allopathic Treatments

## Rabin Cone Contrast Test      ERG and VEP



# Vulnerable to Oxidation

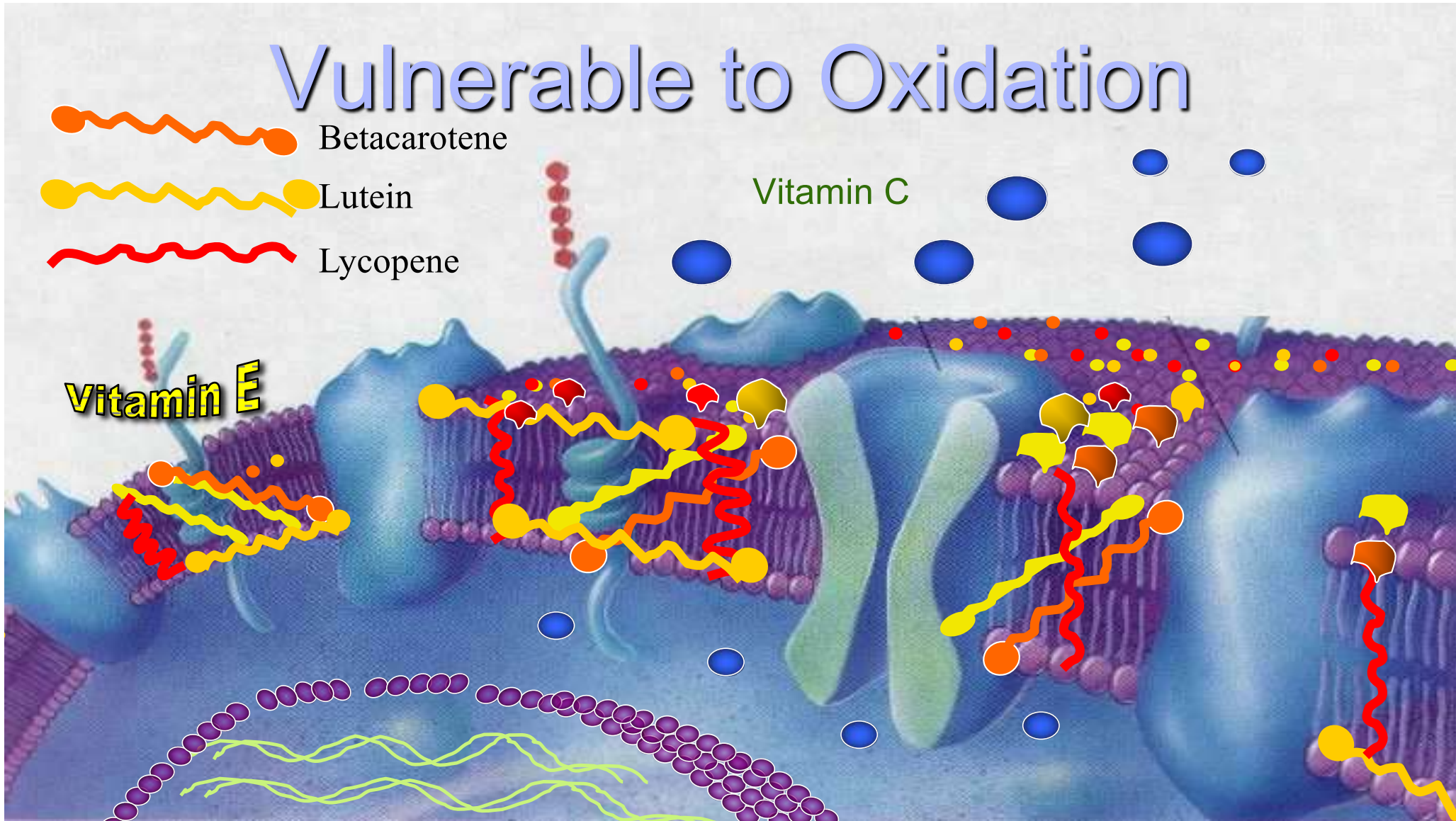
 Betacarotene

 Lutein

 Lycopene

Vitamin C

Vitamin E



# 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?

👁 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”

## 👓 Functional

- ★ Medicine of why, treat the cause

## 👓 Integrative medicine

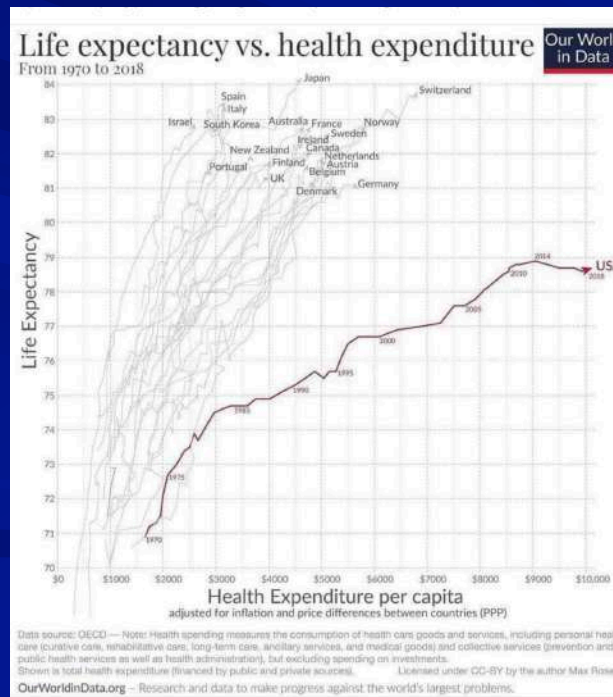
- ★ Complementary medicine - Eastern complimenting Western

### 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.

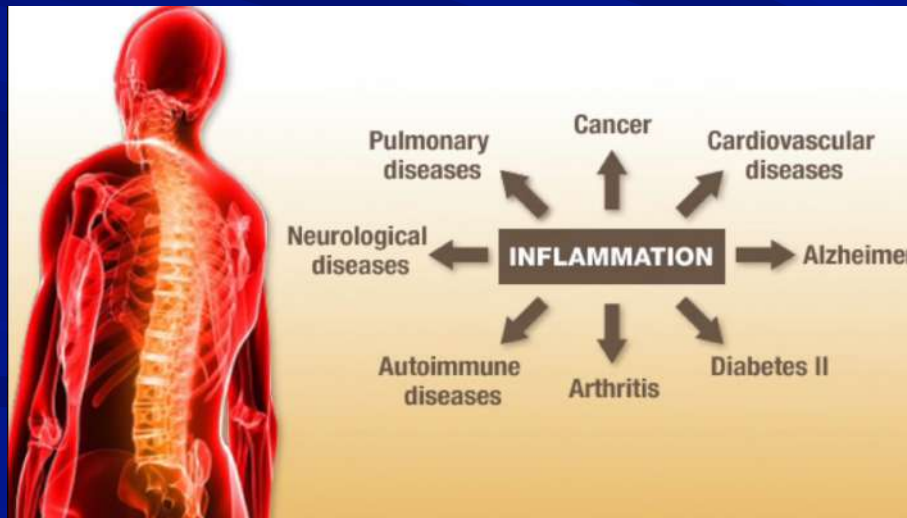
# Chronic and Low-Grade Inflammation

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

- ✍ 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

# 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 – 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?



Annual Review of Nutrition

## Ocular Carotenoid Status in Health and Disease

Lydia Sauer, Binxing Li, and Paul S. Bernstein

Department of Ophthalmology and Visual Sciences, John A. Moran Eye Center, University of Utah, Salt Lake City, Utah 84142, USA; email: lydia.sauer@hsc.utah.edu, Binxing.Li@hsc.utah.edu, paul.bernstein@hsc.utah.edu

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**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 properties 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 ophthalmologists 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.

## 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.

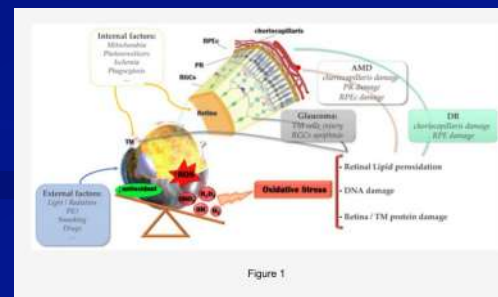
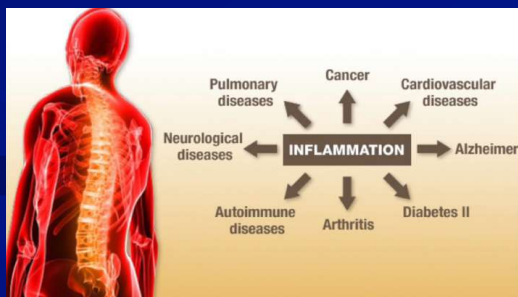
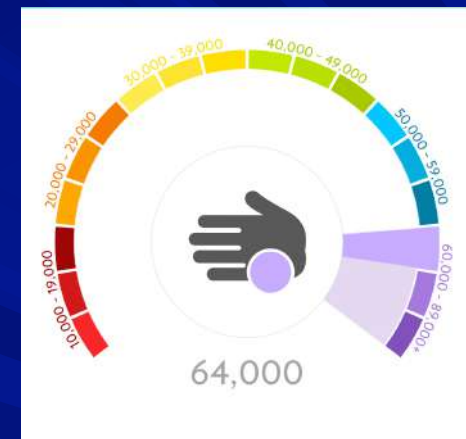
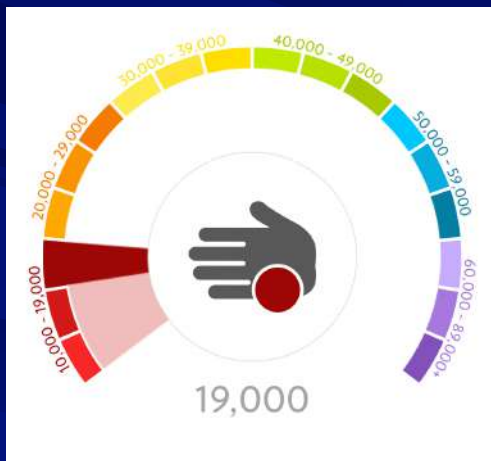
A large variety of methods are used to assess carotenoid status in humans, most of which are focused on the eye, but carotenoids can also be measured in tissue outside of the eye, such as the skin, blood, and the brain. Measurements of ocular carotenoids can be distinguished between subjective (psychophysical) 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

Carotenoids can be assessed noninvasively in the skin 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

(57, 96). Skin RRS and reflectometry are particularly useful to assess the carotenoid status of children, with skin carotenoid levels strongly associated with fruit and vegetable intake (123). 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).

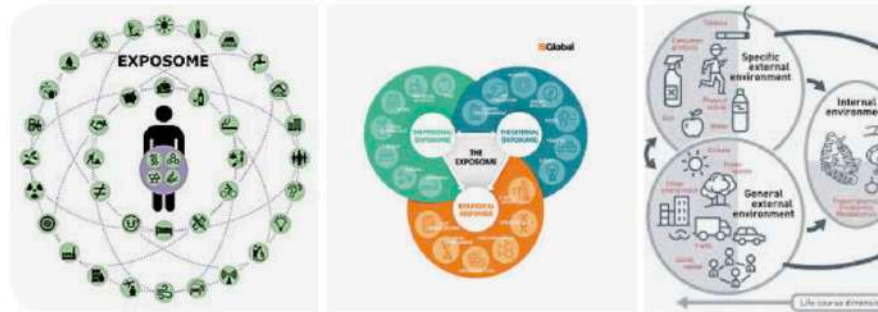
# Chronic and Low-Grade Inflammation



# 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

# 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.

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

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

Google Search Definition

visiblegenomics.slings.io

2 of 3

PATIENT'S RISK OF ED AMD

**LOW**

**CONTRIBUTION TO RISK RESULTS**  
The AMD Lifetime Risk is calculated based upon the patient's genetics, ocular findings, demographic and behavior status. The table below lists the patient's individual factors contributing to their individual risk.

**RISK FACTORS**

PATIENT FACTOR MEASURED	LOWER RISK	MODERATE RISK	HIGHER RISK	PATIENT RESULTS
AMD Grading	0-2 Factors	3 Factors	4 Factors	LOWER
Genetic Markers	Low	Moderate	High	LOWER
Race	Non-White	-	White	HIGHER
Smoking Status	Never	Past	Current	LOWER
BMI Score	<25	25-29	≥30	HIGHER
Gender	Male	-	Female	LOWER
Age (years)	55-64	65-74	≥75	LOWER

Electronically signed by: Date Signed: Order ID: Patient ID: Page 1 of 2

**AMD** LIFETIME RISK REPORT  
age related macular degeneration

**RISK FACTORS**

GENE	SNPS	ALLELE	RISK	PATIENT RESULTS
ARMS2/HTRA1 (HTRA Serine Peptidase 1)	rs10490924	GG	Lower Risk (Reference)	X
		GT	Moderate Risk	
		TT	Higher Risk	
CFH (Complement Factor H)	rs1061170	TT	Highly Protective	X
		CT	Moderately Protective	
		CC	Higher Risk (Reference)	
		rs121913059	CC	
CT	Moderate Risk			
TT	Higher Risk			
rs1410996	AA	Highly Protective	X	
	GA	Moderately Protective		
	GG	Higher Risk (Reference)		
C3 (Complement Component 3)	rs2230199	GG	Lower Risk (Reference)	X
		GC	Moderate Risk	
		CC	Higher Risk	

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CURRENT AGE 80 RISK OF ADVANCED AMD

PATIENT'S PROBABILITY OF ADVANCED AMD

**HIGH**

2 YEARS 18%  
5 YEARS 49%  
10 YEARS 90%  
20 YEARS 100%  
30 YEARS 100%

PROBABILITY OF ADVANCED AMD (%)

YEARS

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**AMD** PROGRESSION REPORT  
age related macular degeneration

**RISK FACTORS**

PATIENT FACTOR MEASURED	LOWER RISK	MODERATE RISK	HIGHER RISK	PATIENT RESULTS
AMD Grading	0-2 Factors	3 Factors	4 Factors	MODERATE
Genetic Markers	Low	Moderate	High	HIGHER
Race	Non-White	-	White	HIGHER
Smoking Status	Never	Past	Current	MODERATE
BMI Score	<25	25-29	≥30	HIGHER
Gender	Male	-	Female	LOWER
Age (years)	55-64	65-74	≥75	HIGHER

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2 of 3

PATIENT'S RISK OF ED AMD

**MODERATE**

**CONTRIBUTION TO RISK RESULTS**  
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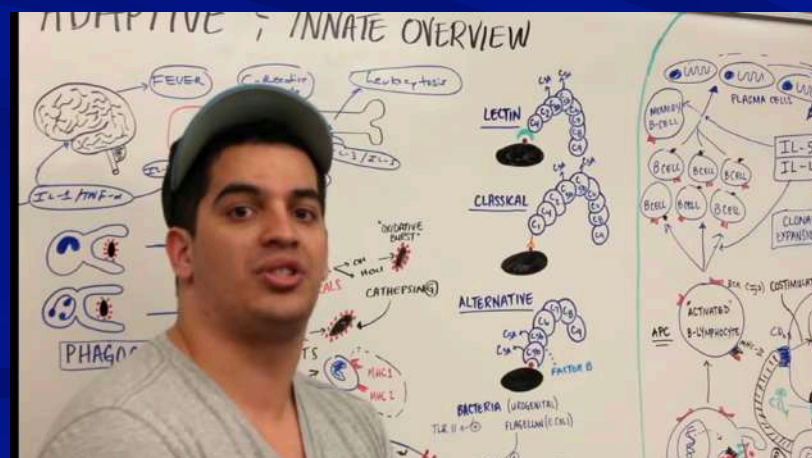
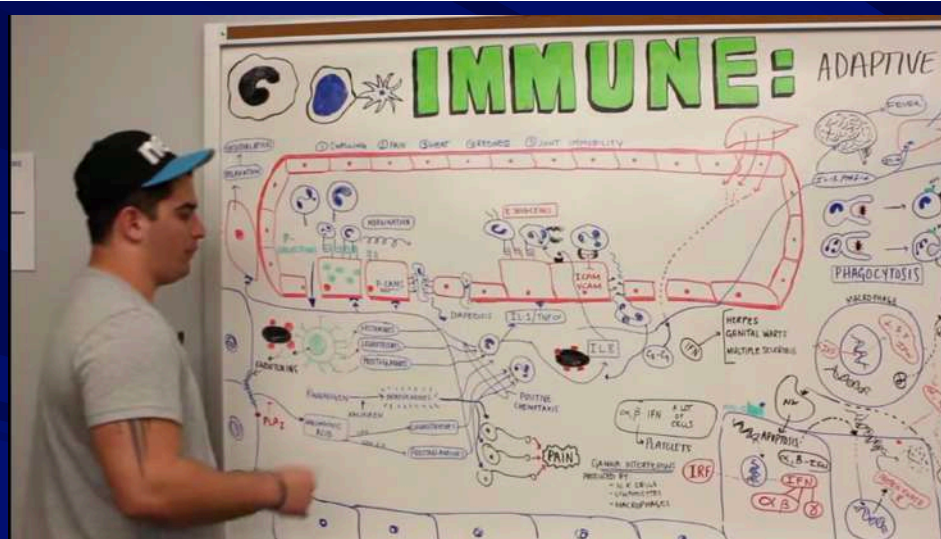
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**AMD** LIFETIME RISK REPORT  
age related macular degeneration

**RISK FACTORS**

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		CC	Higher Risk (Reference)	
		rs121913059	CC	
CT	Moderate Risk			
TT	Higher Risk			
rs1410996	AA	Highly Protective	X	
	GA	Moderately Protective		
	GG	Higher Risk (Reference)		
C3 (Complement Component 3)	rs2230199	GG	Lower Risk (Reference)	X
		GC	Moderate Risk	
		CC	Higher Risk	

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# Complement factor H in AMD: Bridging genetic associations and pathobiology

Christopher B. Toomey <sup>a, b, 1</sup> ... Catherine Bowes Rickman <sup>a, b</sup>  

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<https://doi.org/10.1016/j.preteyeres.2017.09.001>

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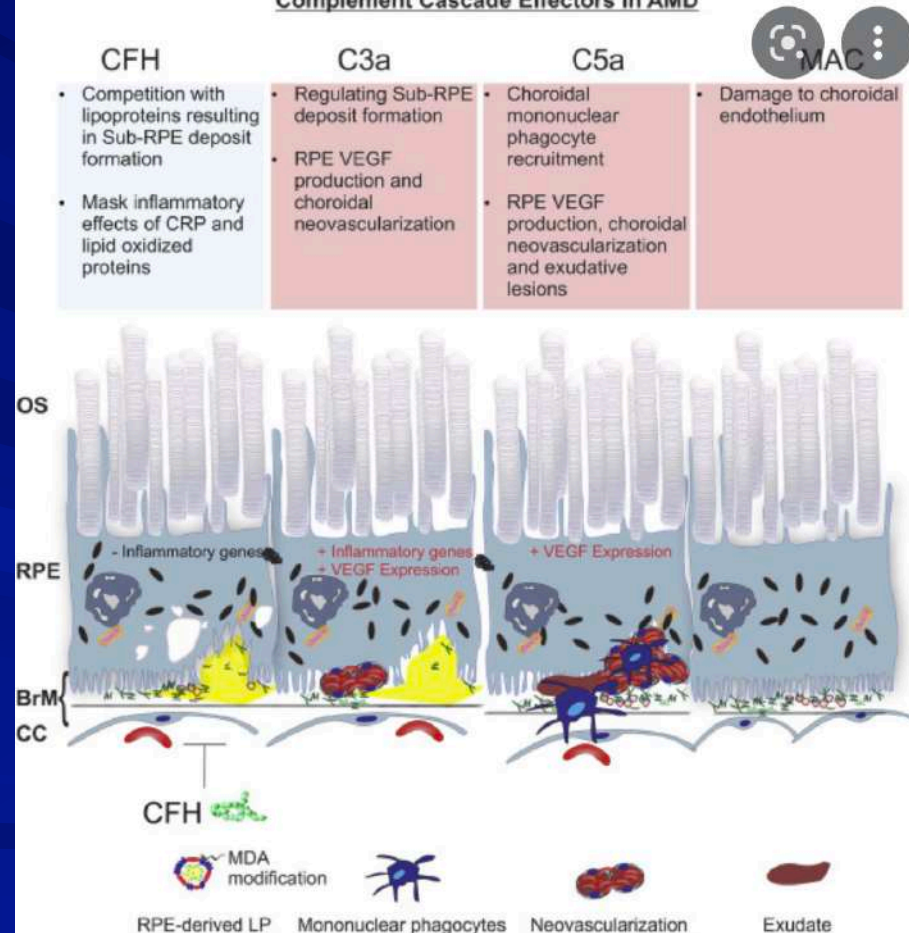
## Abstract

Age-Related Macular Degeneration (AMD) is a complex multifactorial disease characterized in its early stages by lipoprotein accumulations in Bruch's Membrane (BrM), seen on fundoscopic exam as drusen, and in its late forms by neovascularization ("wet") or geographic atrophy 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 Complement Factor H (CFH) and development of AMD. However, the functional significance of the CFH Y402H polymorphism remains elusive. In this

FEEDBACK 

 sciencedirect.com

## Complement Cascade Effectors in AMD



## AREDS/AREDS2 Frequently Asked Questions

### Ingredients

#### Supplement Facts

Serving Size 2 Capsules		Servings per Container 30	
Amount Per Serving			% Daily Value
Vitamin C (Ascorbic Acid)	500 mg		833%
Vitamin E (d-Alpha Tocopheryl Succinate)	200 IU		667%
Zinc (Zinc Gluconate)	25 mg		167%
Copper (Copper Gluconate)	2 mg		100%
Selenium (L-Selenomethionine)	70 mcg		100%
Lutein (from Marigold Flower Extract)	10 mg		*
Zeaxanthin (from Marigold Flower Extract)	2 mg		*

\*Daily Values not established.

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

### 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](#) [↗](#).



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.

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## 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 zinc-containing 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). Seven-year 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.

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RESEARCH ARTICLE | OPEN ACCESS



## CFH and ARMS2 genetic risk determines progression to neovascular age-related macular degeneration after antioxidant and zinc supplementation

Demetrios G. Vavvas, Kent W. Small, Carl C. Awh, and Rafal Kusztal. [Authors Info & Affiliations](#)

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



## 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

Miklos J. Aul, MD,<sup>1,2</sup> Fan Li, MD,<sup>1,2</sup> Ying Wang, PhD,<sup>1,2</sup> Andrew S. Allen, PhD,<sup>1,2</sup> Erik A. Rugeley, PhD,<sup>1,2</sup> Andrew J. Valler, PhD

**Purpose:** Considerable controversy has existed in recent years regarding whether genotyping should be part of standard care for patients with age-related macular degeneration (AMD) who are being considered for treatment with antioxidants and zinc. We aimed to determine whether genotype predicts response to supplements in AMD.

**Design:** Three separate statistical teams reanalyzed data derived from the Age-Related Eye Disease Study (AREDS), receiving data provided by the AREDS investigators and, separately, data from investigators reporting findings that extend the use of genotyping.

**Participants:** The population of interest was AREDS participants with AMD worse than category 1 and genotyping data available. Data from the 2 groups overlap extensively with respect to measurements made; the largest common set involved 879 participants for whom the same CFH and ARMS2 single nucleotide polymorphisms were measured by both groups.

**Methods:** Each team took a separate but complementary approach. One team focused on data concordance between conflicting studies. A second team focused on replicating the key claims of an interaction between genotype and treatment. The third team took a linear model approach in attempting to find baseline predictors of treatment response.

**Main Outcome Measures:** Progression to advanced AMD.

**Results:** The first team aimed to support the initial claim of genotype-treatment interaction. Although we found evidence that high-risk patients had more to gain from treatment, we were unable to replicate any genotype-treatment interactions after adjusting for multiple testing. We tested 3 genotype claims on an independent set of data, with negative results. Even if we assumed that interactions in fact did exist, we did not find evidence to support the claim that supplementation leads to a large increase in the rate of advanced AMD in some genotype subgroups.

**Conclusions:** Patients who meet criteria for supplements to prevent AMD progression should be offered zinc and antioxidants without consideration of genotype. Ophthalmology 2018;125:391-397 © 2017 by the American Academy of Ophthalmology

Supplemental material available at [www.aaojournal.org](http://www.aaojournal.org)

The Age-Related Eye Disease Study (AREDS) was a large, multicenter, double-blind, randomized trial to determine whether high-dose antioxidants, zinc, or their combination could reduce the risk of progression of age-related macular degeneration (AMD) in older patients. Excluding patients in AREDS category 1, for whom the crude rate was less than 1%, the combination of data and antioxidants was found to reduce the rate of progression to

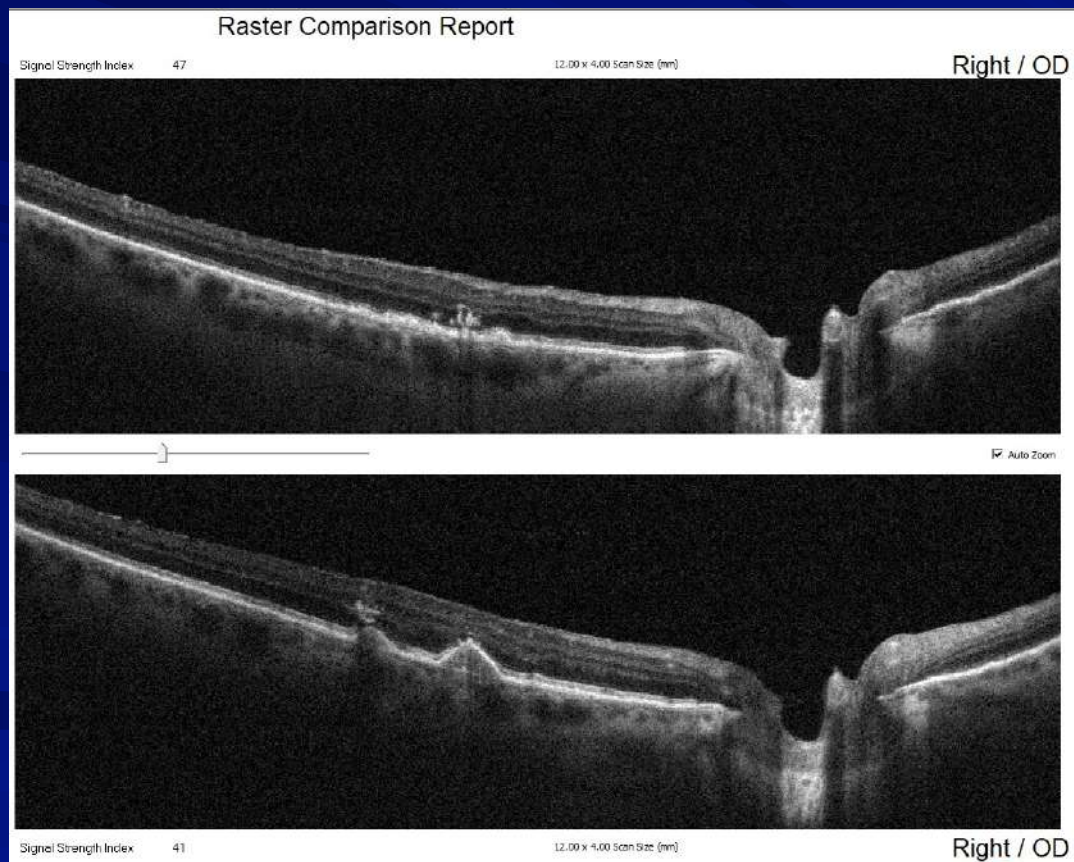
advanced AMD (odds ratio, 0.48; 95% confidence interval [CI], 0.40-0.57; P = 0.002). The publication of the trial results led to rapid changes in practice, with at-risk patients routinely prescribed the zinc and antioxidant combination used in the trial.

In 2010, Klein et al<sup>1</sup> published a pharmacogenetics study regarding the effect of antioxidants and zinc on AMD. In AREDS, may be influenced by genotype,

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ISSN: 0000-6718/18/1250391-07\$36.00/0  
DOI: 10.1016/j.ophtha.2017.09.017

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



Melanie Clemmons, OD  
May 20, 2022 AACO Nashville

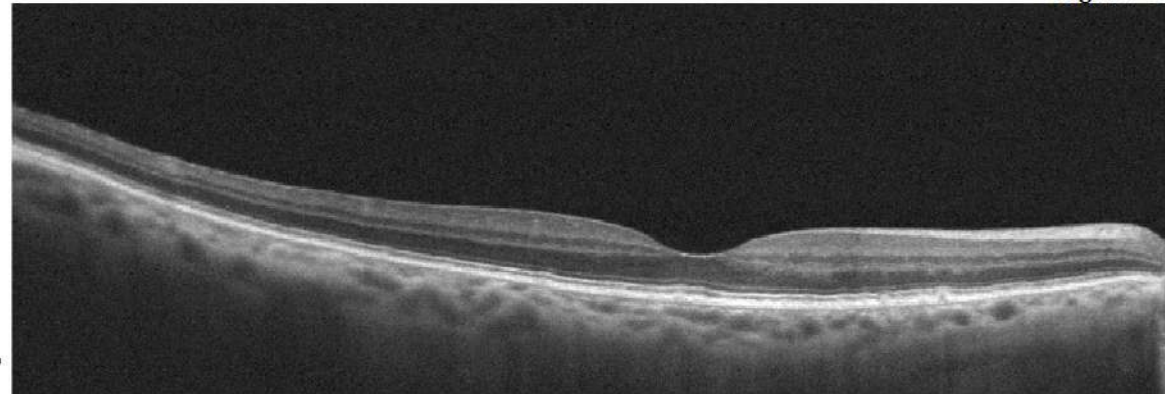
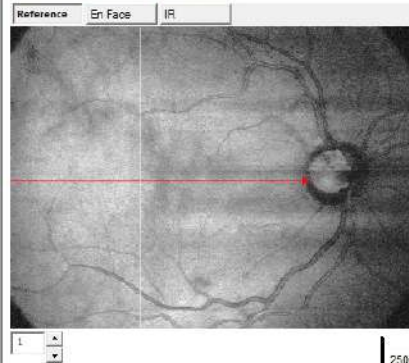
## Cross Line Comparison Report

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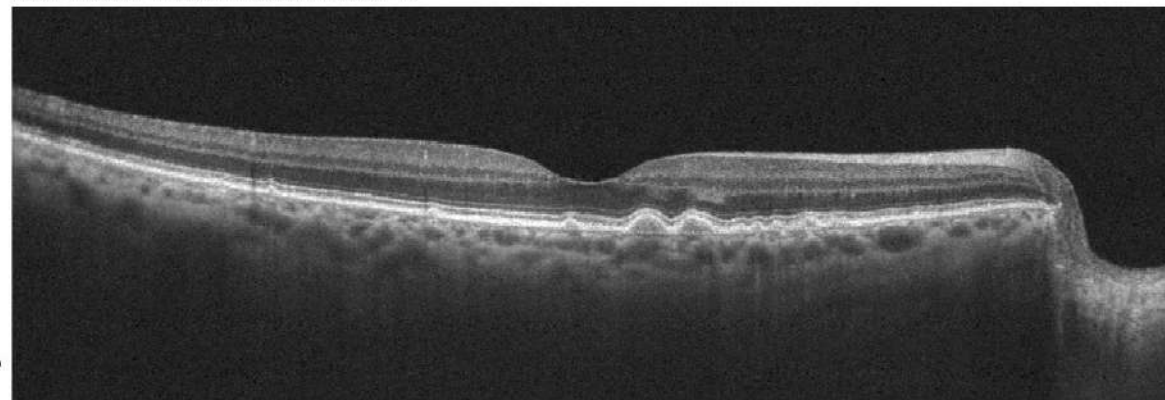
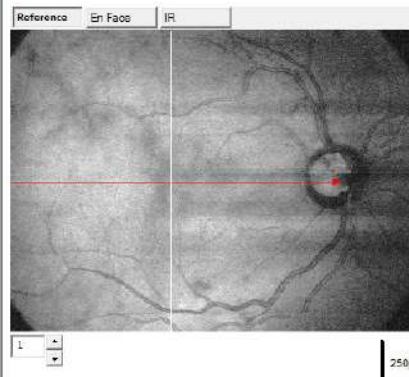
Signal Strength Index 58

10.00 Scan Size (mm)

Right / OD



☒ Auto Zoom



Scan 09/21/2020 10:40:42

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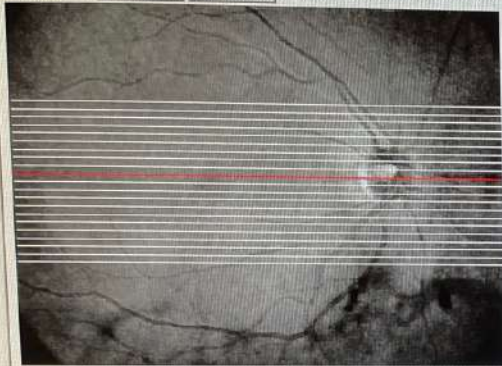
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OU Report

# Raster Comparison Report

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Reference En Face IR



10

250µm

Reference En Face IR



10

250µm

Scan 06/23/2021 10:22:11

Print

OU Report

Signal Strength Index 55

12.00 x 4.00 Scan Size (mm)

Right / OD



Auto Zoom



Signal Strength Index 43

12.00 x 4.00 Scan Size (mm)

Right / OD

CRTVue

49°F Sunny 10:46 AM 6/23/2021

## Ingredients

Ingredients	Amount	% Daily Value
<b>Serving Size: 1 Packet</b>		
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%
Iodine (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 <i>Camellia sinensis</i> 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 <i>Polygonum cuspidatum</i> root extract)	(2.5 mg)	*
Mixed Tocopherols (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, Croscarmellose 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



Oxidative Stress / Inflammation



Hormonal Balance



Stress Hormones



Glucose / Insulin Regulation



GUT integrity and microbiome diversity



Immune Balance



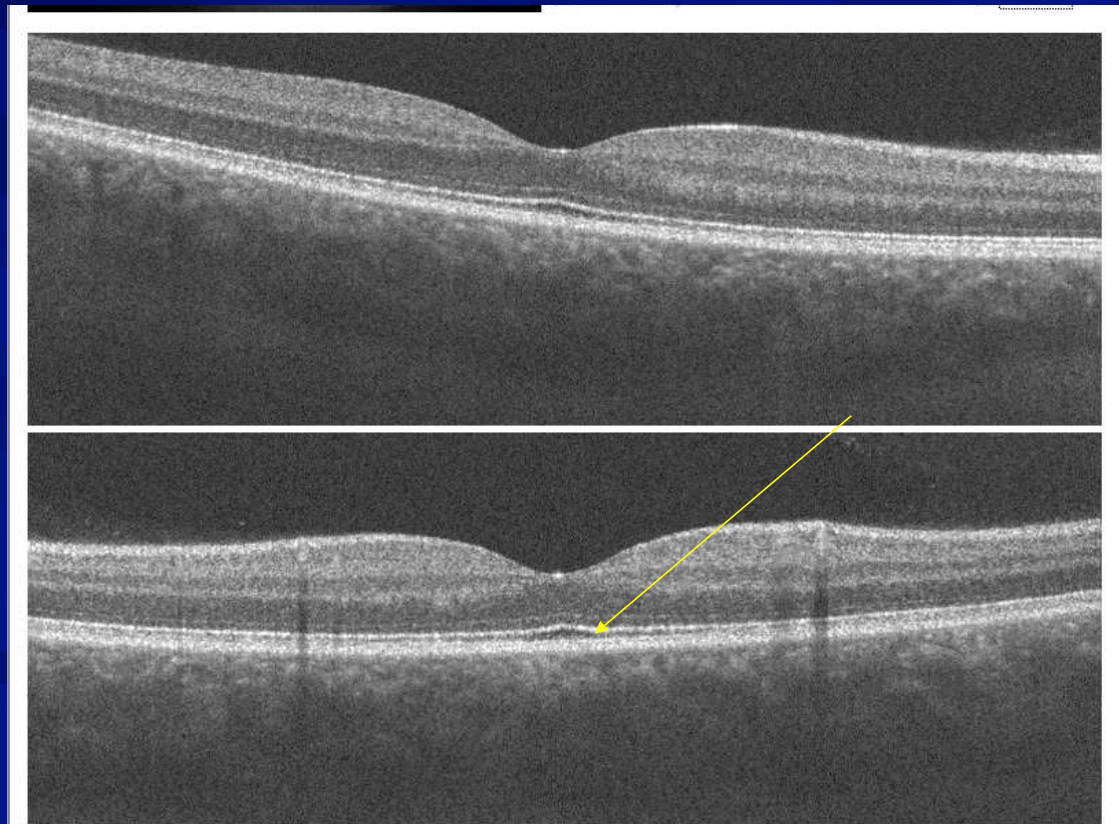
Environmental Exposure/Burden



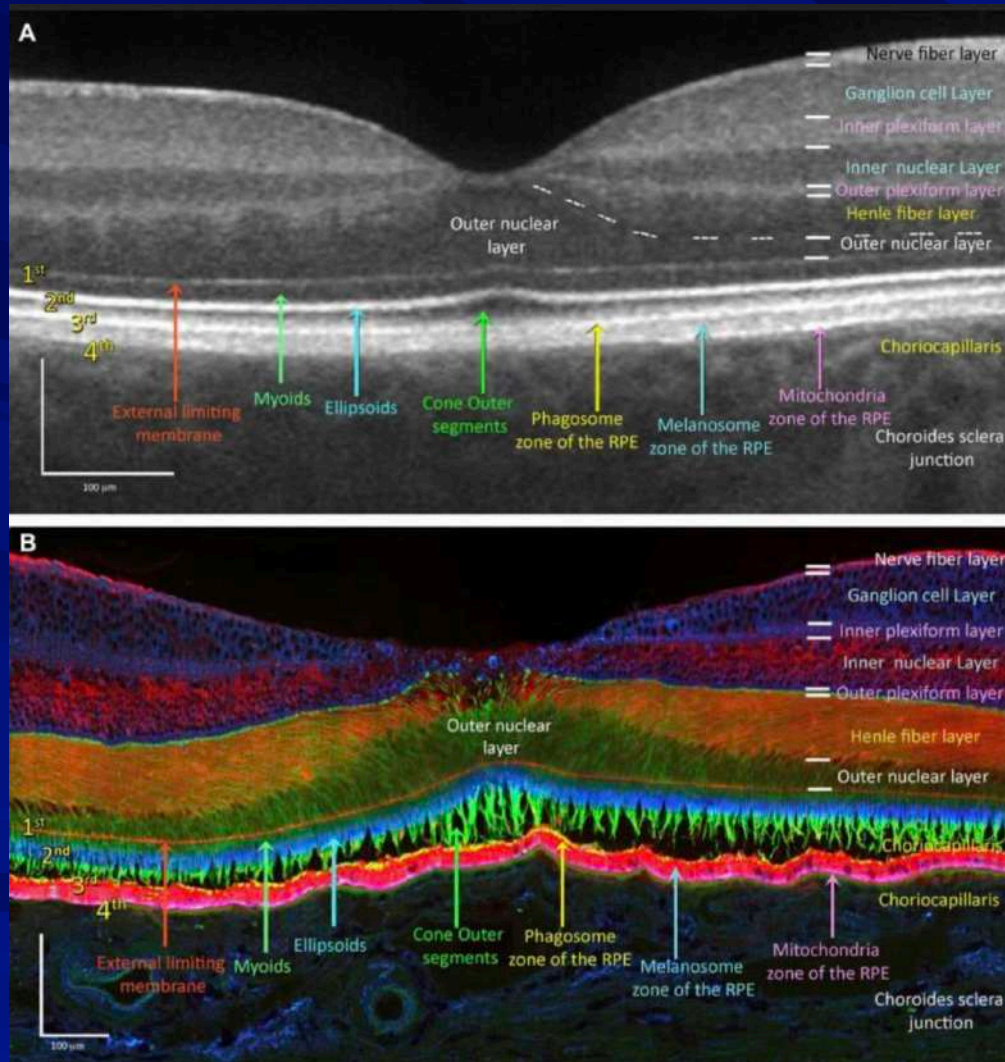
Individuality

Credit to: James LaValle, RPh, CCN

# What is this layer called?







Progress in Retinal and Eye Research

Volume 77, July 2020, 100828

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

Nicolás Cuenca <sup>a, b, 1</sup> ... Isabel Pinilla <sup>f, 1</sup>

Show more

Outline | Share | Cite

<https://doi.org/10.1016/j.preteyeres.2019.100828>

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### Abstract

Optical coherence tomography (OCT) and OCT angiography (OCTA) have been a techn

FEEDBACK

# 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
- 👁 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**



## Inflamm-aging

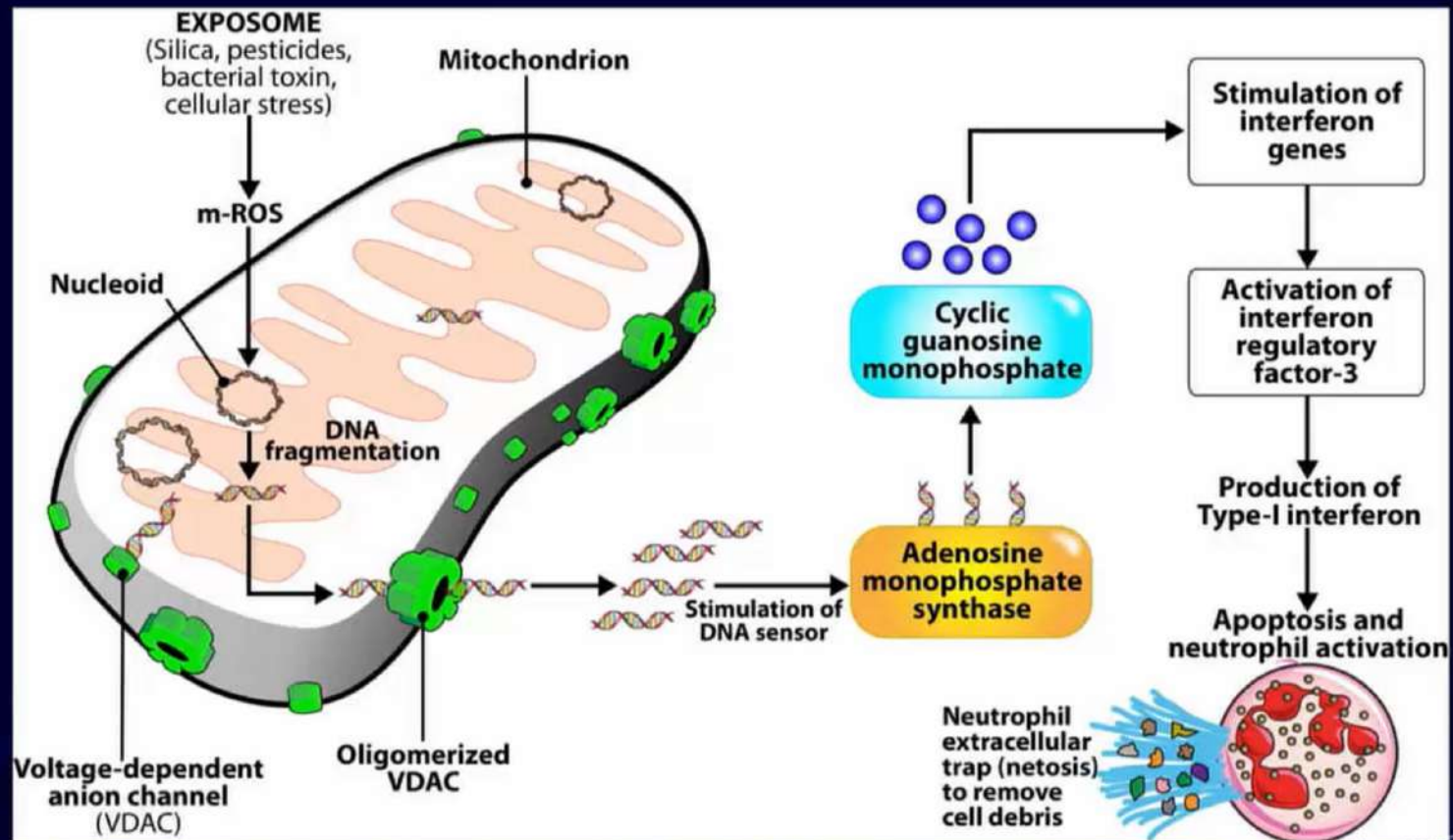
One of the consequences of failing mitochondria due to aging, beyond mtROS, is the release of mtDNA. Plasma levels of mtDNA increase gradually after the fifth decade of life, correlating with elevated levels of pro-inflammatory cytokines (i.e., TNF- $\alpha$ , IL-6, RANTES, and IL-1ra)

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.



**Credit to: Elroy Vojdani, MD -**

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



Mitochondrial exposure to exposomes or endogenous stress by fragmentation of DNA and its release into the cytosol induce inflammation and Autoimmunity. Modified from Crow MK, *Science*, 2019, 366(6472): 1445-1446

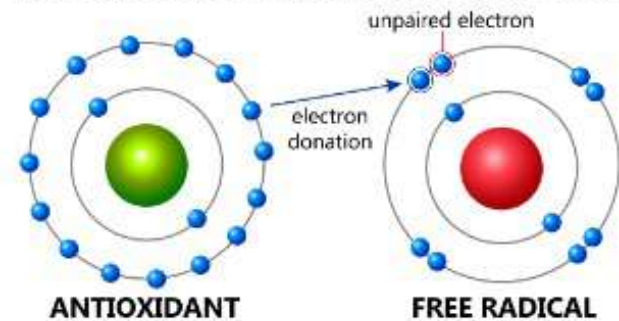
Credit to: Elroy Vojdani, MD -

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

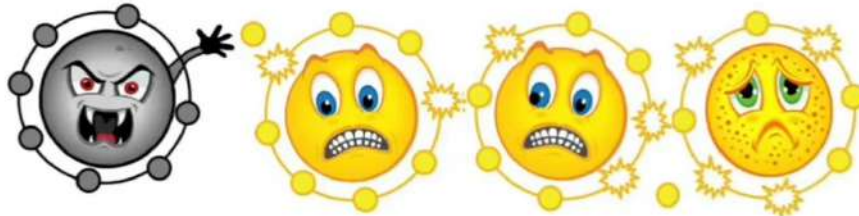
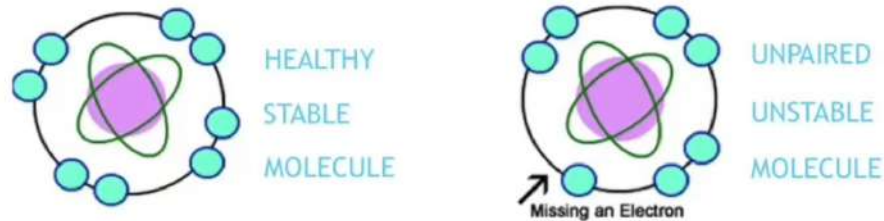
# Free Radicals and Antioxidants



## How antioxidants reduce free radicals

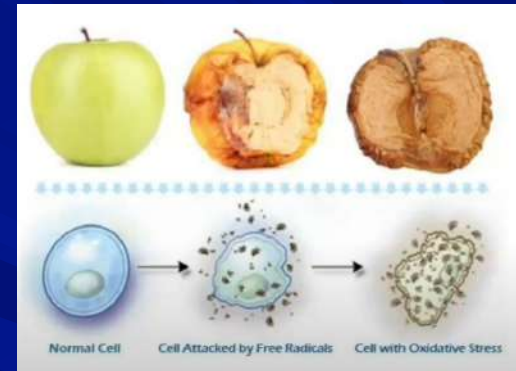


chemically reactive unpaired electron + electron donation:  
stable electron pair is formed, free radical is neutralised



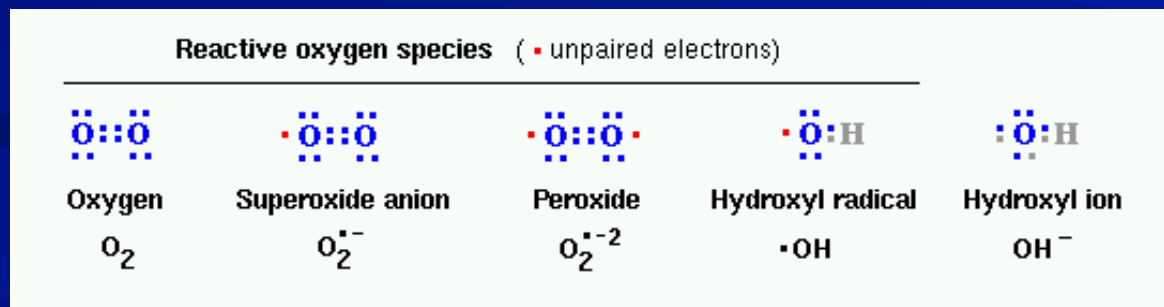
# Oxidative Stress

- 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

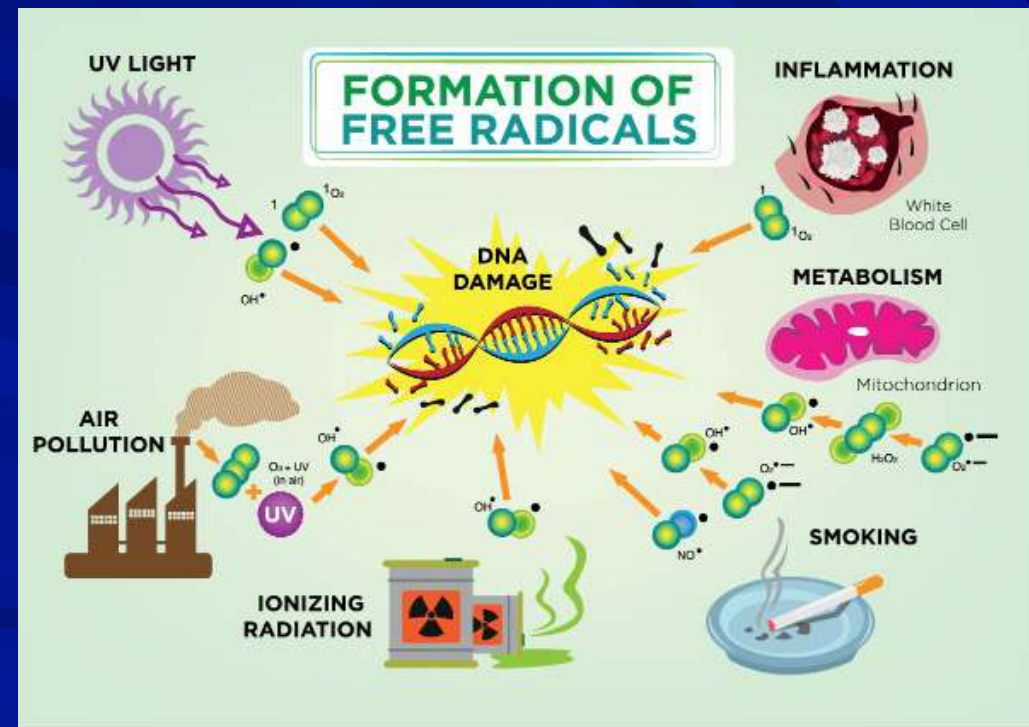
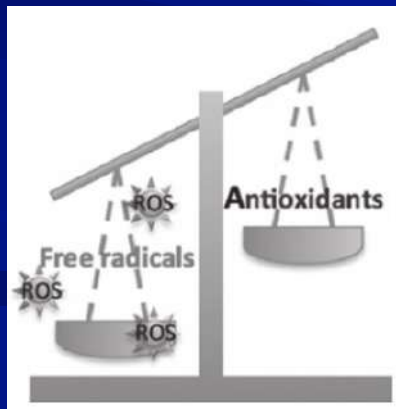
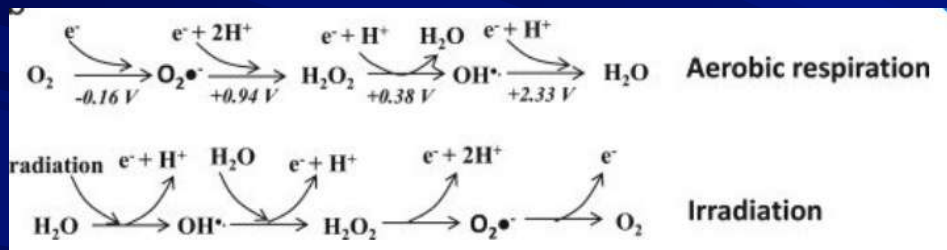


# Free Radicals

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



# Endogenous and Exogenous Free Radial Formation



# 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.

# The Equalizer



# October 23, 2021



# Nutritional Antioxidants

## Exogenous antioxidants

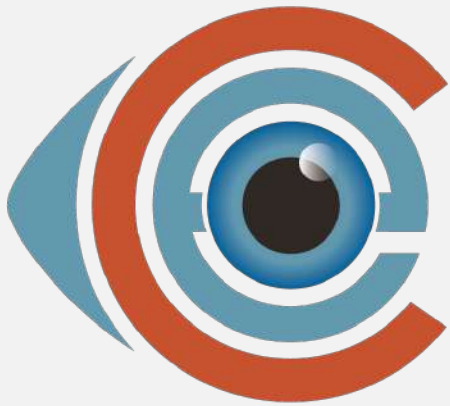
- ★ Tocopherols (E), ascorbic acid (C), carotenoids, ubiquinone, and polyphenols

## Well know antioxidants

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

## 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

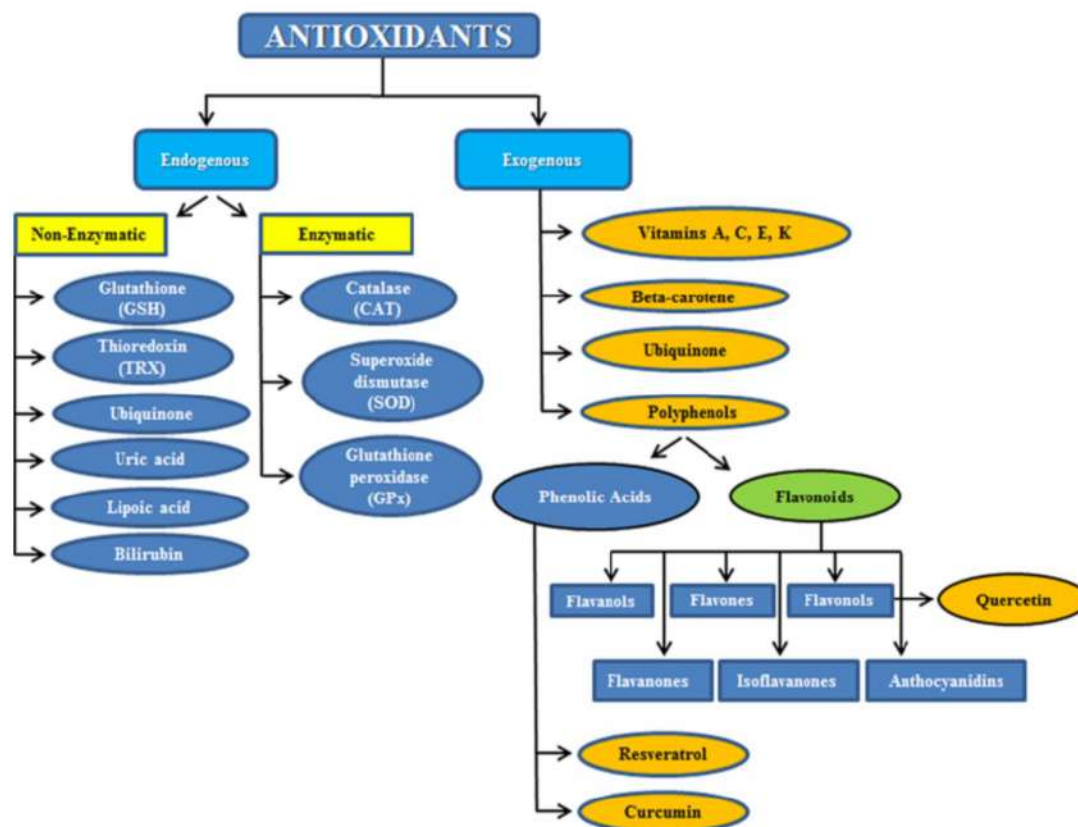


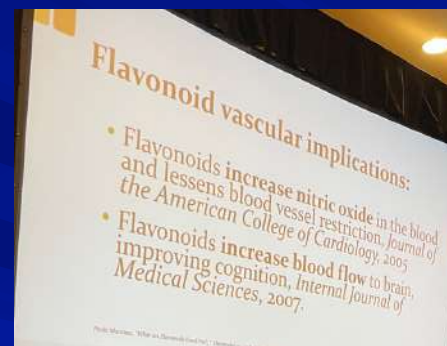
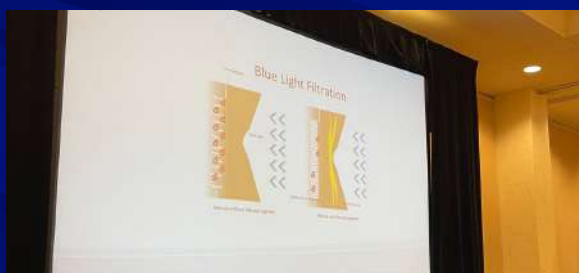
Figure 1: Subdivision between endogenous and exogenous antioxidants.

# 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

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

# Measure?



Annual Review of Nutrition

## Ocular Carotenoid Status in Health and Disease

Lydia Sauer, Binxing Li, and Paul S. Bernstein

Department of Ophthalmology and Visual Sciences, John A. Moran Eye Center, University of Utah, Salt Lake City, Utah 84143, USA; email: lydia.sauer@hsc.utah.edu, Binxing.Li@hsc.utah.edu, paul.bernstein@hsc.utah.edu

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95

Ann. Rev. Nutr. 2019.39:95-120. Downloaded from www.annualreviews.org. Access provided by Dartmouth College - Main Library on 01/12/21. For personal use only.

## 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 skin, blood, and the brain. 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

Carotenoids can be assessed noninvasively in the skin 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 Carotenoid Status in Health and Disease 103

(57, 96). Skin RRS and reflectometry are particularly useful to assess the carotenoid status of children, with skin carotenoid levels strongly associated with fruit and vegetable intake (123). 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).

## Significance of Carotenoids

**High blood levels of the carotenoid alpha-carotene may reduce the risk of dying from cardiovascular disease (CVD), cancer, and all other causes by up to 39 percent.** Results from a 14 year study.

Source: Archives of Internal Medicine  
Published online ahead of print, doi: 10.1001/archinte  
"Serum a-Carotene Concentrations and Risk of Death  
Examination Survey Follow-up Study"  
Authors: C. Li, E.S. Ford, G. Zhao, L.S. Balluz, W.L.

elderly: results of

**AREDS 2: Higher dietary intake of lutein/zeaxanthin was independently associated with decreased risk of having neovascular AMD, geographic atrophy, and large or extensive AMD.**

Arch Ophthalmol. 2008

**Low levels of carotenoids may increase risk of persistent HPV infection**

**Total plasma carotenoids and risk of coronary heart disease: a prospective study**  
British Journal of Nutrition

**Plasma carotenoid levels and cognitive performance in an elderly population: results of the EVA Study.**

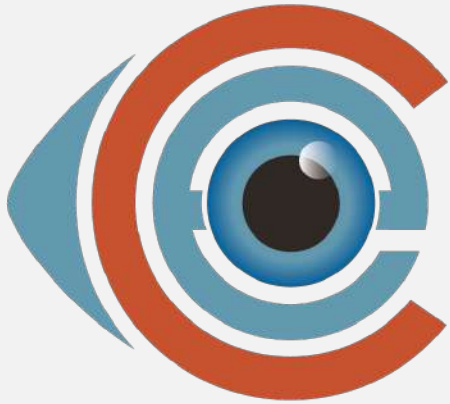
Akbaraly NT<sup>1</sup>, Faure H, Gourlet V, Favier A, Berr C.  
J Gerontol A Biol Sci Med Sci. 2007 Mar;62(3):308-16.

**Epidemiology study**  
Am J Clin Nutr

Search term

**Oxidative stress in rheumatoid arthritis patients: relationship with carotenoid intake and antioxidant activity.**

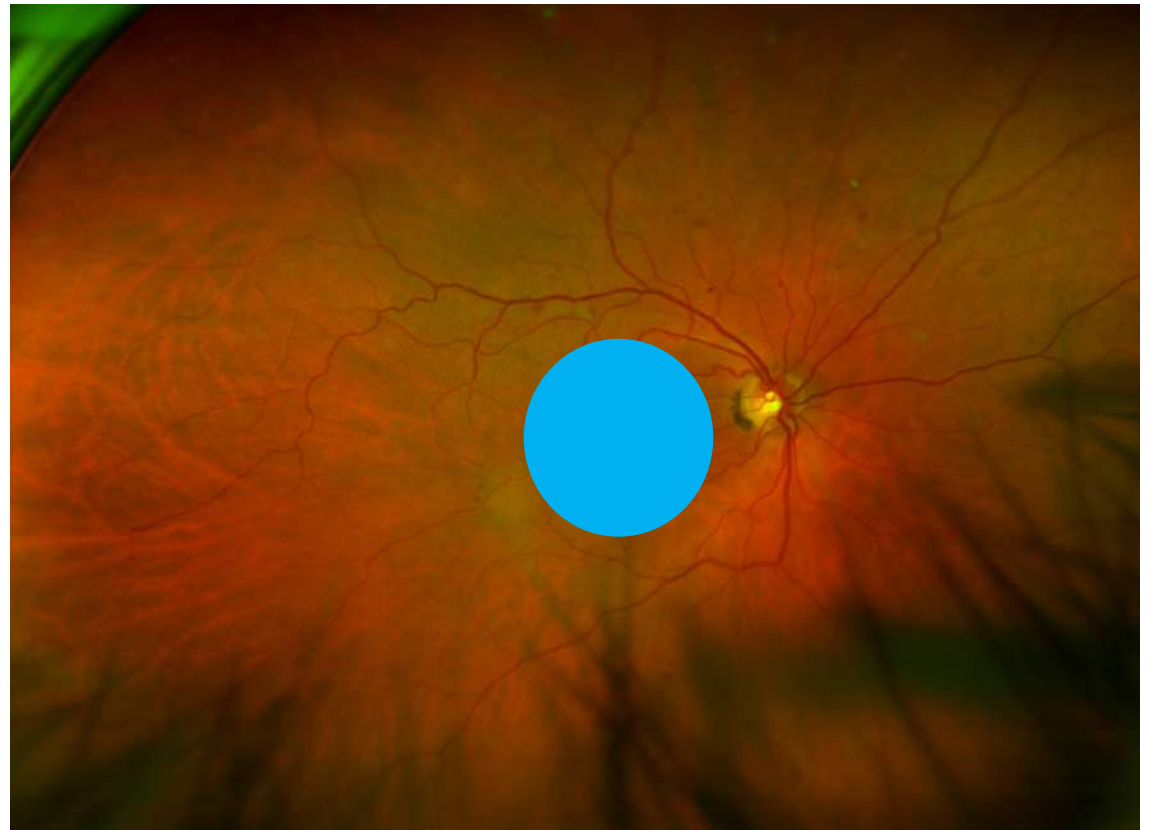
Veselinovic M, et al. [Show all](#)  
Mol Cell Biochem. 2014 Jun;391(1-2):225-32. doi: 10.1007/s11010-014-2006-6. Epub 2014 Mar 9.



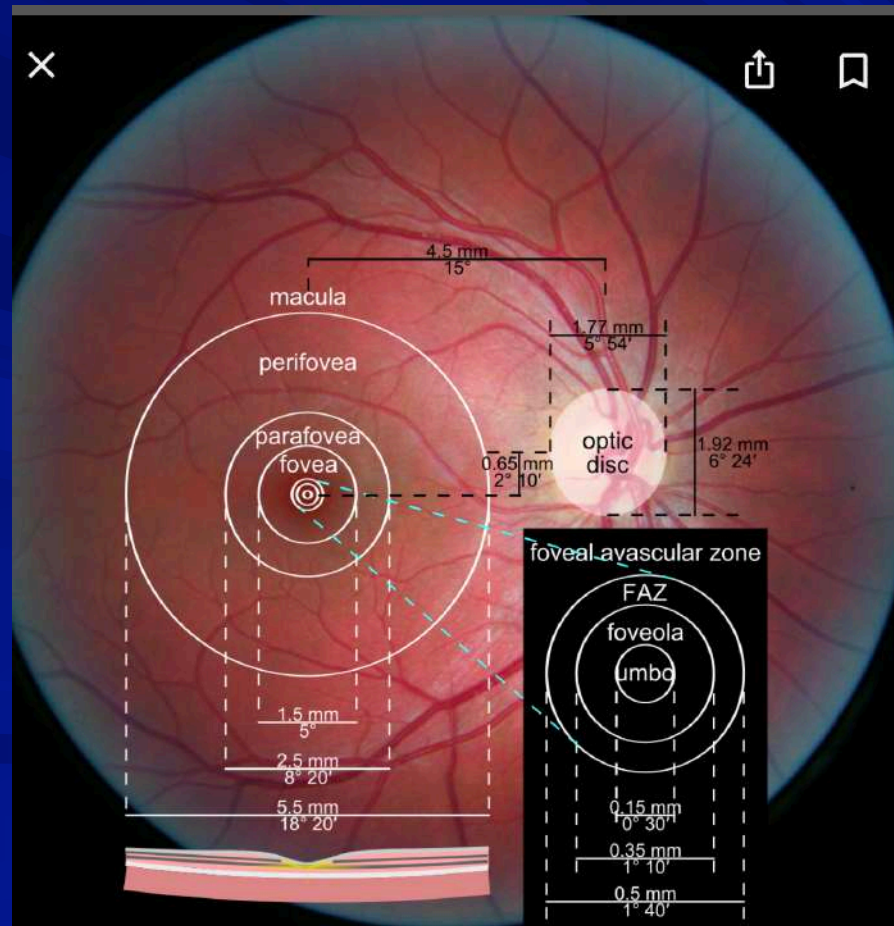
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Education  
Consultants

Where is the macula?

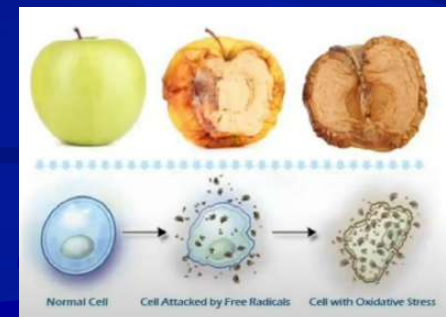
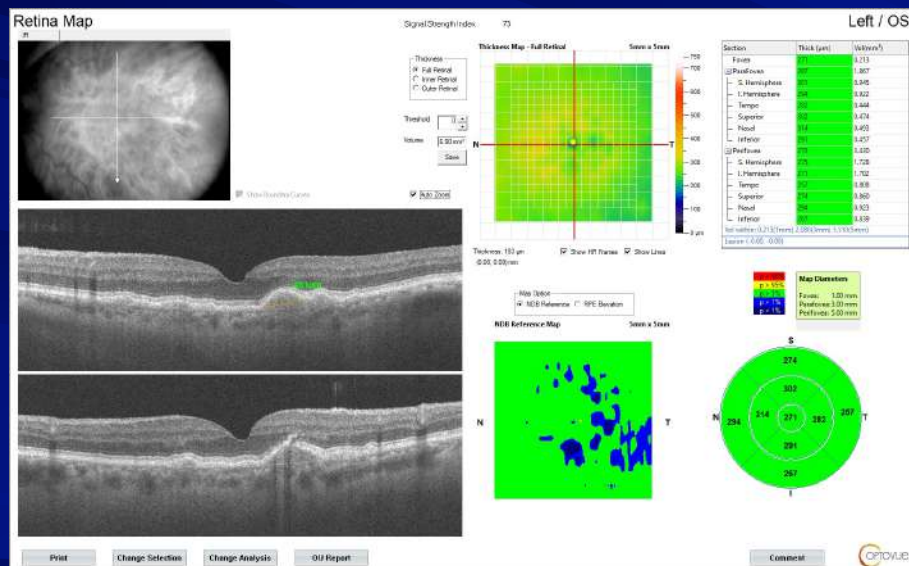
- A. Blue
- B. Orange



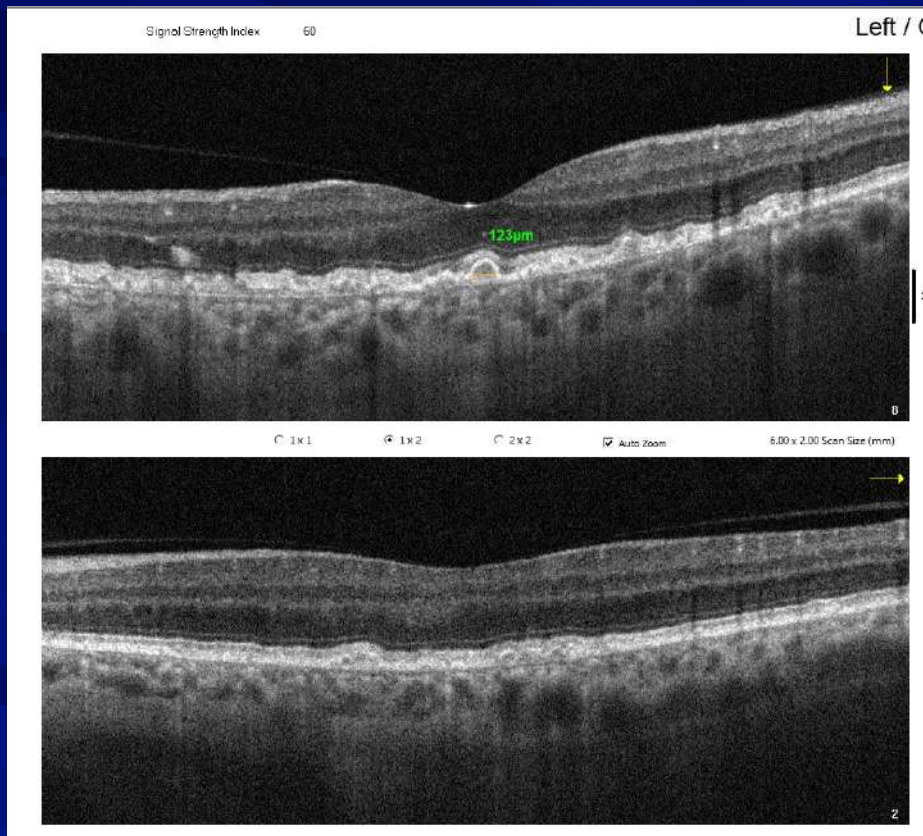
# How large is the macula?



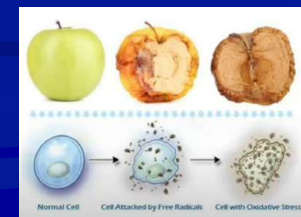
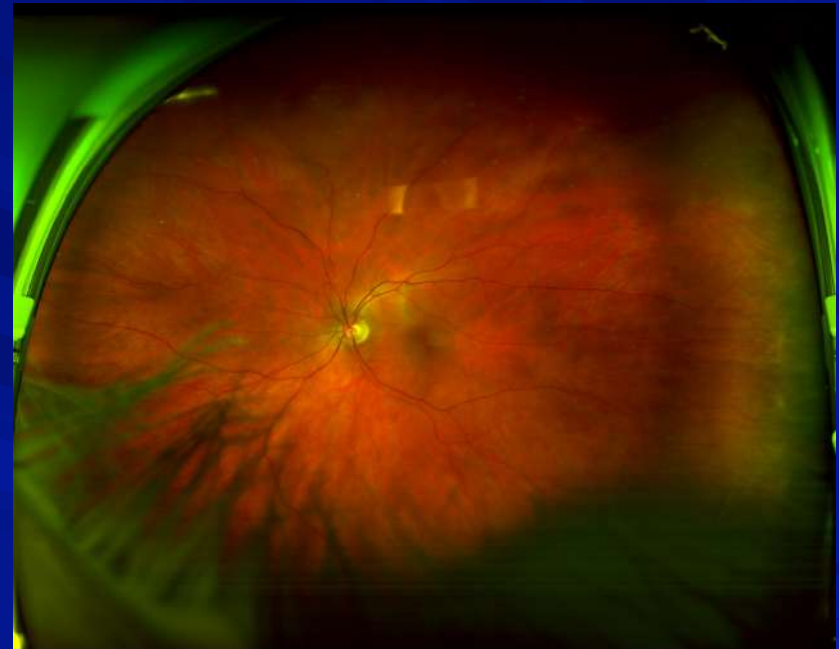
# Oxidative Stress with Your OCT



# Oxidative Stress with Your OCT

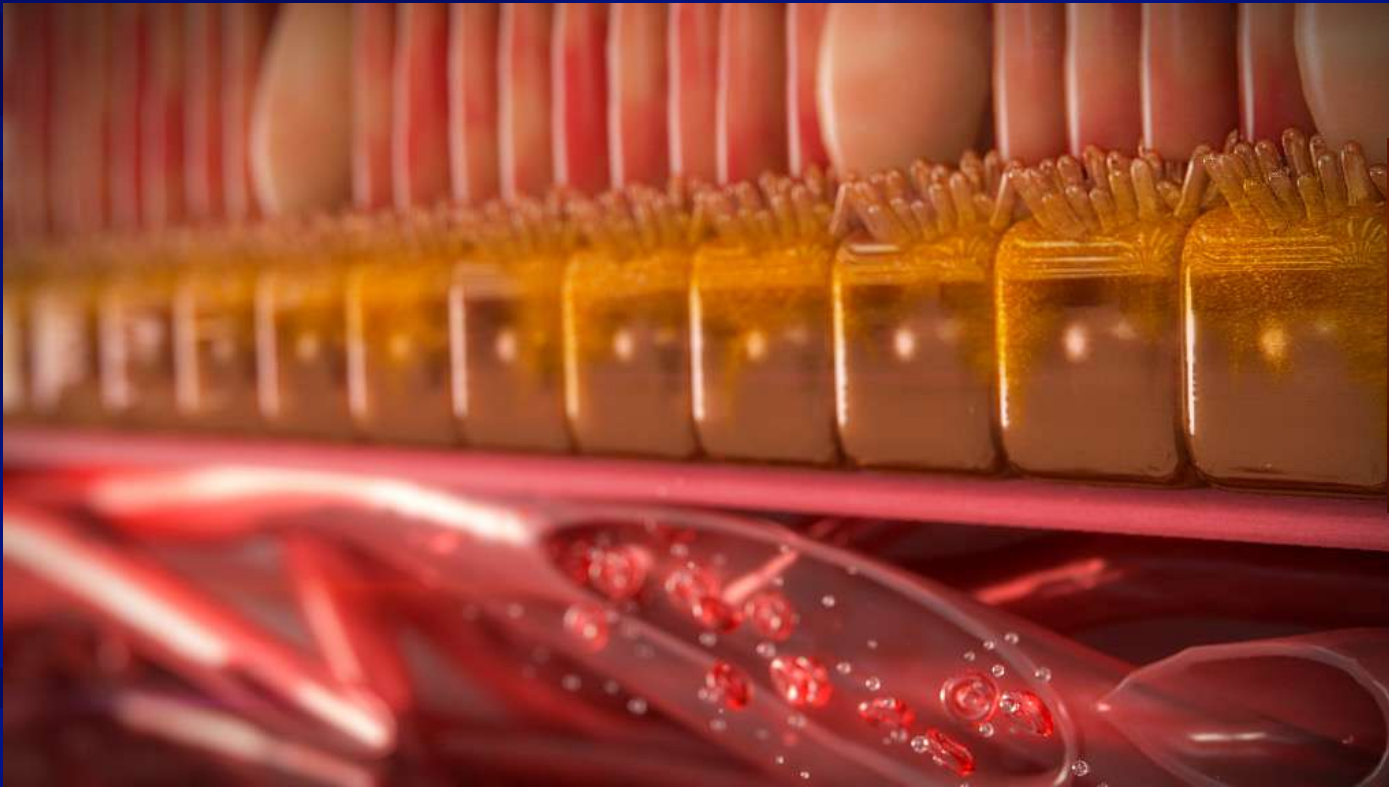


# Oxidative Stress with Your OCT



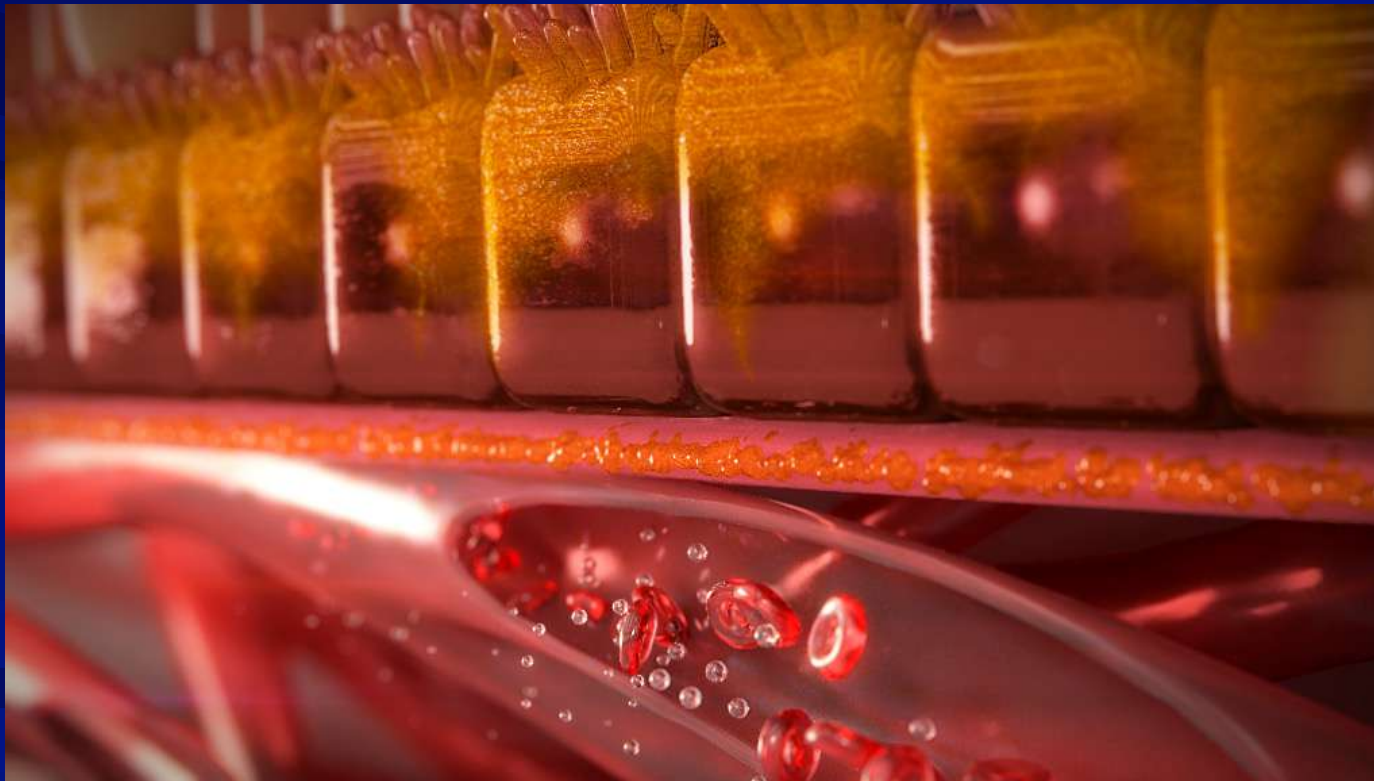
# Healthy choriocapillaris, Bruch's, RPE, and Photoreceptors

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# Cholesterol barrier deposited along Bruch's and RPE

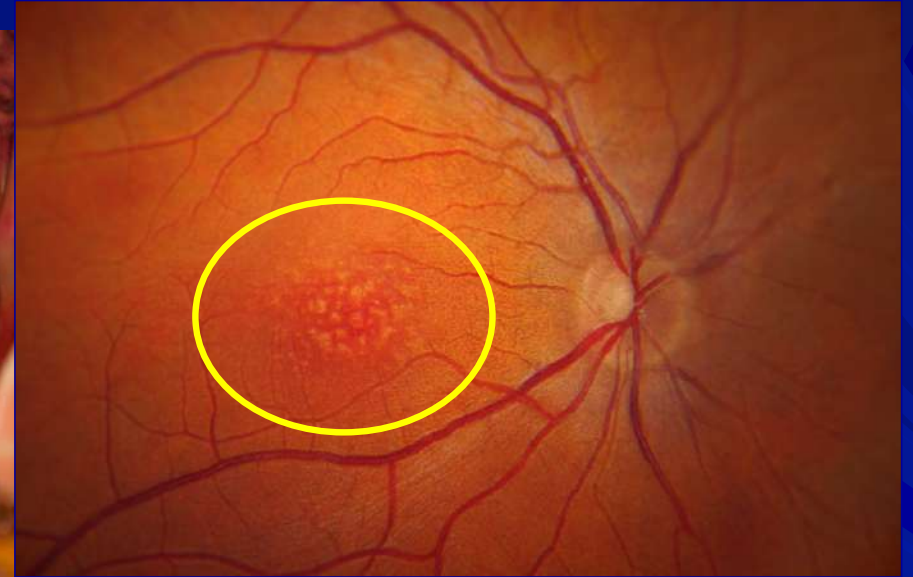
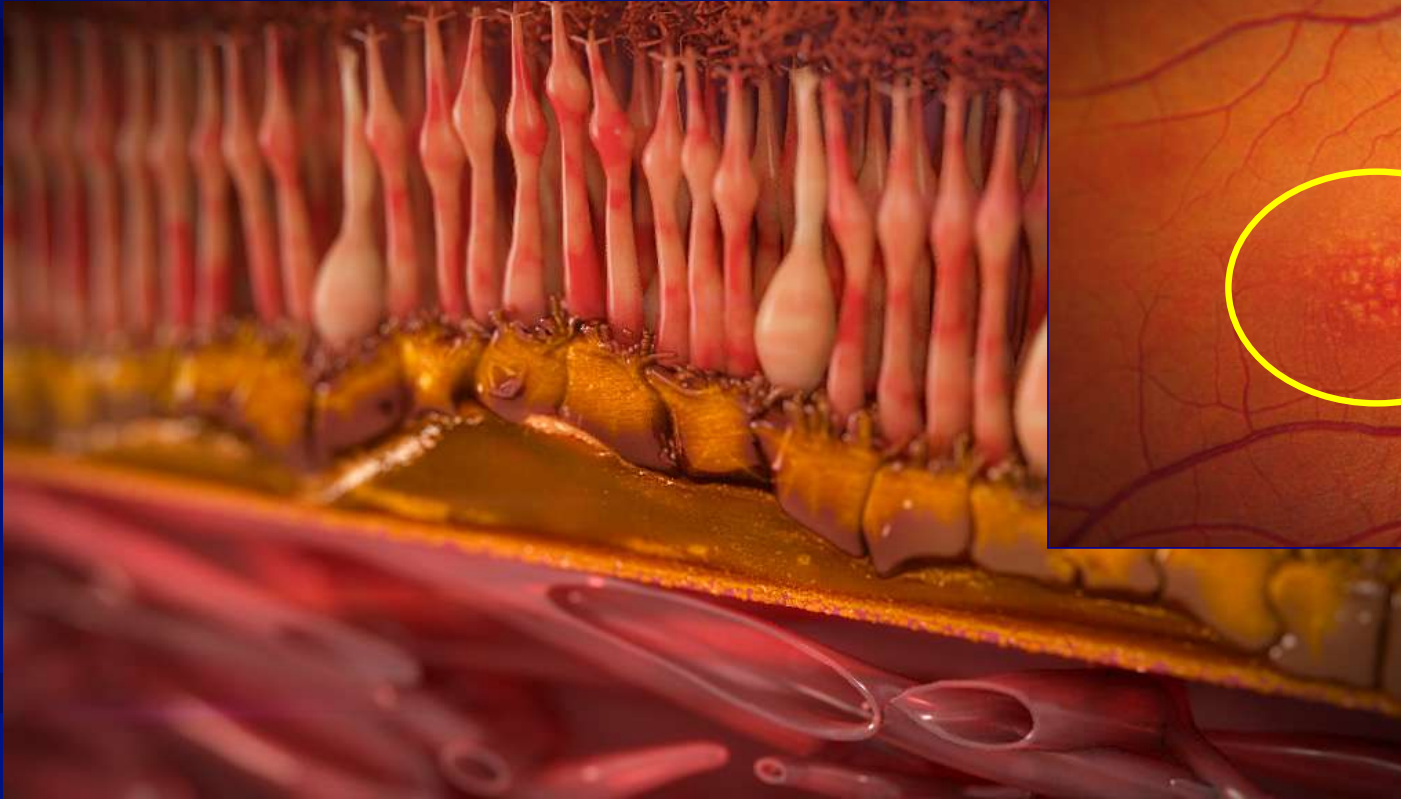
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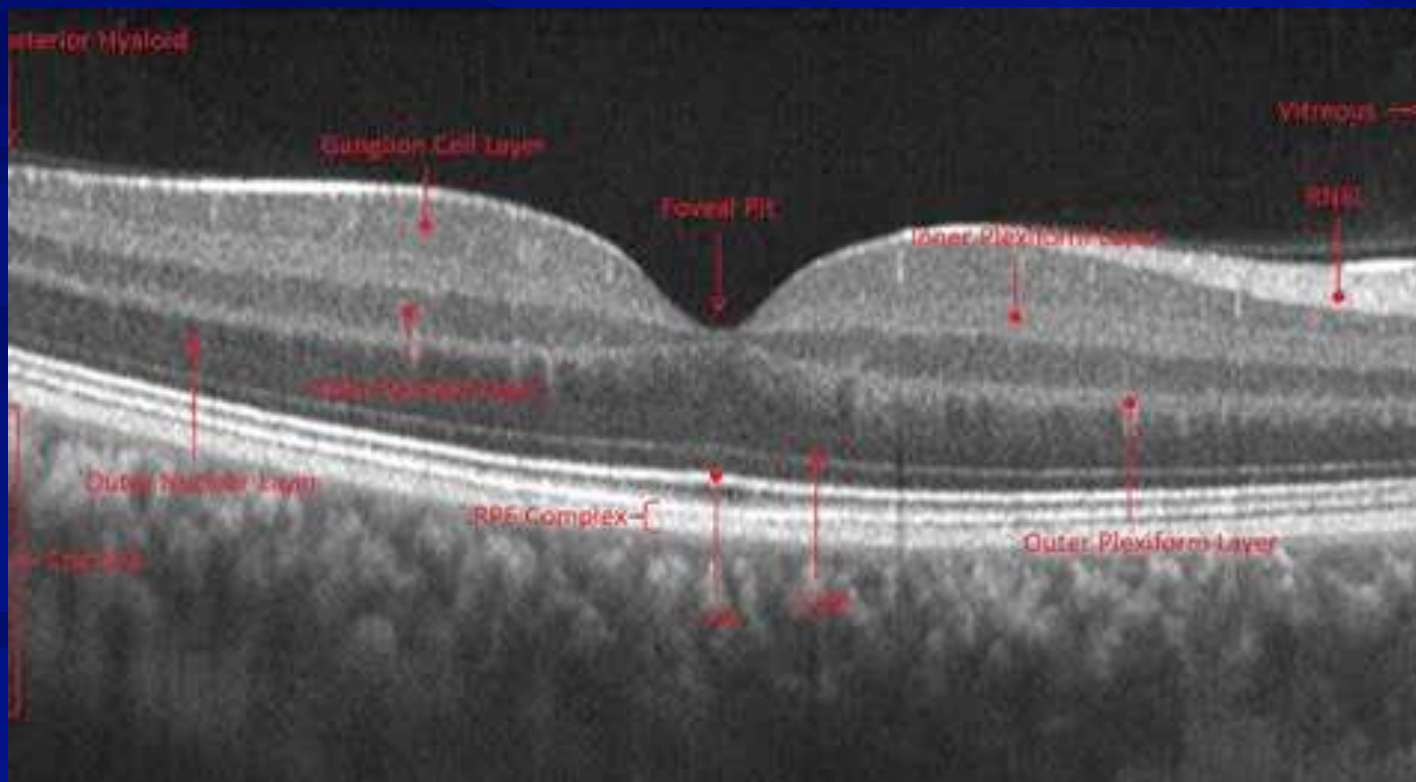
# RPE Secretes even more cholesterol and degenerates

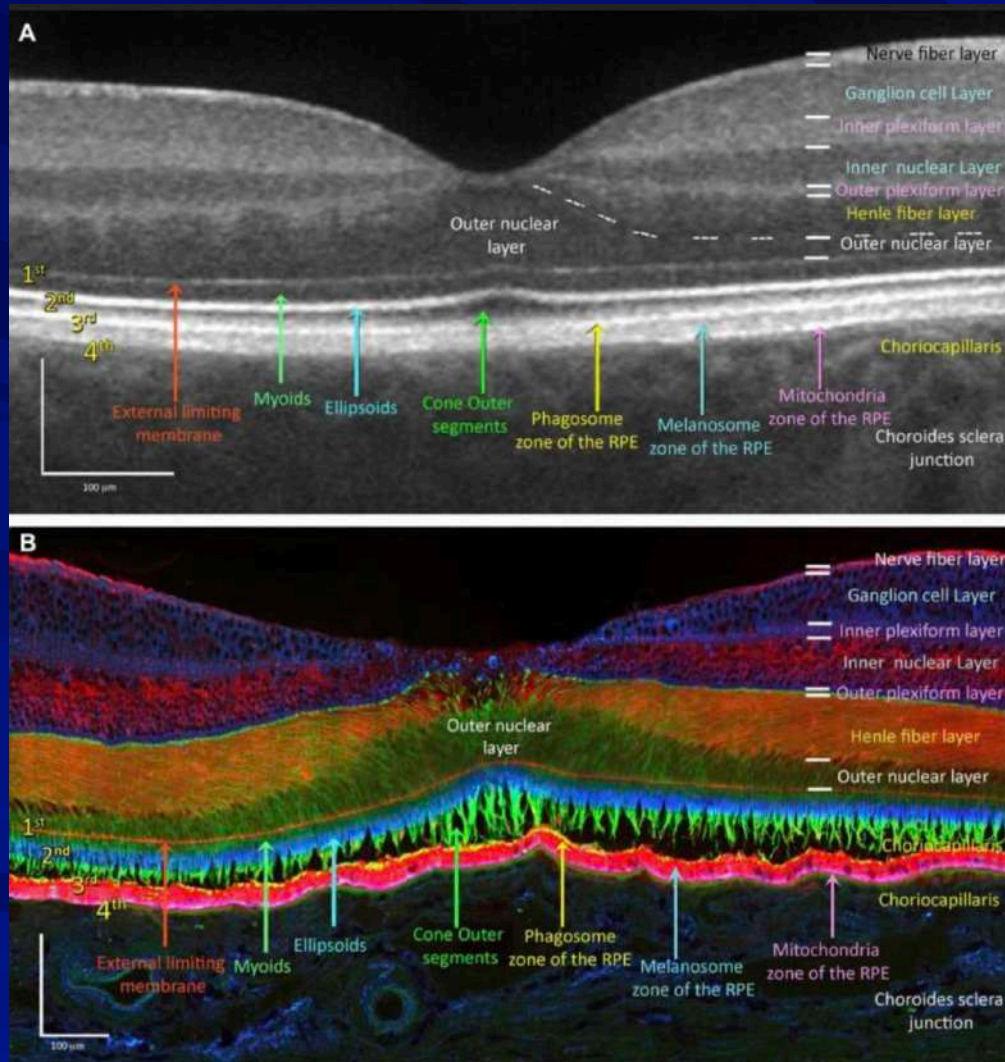


Finally, visibly evident drusen on fundus evaluation



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





Progress in Retinal and Eye Research

Volume 77, July 2020, 100828

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

Nicolás Cuenca <sup>a, b, 1</sup> ... Isabel Pinilla <sup>f, 1</sup>

Show more

Outline | Share | Cite

<https://doi.org/10.1016/j.preteyeres.2019.100828>

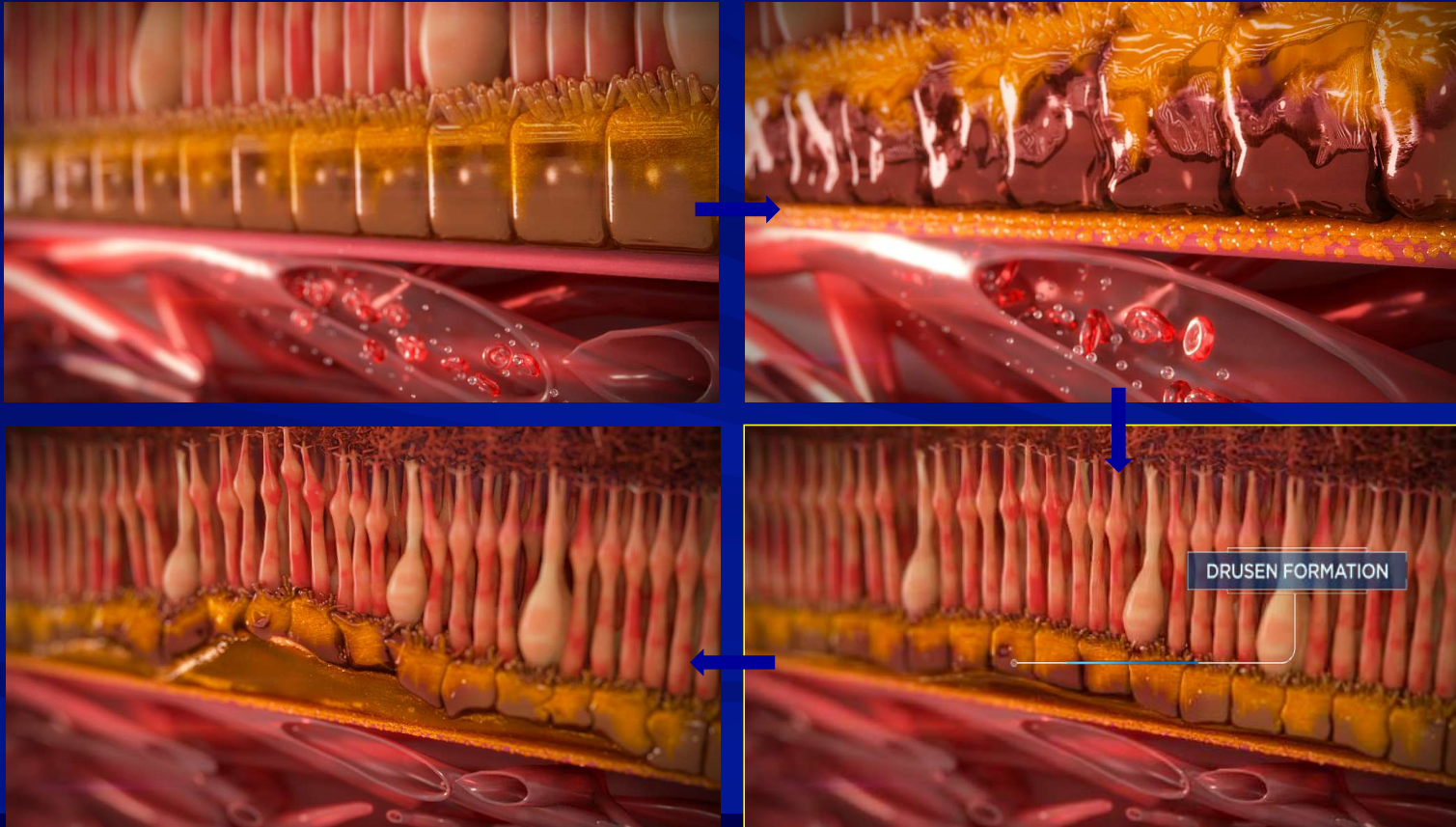
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### Abstract

Optical coherence tomography (OCT) and OCT angiography (OCTA) have been a techn

FEEDBACK

# 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

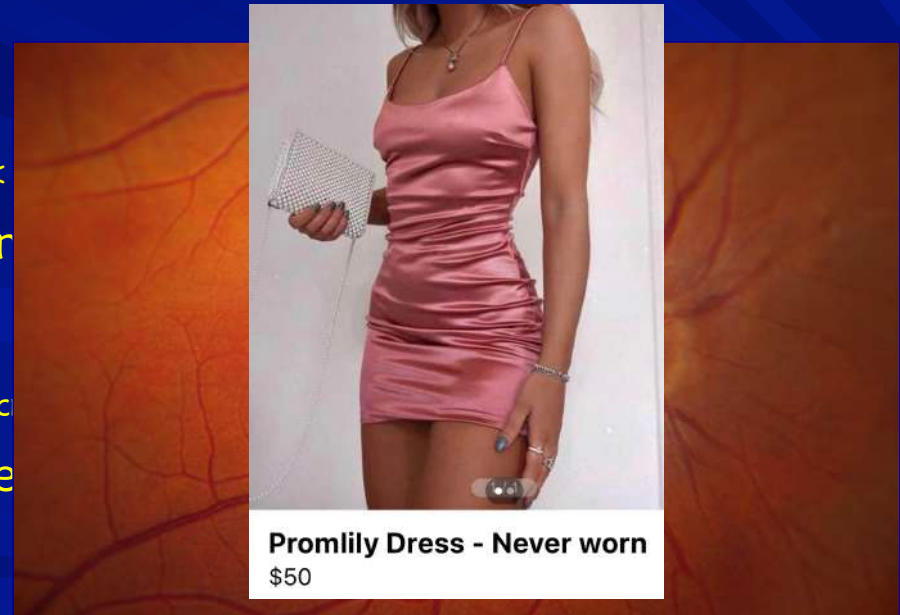
- 📋 None or few small drusen, < 63 microns
- 📋 No AMD pigmentary abnormalities

## ★ Early AMD

- 📋 Medium drusen, > 63 – <125 microns
- 📋 No AMD pigmentary changes

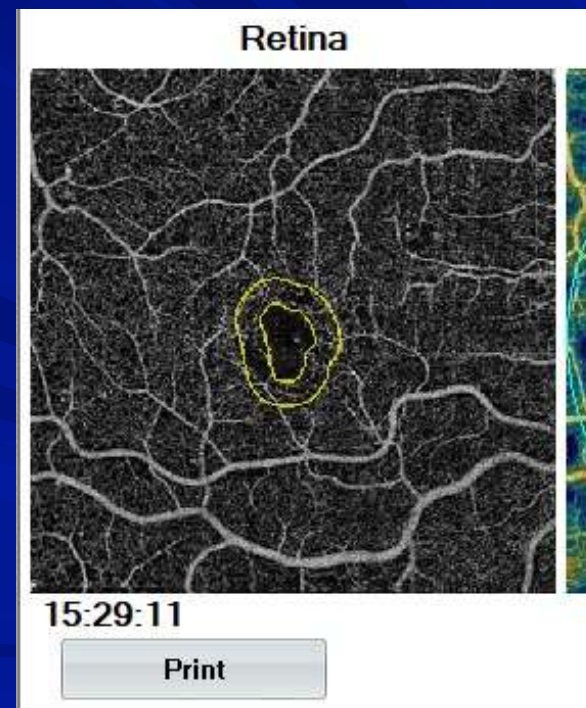
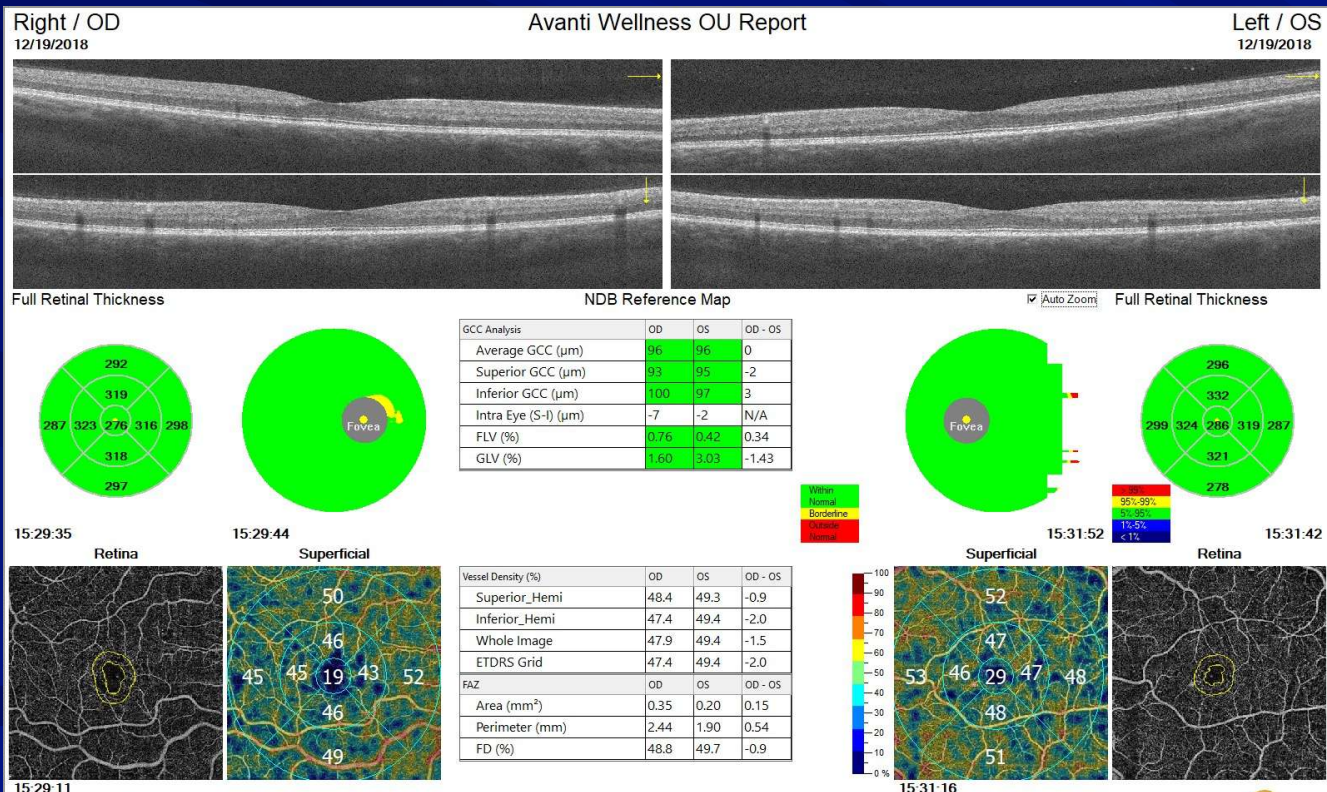
## ★ Intermediate AMD

- 📋 1 large drusen, > 125 microns
- 📋 Any AMD pigmentary changes

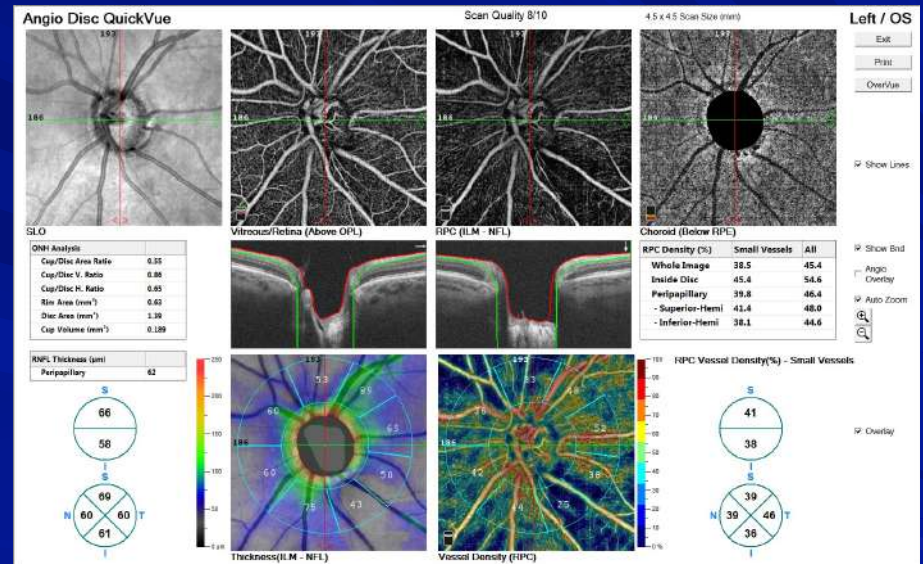
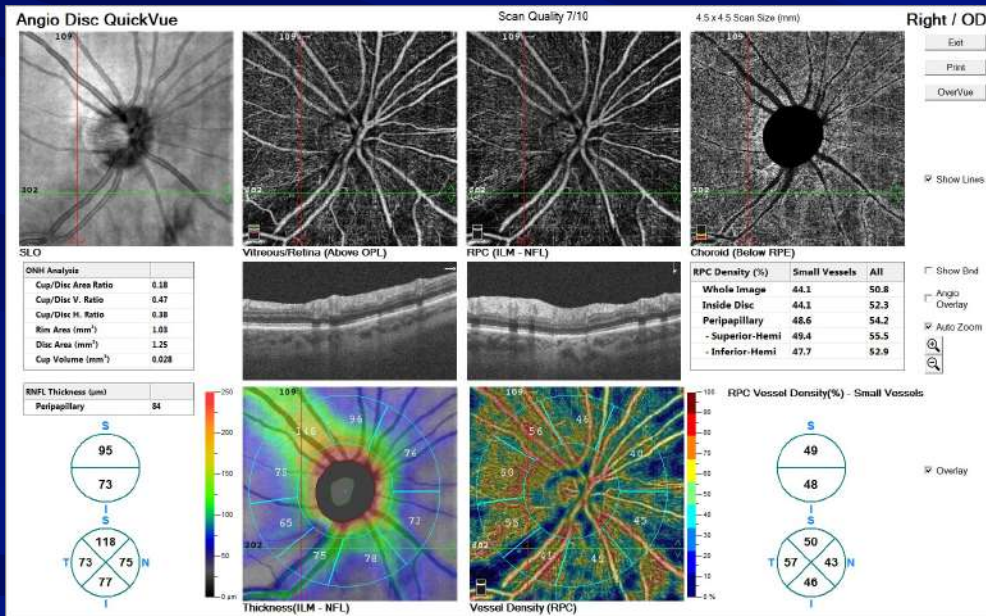


# AngioWellness Report

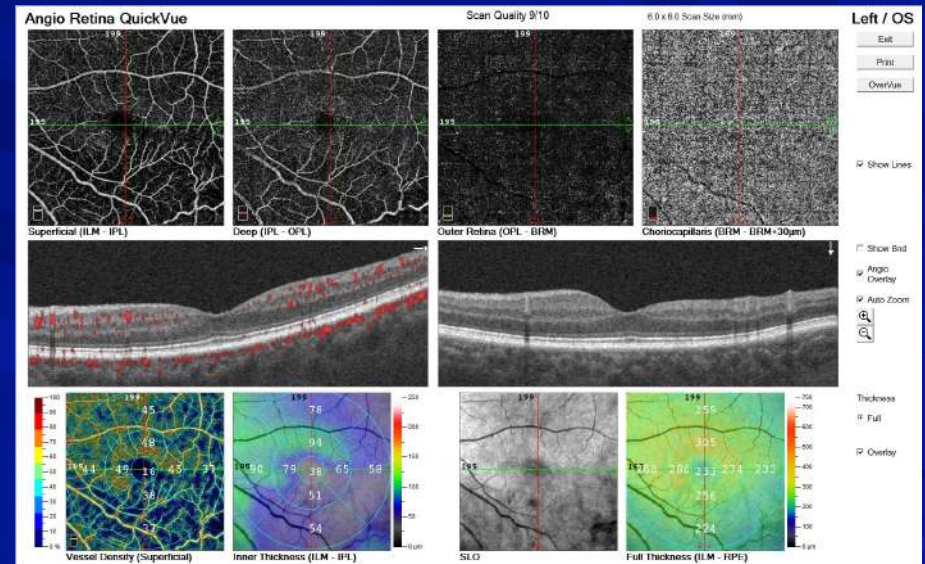
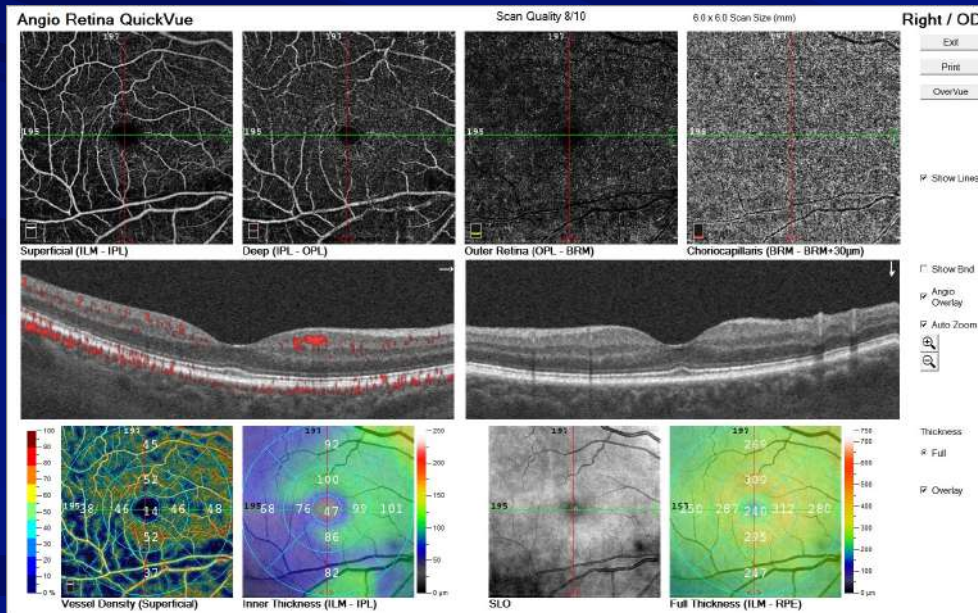
## Patient with Diabetes



# 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>, Jeffrey D Gerson<sup>3</sup>, Renu A Kowluru<sup>4</sup>

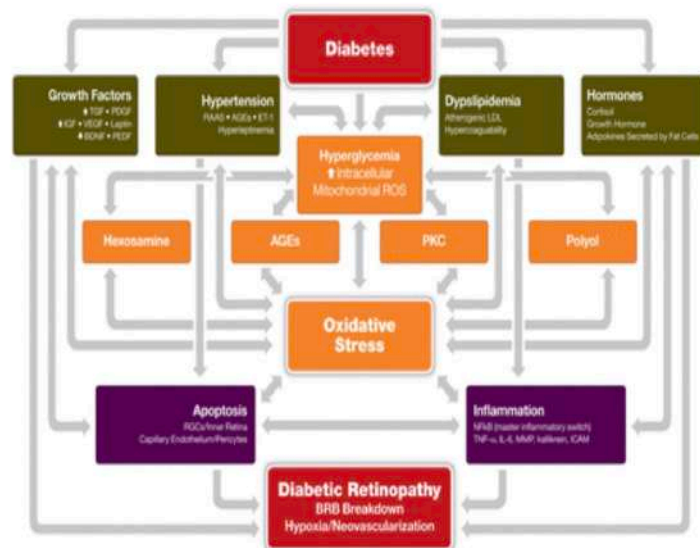
Affiliations + expand

PMID: 26089210 PMCID: PMC4752618 DOI: 10.1136/bjophthalmol-2014-306534

[Free PMC article](#)

### PATHWAYS CONTRIBUTING TO DIABETIC RETINOPATHY

USED WITH PERMISSION  
A. PAUL CHOUS, MD, PhD



DiVFuSS Constituents	Mitigates DR in animal models	Blocks capillary cell apoptosis	Improves retinal capillary fragility	Reduces VEGF	Reduces oxidative stress	Reduces AGE activity	Reduces Polyol activity	Reduces PKC activity	Reduces NF-κB
Alpha-Lipoic Acid	*		*	*	*				*
Berberine	*	*				*	*	*	*
Vitamins C/E	*				*		*		*
Curcumin	*			*	*	*			*
Vitamin D3	*			*					
DHA/EPA	*	*		*	*				
Grape Seed Extract	*	*		*	*	*			
Resveratrol	*	*		*	*				
Green Tea Extract	*			*	*				
N-Acetyl Cysteine	*			*	*				
CoQ10	*			*	*				
Zinc	*			*	*				
Pycnogenol	*		*	*	*				*
Lutein/Zeaxanthin	*		*	*	*				*

DiVFuSS Constituents	Improves visual function in humans	Reduces retinal edema in humans	Improves endothelial dysfunction in humans	Improves retinal blood flow in humans	Reduces HbA1c in humans	Improves Dyslipidemia in humans	Reduces blood pressure in humans	Reduces DPN symptoms in humans
Alpha-Lipoic Acid			*	*				*
Berberine			*	*		*		*
Vitamins C/E			*	*		*		*
Curcumin	*	*	*	*		*		*
Vitamin D3			*	*	*	*	*	*
DHA/EPA			*	*	*	*	*	*
Grape Seed Extract			*	*	*	*	*	*
Resveratrol			*	*	*	*	*	*
Green Tea Extract			*	*	*	*	*	*
N-Acetyl Cysteine			*	*	*	*	*	*
CoQ10			*	*	*	*	*	*
Zinc			*	*	*	*	*	*
Pycnogenol	*	*	*	*	*	*	*	*
Lutein/Zeaxanthin	*	*	*	*	*	*	*	*

Note: Suggested improvements marked by \* include published evidence in animal and/or cell models, except as specifically noted, but do not reflect grading of that evidence.

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>

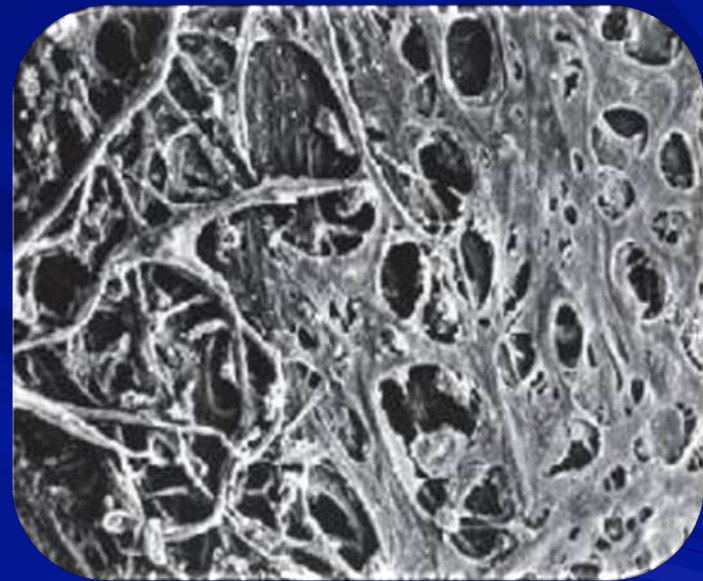
Healthy TM  
Normal IOP



Cellular Damage  
(eg, Oxidative Stress)



POAG TM Stiffness  
Elevated IOP



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

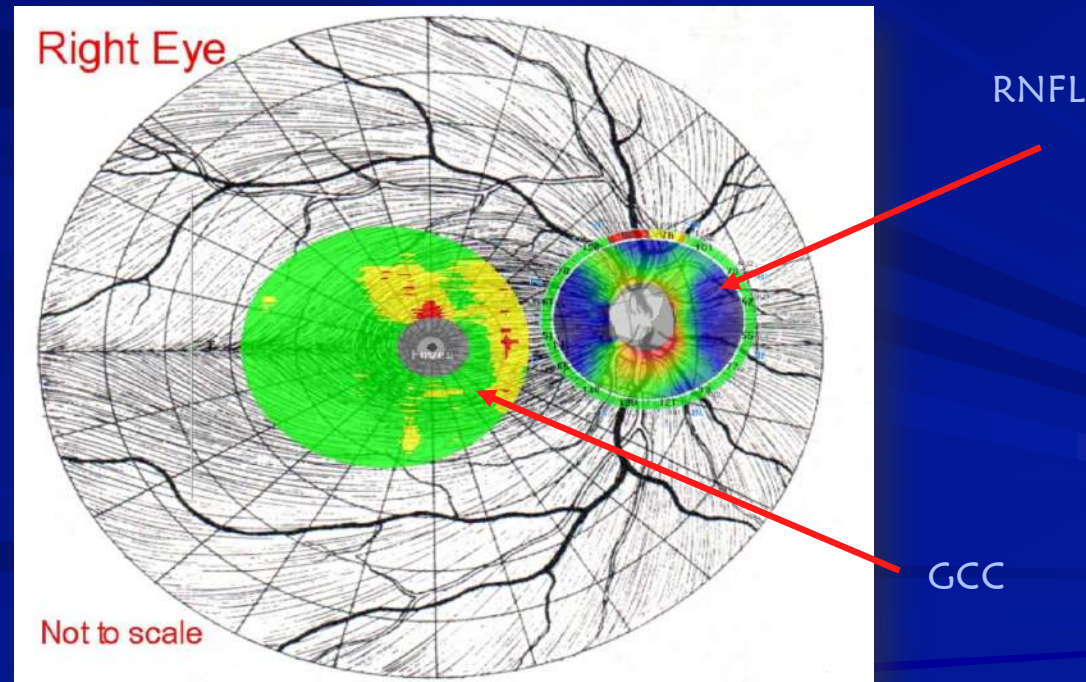
PERSPECTIVES ON GLAUCOMA

## Antioxidants enhance ocular perfusion in Open Angle Glaucoma

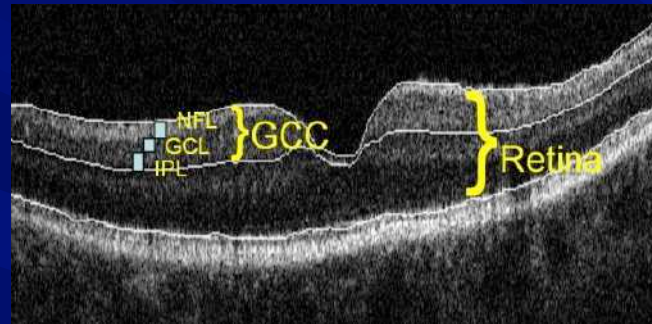
Harris A, et al. Acta Ophthalmol. 2018;doi:10.1111/aos.13530.

“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 [oral antioxidant supplementation](#) may decrease vascular resistance over a longer period of time than previous trials investigated.”

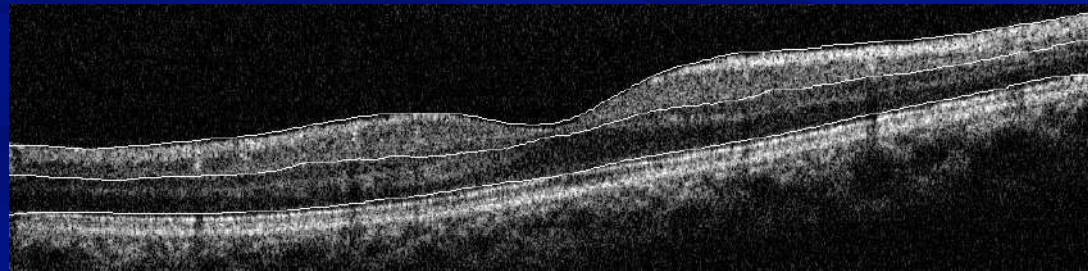
# Overlay of the RNFL and GCC



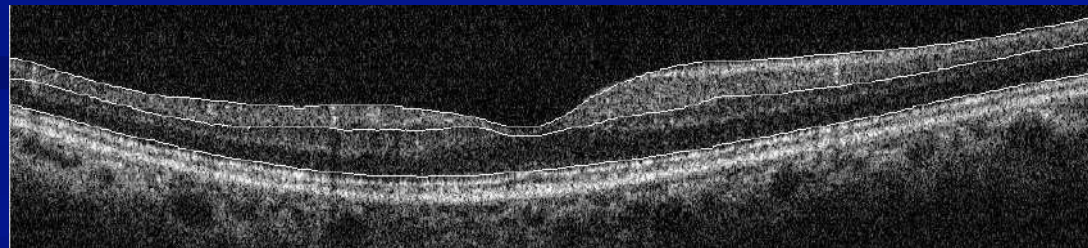
# GCC Thinning in Glaucoma

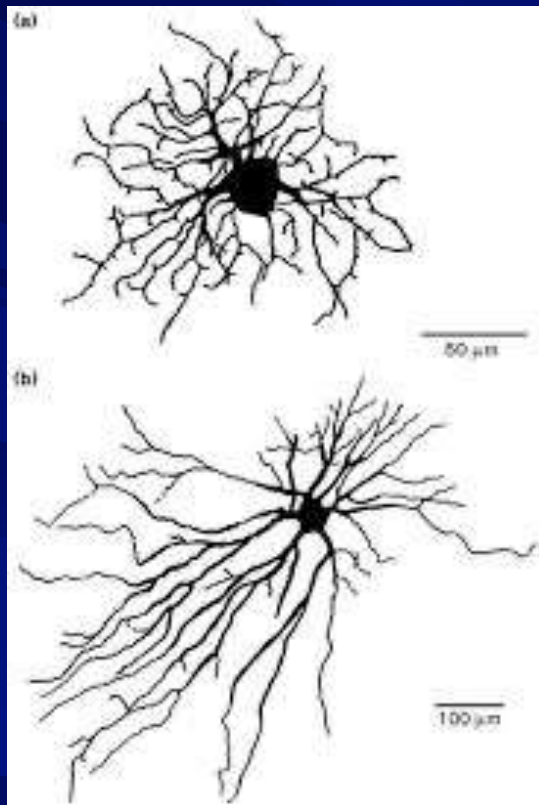


Normal

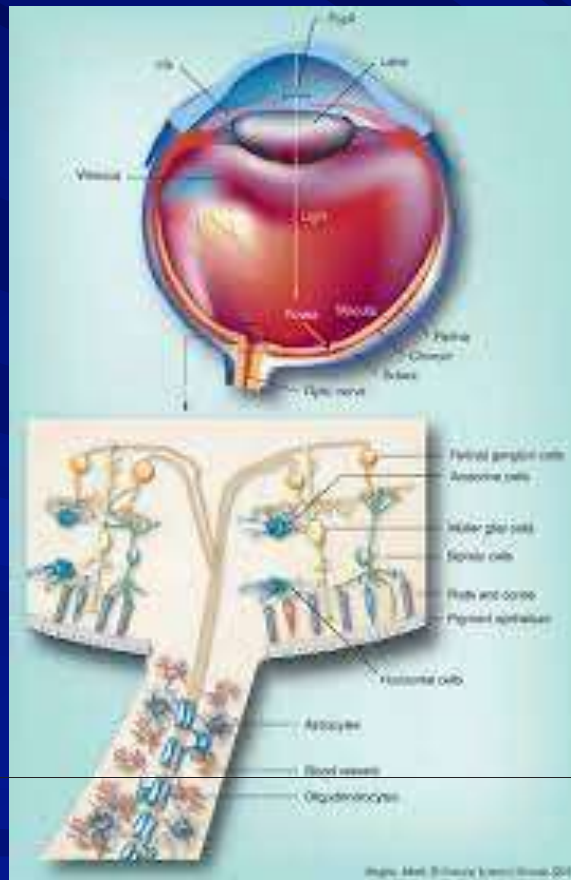


Glaucoma with thinner GCC

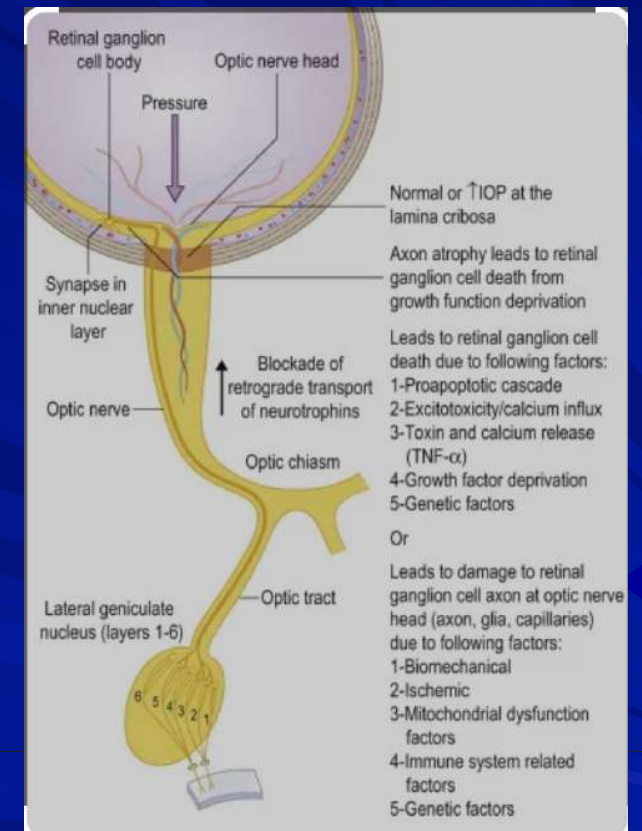




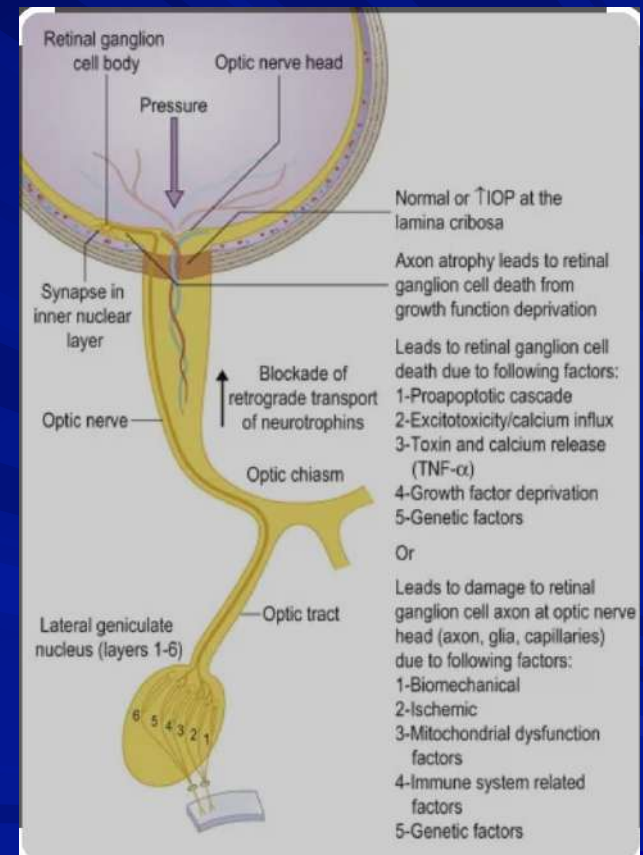
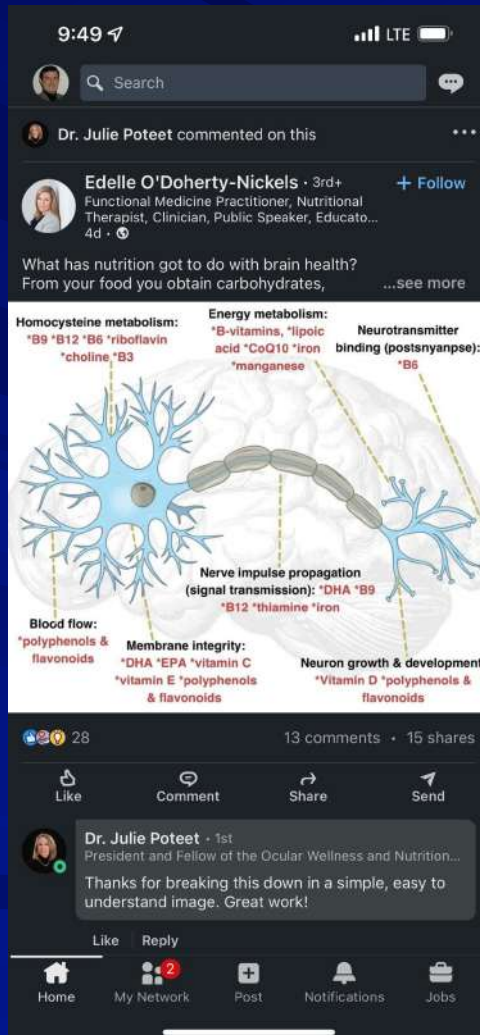
[alpha and beta retinal ganglion cells ... cell.com](#)



[retinal ganglion cell regeneration ...futuremedicine.com](#)



[Pu Eble Rino](#)  
[Retinal Ganglion Cells Optic Nerve](#)





Sissy D. Johns · 2nd

1w · 🌐

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

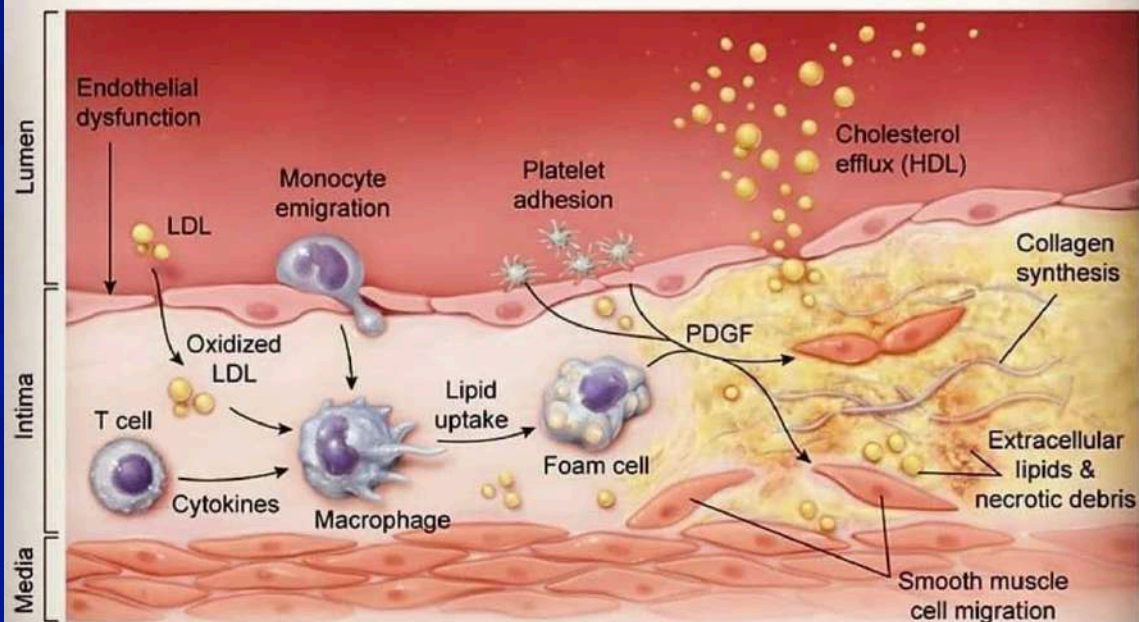
Initially, factors including hyperlipidemia, hypertension, hyperglycemia, and smoking trigger endothelial injury and/or dysfunction. This leads to increased vascular permeability, enhanced leukocyte adhesion, and a higher propensity for thrombosis.

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

## Formation of atheroma



PDGF = platelet-derived growth factor.

# Treatments for AMD

🕒 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

# AREDS/AREDS2 Frequently Asked Questions

On this page: [AREDS formulas](#) | [Formulation components](#) | [Risks and side-effects](#) | [About the trials](#) | [Genetic testing](#) | [References](#) | [Definitions](#)

## 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

[Age-Related Eye Disease Studies](#) ➤

[AREDS/AREDS2 - Background and Design](#) ➤

[AREDS/AREDS2 Nutritional Supplements](#) ➤

[AREDS/AREDS2 News](#) ➤

##### Information about AMD

[Age-Related Macular Degeneration](#)

## **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.

## **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.

# Treatment for AMD

## 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
  - 📋 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
  - 📋 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

# An Evening with Dr. Paul Bernstein

## Measurement of Macular Pigment



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



## High Performance Liquid Chromatography



# 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.

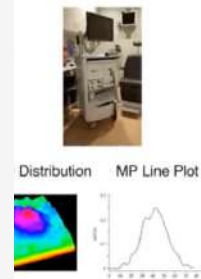
# An Evening with Dr. Paul Bernstein

## 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



RetCam® Blue Light  
Reflectance Imaging of MP



Do Prenatal supplements with  
lutein & zeaxanthin benefit  
pregnant mothers and their infants?

**RESEARCH VOLUNTEERS NEEDED**

We are seeking for supporting mothers after age:  
• 18 or older  
• 1st trimester of pregnancy  
• Residing in the US or its territories

Participants will receive a supply of prenatal supplements, 1 dose for the duration of the pregnancy, after a study group their pregnancy outcomes to provide.

**CAROTENOID SUPPLEMENTATION DURING PREGNANCY**

For more information, contact:  
Dr. Paul Bernstein  
NIH/NINDS  
401 Convent Ave.  
Bldg. 35, Room 3A01  
Bethesda, MD 20894  
Tel: 301-495-4444  
Fax: 301-495-4444

**NIH HEALTH**



# An Evening with Dr. Paul Bernstein

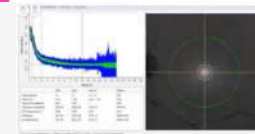
## The Moran AMD Genetic Testing Assessment Study: The **Magenta** Study

- 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

Skin Carotenoid Resonance Raman Spectroscopy



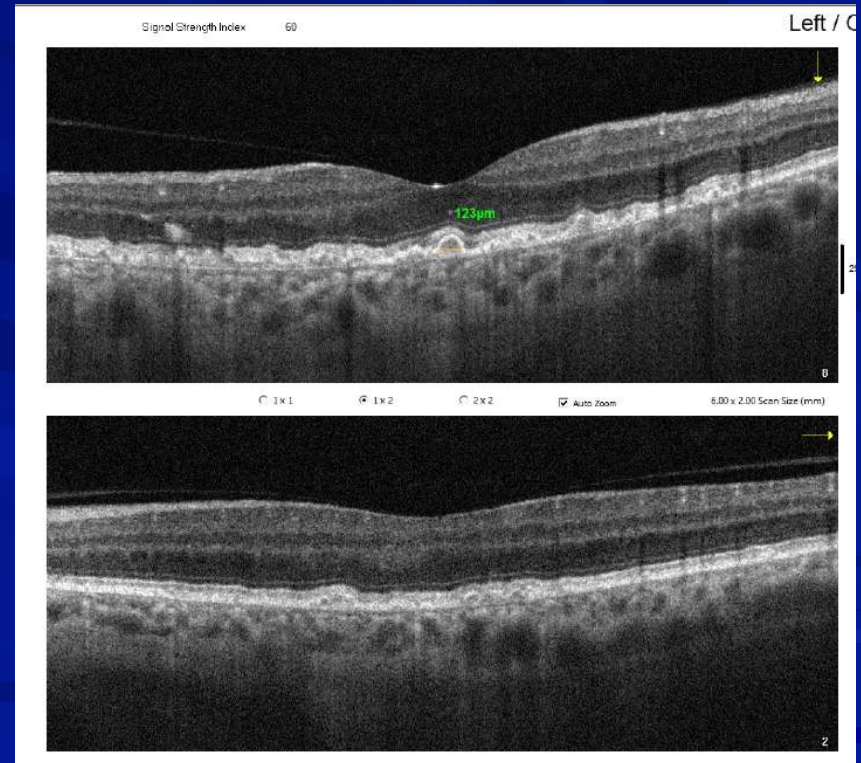
Spectralis® Autofluorescence Attenuation Imaging of MP



Skin Carotenoid reflectance Spectroscopy with the Veggie Meter®



# Macular Pigment

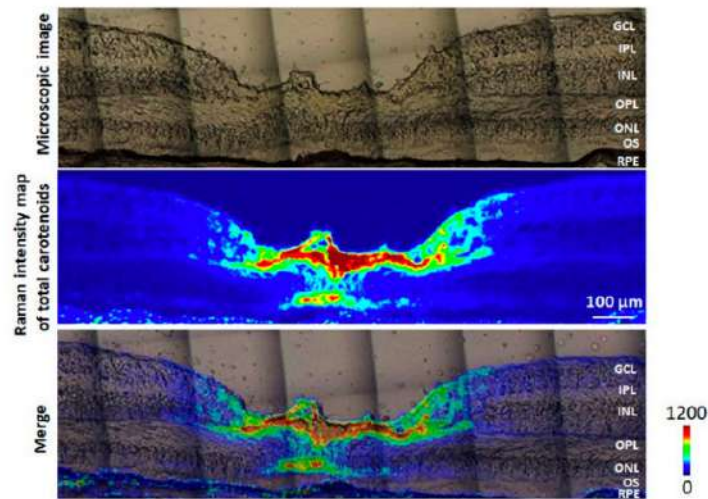


# Macular Pigment

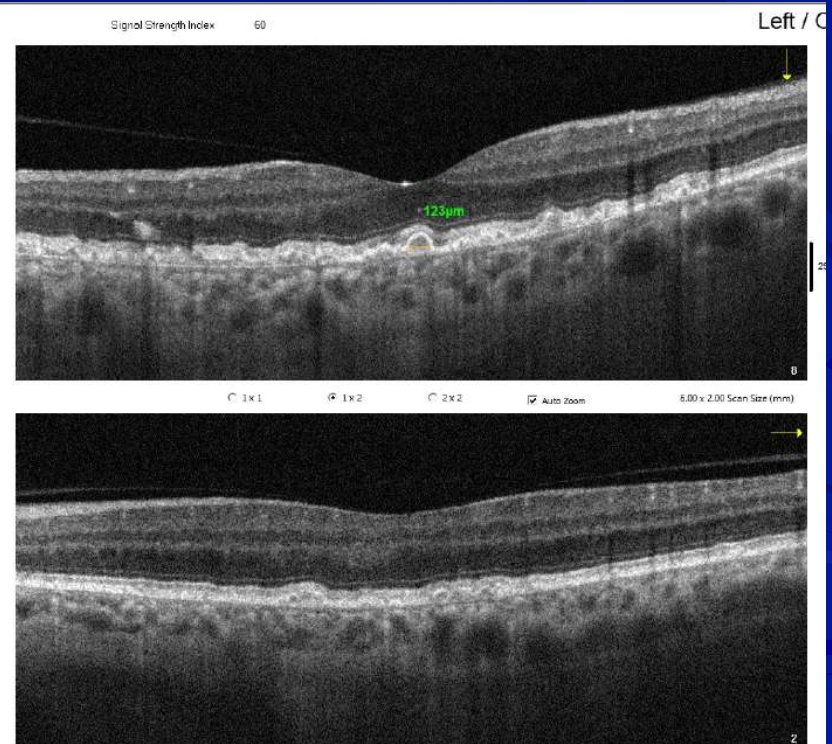
## Imaging lutein and zeaxanthin in the human retina with confocal resonance Raman microscopy

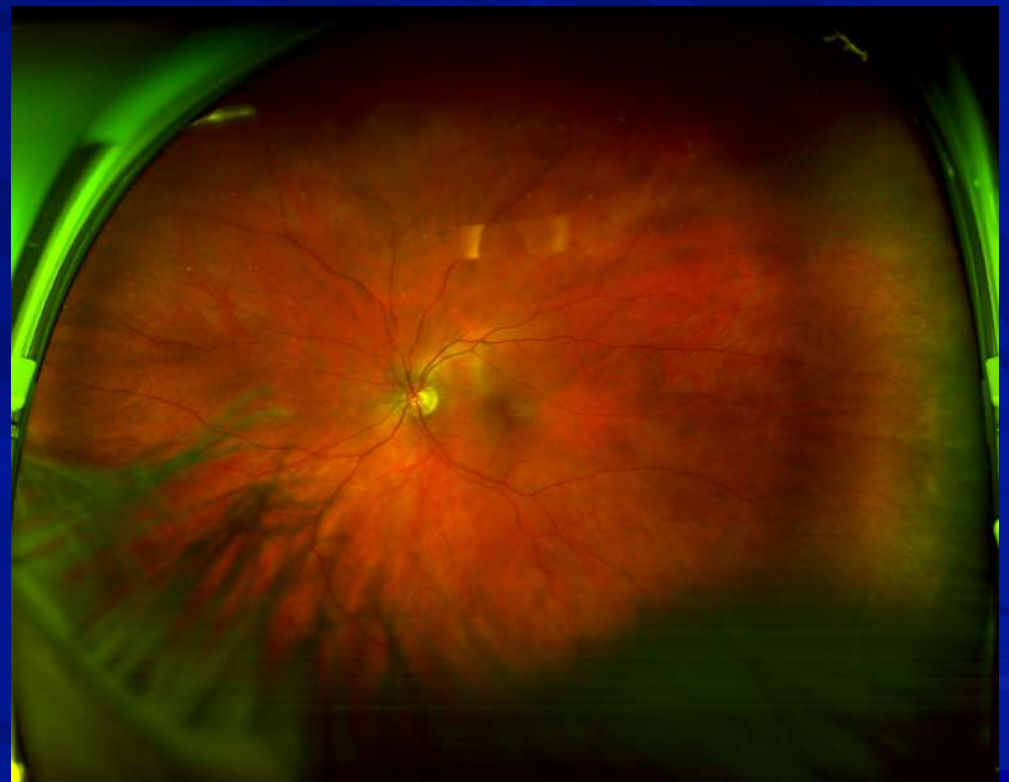
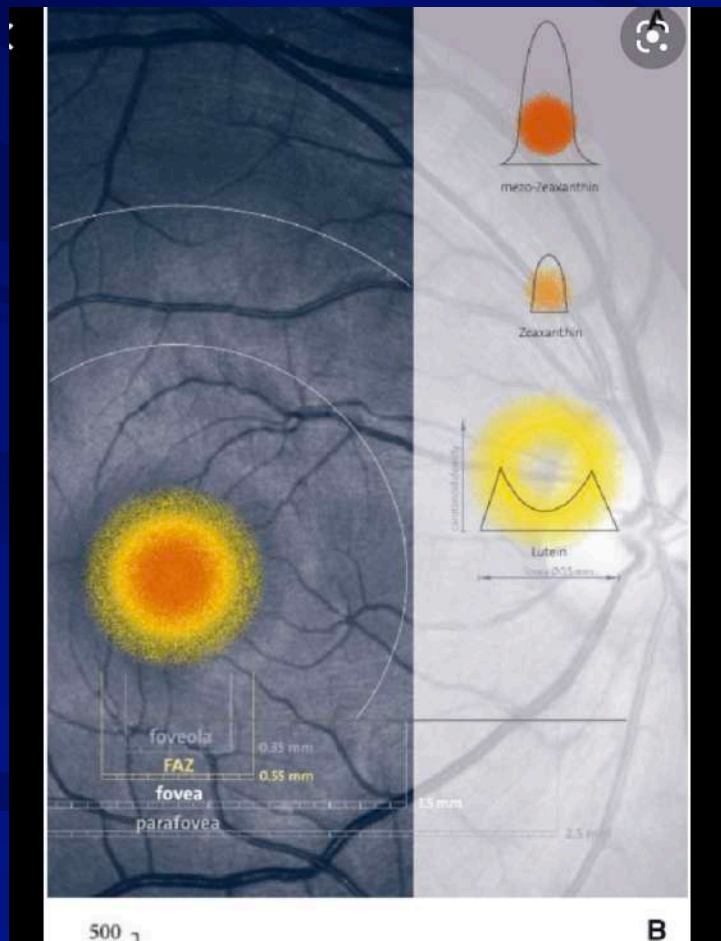
Binxing Li<sup>a</sup>, Evan W. George<sup>a</sup>, Gregory T. Rognon<sup>a</sup>, Aruna Gorusupudi<sup>a</sup>, Arunkumar Ranganathan<sup>a</sup>, Fu-Yen Chang<sup>a</sup>, Linjia Shi<sup>a</sup>, Jeanne M. Frederick<sup>a</sup>, and Paul S. Bernstein<sup>a,1</sup>

<sup>a</sup>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





# Question

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

★ Yes

★ No

# Why Are We Only Treating Half the Retina?



*Oxid Med Cell Longev*. 2019; 2019: 9783429.

PMCID: PMC6390265

Published online 2019 Feb 12. doi: [10.1155/2019/9783429](https://doi.org/10.1155/2019/9783429)

PMID: [30891116](https://pubmed.ncbi.nlm.nih.gov/30891116/)

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

Simona Bungau,<sup>1</sup> Mohamed M. Abdel-Daim,<sup>2,3</sup> Delia Mirela Tit,<sup>1</sup> Esraa Ghanem,<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>

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### Abstract

Go to:

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 mezoanthin) 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-1 $\alpha$ , 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.

# Carotenoids and Polyphenols

www.oncotarget.com

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

Review

## 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>

<sup>1</sup>Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy

<sup>2</sup>Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

<sup>3</sup>Department of Medicine and Surgery, University of Parma, Parma, Italy

<sup>4</sup>CoreLab, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy

<sup>5</sup>Department of Life Sciences and Biotechnology, Pharmaceutical Biology Laboratory, University of Ferrara, Ferrara, Italy

Correspondence to: Luca M. Neri, email: luca.neri@unife.it

Keywords: exercise training; nutraceuticals; flavonoids intake; aging; antioxidant supplementation

Received: January 26, 2018

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Published: March 30, 2018

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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

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].

It is reported that also curcumin possesses anti-

## 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 skin, blood, and the brain. 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

read study

👓 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 City, UT 84132, USA; paul.bernstein@hsc.utah.edu.

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Citation: Conrady CD, Bell JP, Besch BM, et al. Correlations between macular, skin, and serum carotenoids. *Invest Ophthalmol Vis Sci*. 2017;58:3616–3627. DOI:10.1167/ios.17.21818

**Purpose.** 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 (AFI) of macular pigment with skin resonance Raman spectroscopy (RRS) and serum carotenoid levels in a clinic-based population.

**Methods.** Eighty-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 telangiectasia (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.

**Conclusions.** 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



**Quick Test**  
(approx. 30 sec)

**Portable**

**Cost Effective**

**Remeasure in 60 days**

**Reassurance to you and patient**

# Raman Spectroscopy



# 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>a</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, ND 58203, USA

<sup>d</sup> Department of Physics and Astronomy, University of Utah, Salt Lake City, UT 84142, USA

## ARTICLE INFO

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Keywords:

Carotenoids

Skin

Resonance Raman spectroscopy

Beta-carotene

Biomarker

## ABSTRACT

Resonance Raman spectroscopy (RRS) is a non-invasive method that has been developed to assess carotenoid status in human tissues including human skin *in vivo*. Skin carotenoid status has been suggested as a promising biomarker for human studies. This manuscript describes research done relevant to the development of this biomarker, including its reproducibility, validity, feasibility for use in field settings, and factors that affect the biomarker such as diet, smoking, and adiposity. Recent studies have evaluated the response of the biomarker to controlled carotenoid interventions, both supplement-based and dietary [e.g., provision of a high-carotenoid fruit and vegetable (F/V)-enriched diet], demonstrating consistent response to intervention. The totality of evidence supports the use of skin carotenoid status as an objective biomarker of F/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

## 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.

# Vulnerable to Oxidation

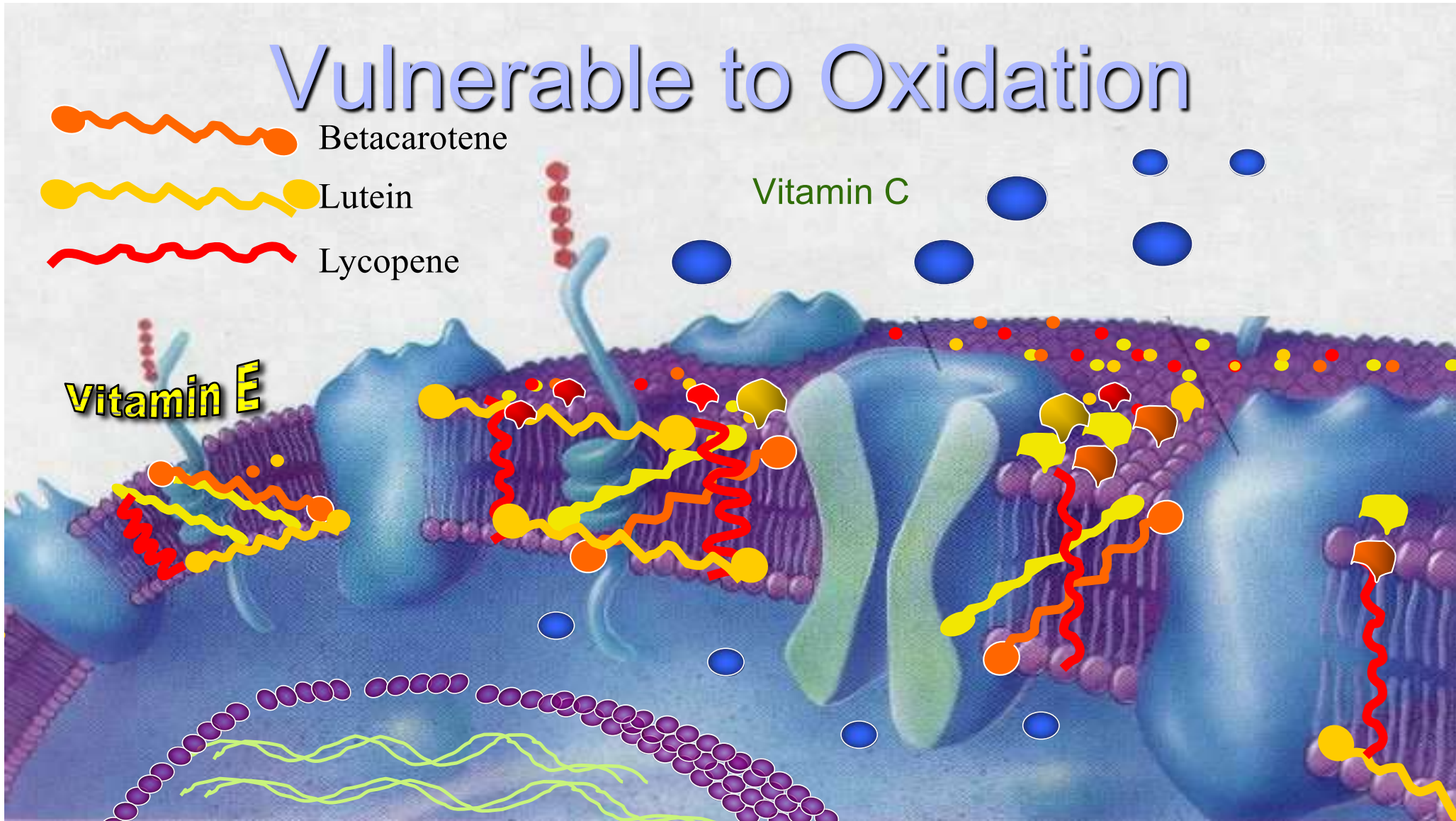
 Betacarotene

 Lutein

 Lycopene

Vitamin C

Vitamin E



Are you taking a supplement?

# 53-year-old man

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

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

Dear [REDACTED]

Recently, on 12/15/2020, you met with me and I scanned the palm of your hand with the [REDACTED] 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
<b>Serving Size: 1 Packet</b>		
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%
Iodine (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 <i>Camellia sinensis</i> 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 <i>Polygonum cuspidatum</i> root extract)	(2.5 mg)	*
Mixed Tocopherols (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, Croscarmellose 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 Container 60

Amount Per Serving		% DV
Total Calories	15	
Total Fat	1 g	1%*
Saturated Fat	0 g	0%*
Trans Fat	0 g	
Vitamin D <sub>3</sub> (as cholecalciferol)	12.5 mcg (500 IU)	63%
Vitamin K <sub>2</sub> (as menaquinone-7)	20 mcg	17%
Ultra-pure fish oil concentrate:	1055 mg	**
EPA (Eicosapentaenoic acid)	300 mg	**
DHA (Docosahexaenoic acid)	200 mg	**
Citrus Bioflavonoids	100 mg	**
(including hesperidin and naringin)		
Purple corn ( <i>Zea mays</i> L.) cob extract	66.67 mg	**
including anthocyanins		
Alpha Lipoic Acid	50 mg	**
Quercetin (from <i>Dimorphandra mollis</i> fruit extract)	37.5 mg	**
D-Limonene (from <i>Citrus sinensis</i> peel)	25 mg	**
Rosemary ( <i>Rosmarinus officinalis</i> L.) leaf extract	18.75 mg	**
including carnosic acid		
Resveratrol (from <i>Polygonum cuspidatum</i> root)	15 mg	**
Coenzyme Q10	15 mg	**
Lycopene	2.5 mg	**
Lutein (from marigold flower ( <i>Tagetes erecta</i> ))	2 mg	**
Astaxanthin (from <i>Haematococcus pluvialis</i> algae)	0.5 mg	**

\* 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 [REDACTED]

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 [REDACTED]

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

Reference En Face IR



10

250µm

Signal Strength Index

55

12.00 x 4.00 Scan Size (mm)

Right / OD



Auto Zoom

Reference En Face IR



10

250µm

Signal Strength Index

43

12.00 x 4.00 Scan Size (mm)

Right / OD

Optovue

Scan 06/23/2021 10:22:11

Print

OU Report

49°F Sunny 10:46 AM 6/23/2021

N of 3  
So Far

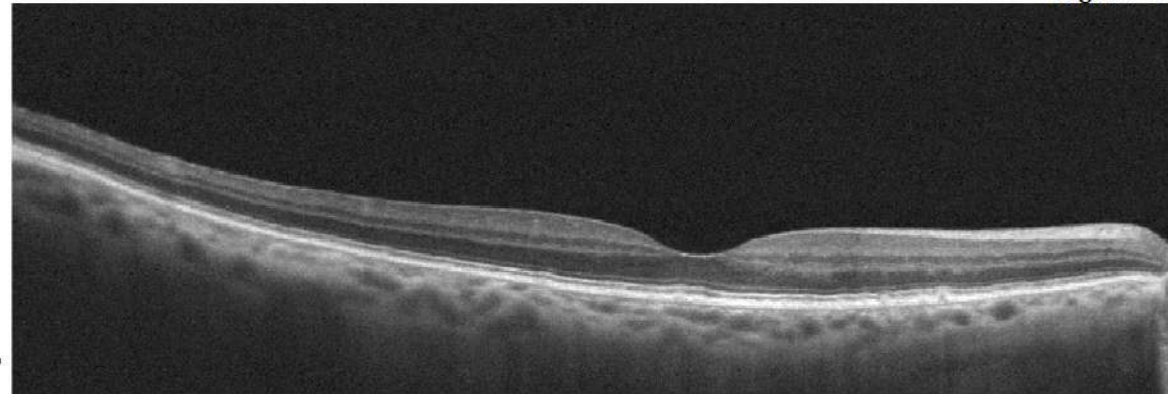
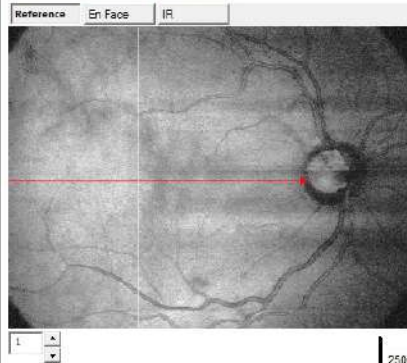
## Cross Line Comparison Report

Scan 04/05/2021 14:33:33

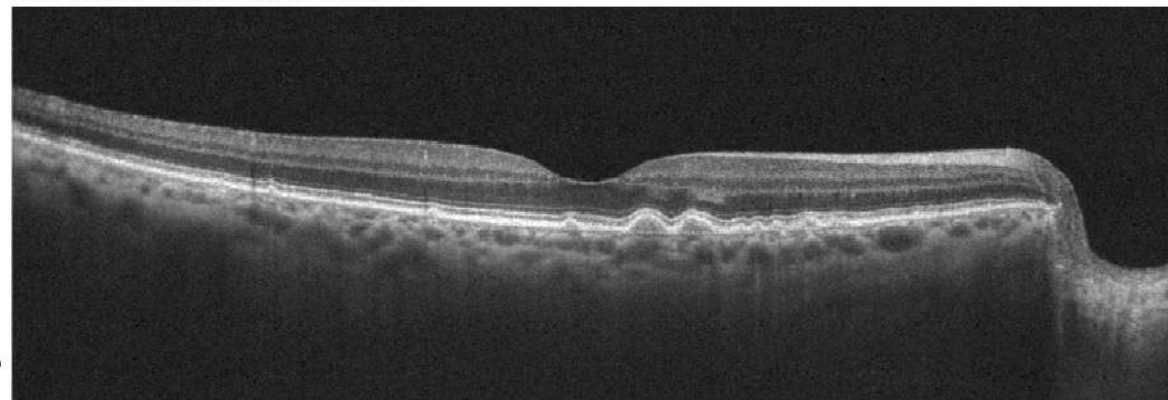
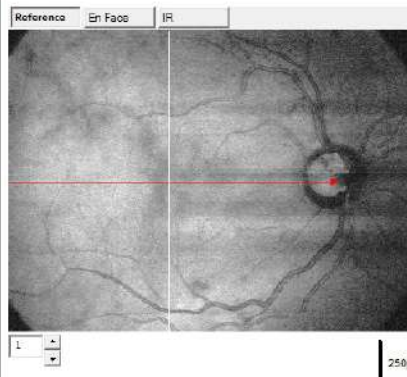
Signal Strength Index 58

10.00 Scan Size (mm)

Right / OD



☒ Auto Zoom



Scan 09/21/2020 10:40:42

Signal Strength Index 59

10.00 Scan Size (mm)

Right / OD

Print

OU Report

## Ingredients

Ingredients	Amount	% Daily Value
<b>Serving Size: 1 Packet</b>		
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%
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Molybdenum (as Molybdenum Bisglycinate)	37.5 mcg	83%
Polyphenol and Flavonoid Blend	97.5 mg	*
Catechins (from <i>Camellia sinensis</i> 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 <i>Polygonum cuspidatum</i> root extract)	(2.5 mg)	*
Mixed Tocopherols (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, Croscarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

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

# Treat and Extend!

**Comment:**

Mr. Burke 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.**

CC: Julie Lesneski CRNP

Phone: 412-683-5300  
800-456-4393

**PITTSBURGH**  
300 Oxford Drive  
Suite 300

2000 Oxford Drive  
Suite 670  
Pittsburgh, PA 15107

Cloverleaf 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
- 👓 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...



1:16 PM Sat Oct 23

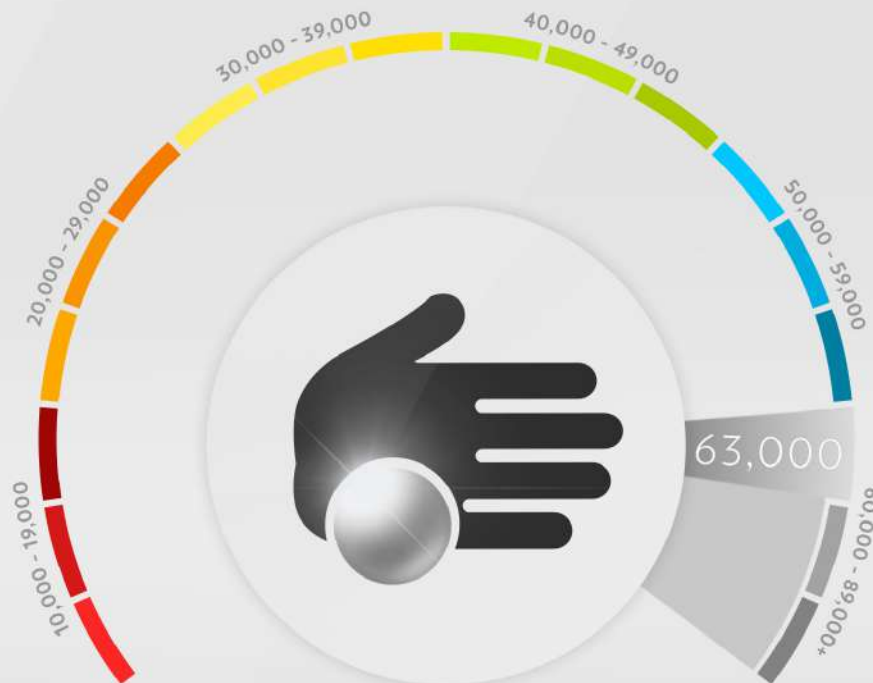
88%

GREG CALDWELL  
grubc@aol.com

5200953148879799



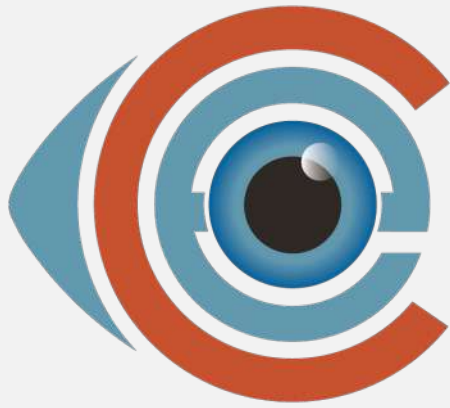
CANCEL



NEXT

SCAN COMPLETE





Optometric  
Education  
Consultants

Questions and Thank You!

Integrative and Functional Medicine

New Opportunities for Optometry

Greg Caldwell, OD, FAAO

Sunshine State Summer Conference  
Optometric Education Consultants

Friday, June 16, 2023

