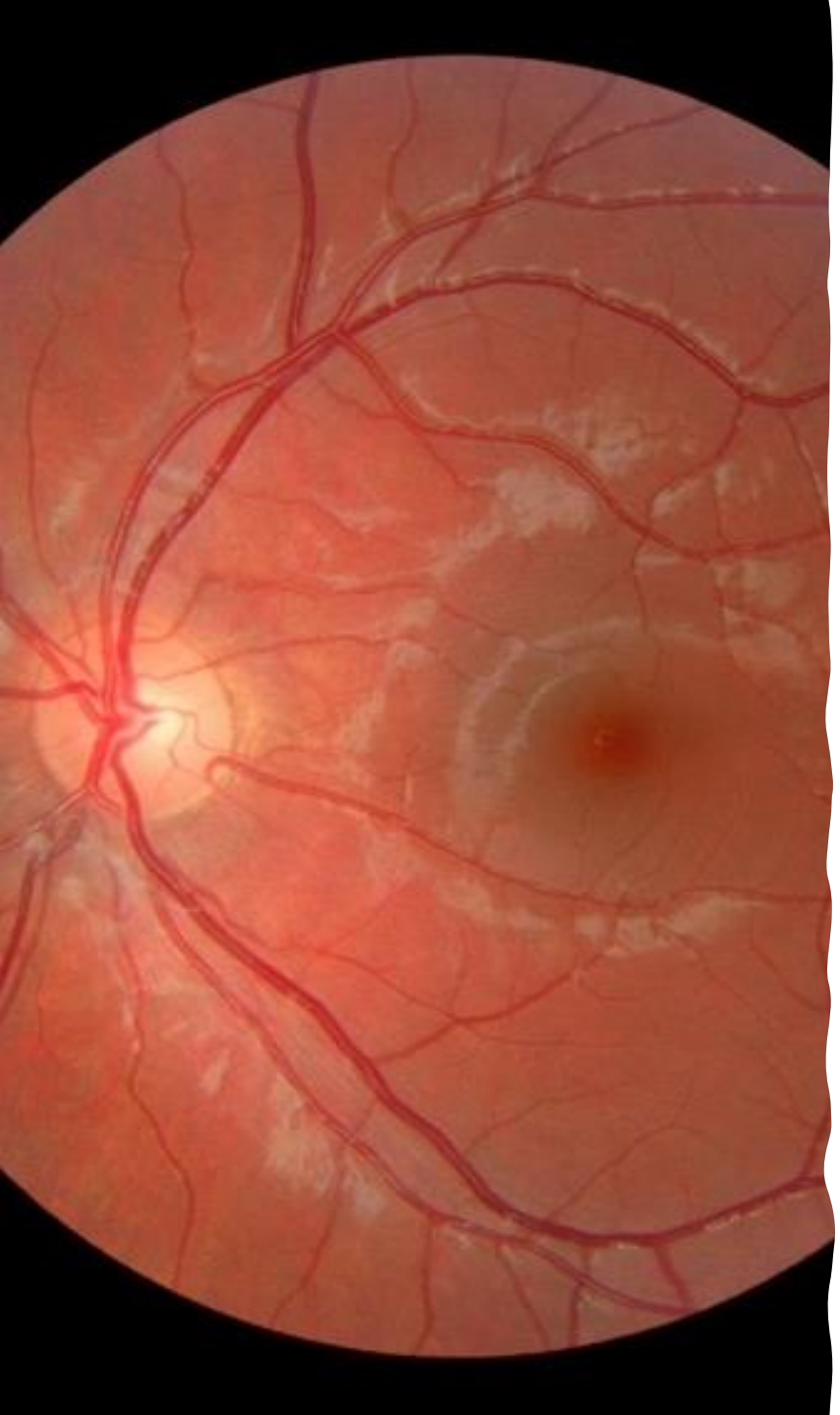


OCULAR HEALTH: IT'S MORE THAN MEETS THE EYE

THE SIGHT-SAVING POWER OF NUTRITION

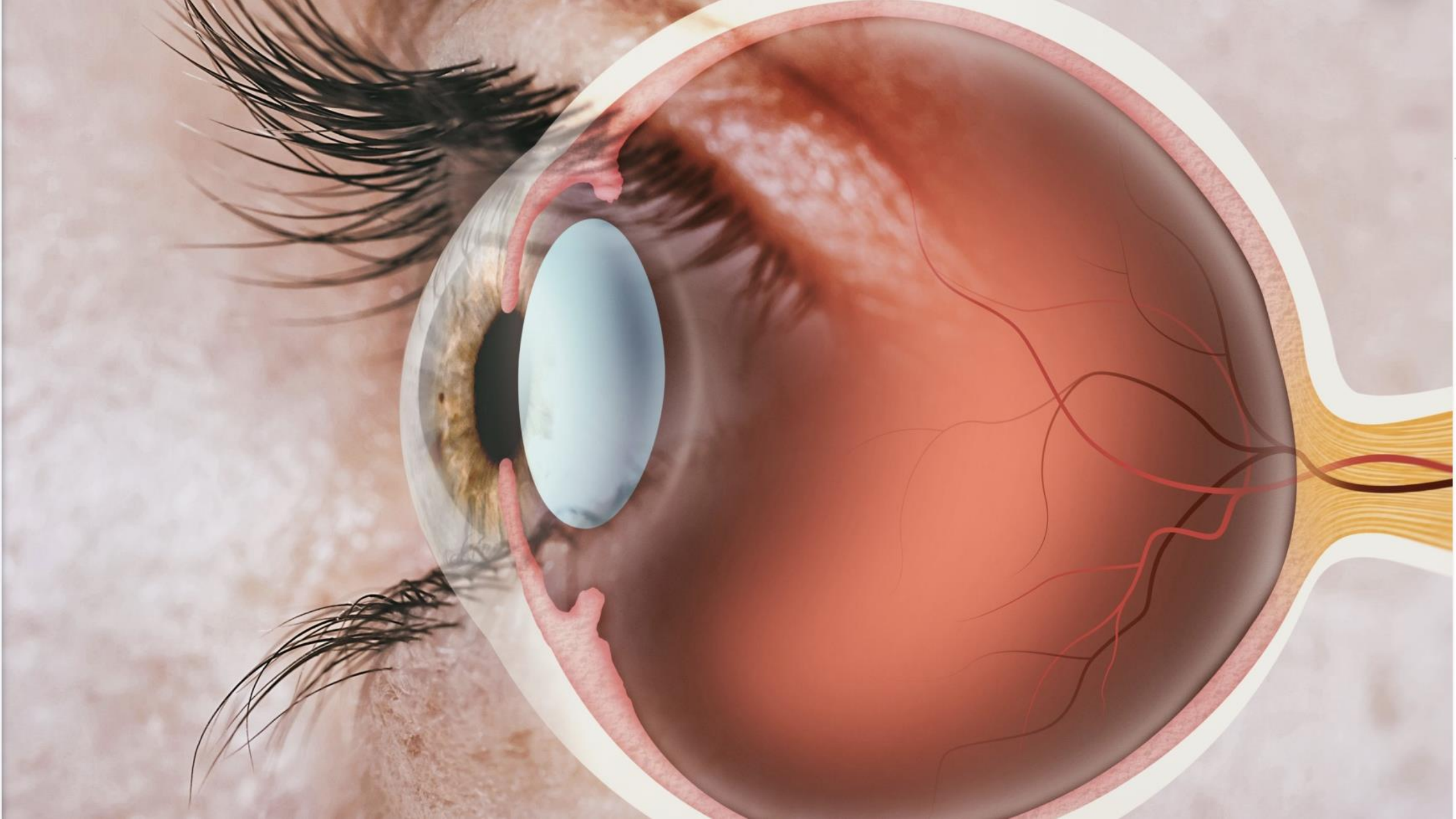
Julie Poteet, OD, MS, CNS, FOWNS

Financial Disclosures

- Part-time consultant for nutraceuticals by Bausch & Lomb
- Nutrition Writer and Clinical Editor for the journal *Presbyopia and the Aging Eye*
- Frequent lecturer on nutrition and wellness for eye doctors

Presentation Learning Objectives

- Identify diet as a driver of many chronic diseases including ocular diseases such as dry eye disease and macular degeneration, two frequently encountered diseases for which nutraceuticals are often prescribed in eye care
- Describe the evidence behind using nutraceuticals for dry eye disease
- Describe the history behind prescribing nutraceuticals as the standard of care for certain stages of macular degeneration based on the NIH/NEI Age Related Eye Disease Studies (AREDS)
- Describe the post hoc analysis of the AREDS trials that showed that a Mediterranean Diet is protective against all stages of macular degeneration
- Describe the importance of the dietary carotenoids lutein, zeaxanthin, and mesozeaxanthin in eye and brain health
- Describe ophthalmic manifestations of nutritional deficiencies
- Identify strategies for bringing the discussion of nutrition into clinical care

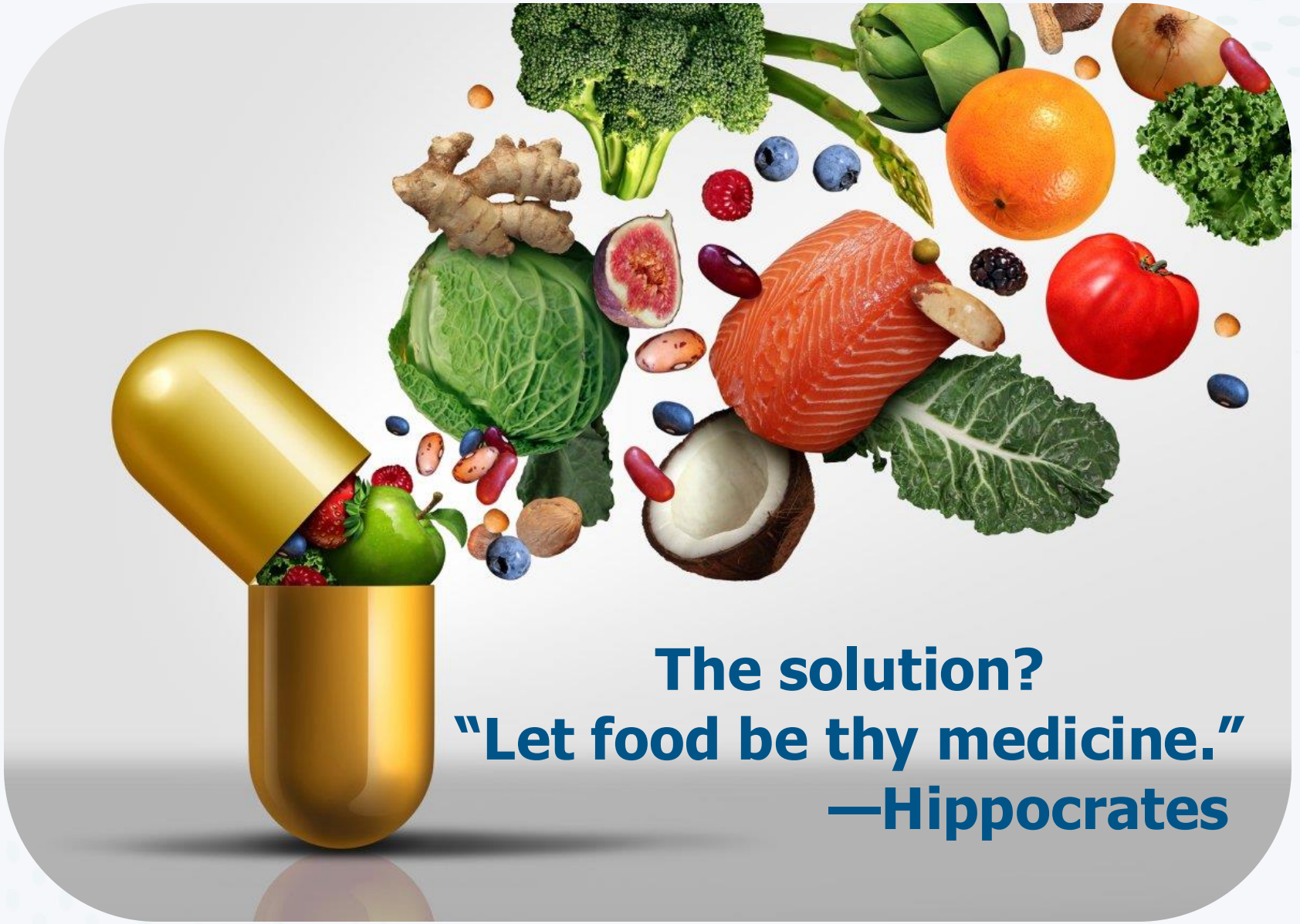


- Public health defined by Winslow in 1920 at Yale was defined as the art of preventing diseases (not just curing them) through lifestyle, food, hygiene, and environmental health...

New York Times opinion piece: Our food is killing too many of us.

"Poor diet is the *leading cause* of mortality in the United States, causing more than half a million deaths per year."

Our Food is Killing Too Many of Us. *The New York Times*. August 26, 2019. Accessed June 16, 2024. https://www.nytimes.com/2019/08/26/opinion/food-nutrition-health-care.html



The solution?
"Let food be thy medicine."
—Hippocrates

PUFA = polyunsaturated fatty acid.
Micha R, et al. *JAMA.* 2017;317(9):912-924.

Consumption of 10 foods/nutrients associated with cardiometabolic disease:

LOW:

- Nuts & seeds
- Seafood omega-3 fats
- Vegetables
- Fruits
- Whole grains
- PUFAs replacing carbohydrates or saturated fats

HIGH:

- Sodium
- Processed meats
- Sugar-sweetened beverages
- Red meats, unprocessed

AAPS PharmSci 2003; 5 (3) Article 25 (http://www.pharmsci.org).

Nutraceutical - Definition and Introduction

Submitted: April 15, 2003; Accepted: July 28, 2003; Published: September 3, 2003

Ekta K. Kal

[1]Nagpur Co

The term "nutraceutical" was coined from "nutrition" and "pharmaceutical" in 1989 by Stephen DeFelice, MD, founder and chairman of the Foundation for Innovation in Medicine, in 1989. According to DeFelice, nutraceutical can be defined as, "a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease." However, the term nutraceutical as commonly used in marketing has no regulatory definition.

ABSTRACT

Dr Stephen tion and/or from "Nutri other than term nutrace most of the ing but has ther as anti- define nutrac ered so as to this article. The vo terms, func- guish between functional foods, nutraceuticals, and dietary supplements. The advantages and disadvantages of nutr ticals ar also briefly disc sed.

tional food and nutraceutical.) Thus, a functional food for one consumer can act as a nutraceutical for another cons Examples of nutraceuticals include fortified

BUSINESS BUILDING

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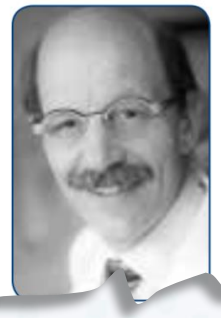
"In a recent national study, 3 out of 4 Americans said they'd prefer to fill their prescriptions in doctor's office instead of pharmacy."

"One study found that new prescriptions for common maintenance medications went unfilled from 20%-30% of the time."

"**Doctors must understand the science behind them** and have a strong conviction that they work."



Patients are focused on health and wellness today more than ever before. Many of our patients are interested in vitamins and nutraceuticals to promote eye health and general well-being, although there are some skeptics who question their effectiveness. With their interest in leading healthier lifestyles, vitamin

consider. In a recent national study, three out of four Americans said that they would prefer to fill their therapeutic prescriptions in a doctor's office instead of having to go to a pharmacy.[2] Unfortunately, most people are not given that choice.

Office-based dispensing guarantees that patients have the recommended or prescribed therapeutic products in hand before leaving the office. Going to a pharmacy, patients always

Vitamin Usage

- About one-third of people aged 18 to 29 years say they regularly take vitamins or mineral supplements.
- Vitamin use increases among older patients, reaching higher than 50% in the 50- to 64-year age group and continuing upward to 68% for seniors.
- Vitamin use increases with education.
- Vitamin use increases with income and is more prevalent among women.

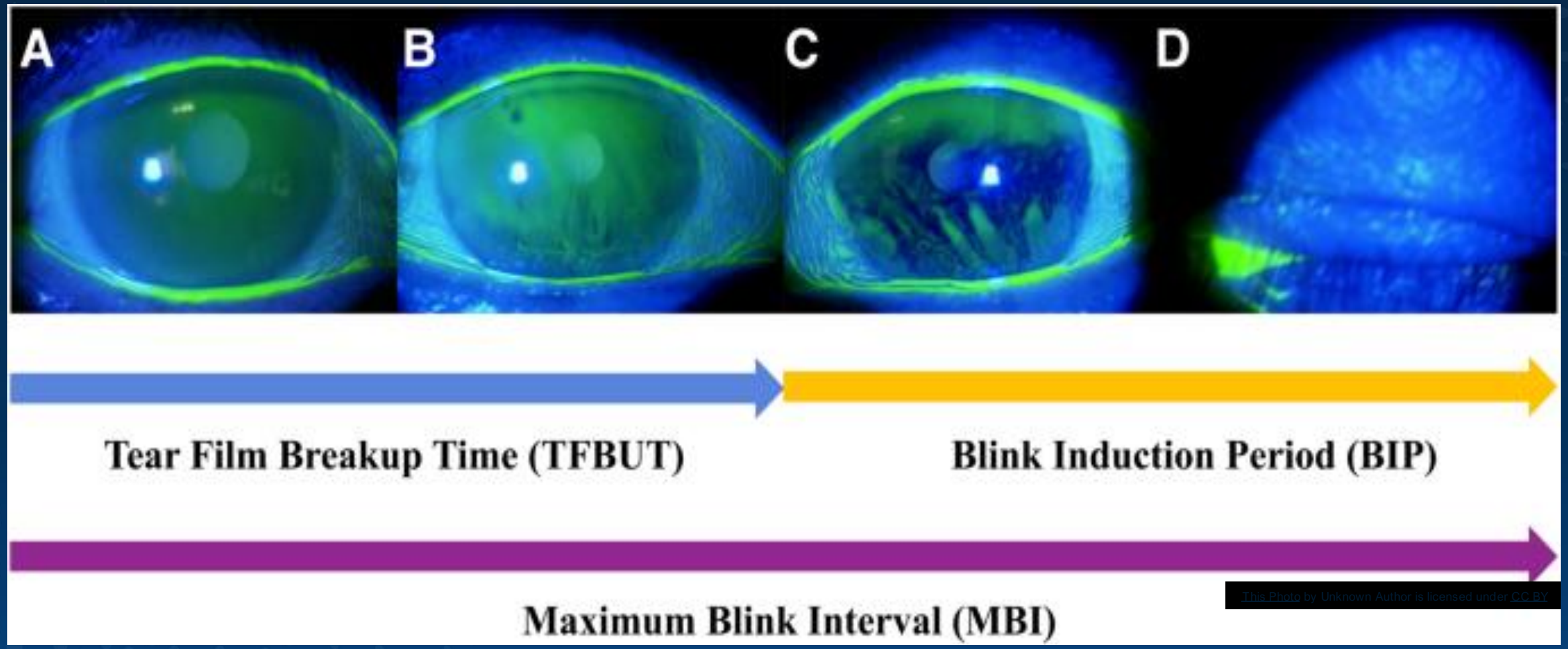
TABLE: DEMOGRAPHIC DIFFERENCES IN VITAMIN USAGE

	Yes, Take a Vitamin (%)	No, Do Not Take a Vitamin (%)
Age		
18-29	36	60
30-49	43	54
50-64	58	41
≥65		
Education		
High School	43	53
Some College	51	48
College Graduate	55	44
Postgraduate	65	34
Household Income ($)		
<24,000	41	59
24,000-60,000	52	48
60,000-90,000	55	46
90,000+	56	44
Sex		
Men	46	52
Women	54	43

Source: Gallup, 2013

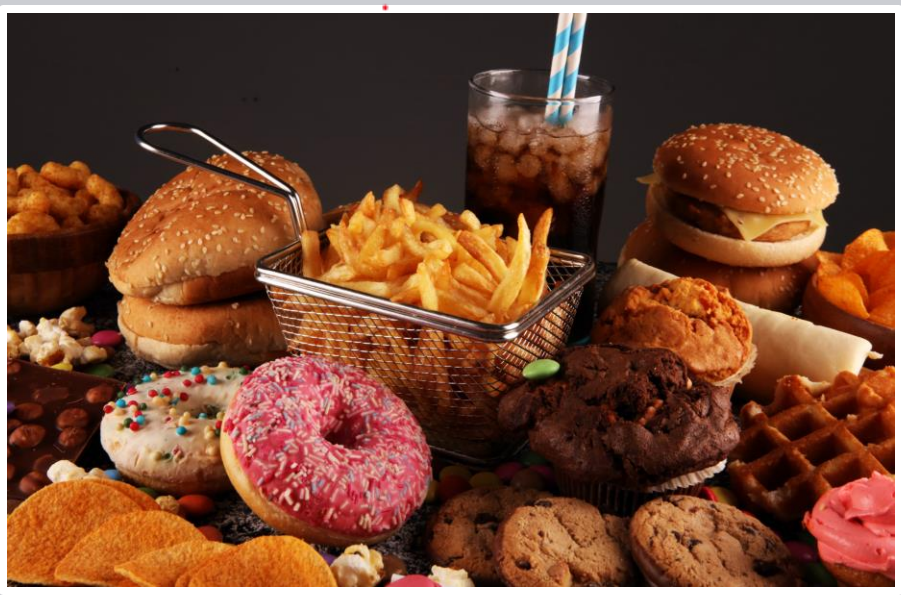
Davis R. *Advanced Ocular Care.* Jan/Feb 2017.

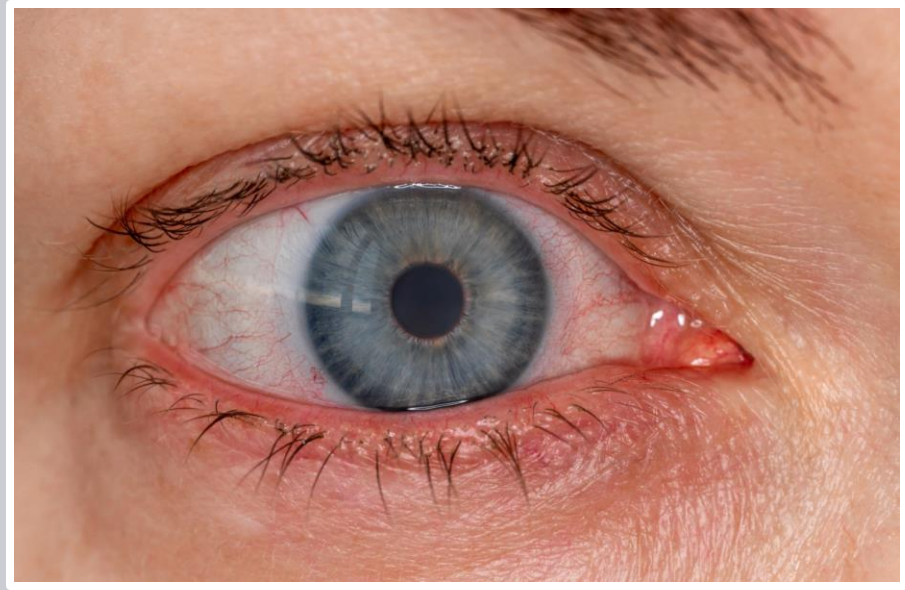
Dry Eye Disease



How Nutrition Can Impact the Severity of Dry Eye Disease

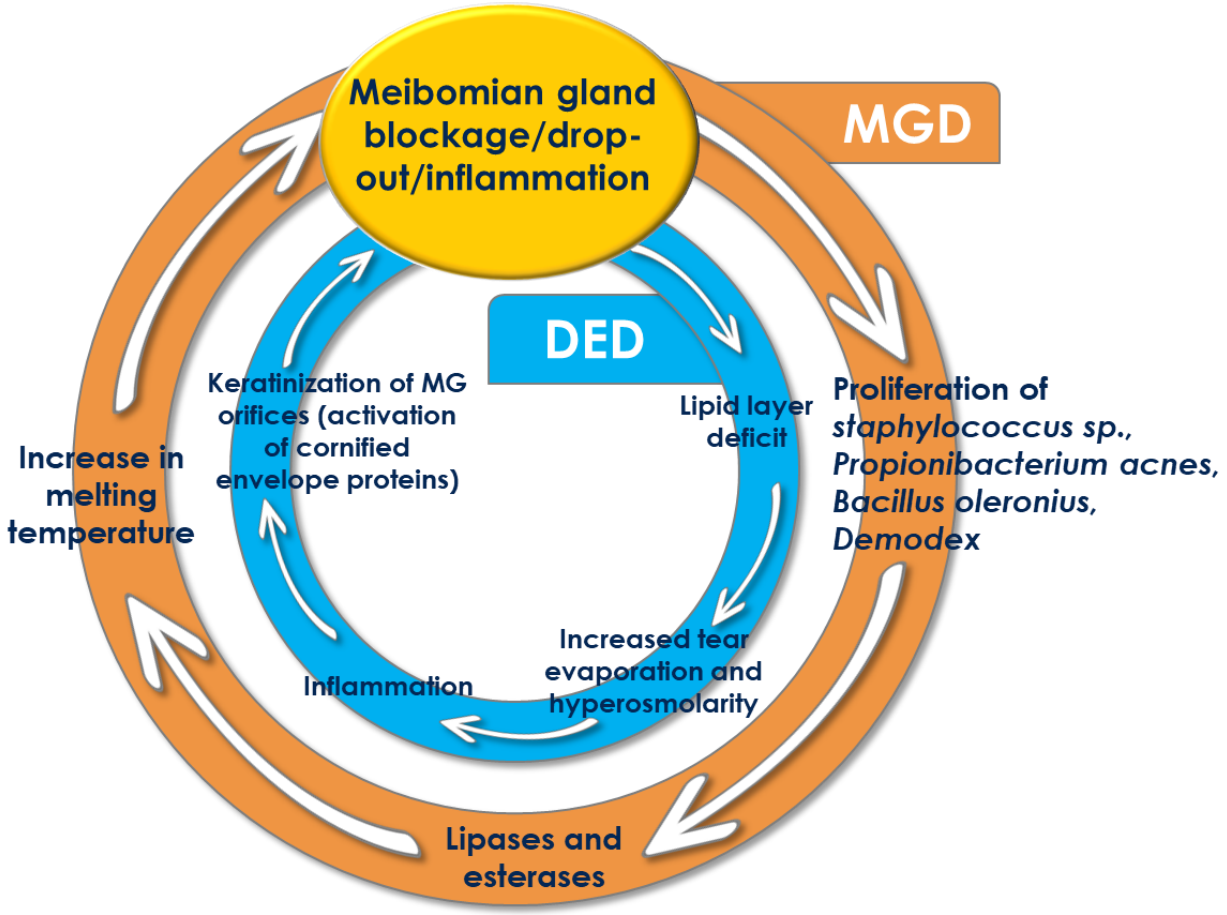
American diet appears to be a major contributor to **meibomian gland dysfunction** and **dry eyes.**





Markoulli M, et al. *Ocul Surf*. 2023;29:226-271.

Mechanism of Disease



- Lipids from meibomian glands necessary for ocular surface health and integrity.[1]
- Blocked meibomian glands lead to gland dilation, atrophy, low secretion, gland dropout, and compromised tear film.[1]
- **Meibomian gland health is integral to a healthy tearfilm.[2]**

MGD = meibomian gland dysfunction.

1. Baudouin C, et al. *Br J Ophthalmol*. 2016;100(3):300-306; 2. Zhang X, et al. *Int J Mol Sci*. 2017; 18(7):1398.

Study Finds Most US Adults and Children Have Low Blood Serum Levels of Omega-3s

- 2/3 of US adults and 95% of US children do not consume enough omega-3s in their daily diet to meet their nutritional needs.
- Essential omega-3s reduce inflammation in the body and prevent disease.
- Chronic DED is a disease of inflammation.
- "*Healthcare practitioners need to ensure their patients are consuming enough omega-3 fatty acids in their daily diet, and if they are not, they need to* ***consider the role of supplementation***…"

Murphy RA, et al. *BMJ Open.* 2021;11:e043301.

Relation Between Dietary N-3 And N-6 Fatty Acids and Dry Eye Syndrome in Women

- 32,470 female health professionals in the WHS aged 45-84 years evaluated for ω-3 intake and incidence of DED.
- Higher intake of n-3 FAs associated with decreased incidence of DED in women.
- Findings consistent with anecdotal clinical observations and postulated biological mechanisms.

Table: Relative risks of DES among WHS participants according to dietary intake of n-3 and n-6 FAs

Quintile of dietary intake (mean intake)	No. of subjects	No. with DES	Model 1:[1] OR (95% CI)
	n	*n*	
n−3 Fatty acids			
Quintile 1 (0.92 g)	6473	329	1.0
Quintile 2 (1.17 g)	6396	296	0.89 (0.76, 1.05)
Quintile 3 (1.34 g)	6606	318	0.92 (0.78, 1.08)
Quintile 4 (1.55 g)	6572	314	0.90 (0.76, 1.06)
Quintile 5 (1.99 g)	6423	289	0.83 (0.70, 0.98)
P for trend			0.05
n−6 Fatty acids			
Quintile 1 (7.15 g)	6447	329	1.0
Quintile 2 (9.12 g)	6498	304	0.92 (0.78, 1.09)
Quintile 3 (10.50 g)	6512	306	0.95 (0.80, 1.12)
Quintile 4 (12.03 g)	6516	307	0.94 (0.78, 1.12)
Quintile 5 (15.25 g)	6497	300	0.91 (0.75, 1.11)
P for trend			0.72

ω-3 = omega-3; FAs = fatty acids; WHS = Women's Health Study

Miljanović B, et al. *Am J Clin Nutr.* 2005;82(4):887-893.

Decreasing Ocular Surface Inflammation

Omega-3 Fatty Acids

- Decrease inflammation; increase quality of tear film[1]
- Reduction of dry eye symptoms[1]
- Faster epithelial healing and visual recovery with PRK[2]
- Regeneration of corneal nerves[3]

PRK = photorefractive keratectomy.

1. Epitropoulos AT, et al. Cornea. 2016;35(9):1185-1196; 2. Ong NH, et al. Cornea. 2013;32(6):761-765;
3. He J, et al. Prostaglandins Leukot Essent Fatty Acids. 2010;82(4-6):319-325.

Highlights from TFOS Lifestyle Reports

Omega-3 Fatty Acids

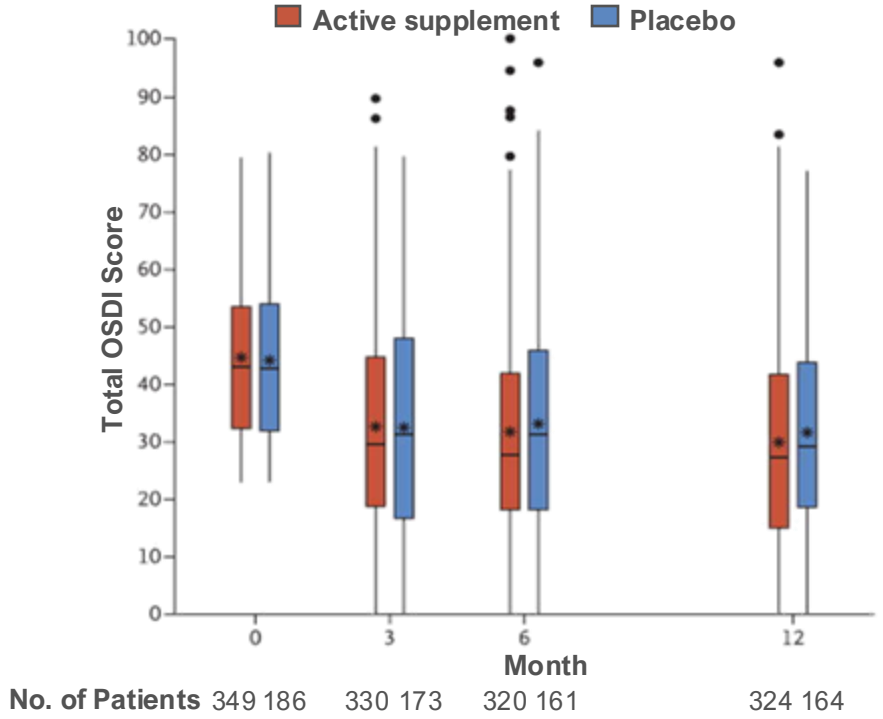
- A higher ratio of omega-6s to omega-3s found to be proinflammatory; lower ratio anti-inflammatory.
- Increasing omega-6 intake conferred ~2.5x's higher risk for dry eye symptoms.
- Every gram of omega-3 consumed associated with a 30% reduction in dry eye risk.
- The **ideal ratio of omega-3 to omega-6 reported was 4:1**

Craig JP, et al. *Ocul Surf*. 2023:30:240-253.

DREAM Study

Omega-3 supplementation in moderate-to- severe DED

- Prospective, multi-center, double masked RCT
- 535 patients: 349 active group; 186 placebo group
- 3g omega-3 vs 5g olive oil (placebo)
- 2:1 ratio of EPA to DHA
- Omega-3s in re-esterified triglyceride form
- Primary Outcome: Change from baseline in OSDI score at 6 and 12 months



Found omega-3 supplements to be no more effective than placebo in DED.

DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; OSDI = ocular surface disease index; RCT = randomized clinical trial

Dry Eye Assessment and Management Study Research Group, et al. *N Engl J Med*. 2018;378(18):1681-1690.

Uncontrolled Study = "Real World"?

Only 6% of patients met a more focused traditional definition of DED.

Patients were allowed to use a wide variety of other therapies:

- Artificial tears and gels (79.4%)
- Cyclosporine drops (38%)
- Warm soaks (22.9%)
- Lid scrubs or baby shampoo (16%)
- **Omega-3s: up to 1200 mg/day**
- Systemic medications that cause dryness
- Systemic steroids
- Other immune suppressive agents

Tx compared with baseline	Omega-3	Placebo
Stopped ≥1 treatment	53%	57%
No change	25%	22%
Changed ≥1 treatments	12%	13%
Added Treatments	10%	8%
Patients who changed treatments, %	75%	78%

Tx = treatment.

Dry Eye Assessment and Management Study Research Group, et al. *N Engl J Med*. 2018;378(18):1681-1690.

Misleading Headlines

Patients find cherry-picked headlines when they search online.

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NEWS RELEASES

Friday, April 13, 2018

Omega-3s from fish oil supplements no better than placebo for dry eye

NIH-funded study finds omega-3 fails to yield beneficial results in the clinic.

Institute/Center

National Eye Institute (NEI)

Contact

National Eye Institute

301-496-5248

AMERICAN
OF OPHTHA

For Ophthalmologists For Practice

JUN 17, 2022

Week in revie
dry eye, early-onset glaucoma predictors, new femto laser cataract system

By Stephanie Leveene, ELS

Cataract/Anterior Segment, Comprehensive Ophthalmology, Cornea/External Disease, Glaucoma

A weekly roundup of ophthalmic news from around the web.

No need to take those fish oil pills if you have dry eye disease. An ancillary study of the randomized, double-blind, placebo-controlled Vitamin D and Omega-3 Trial (VITAL), VITAL-Dry Eye evaluated the role of vitamin D and marine omega-3 fatty acid supplements in incident dry eye disease (DED). Patients included in VITAL-Dry Eye were those enrolled in VITAL who had not been previously diagnosed with DED or who were not currently experiencing dry eye symptoms. Over a median of 5.3 years, there was no difference in diagnosed DED or in incident DED plus incident severe DED symptoms between those given omega-3 fatty acids (1 g/day) and those given placebo. Therefore, the authors conclude that "These results do not support recommending marine omega-3 fatty acid supplementation to reduce the incidence of DED." *JAMA Ophthalmology*

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Feedback

DRY EYE

Marine ω-3 fatty acid supplementation doesn't reduce DED incidence

Conflicting Data???

What do we tell our patients? We have to follow the science and be evidence-based in our recommendations…

Bhargava 2023 - India Study

O3FA Group (n=470)

Placebo Group (n=480)

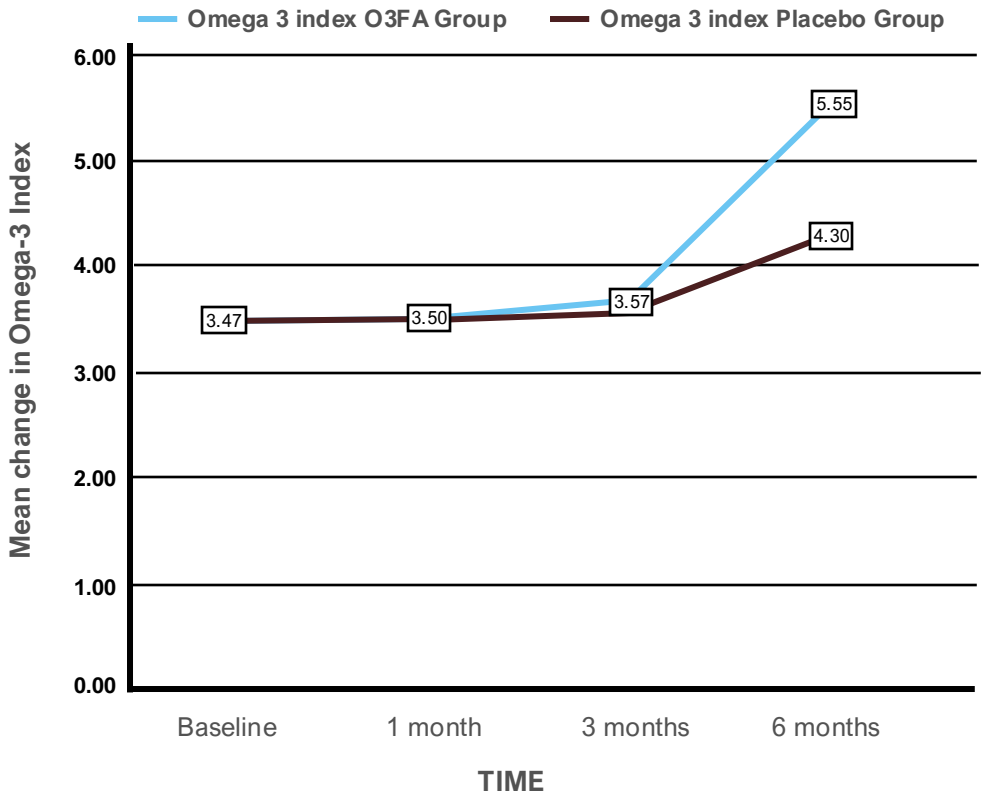
2.4 g omega-3 (1.5:1 ratio of EPA to DHA) BID for 6 months

Olive oil BID for 6 months

Patients evaluated at baseline, 1 month, 3 months, and 6 months

Primary outcome:
Change from baseline in omega-3 index

Secondary outcome:
Change from baseline in dry eye symptoms, Schirmer, TBUT, TFO, Nelson grade and Goblet cell density

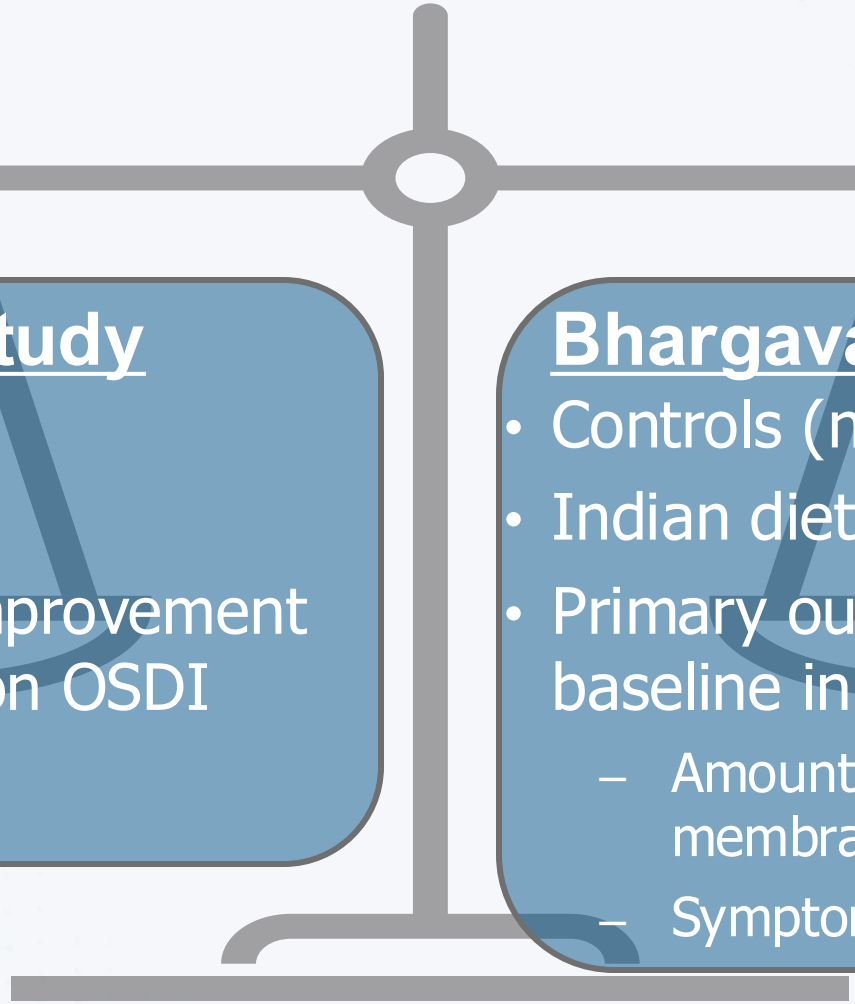


Omega-3 fatty acids are effective in relieving dry eye indices in symptomatic VDT users

BID = twice daily; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; VDT = video display terminal.

Bhargava R, et al. *Indian J Ophthalmol*. 2023;71(4):1619-1625.

DREAM Study vs India Study



DREAM Study

- Controls (n=186)
- American diet
- Primary outcome: Improvement in symptoms based on OSDI scale

Bhargava 2023 – India Study

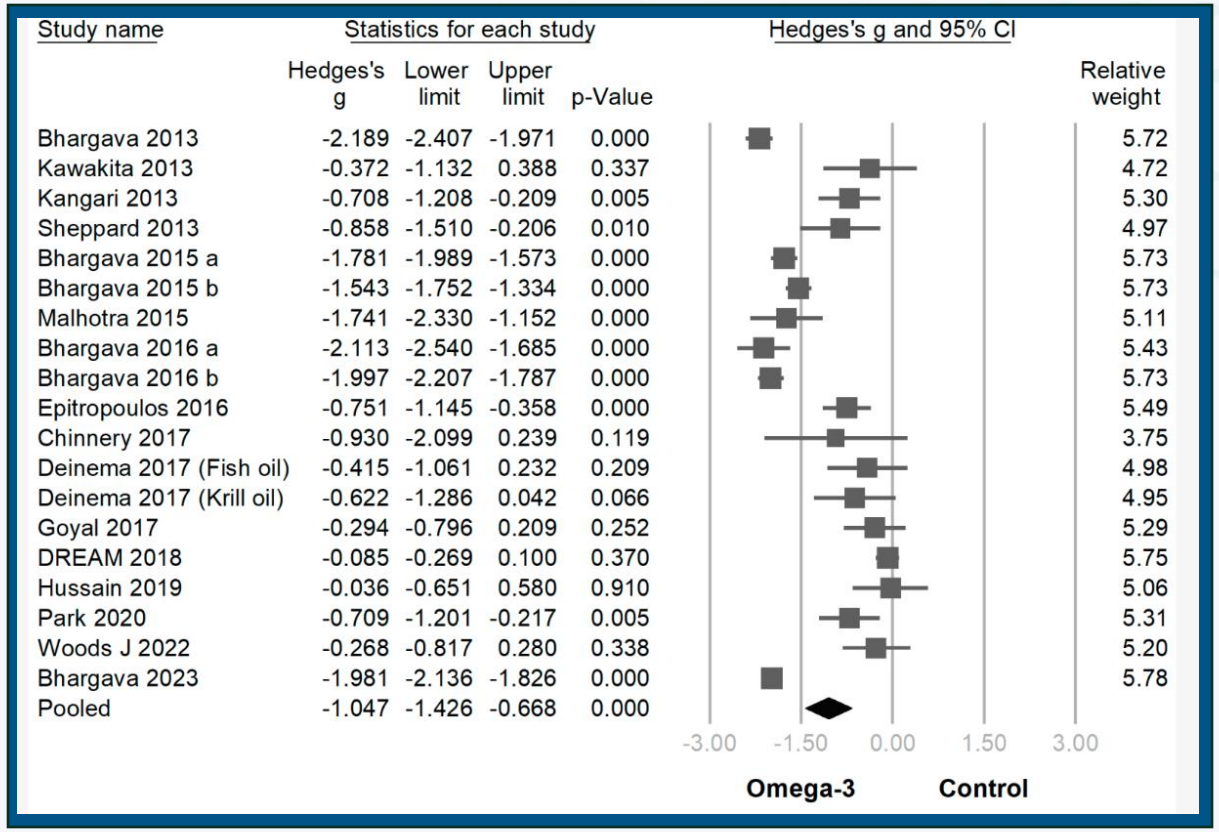
- Controls (n=480)
- Indian diet
- Primary outcome: Change from baseline in omega-3 index
  - Amount of EPA and DHA in the RBC membranes
  - Symptom scale as secondary outcome

OSDI = Ocular Surface Disease Index; RBC = red blood cell.

Bhargava R, et al. *Indian J Ophthalmol*. 2023;71(4):1619-1625.

Omega-3 Intake in Managing Dry Eye Disease: 2023 Systematic Review and Meta-Analysis of RCTs

- 19 RCTs; 4246 subjects with different types of DED
- Omega-3s significantly alleviated symptoms
  - Confirmed by dry eye scores, TBUT, Schirmer test, osmolarity, and CFS
- Statistical significance consistent across sensitivity analysis.
- Treatment duration, dosage, and percentage of EPA correlated with more substantial decrease in symptoms and improvement in outcome measures.



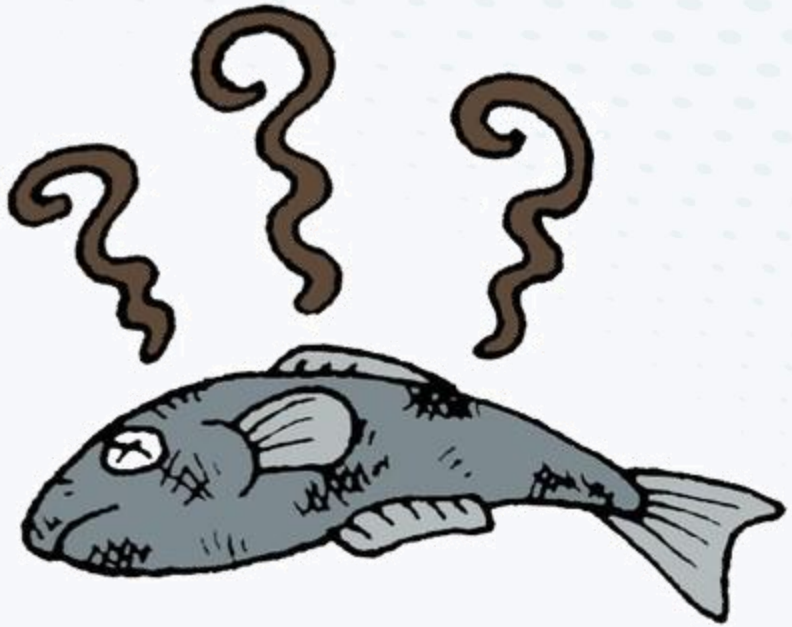
Conclusion: Omega-3 FA supplementation is suggested for clinical use in the management of DED.

CFS = corneal fluorescein staining

Wang WX, et al. *J Clin Med*. 2023;12(22):7026.

Quality Matters: Rancidity Analysis of Marine and Microalgal Oil Omega-3's

- 72 OTC omega-3 supplements sampled from 2014 – 2020
- Most were found to be oxidized and/or rancid
- 68% of the flavored supplements and 13% of the unflavored supplements exceeded TOTOX upper limit
- Fishy odors were noted in the rancid supplements



OTC = over-the-counter; TOTOX = total oxidation value

Hands JM, et al. *J Diet Suppl*. 2024;21(2):195-206.

First, Do No Harm

- The STRENGTH, OMEMI, and REDUCE-IT studies have shown a small risk for new-onset atrial fibrillation associated with high doses of omega-3s.
- No increased incidence of stroke was observed in these trials.
- Clinicians should consider the relatively small increased risk for new-onset atrial fibrillation when prescribing any high-dose omega-3 formulations
- **A less bioavailable, synthetic ethyl ester was used in these studies (*not* the triglyceride form found in our diets and some other supplements).**

Nicholls SJ, et al. *JAMA*. 2020;324(22):2268-2280; Kalstad AA, et al. *Circulation*. 2021;143(6):528-539; Byatt DL, et al. *N Engl J Med.* 2019;380(1):11-22.

Omega-3 Takeaways

- Fatty fish (which are abundant in anti-inflammatory omega-3s) twice a week is recommended for cardiovascular, neurological, and ocular health (SMASH: salmon, mackerel, anchovies, sardines, herring).
- Omega-3s have been shown in studies to decrease ocular surface inflammation, increase quality of the tear film, reduce dry eye symptoms, regenerate corneal nerves, and promote faster epithelial healing and visual recovery with PRK.
- The type, amount, and duration of omega-3 supplementation matter. Oxidation and rancidity have been found in many commercial products.
- Conflicting data exist on the benefits of omega-3 supplementation in dry eyes (DREAM study).
- Very slight risk for atrial fibrillation in patients who have never experienced it before???

Other nutrients have been shown to decrease ocular surface inflammation.

Other Nutrients Have Been Shown to Decrease Ocular Surface Inflammation

Vitamins A and C

Vitamin A

Deficiency can lead to DED by causing goblet cell loss, leading to mucin deficiency and corneal epitheliopathy. Long-term deficiency may result in metaplasia and the keratinization of the corneal and conjunctival epithelial cells. Supplementation has been shown to be helpful for improving ocular surface damage and DED.

Vitamin C

Present in every ocular tissue at 20x to 30x serum concentration, vitamin C has antioxidant, anti-inflammatory, and immunomodulatory functions, which can be helpful for the prevention of DED. It has a therapeutic role in corneal wound repair. An experimental study using a rat model recently showed that vitamin C improved corneal edema and alleviated inflammation after corneal injury caused by ultraviolet B exposure.[1] A recent study by Nguyen et al. showed that oral vitamin C supplementation slightly increased the risk for DED.[2]

Hyon JY, et al. *Applied Sciences*. 2022;12(9). Accessed June 10, 2024. https://www.mdpi.com/2076-3417/12/9/4567;
Nguyen L, et al. *Invest Ophthal Vis Sci*. 2023;64(8). Accessed June 10, 2024. https://iovs.arvojournals.org/article.aspx?articleid=2790799

Effects of Vitamin A on Tear Film in Dry Eye

Clinical Ophthalmology

Dovepress

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ORIGINAL RESEARCH

Effects of short-term oral vitamin A supplementation on the ocular tear film in patients with dry eye

This article was published in the following Dove Medical Press journal:
Clinical Ophthalmology

Saud A Alanazi
Gamal A El-Hiti
Abdulaziz A Al-Baloud
Mohamed I Alfarhan
Ammar Al-Shahrani
Abdulkareem A Albakri
Saad Alqahtani
Ali M Masmali

Cornea Research Chair, Department of Optometry, College of Applied Medical Sciences, King Saud University, Riyadh 11433, Saudi A...

Objective: To investigate the effects of short-term oral vitamin A supplementation on the ocular tear film in patients with dry eye.

Methods: In total, 30 male patients with dry eye (age range, 18–38 years; mean age, 25.2±2.8 years) who did not wear contact lenses or exhibit any ocular (other than dry eye) or systemic diseases were included, along with 30 age-matched men (control group; mean age, 24.5±2.3 years) with healthy eyes. Subject exclusion was based on the findings of the McMonnies questionnaire (cutoff score for dry eye: 14.5) and slit-lamp biomicroscopy. All subjects received an oral vitamin A supplement at a daily dose of 1,500 mg for 3 consecutive days. The phenol red thread (PRT) test was performed along with assessments of tear ferning (TF), tear osmolarity, and the tear break-up time (TBUT) before and 24 hours after the third dose of the vitamin A supplement. A 10-minute interval was observed between different tests.

Resu... the dry eye group, the TF grade (Wilcoxon test, $P=0.01$) exhibited a signif...

Test	Before vitamin A	After vitamin A
TF*	2.4 (0.5)	1.4 (1.1)
PRT (mm)	27.9 (5.8)	30.7 (4.2)
TBUT (s)	7.8±3.3	8.8±4.5
Osmolarity* (mOsm/L)	293.0±8.9	303.0±9.3

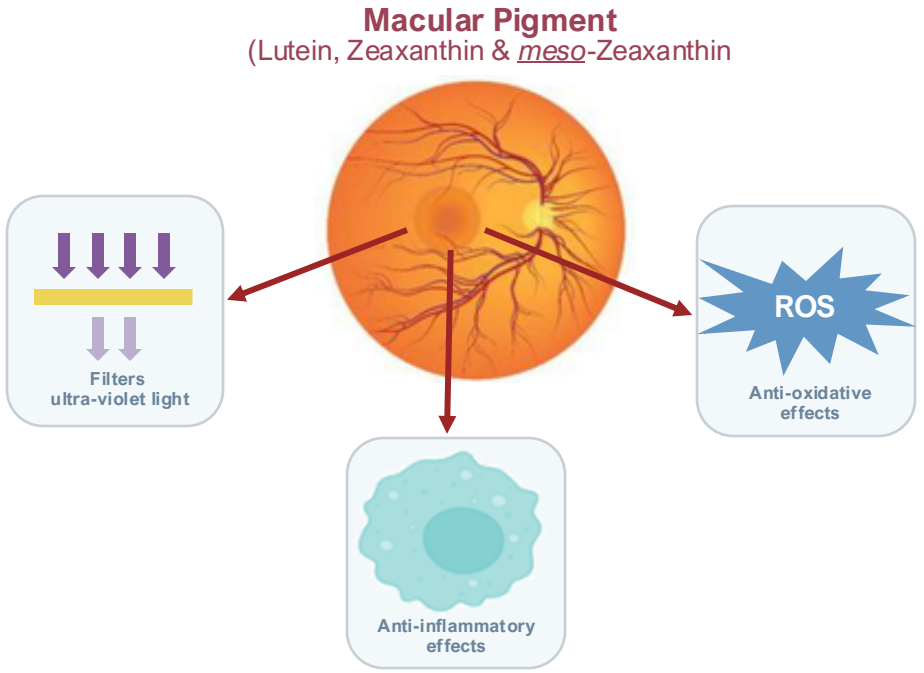
Table: TF grades, PRT test results, TBUT values, and osmolarity values for patients with dry eye who received short-term vitamin A supplementation

PRT = phenol red thread; TBUT = tear break-up time; TF = tear ferning.
Alanazi SA., et al. *Clin Ophthalmol*. 2019;13:599-604.

Profound xerophthalmia due to vitamin A deficiency

Lutein and Zeaxanthin

- Antioxidant and anti-inflammatory nutrients that defend against free radicals and oxidative stress
  - Modulate gene expression related to inflammation and cytokine production
- Mitigate the inflammatory response within ocular tissues
- Linked to the reduction of factor D
  - Enzyme associated with the alternative complement activation pathway
- Contribute to regulating systemic inflammation



Addo EK, Bernstein PS. Carotenoids in eye health. Review of Presbyopia and the Aging Eye. Ocular Health and Wellness Supplement 2024

Vitamin D

- Potent modulator of the innate and adaptive immune system in the eye.
- Inhibits corneal inflammation by:
  - Suppressing the migration of Langerhans cells into the cornea
  - Curbing the excessive production of proinflammatory mediators (i.e., IL's and TNF-α)
- Significant association between low serum concentrations of vitamin D and DED occurrence has been established.

Table: Effects of vitamin D treatment on ocular surface parameters

		After vitamin D supplementation				
	Baseline	8 weeks		12 weeks		24 weeks	
	Mean ± SD	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Eyelid margin score	1.65 ± 1.27	1.60 ± 1.24	0.160	1.33 ± 1.02	0.000*	1.28 ±1.01	0.000*
Meibomian gland expressibility score	0.93 ± 0.94	0.83 ± 0.81	0.044*	0.73 ± 0.78	0.003*	0.70 ± 0.79	0.005*
Oxford grading	0.55 ± 0.68	0.43 ± 0.59	0.058	0.33 ± 0.57	0.002*	0.33 ± 0.57	0.002*
Schirmer I tear secretion test (mm)	13.10 ± 8.01	15.03 ± 7.80	0.002*	16.55 ± 7.26	0.000*	17.33 ± 7.29	0.000*
TBUT (s)	5.53 ± 3.12	6.90 ± 2.72	0.000*	8.30 ± 2.66	0.000*	9.13 ± 3.01	0.000*
Tear osmolarity	307.4 ± 15.4	304.1 ± 11.8	0.000*	303.5 ± 12.1	0.000*	302.7 ± 10.6	0.000*
OSDI score	36.4 ± 22.1	27.40 ± 18.2	0.000*	21.97 ± 13.9	0.000*	19.12 ± 11.9	0.000*

Vitamin D replacement appears to improve ocular surface health in patients with vitamin D deficiency

IL's = interleukins; TNF-α = tumor necrosis factor alpha.

Rolando M, et al. *Int J Mol Sci*. 2023;24(2):1458; Karaca EE, et al. *Arq Bras Oftalmol*. 2020;83(4):312-317.

Curcumin

- Restores the balance of the ocular surface by:
  - Diminishing the presence of ROS
  - Suppressing the expression of inflammatory mediators
  - Enhancing the levels of neurotrophic factors
- Curcumin tablets as a replacement for tear substitutes for DED demonstrated significant improvements in Schirmer testing, OSDI, TBUT, SPEED, ocular staining scores, tear osmolarity, and MMP-9.
- Reduced frequency of artificial tear use compared with placebo.

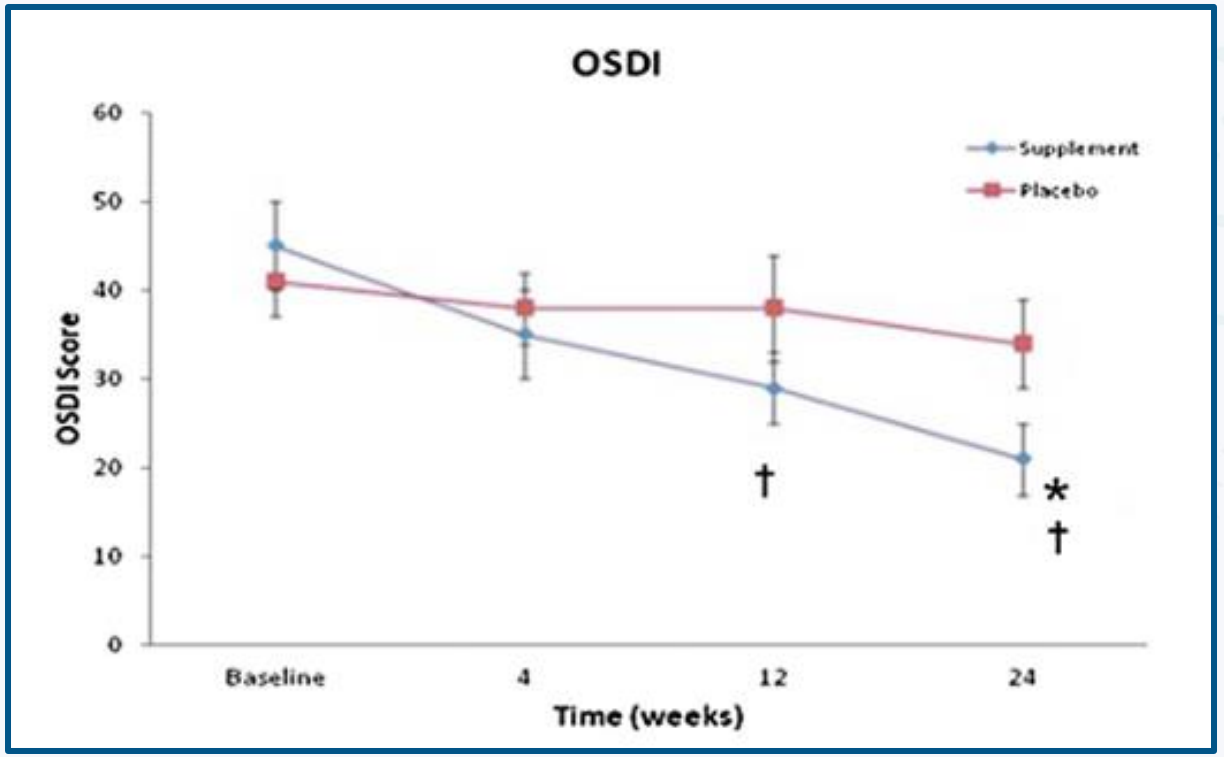
Addition of a curcumin supplement in DED may facilitate a greater improvement in ocular discomfort symptoms than tear substitutes alone, **especially in severe cases**

MMP-9 = matrix metalloproteinase-9; ROS = reactive oxygen species; SPEED = Standard Patient Evaluation of Eye Dryness.
Radkar P, et al. Ophthalmol Ther. 2010;10(3):581-599. Borselli, M. et al. Front. Ophthalmol. 2023;3:1236525.

Nutrients Act Synergistically

Long-term Supplementation with GLA and n-3 PUFAs Improves Moderate-to-Severe Keratoconjunctivitis Sicca

- Multicenter, double-masked placebo-controlled RCT
- 38 patients (both eyes) with tear dysfunction
- Randomized to **supplemental GLA + n-3 PUFAs** or placebo for 6 months and assessed at baseline, 4, 12, and 24 weeks.
- Efficacy outcomes/parameters: OSDI, Schirmer test, TBUT, conjunctival fluorescein and lissamine green staining, and topographic corneal smoothness indexes



Supplemental GLA and n-3 PUFAs for 6 months improved ocular irritation symptoms, maintained corneal surface smoothness, and inhibited conjunctival dendritic cell maturation in patients with keratoconjunctivitis sicca.

†Significant improvement when compared to baseline; *Significant improvement compared to placebo

Sheppard JD Jr, et al. *Cornea*. 2013;32(10):1297-1304.

Kan 2020: Botanical Formula Improves Eye Fatigue and Dry Eye

- Double-blind, placebo-controlled RCT.
- Participants: 360 patients with self-reported eye fatigue symptoms
- Assigned to 1 of 4 arms:
  - Placebo, 6 mg, 10 mg or 14 mg of botanical formula QD for 90 days.
- Supplement consisted of **lutein ester, zeaxanthin, and extracts of blackcurrant, chrysanthemum, and goji berry**
- Participants had 3 visits: Baseline, 45 days, and 90 days

Table: Differences in keratography results at baseline and 90 d

		6-mg group, n = 69		
Outcome	**Eye**	**V1**	**V3**	***P* value for visit**
First tear break-up time, s	Left	6.20 ± 3.08	6.92 ± 3.42	0.0002
	Right	5.93 ± 3.38	6.59 ± 3.45	
Average tear break-up time, s	Left	7.97 ± 2.81	8.69 ± 3.19	0.001
	Right	7.71 ± 3.12	8.29 ± 3.45	
Tear meniscus height, mm	Left	0.19 ± 0.06	0.21 ± 0.06	0.0003
	Right	0.21 ± 0.08	0.22 ± 0.08	

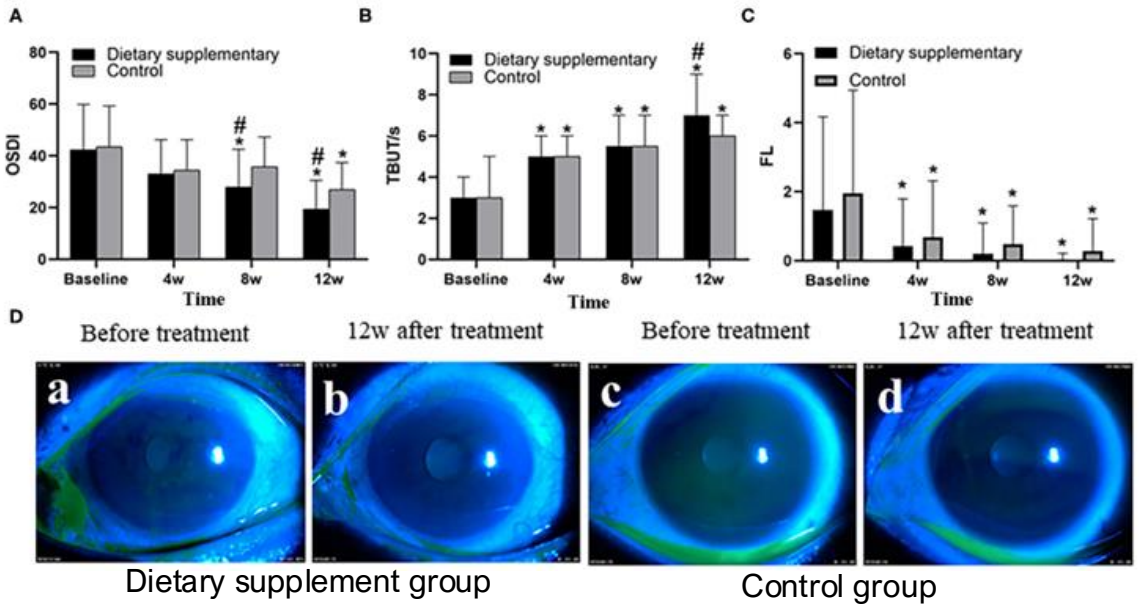
Novel botanical formula could improve eye fatigue symptom scores, visuognosis persistence, Schirmer test, and MPOD.

d = days; QD = once daily

Kan J, et al. *Am J Clin Nutr*. 2020;112(2):334-342.

Liu 2021: Supplement Blend Improved Dry Eye Symptoms in MGD

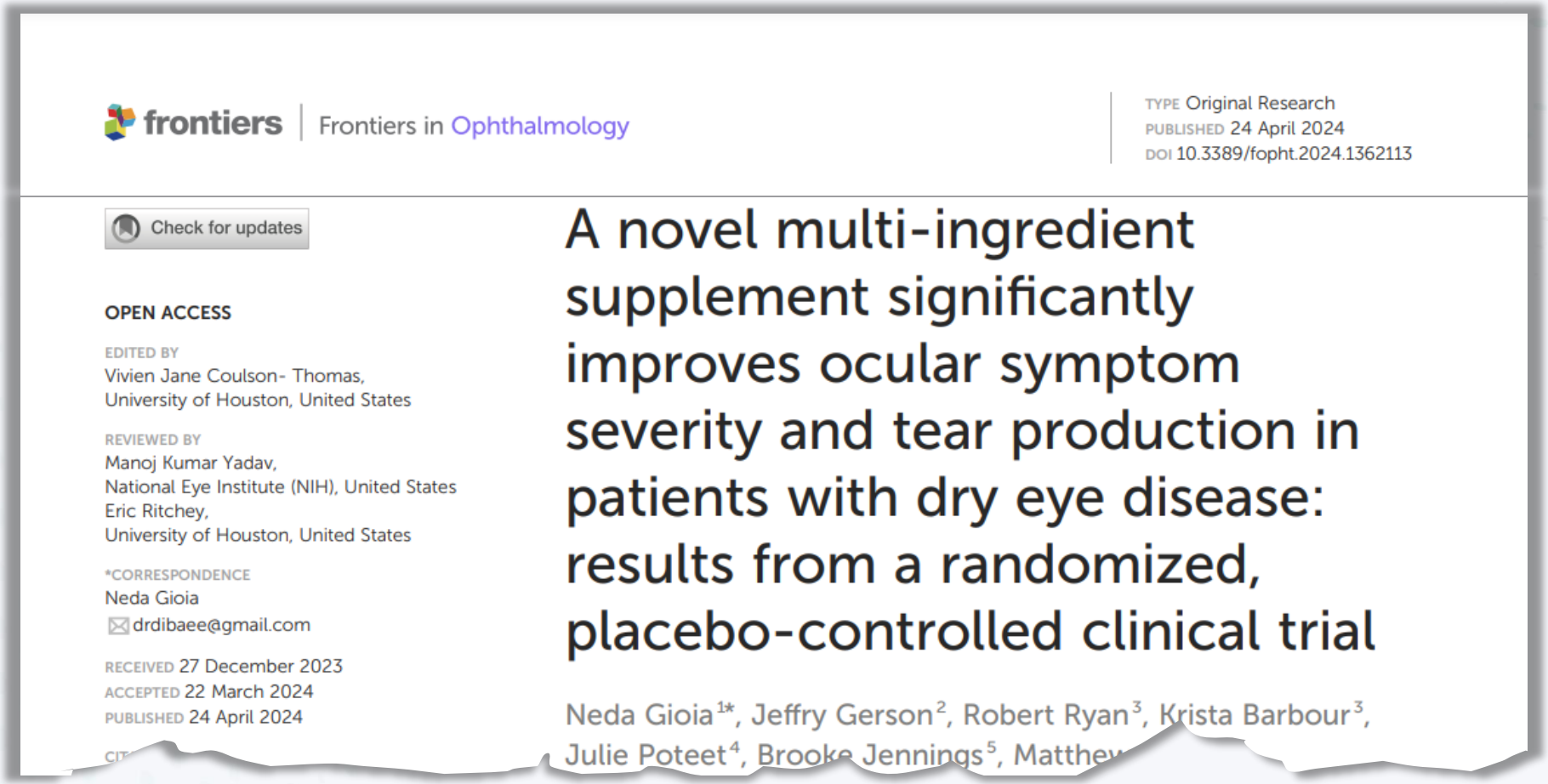
- Prospective, randomized, placebo-controlled study recruited 60 patients with MGD-related dry eye
- Subjects were treated with eye hot compress, artificial tears, and antibiotic ointment.
- Received dietary supplement or placebo daily for 12 weeks.
  - Supplement ingredients include **omega-3, lutein, aronia extract, vitamin C, and vitamin E**
- Patients were assessed at 4, 8, and 12 weeks after the treatment.



Addition of dietary supplement can improve dry eye, reduce the inflammatory response of MG, restore glandular structure, and improve visual quality without systemic or local adverse reactions

Liu K., et al. *Front Med (Lausanne)*. 2021;8:769132.

Gioia, et al. 2024: A Combination of Nutrients Successfully Treats Dry Eyes in RCT



frontiers | Frontiers in Ophthalmology

TYPE Original Research
PUBLISHED 24 April 2024
DOI 10.3389/fopht.2024.1362113

Check for updates

OPEN ACCESS

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RECEIVED 27 December 2023
ACCEPTED 22 March 2024
PUBLISHED 24 April 2024

A novel multi-ingredient supplement significantly improves ocular symptom severity and tear production in patients with dry eye disease: results from a randomized, placebo-controlled clinical trial

Neda Gioia[1*], Jeffry Gerson[2], Robert Ryan[3], Krista Barbour[3], Julie Poteet[4], Brooke Jennings[5], Matthe

Gioia N, et al. Front Ophthalmol. April 23, 2024. Accessed June 10, 2024. https://www.frontiersin.org/journals/ophthalmology/articles/10.3389/fopht.2024.1362113/full

Gioia, et al. 2024: A Combination of Nutrients Successfully Treats Dry Eyes in RCT

Study Design

- Double-blind, placebo-controlled, parallel, multicenter RCT
- 116 healthy participants: 40%-47% males
- Aged 18-65 years: mean, 41.53 years (treatment group), and 42.17 years (placebo group)
- 56-day study (8 weeks)
- **Intervention:**
- **20 mg lutein, 4 mg zeaxanthin isomers, 200 mg curcuminoids, 600 IU vitamin D3**
- Placebo: **Soybean oil**
- Study visits: Days 14, 28, 56

Parameter	What was measured
Eye hydration and moisture	Tear volume, breakup time, osmolarity
Discomfort and inflammation	Symptom severity (OSDI score), symptom progression (SPEED score), ocular surface damage (corneal/conjunctival staining), tear inflammation (MMP-9)
Use of artificial tears	Number of patients using AT and frequency of use of AT (times/day)

Gioia N, et al. *Front Ophthalmol*. April 23, 2024. Accessed June 10, 2024. https://www.frontiersin.org/journals/ophthalmology/articles/10.3389/fopht.2024.1362113/full

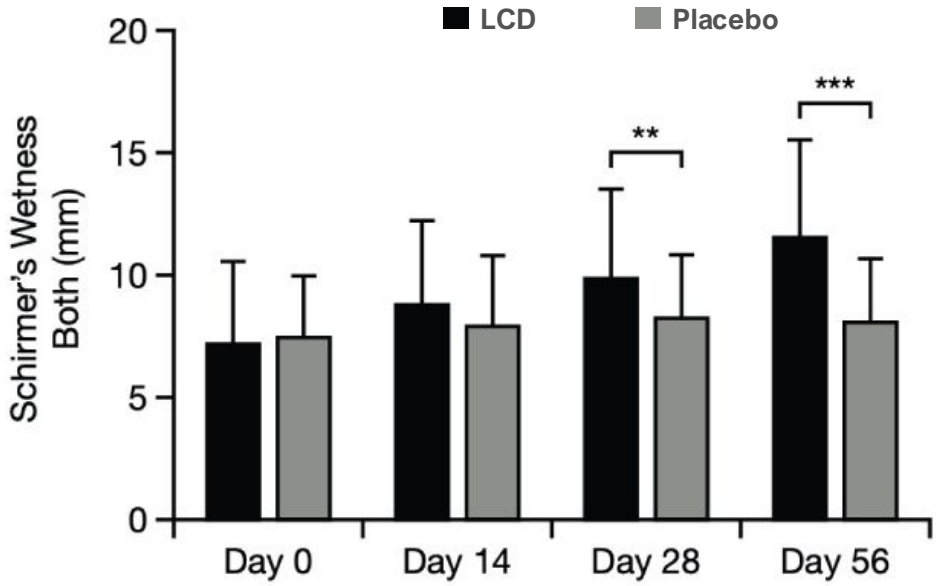
Gioia 2023: A Combination of Nutrients Successfully Treats Dry Eyes in RCT

Parameter	Primary outcome
Tear volume	Mean tear volume of both eyes was significantly better in the treatment group than in the placebo group at days 28 and 56 ($P<0.05$ and $P<0.001$, respectively)
OSDI total scores	Improvement from baseline in total OSDI score was significantly better (lower scores) in the treatment group than in the placebo group by day 14 ($P<0.001$)

Parameter	Secondary outcome
TBUT	Mean TBUT values were significantly improved in the treatment group compared with the placebo group by day 56 ($P<0.001$)
Tear osmolarity	Tear osmolarity (measured by TearLab Osmolarity system) was significantly improved in the treatment group vs the placebo group at day 56 ($P<0.001$)
Inflammatory biomarker: MMP-9	Incidence of positive MMP-9 decreased from baseline in the treatment group but did not decrease for the placebo group (measured using InflammaDry)
SPEED scores	Treatment group saw significantly reduced progression of symptoms by day 14 with symptom reduction increasing continuously to day 56

Gioia N, et al. *Front Ophthalmol*. April 23, 2024. Accessed June 10, 2024. https://www.frontiersin.org/journals/ophthalmology/articles/10.3389/fopht.2024.1362113/full

Combination of Nutrients Successfully Treats Dry Eyes: Summary of RCT



- Increased tear volume and stability
- Reduced tear osmolarity
- Improved ocular surface structure with less inflammation
- Reduced dry eye discomfort
- Treatment did not significantly alter blood safety metrics or resting vital signs and was well tolerated

Significant and clinically meaningful benefits for the management of dry eye symptoms vs placebo

LCD = lutein, zeaxanthin isomers, curcumin, and vitamin D3

Gioia N, et al. *Front Ophthalmol*. April 23, 2024. Accessed June 10, 2024. https://www.frontiersin.org/journals/ophthalmology/articles/10.3389/fopht.2024.1362113/full

Conclusions

- Dry eye disease is a multifactorial, chronic, common problem that significantly impacts quality of life
- Poor diet is one of the leading causes of dry eye disease
- Omega-3 fatty acids are anti-inflammatory but inconsistent data exist on the efficacy of omega-3 supplements in the treatment of dry eye disease
- Other nutrients have been shown in clinical studies to be effective treatments for dry eye symptoms and signs

From the Front of the Eye to the Back:

Nutraceuticals and diet for macular degeneration and beyond

Leafy Greens as the “Carrots” of Healthy Vision

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

The inflammatory potential of diet is associated with the risk of age-related eye diseases

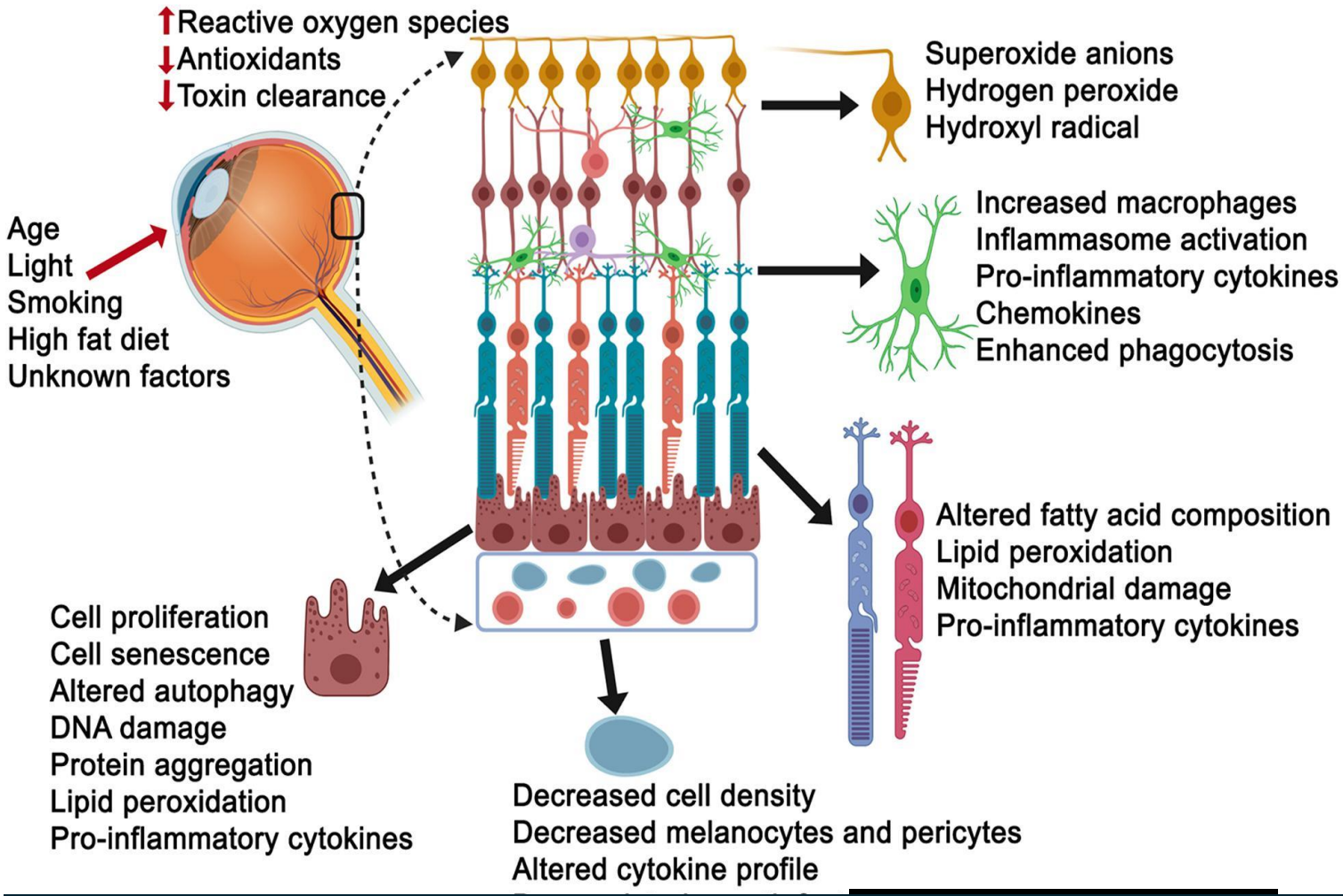
Joëlle E. Vergroesen [a, b], Eric F. Thee [a, b, c], Tosca O.E. de Crom [b], Jessica C. Kiefte-de Jong [d], Magda A. Meester-Smoor [a, b], Trudy Voortman [b, e], Caroline C.W. Klaver [a, b, c, f, g], Wishal D. Ramdas [a, *]

Conclusions: A pro-inflammatory diet was associated with increased risks of cataract and AMD. Particularly the NLR, a marker of subclinical inflammation, appears to be implicated. These findings are relevant for patients with AMD and substantiate the current recommendations to strive for a healthy lifestyle to prevent blindness.

Reactive Oxygen Intermediates and Cellular Damage

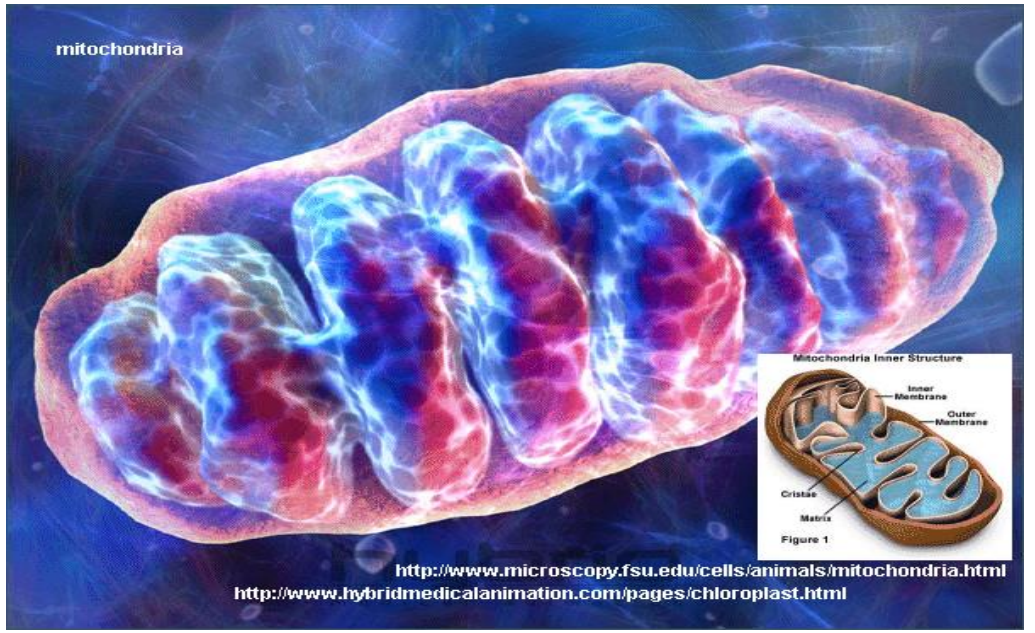
Every component of the eye is vulnerable to damage from ROI – particularly retina There are several reasons for the vulnerability of the retina, including:

- high concentrations of polyunsaturated fatty acid (PUFA)
- constant exposure to visible light
- high consumption of oxygen
- an abundance of photosensitisers in the neurosensory retina and the RPE
- the process of phagocytosis by the RPE, which is known to generate hydrogen peroxide.



The Eye is a Highly Metabolic Tissue Prone to Oxidative Stress

Oxidative Processes



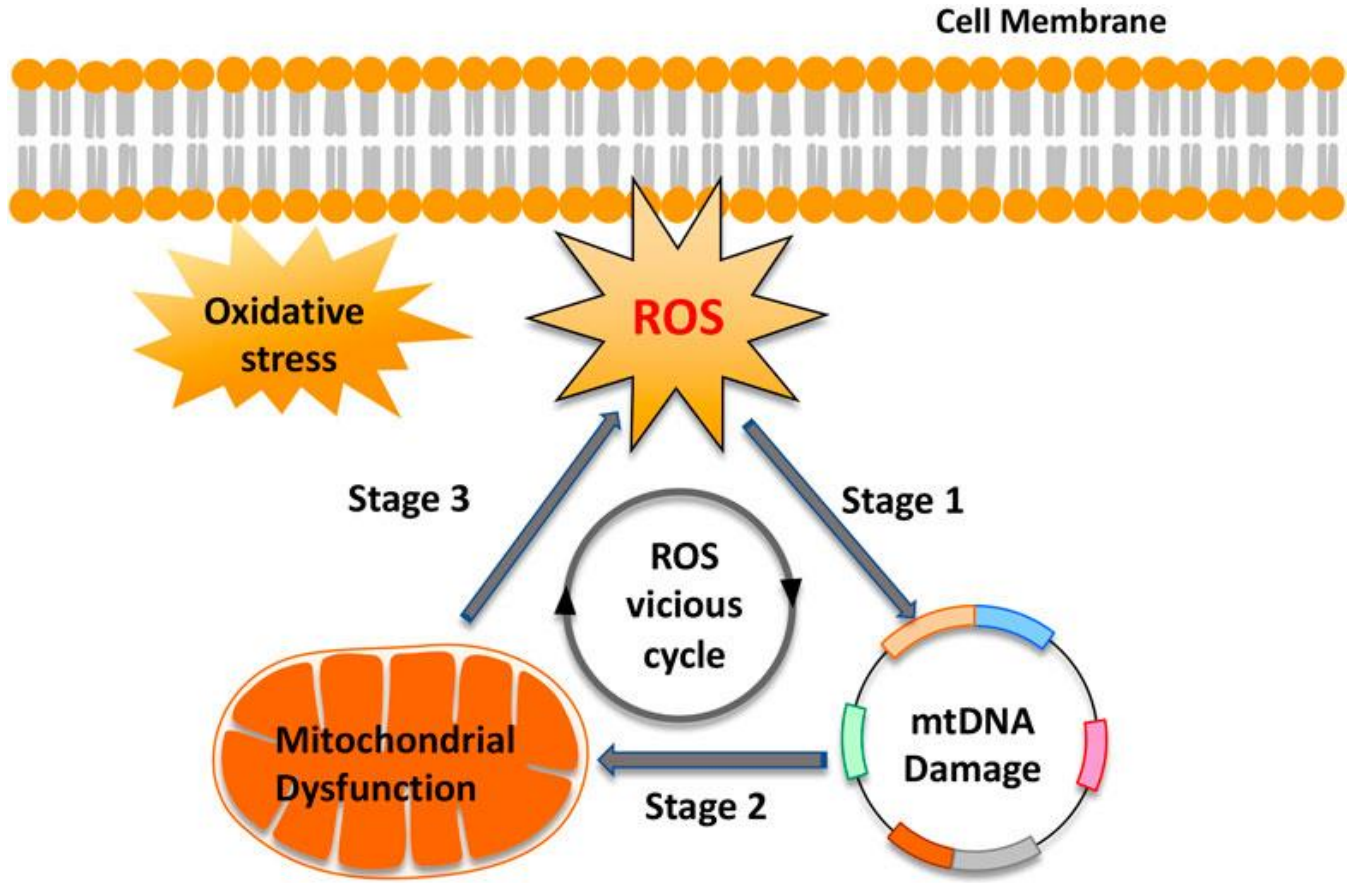
Oxidative phosphorylation occurs in the mitochondrion and is catalysed by ATP synthase.

The electron transport chain accounts for approximately 90% of our total O2 consumption, the remainder being utilized by reactions involving oxidases or oxygenases.

The majority of ROI are formed during energy generation from mitochondria, or during the detoxifying reactions involving the liver cytochrome P450 enzyme system.

Reactive Oxygen Intermediates

- Most ROI are the inevitable byproducts of normal and essential metabolic reactions, such as energy generation from mitochondria
- Pollution
- Asbestos
- fungal or viral infections
- Excess consumption of alcohol
- **Irradiation (mainly blue wavelength light)**
- Inflammation and aging are all known to be associated with increased production of ROI



ROI and Cellular Damage

Every component of the eye is vulnerable to damage from ROI – particularly retina There are several reasons for the vulnerability of the retina, including

1. high concentrations of polyunsaturated fatty acid (PUFA)
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4. an abundance of photosensitisers in the neurosensory retina and the RPE
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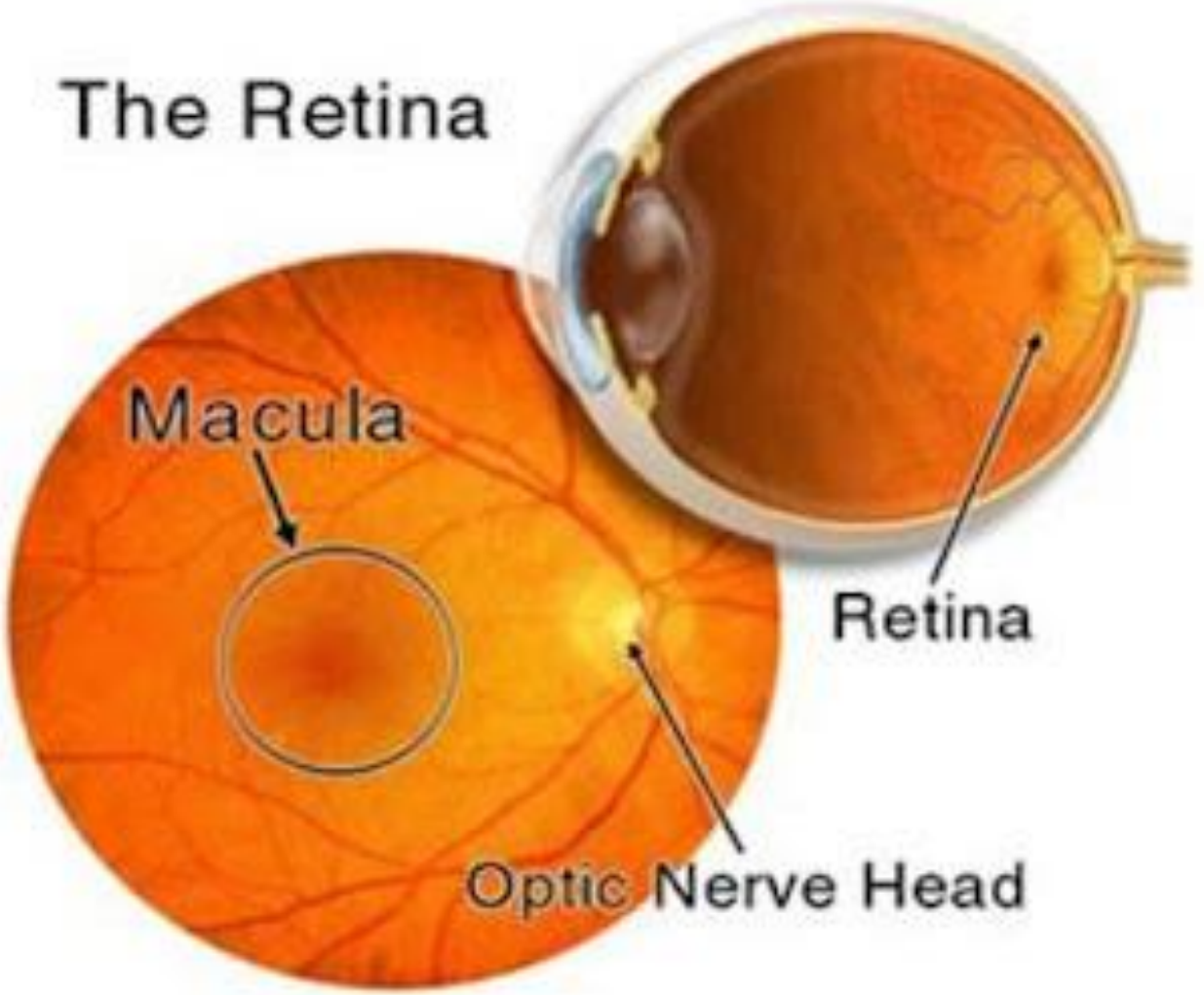


ROI and Cellular Damage

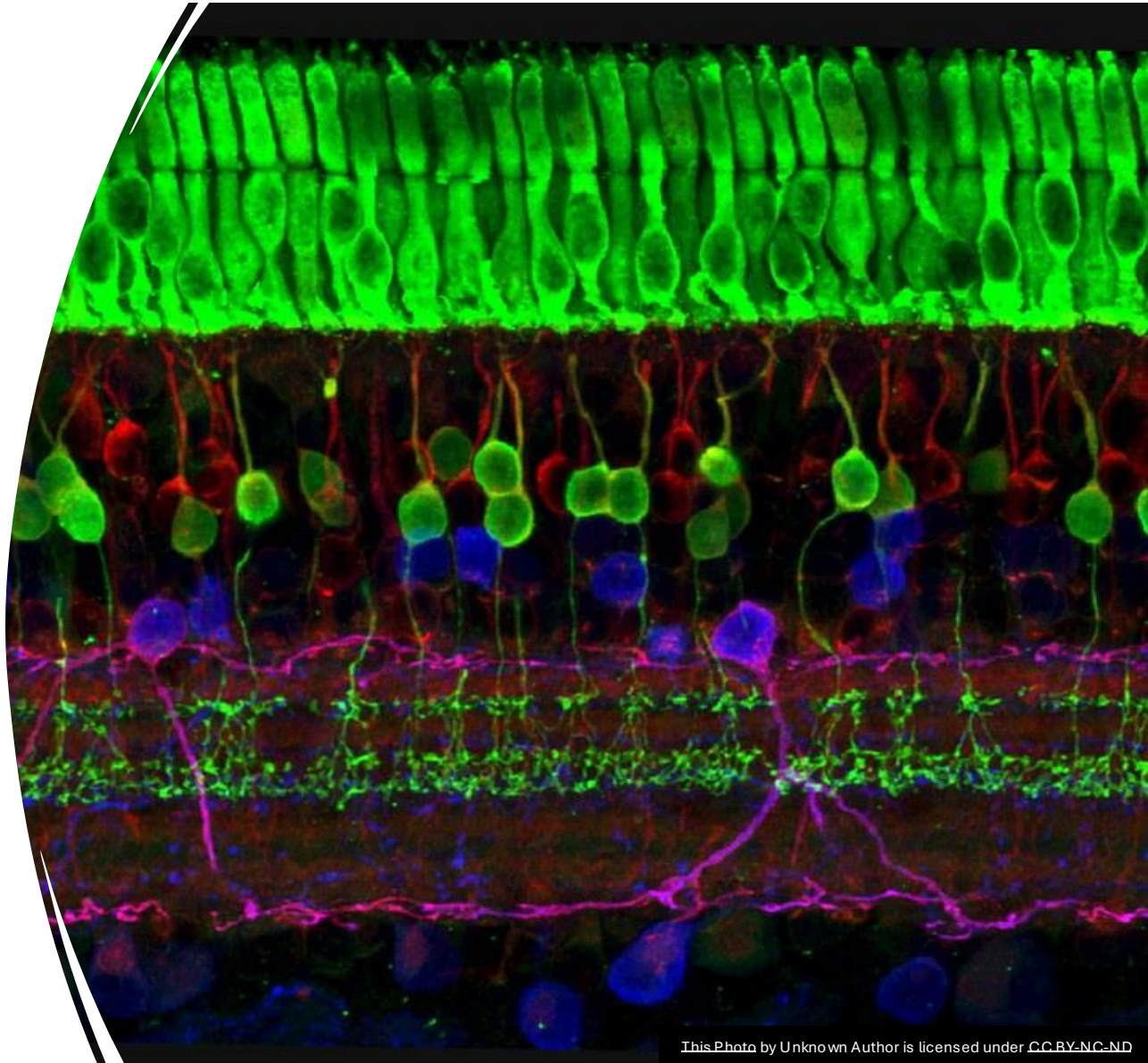
- The high concentrations of PUFA (50%) are found in the lipid bilayer of the outer segment of the rod photoreceptors, and DHA accounts for approx. 50% of the vertebrate rod photoreceptor phospholipids
- The susceptibility of an unsaturated fatty acid to oxidation correlates directly with the number of its double bonds
- PUFAs are particularly susceptible to free radical damage because their conjugated double bonds are convenient sources of hydrogen atoms, which contain one electron
- The lipid radical thus formed then combines with oxygen to form lipid peroxyl radicals and lipid peroxides, which can only be stabilized by acquiring a quenching electron, probably from an adjacent PUFA

ROI and Cellular Damage

- A series of special conditions imposed upon photoreceptors puts them in what can only be termed a high-risk, pro-oxidant environment

- Rod photoreceptor outer segments contain a high proportion of PUFAs which are readily oxidized, while the inner segments contain a considerable number of mitochondria, which leak a small but significant fraction of newly formed ROI

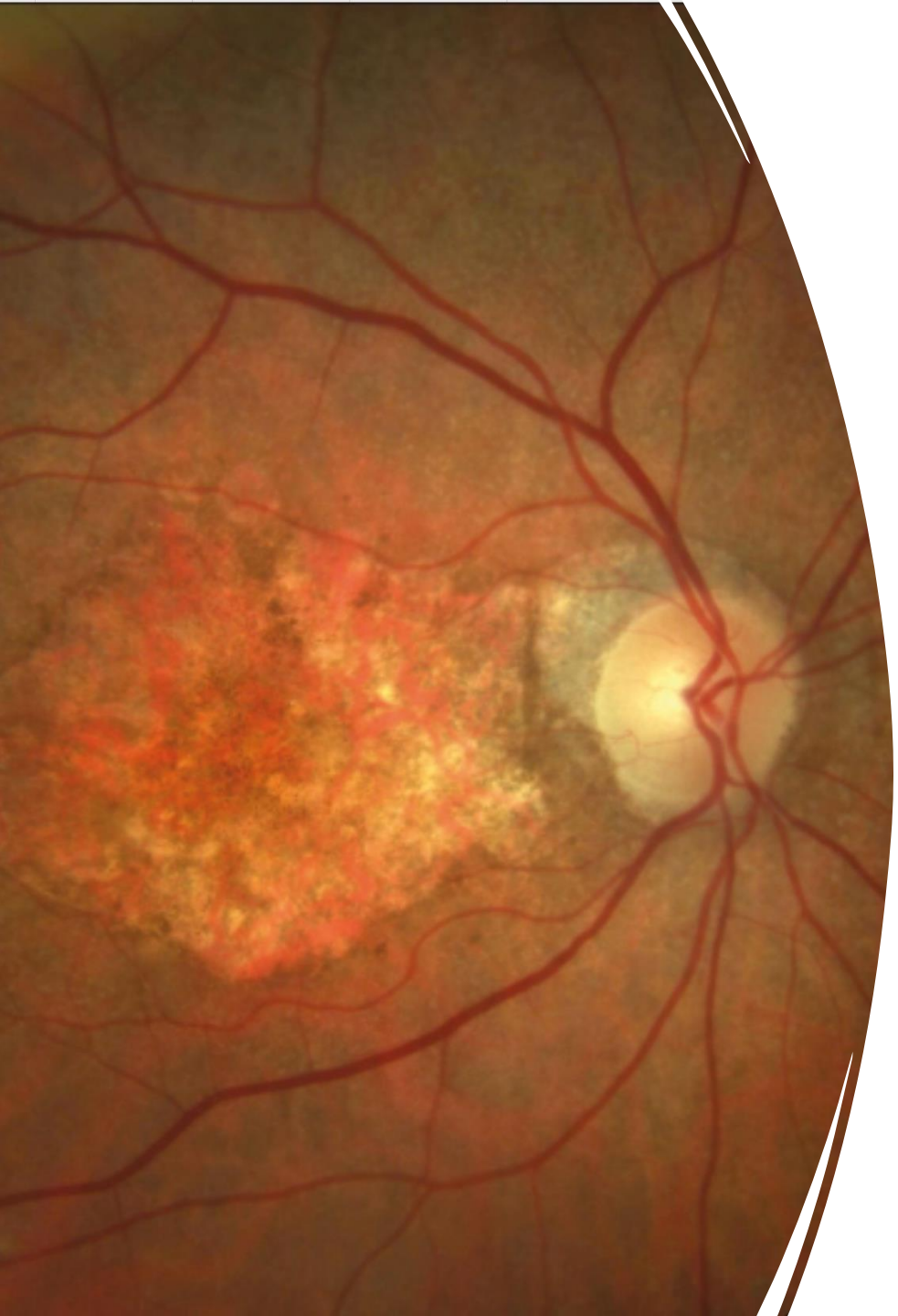
- Also, it has been shown that the partial pressure in this environment is higher than found elsewhere in the body



Oxidative Stress and AMD

- Evidence of oxidative stress can be seen in the RPE and in the neurosensory retina with increasing age, and this damage is most prominent in the region of the retina where early AMD changes are seen
- It has been shown that the concentration of lipofuscin in the RPE increases with increasing age
- Lipofuscin consists of lipid/ protein byproducts resulting from oxidatively damaged photoreceptor outer segments
- it has been shown that lipofuscin compromises RPE cellular function
- lipofuscin generates ROI in response to irradiation with blue light, and therefore contributes further to oxidative stress in the local environment
- RPE dysfunction contributes to the pathogenesis of ARM/AMD, and that this dysfunction is related to lipofuscin accumulation, which, in turn, is related to oxidative injury

Macular Degeneration



Prevalence

- Most common cause of irreversible vision loss in the western world in individuals over 50 years of age.
- 65-75 years- 11% some central vision loss
- >75 years- 30%
- Two Types:
    - -Dry (atrophic) most common form 85-90%
    - -Wet (exudative or neovascular) 10-15%

Chronic disease- AMD

- **AMD in USA** 3.5 million 2020
- Increasing to 5.44 million by year 2050
- AMD # 1 cause of legal blindness in the developed world.
- 7.1% of individuals over the age 75 years have late-stage AMD
- 196 million worldwide 2020; 288 million 2040

Risk Factors

- **Age**
- **Family History, AMD** is, at least in part, an inherited disease (Relative with AMD then life time risk increases from 12% to 50%
- **Smoking, Current smokers have a 2-3 fold increased risk of AMD with vision** loss compared with people that have never smoked.
- **Hypertension**. Association between hypertension and wet AMD.
- **Race**. AMD is more common in Caucasians.
- **Female Gender**. Wet AMD is more common in women.

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Journal of Nutritional Health & Food Engineering

Opinion

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Genetics loads the gun, lifestyle pulls the trigger

Volume 3 Issue 2 - 2015

Opinion

I just finished watching a presentation by Barbara O'Neill called The True Cause of Diseases. Pretty amazing presentation but one of her statements, amongst many, really grabbed my attention: "Genetics Loads the Gun, Lifestyle Pulls the Trigger". What a profound statement, just THINK about it's implications!

Most people think that Lifestyle means the lives of the rich and famous and never think about how they live their lives. That is lifestyle, how you choose to live your life on a daily basis. What you do, what you eat, how you interact with others; that is Lifestyle. It is the force, an energy that defines all living things, that surrounds and penetrates living beings and is structured by the genetic code and fueled/directed by what you eat. Lifestyle is focused by how you act, how you interact with your environment and how active you are.

Genes are not always destiny. For multi-genetic diseases like AMD, lifestyle can modulate gene expression. Hence the science of Epigenetics.

nutrients

MDPI

Nutrients. 2018 Nov; 10(11): 1677.
Published online 2018 Nov 5. doi: 10.3390/nu10111677

PMCID: PMC6267253
PMID: 30400586

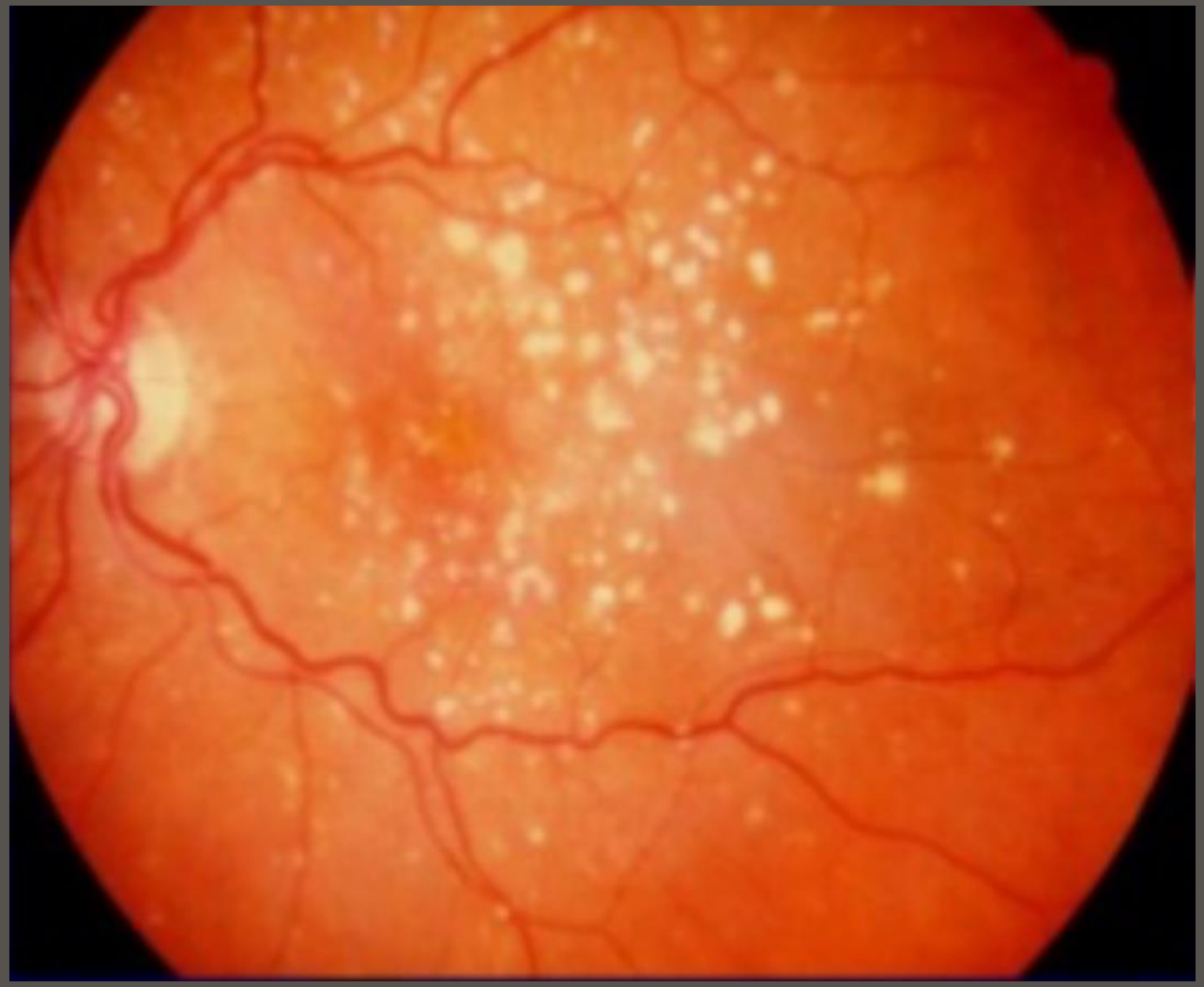
The Role of Diet, Micronutrients and the Gut Microbiota in Age-Related Macular Degeneration: New Perspectives from the Gut–Retina Axis

"Low-grade inflammation, sustained by dysbiosis and a leaky gut, has been shown to contribute to the development of AMD"

Abstract

Go to:

Age-related macular degeneration (AMD) is a complex multifactorial disease and the primary cause of legal and irreversible blindness among individuals aged ≥65 years in developed countries. Globally, it affects 30–50 million individuals, with an estimated increase of approximately 200 million by 2020 and approximately 300 million by 2040. Currently, the neovascular form may be able to be treated with the use of anti-VEGF drugs, while no effective treatments are available for the dry form. Many studies, such as the randomized controlled trials (RCTs) Age-Related Eye Disease Study (AREDS) and AREDS 2, have shown a potential role of micronutrient supplementation in lowering the risk of progression of the early stages of AMD. Recently, low-grade inflammation, sustained by dysbiosis and a leaky gut, has been shown to contribute to the development of AMD. Given the ascertained influence of the gut microbiota in systemic low-grade inflammation and its potential modulation by macro- and micro-nutrients, a potential role of diet in AMD has been proposed.



Drusen: Small yellow or white deposits of lipid and calcium that build up in Bruch's membrane. Amyloid-beta plaques that form in the brains of Alzheimer's patients have a similar composition of protein and fats and utilize the same mechanisms to damage surrounding tissue.

Nutrition and AMD: NHANES

Factors associated with age-related macular degeneration. An analysis of data from the first National Health and Nutrition Examination Survey (NHANES) survey

Am J Epid. 1988;128:700-10

A diet rich in fruits and vegetables with vitamins A and C, was inversely associated with AMD

Goldberg J, Flowerdew J, Smith E, Brody JA, Tso MO

The Age-Related Eye Disease Study

The Age-Related Eye Disease Study

1992-2001-Clinical Trial of Micronutrients for AMD (n=4757)
2001-2005-Epidemiologic Follow-up Study

NIH National Eye Institute

The Age-Related Eye Disease Study

AREDS Formulation Recommended:

- patients with intermediate AMD (bilateral large drusen)
- patients with late AMD in 1 eye
- NOT for current smokers (beta-carotene increased the risk of lung cancer in smokers in 2 NIH studies)
- NOT for unaffected children of individuals with AMD
  -only effective in those with intermediate AMD

Arch Ophthalmol. 2001;119(10):1417-36.

AREDS2

Age-Related Eye Disease Study 2

The Lutein/Zeaxanthin and Omega-3 Supplementation Trial

1° Randomization: 1° Analyses: Progression to Late AMD (neovascular or Central GA)

Omega 3 Fatty acids (DHA/EPA): neither beneficial nor harmful

Lutein/zeaxanthin (L/Z): incremental increase in benefits (reduction of progression to late AMD)

2° analyses: In those with low dietary intake of L/Z, **25% reduction** in development of late AMD with **L/Z (beneficial)**

Direct comparisons with beta-carotene showed a >20% increase in beneficial effects of L/Z (**Lutein/zeaxanthin favored over beta-carotene)**

JAMA. 2013 May 15;309(19):2005-15

Age-Related Eye Disease Study 2

The Lutein/Zeaxanthin and Omega-3 Supplementation Trial

AREDS2 Formulation

Vitamin C (500 mg)

Vitamin E (400 IU)

~~Beta-Carotene (15 mg)~~

Lutein (10 mg)/Zeaxanthin (2 mg)

Zinc (80 mg zinc oxide)

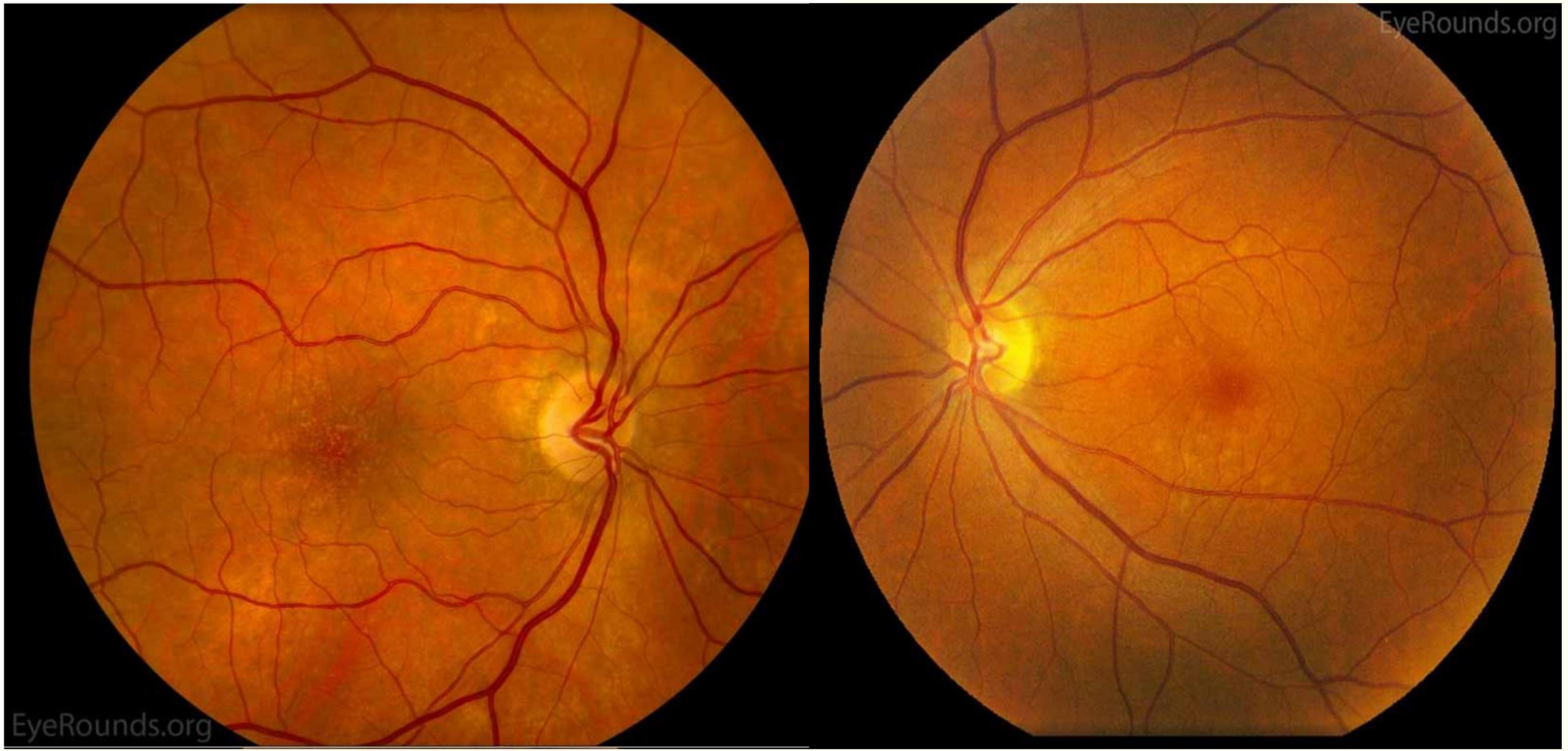
Copper (2 mg cupric oxide)

~~Omega-3 fatty acids (DHA/EPA)~~

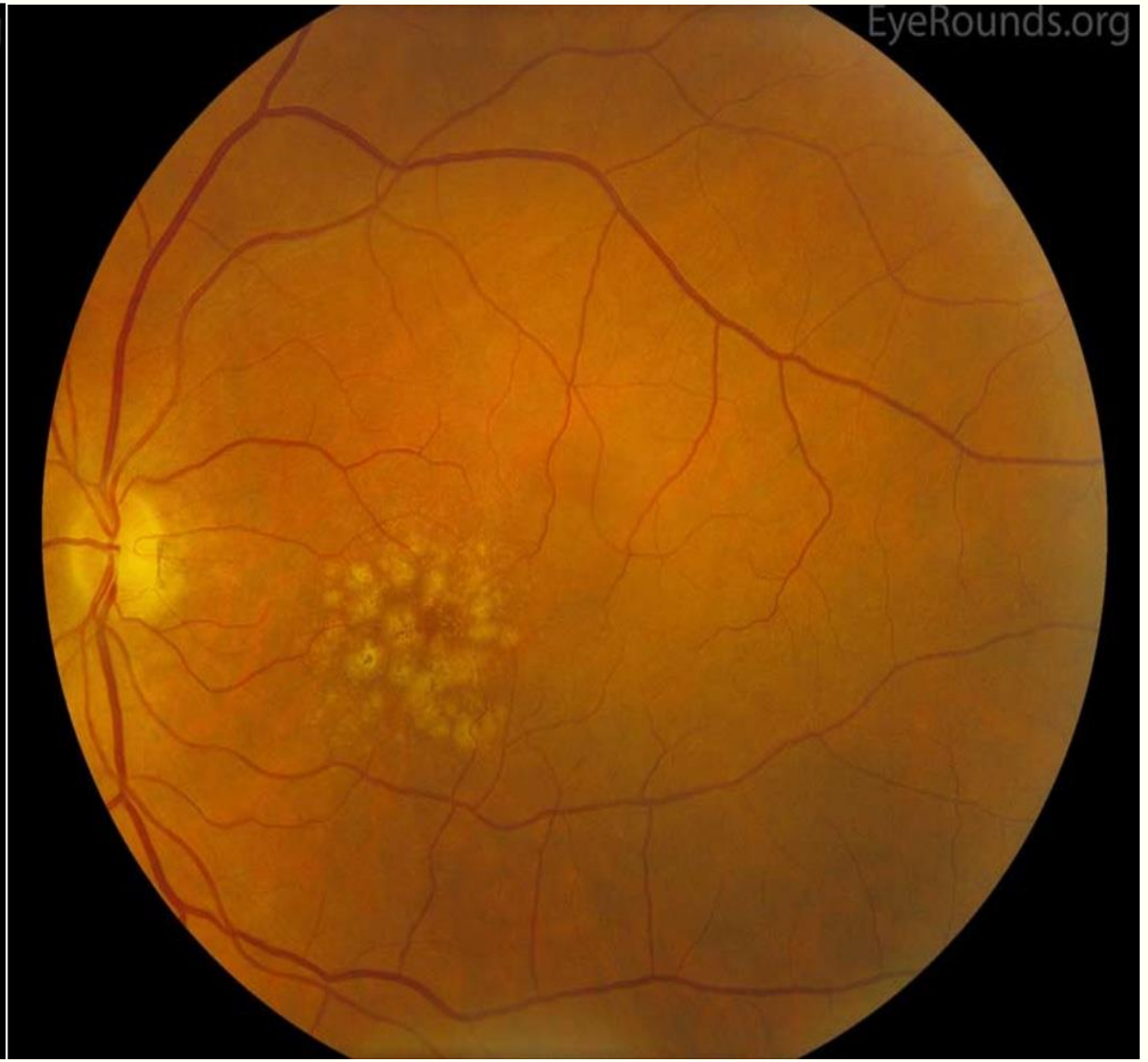
AMD has been categorized by The Age-Related Eye Disease Study (AREDS) based on exam findings of hard drusen, soft drusen, RPE abnormalities, atrophy, and choroidal neovascularization. The AREDS categories are as follows:

Category 1	Category 2	Category 3	Category 4
No AMD	*Early Stage AMD*	*Intermediate AMD*	*Advanced AMD*
A few small or no drusen	Several small drusen or a few medium-sized drusen in one or both eyes	Many medium-sized drusen or one or more large drusen in one or both eyes	In one eye only, either a break-down of light-sensitive cells and supporting tissue in the central retinal area (advanced dry form), or abnormal and fragile blood vessels under the retina (wet form)

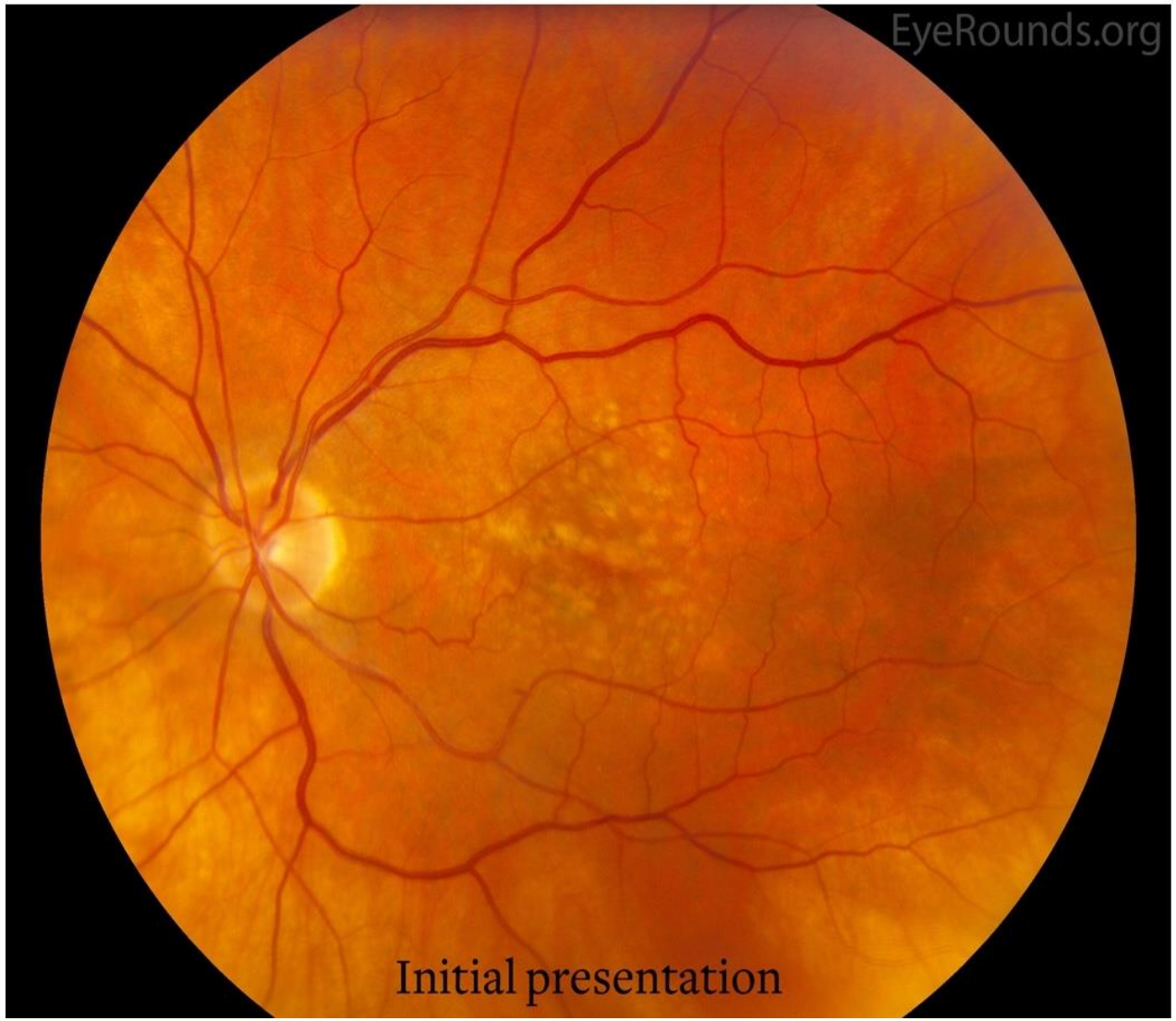
Early AMD (AREDS Category 2)



Intermediate AMD (AREDS Category 3)



Transition to Advanced Unilateral AMD (AREDS Category 4)



Advanced Bilateral AMD

Mediterranean Diet and Cardiovascular Disease

Randomized Clinical Trial of Mediterranean Diet

- **PREvención con Dieta MEDiterránea (PREDIMED) trial-RCT**
- Multicenter trial in Spain: persons at high risk for cardiovascular disease (n=7,447) randomly assigned:
  - 1. Mediterranean diet supplemented with mixed nuts
  - 2. Mediterranean diet supplemented with extra virgin olive oil
  - 3. Control diet (low fat)

Mediterranean diet is beneficial in reducing cardiovascular disease by as much as 30%

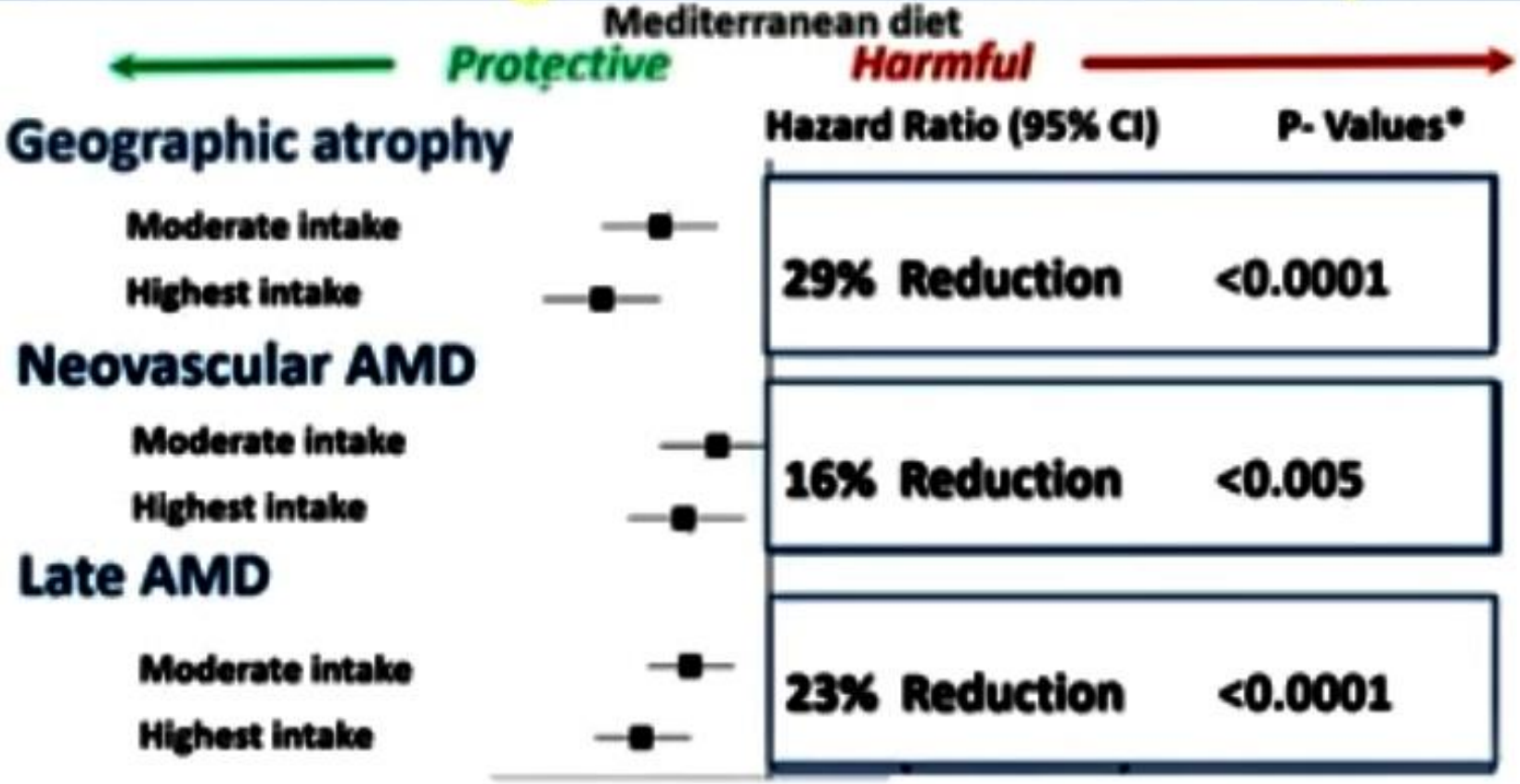
Mediterranean Diet & AMD

Research Question:

- **What is the association of Mediterranean diet with AMD?**
- Previous longitudinal studies of Mediterranean diet & AMD:
  - AREDS data (Merle BM, Silver RE, Rosner B, Seddon JM)
  - EYE-Risk Consortium (Merle BM, et al....Korobelnik JF, Klaver C, Delcourt C)
- Cross sectional evaluations: Colimbra, European Eye Study, etc.

High Mediterranean diet adherence associated with less progression to late AMD by 25-40%

Mediterranean Diet for AREDS & AREDS2
Results of Progression to Late AMD (NV & GA)



Higher intake of Mediterranean diet associated with decreased risk of progression to late AMD, both neovascular and GA

Mediterranean Diet: ***AREDS*** Component Analysis for Geographic atrophy

Fish

Highest Intake HR: 0.69 p-value 0.001*

***Statistically significant after Bonferroni correction**

Fish is the component of the Mediterranean diet associated with 31% decreased risk of progression to GA

Multicenter Study > Ophthalmology. 2019 Mar;126(3):381-390.
doi: 10.1016/j.ophtha.2018.08.006. Epub 2018 Aug 13.

Mediterranean Diet and Incidence of Advanced Age-Related Macular Degeneration: The EYE-RISK Consortium

Abstract

Purpose: To investigate associations of adherence to the Mediterranean diet (MeDi) with incidence of advanced age-related macular degeneration (AMD; the symptomatic form of AMD) in 2 European population-based prospective cohorts.

Conclusions: Pooling data from the RS-I and Alienor Study, higher adherence to the MeDi was associated with a 41% reduced risk of incident advanced AMD. These findings support the role of a diet rich in healthful nutrient-rich foods such as fruits, vegetables, legumes, and fish in the prevention of AMD.

LATEST AREDS DATA

New data from the NEI 10-year follow-up post hoc analysis of the age-related eye disease study (AREDS) and AREDS2 which was presented at ARVO's annual meeting
May 7, 2021.

Clinical Trial > Ophthalmology. 2021 Mar;128(3):425-442. doi: 10.1016/j.ophtha.2020.08.018. Epub 2020 Aug 25.

Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2

Elvira Agrón [1], Julie Mares [2], Traci E Clemons [3], Anand Swaroop [4], Emily Y Chew [5], Tiarnan D L Keenan [6], AREDS and AREDS2 Research Groups

Affiliations + expand

PMID: 32858063 PMCID: PMC7902480 (available on 2022-03-01)
DOI: 10.1016/j.ophtha.2020.08.018

Abstract

Purpose: To analyze associations between the dietary intake of multiple nutrients and risk of progression to late age-related macular degeneration (AMD), its subtypes, and large drusen.

Design: Post hoc analysis of 2 controlled clinical trial cohorts: Age-Related Eye Disease Study (AREDS) and AREDS2.

Findings:

Decreased risk

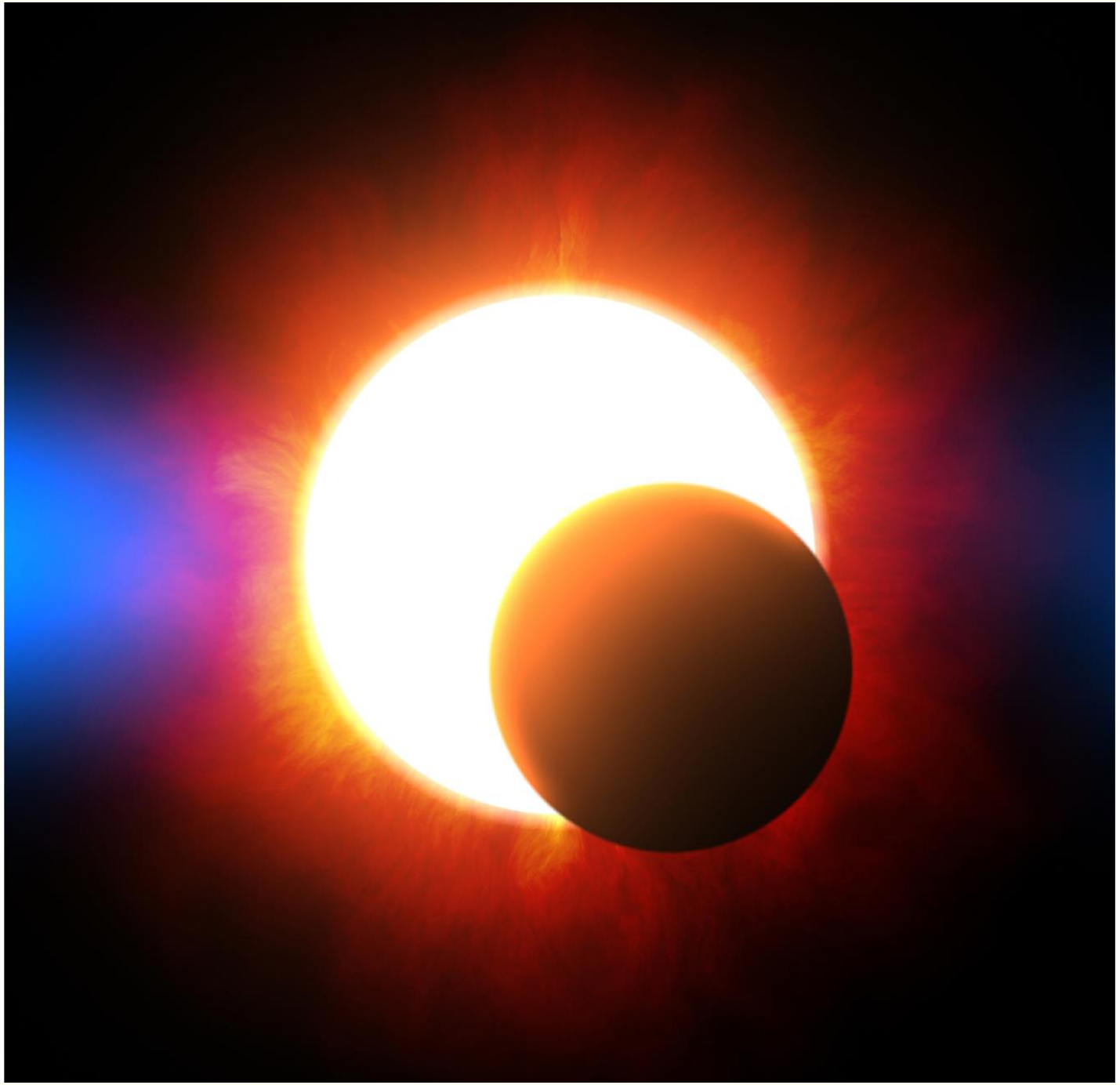
- Vitamins A, D, E, C
- B vitamins such as folate, B6, B12, thiamine, riboflavin, niacin
- Carotenoids such as alpha and beta-carotene, lutein, zeaxanthin, lycopene
- Minerals such as magnesium, calcium, zinc, iron, and copper
- Fatty acids EPA & DHA from fish or algae sources

Increased Risk

- Cholesterol
- Saturated fats
- Monounsaturated fats (meat/dairy sources)
- Omega 6's
- ALA (vegetable omega 3's such as flax seeds, chia, and soy oil)
- Arachidonic acid

What the data showed about eating a Mediterranean Type Diet

- Eating a Mediterranean diet, particularly a lot of fish, may be beneficial for those with early or even intermediate age-related macular degeneration (AMD)
- A diet high in fish can reduce the chances of developing late AMD by 65% for patients who also have protective genes
- In the general AMD population, a high fish diet reduced progression of intermediate AMD, with bilateral large drusen, to geographic atrophy by 31%.
- High adherence to a Mediterranean diet reduced progression from intermediate to late AMD, with geographic atrophy or neovascularization, by 25-to-40%.



Eclipse 2017

c&en

Log In

Volume 95 Issue 33 | pp. 31-33
Issue Date: August 21, 2017 | Web Date: August 14, 2017

Chemistry explains why you shouldn't stare at the solar eclipse without protection

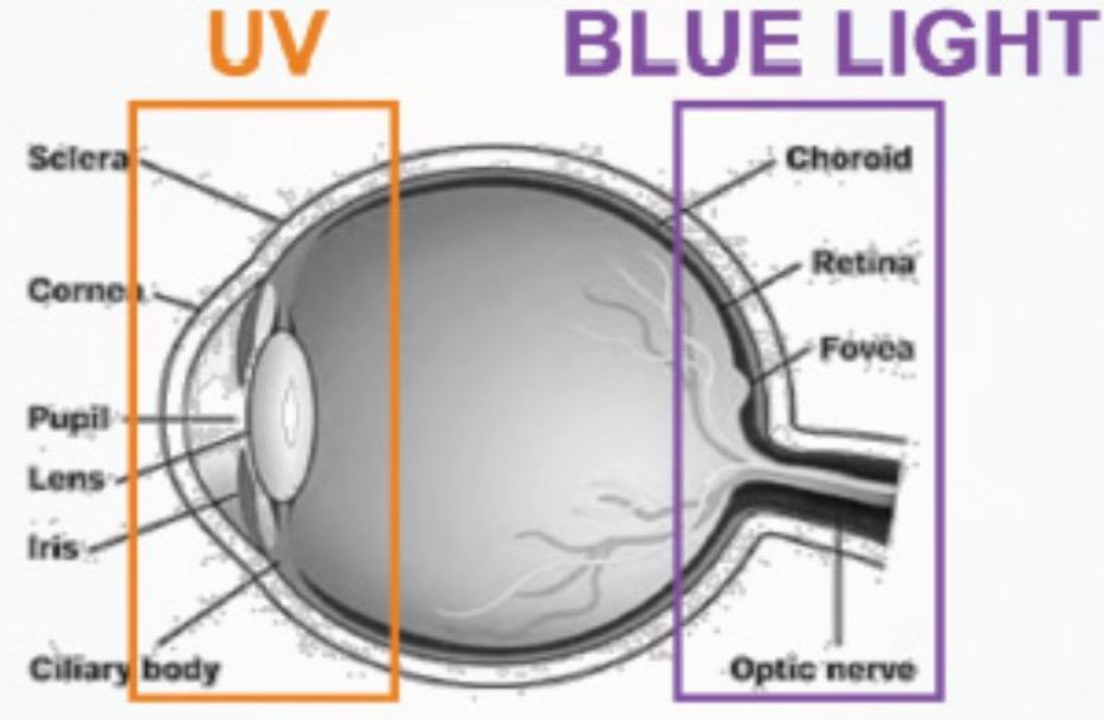
Looking at the sun can set off damaging radical reactions in the eye

By ***Tien Nguyen***

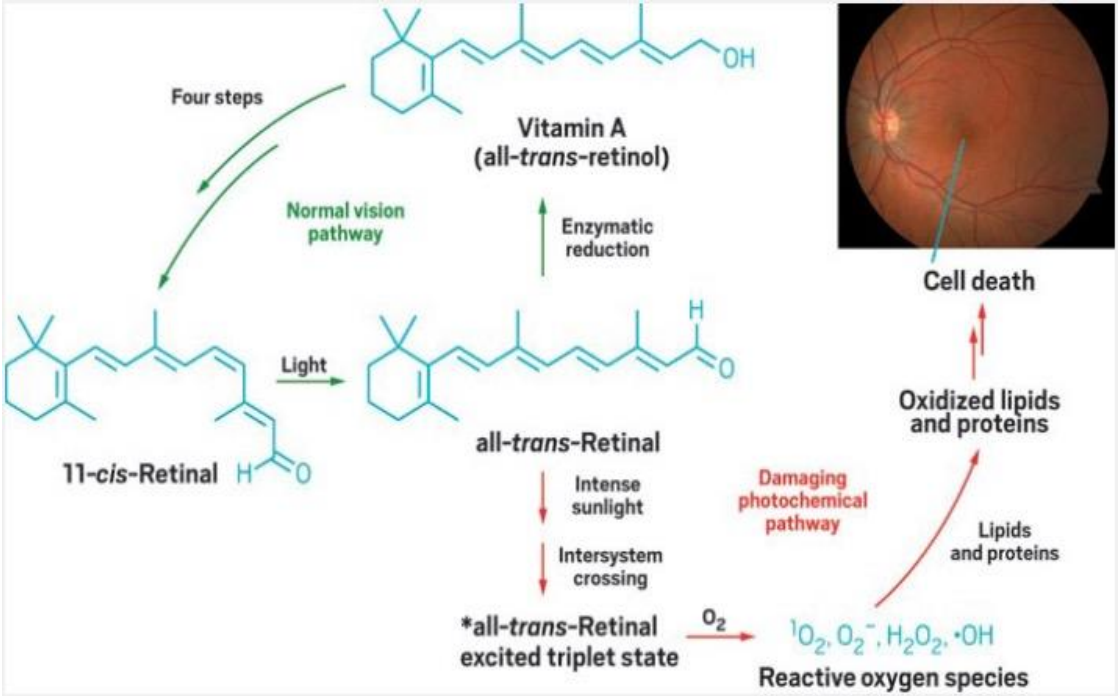
Chemical & Engineering News. 2017;95: 31-33

Sun related retinal damage is not caused by heat (thermal) but rather metabolic poisoning (accumulation of waste products from biochemical processes in cells)

This photochemical nature of light induced damage to the retina comes at wavelengths in the blue light spectrum from 415-450 nm



Chemical & Engineering News. 2017;95: 31-33



Staring at the sun can derail healthy chemical pathways, causing blurred vision or even blind spots.
Credit: Theodore Leng/ASRS Retina Image Bank

Unchecked oxidation can lead to cell death and retinal damage.

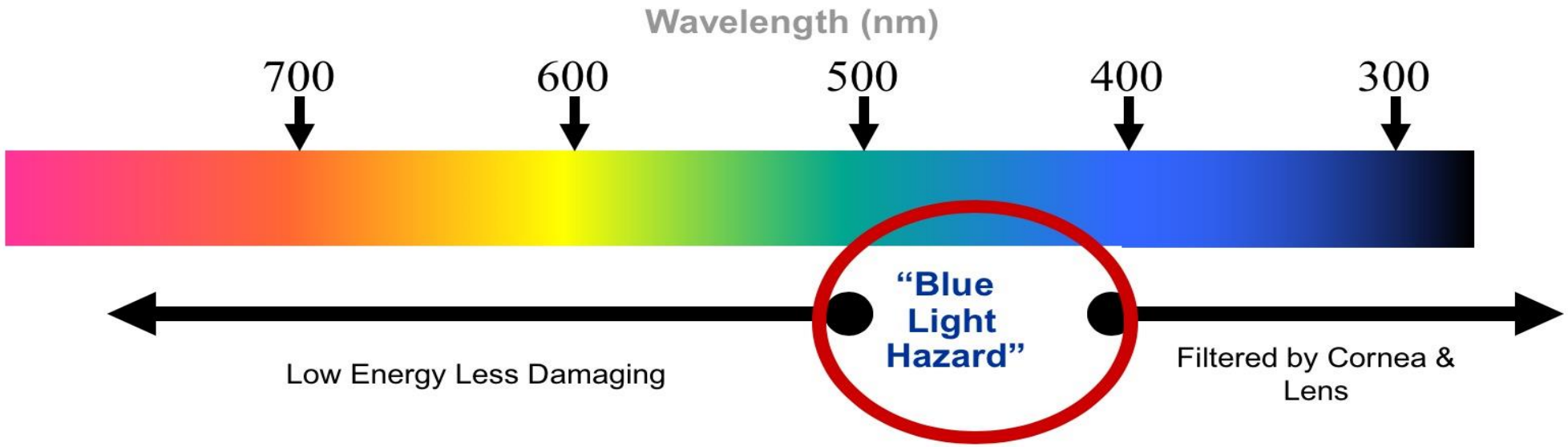
The Macula

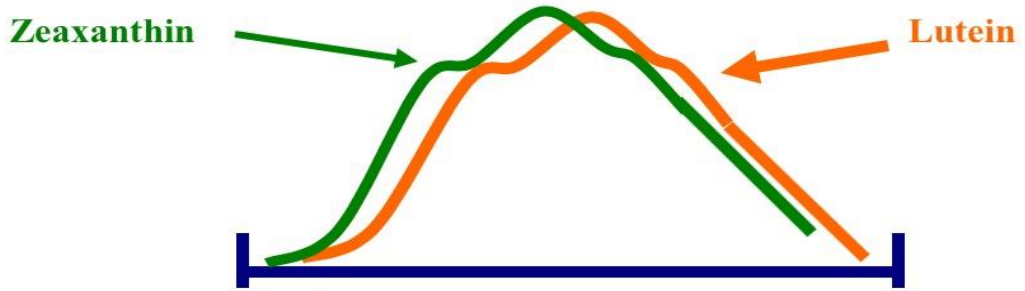
Highest density of photoreceptor cells in the entire eye

Because the macula is yellow in color it absorbs excess blue light and UV light

The yellow color comes from its content of lutein and zeaxanthin

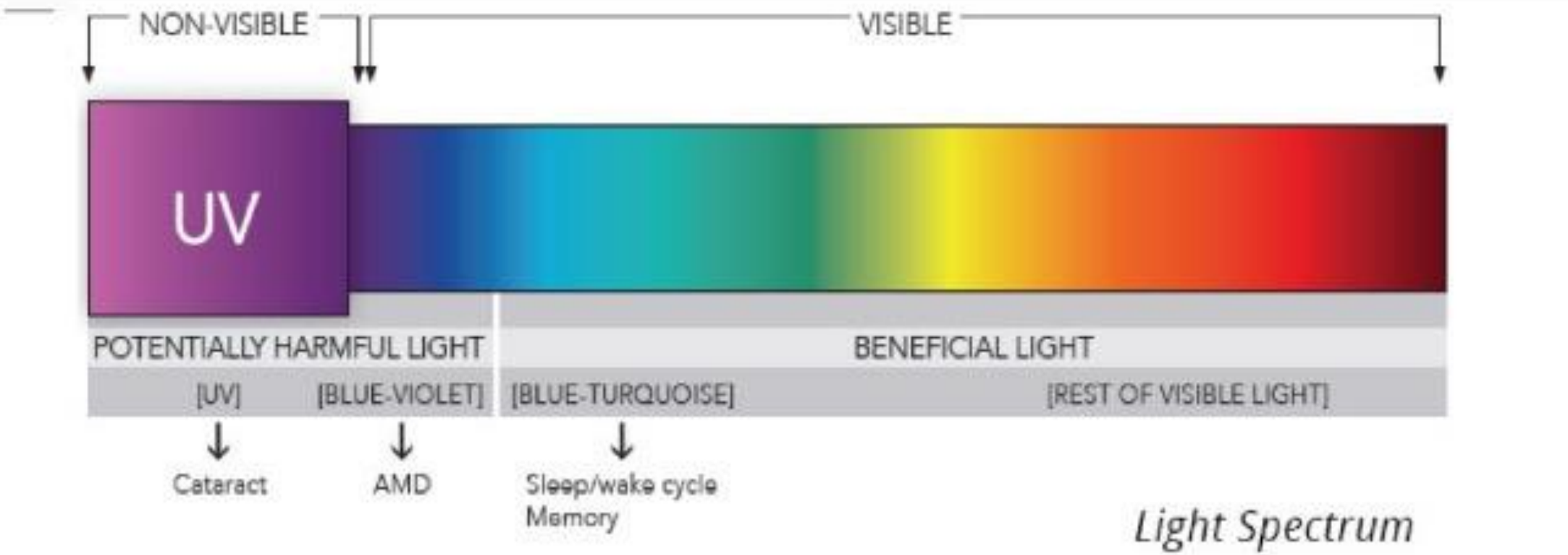
Macular Pigments Filter Blue Light





UV/VIS Spectrum of Lutein & Zeaxanthin

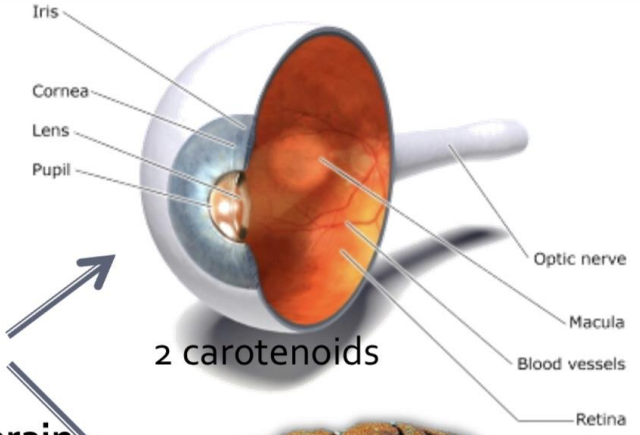
The Light Spectrum: Note the wavelengths associated with Cataracts, Age Related Macular Degeneration (AMD), and the Sleep/Wake Cycle Memory



Light Spectrum

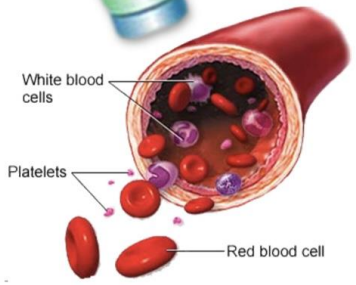
Carotenoids

750 in nature



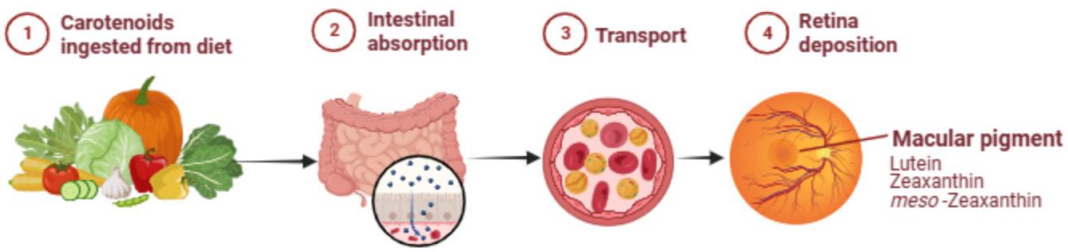
Lutein and zeaxanthin concentrate in the eye and brain

2 carotenoids

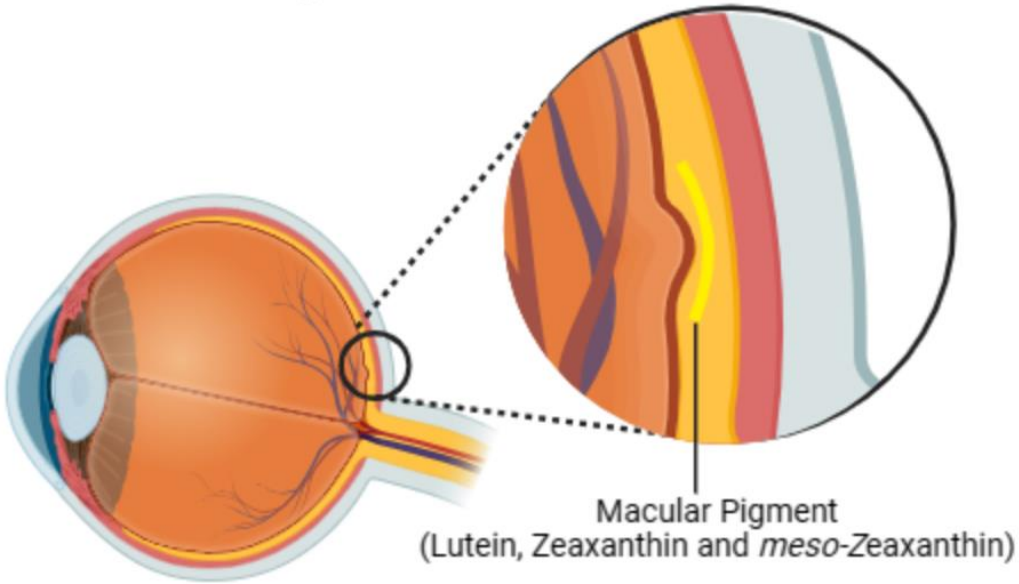


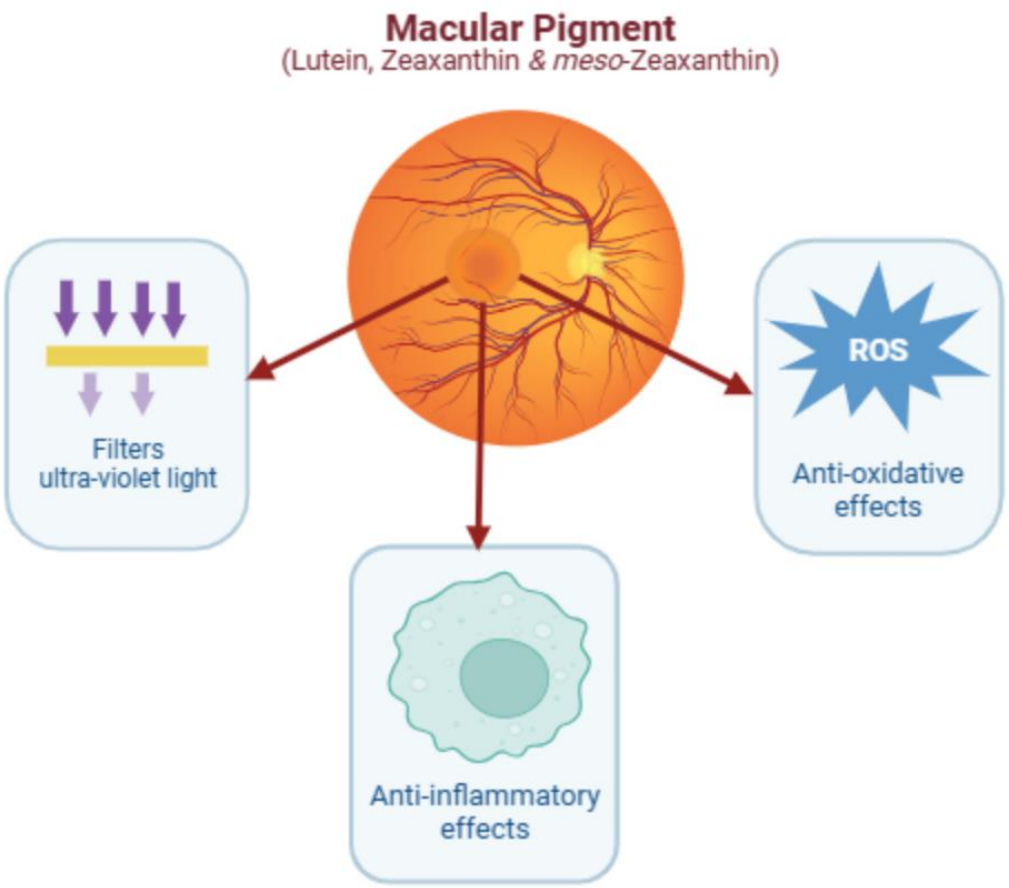
~20 in blood

Carotenoid Metabolism



Macular Pigment Localization in the Eye




Macular Pigment
(Lutein, Zeaxanthin & meso-Zeaxanthin)
Filters
ultra-violet light
ROS
Anti-oxidative
effects
Anti-inflammatory
effects

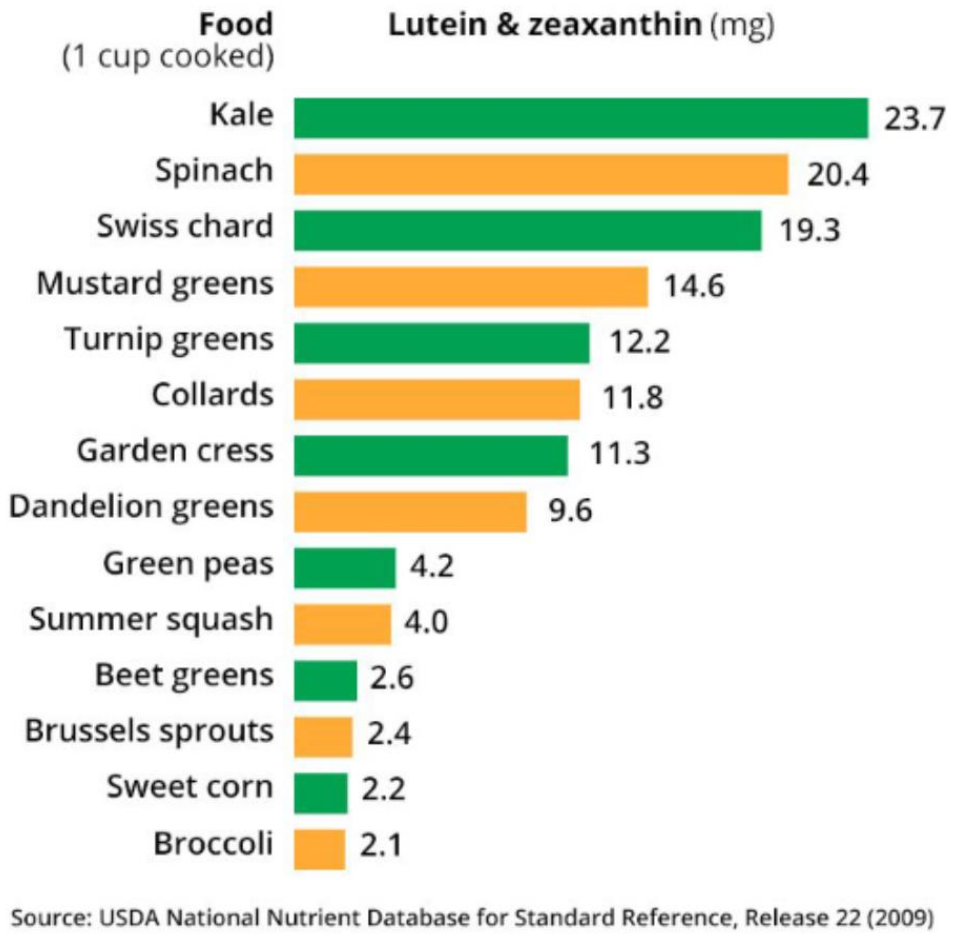
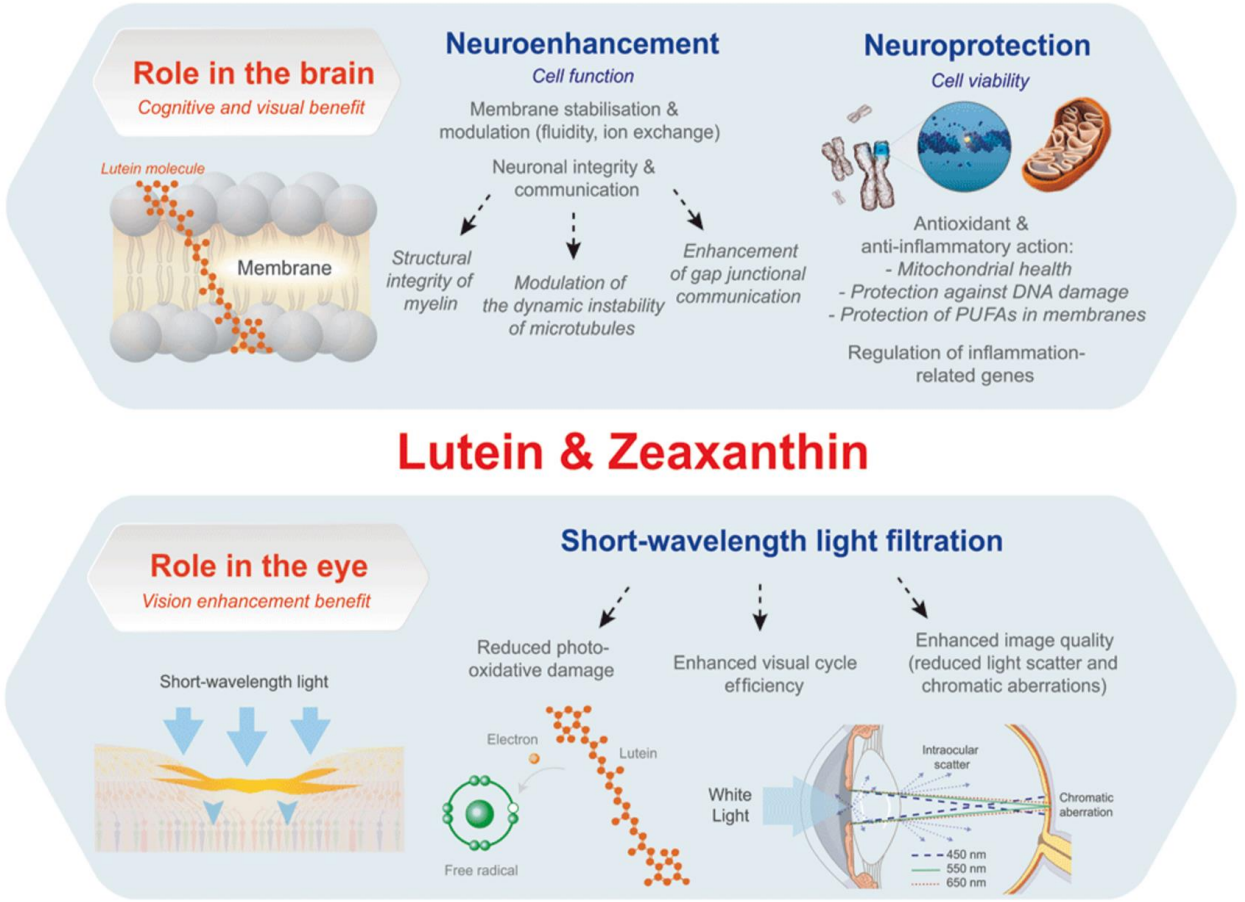

Food
(1 cup cooked)
Lutein & zeaxanthin (mg)
Kale 23.7
Spinach 20.4
Swiss chard 19.3
Mustard greens 14.6
Turnip greens 12.2
Collards 11.8
Garden cress 11.3
Dandelion greens 9.6
Green peas 4.2
Summer squash 4.0
Beet greens 2.6
Brussels sprouts 2.4
Sweet corn 2.2
Broccoli 2.1
Source: USDA National Nutrient Database for Standard Reference, Release 22 (2009)

Figure 2. Schematic of the proposed mechanistic processes through which lutein and zeaxanthin might influence...

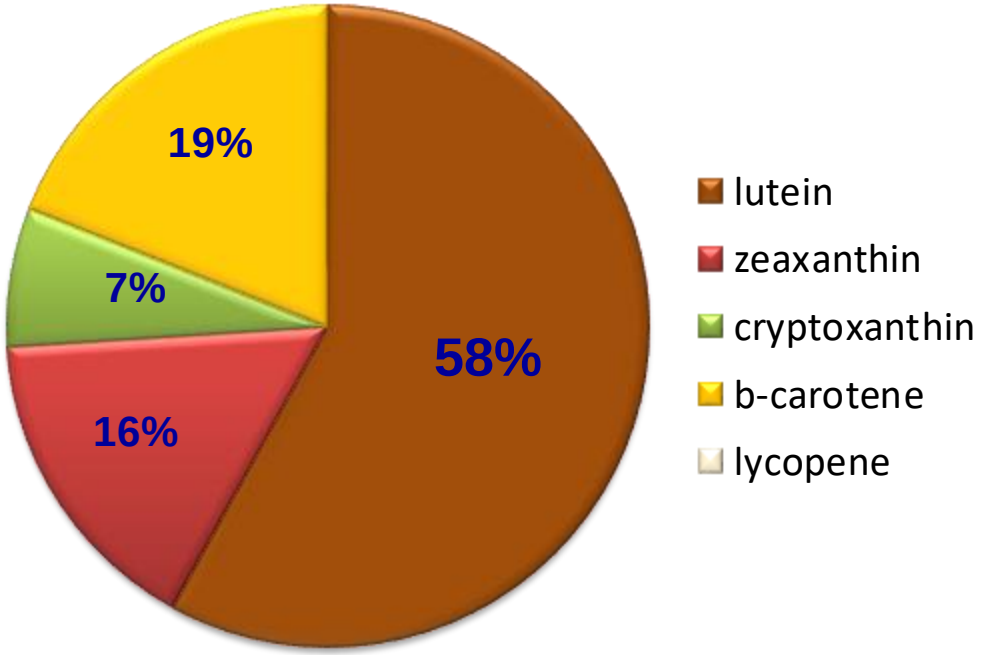


Loskutova E, Shah K, Flitcroft ID et al. Lutein and zeaxanthin: The possible contribution, mechanisms of action and implications of modern dietary intake for cognitive development in children. [version 1]. HRB Open Res 2019, 2:8 (doi: 10.12688/hrbopenres.12903.1)

HRB Open Research

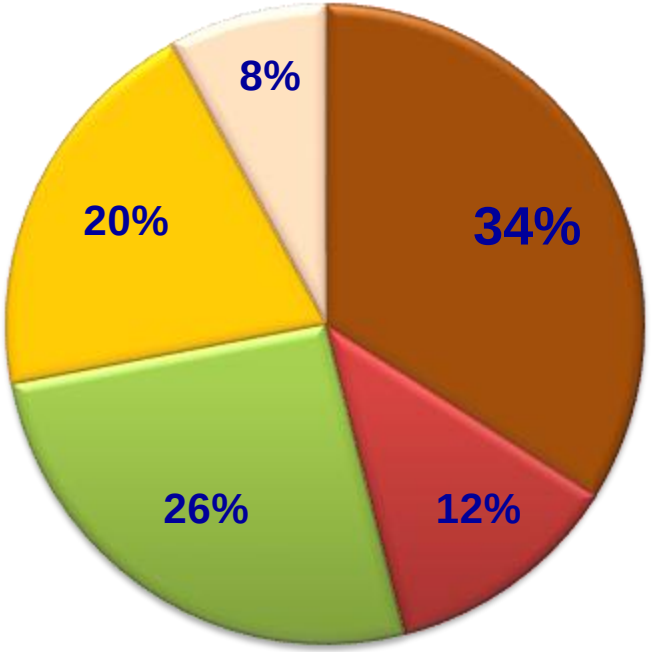
Brain carotenoid profile in infants and centenarians

Infant Brain (n=30)



Vishwanathan et al, 2014

Centenarian Brain (n=48)



Johnson EJ et al. 2013

Screen time stress and cognitive performance

Journal
Nutritional Neuroscience ›
An International Journal on Nutrition, Diet and Nervous System
Volume 21, 2018 - Issue 9

Original Articles

Macular pigment optical density is positively associated with academic performance among preadolescent children

Sasha M. Barnett, Naiman A. Khan, Anne M. Walk, Lauren B. Raine, Christopher Moulton, Neal J. Cohen,
...show all

Pages 632-640 | Published online: 23 May 2017

Results: The regression analyses revealed that MPOD improved the model, beyond the covariates, for overall academic achievement ($\Delta R^2 = 0.10$, $P < 0.01$), mathematics ($\Delta R^2 = 0.07$, $P = 0.02$), and written language composite standard scores ($\Delta R^2 = 0.15$, $P < 0.01$).

Discussion: This is the first study to demonstrate that retinal L and Z, measured as MPOD, is positively related to academic achievement in children, even after accounting for the robust effects of IQ and other demographic factors. These findings extend the positive associations observed between MPOD and cognitive abilities to a pediatric population.

Contents lists available at ScienceDirect

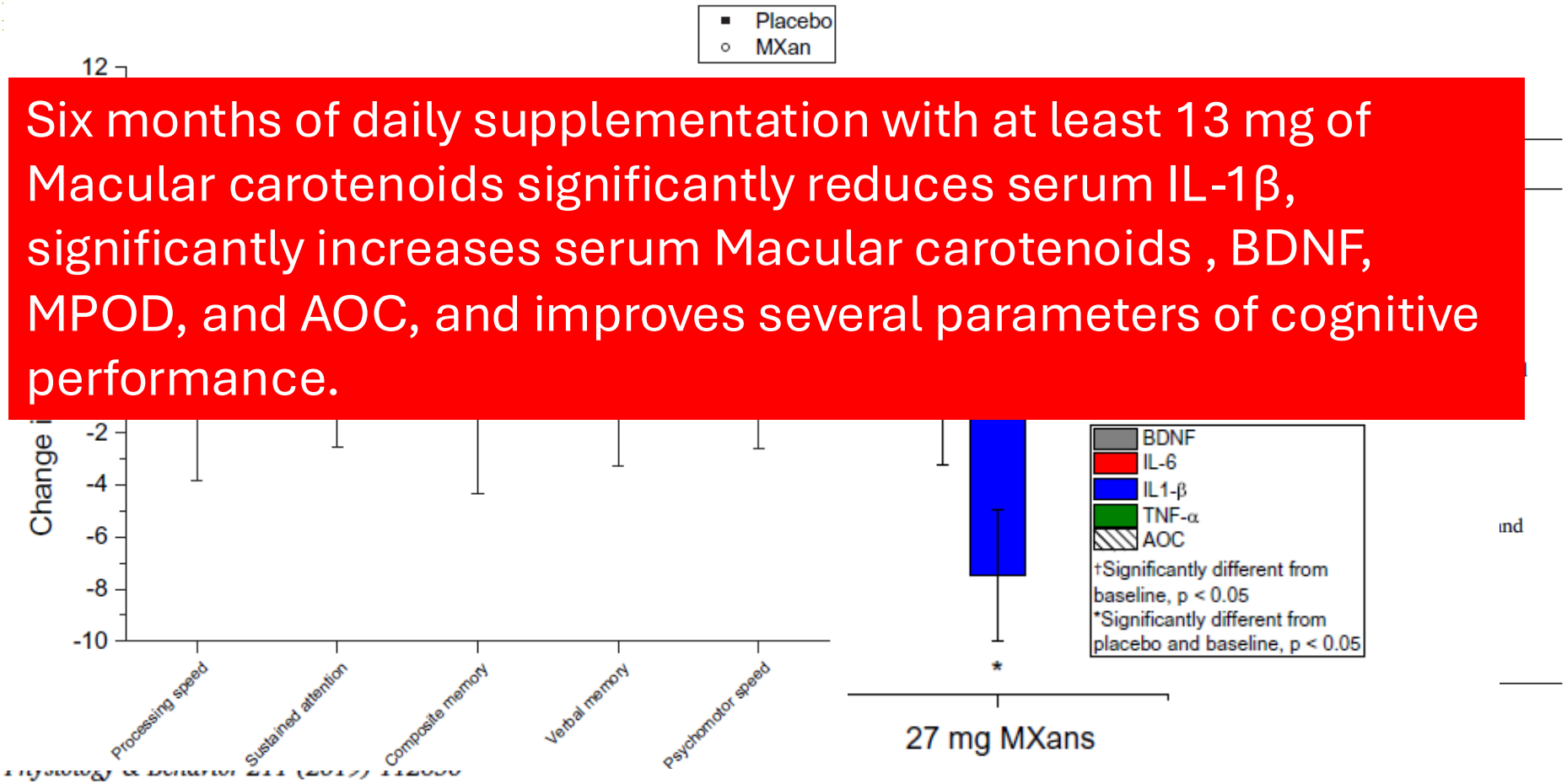
Physiology & Behavior

journal homepage: www.elsevier.com/locate/physbeh

Effects of macular xanthophyll supplementation on brain-derived neurotrophic factor, pro-inflammatory cytokines, and cognitive performance

Nicole T. Stringham[a,b,*], Philip V. Holmes[a,b], James M. Stringham[c]

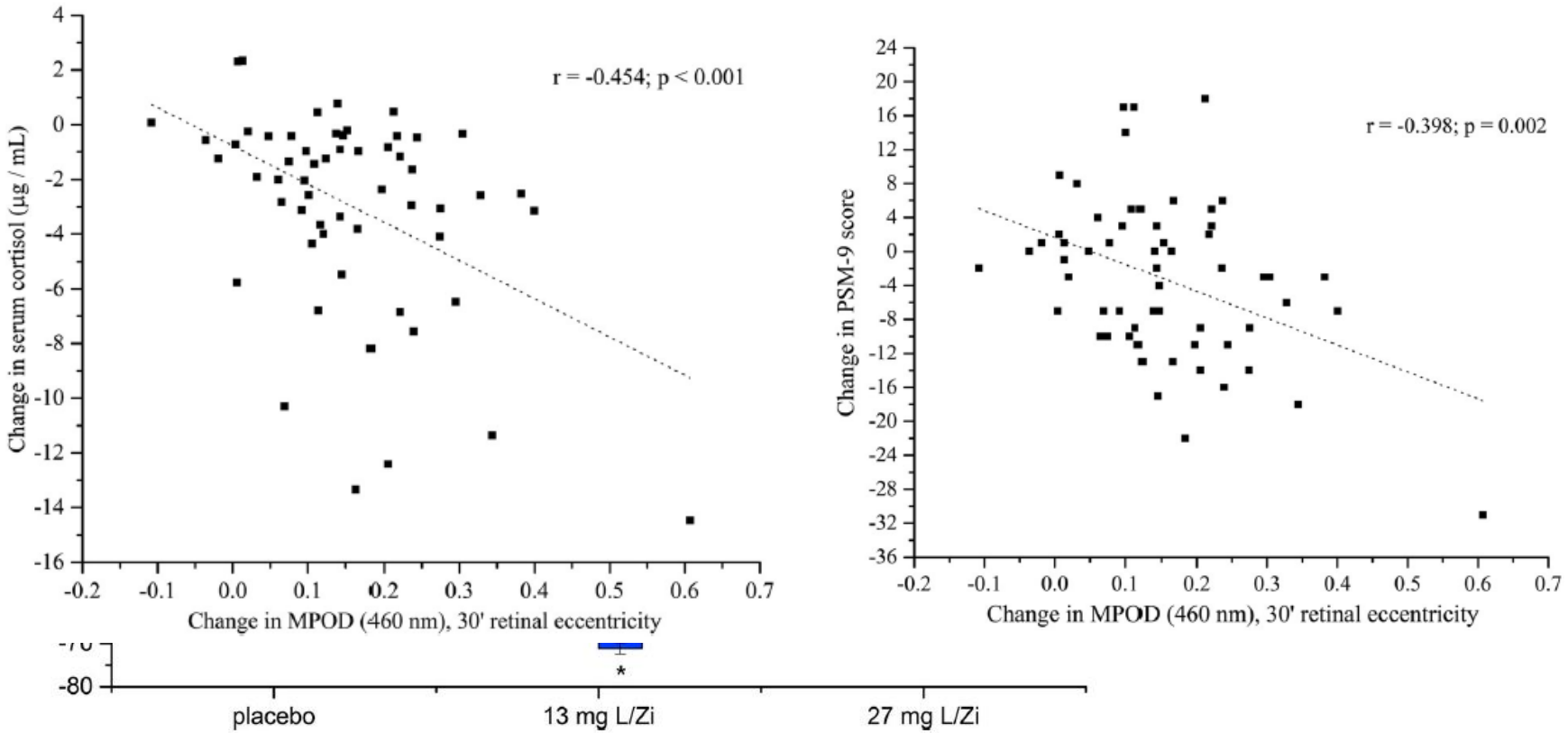
Six months of daily supplementation with at least 13 mg of Macular carotenoids significantly reduces serum IL-1β, significantly increases serum Macular carotenoids , BDNF, MPOD, and AOC, and improves several parameters of cognitive performance.



Supplementation with macular carotenoids reduces psychological stress, serum cortisol, and sub-optimal symptoms of physical and emotional health in young adults

Nicole Tressa Stringham [1,2], Philip V. Holmes[1,2], James M. Stringham [2]

[1]Interdisciplinary Neuroscience Program, Biomedical and Health Sciences Institute, University of Georgia, Athens, GA 30602, USA, [2]Department of Psychology, University of Georgia, Athens, GA 30602, USA



Nutritional Neuroscience 2018 VOL. 21 NO. 4

foods

MDPI

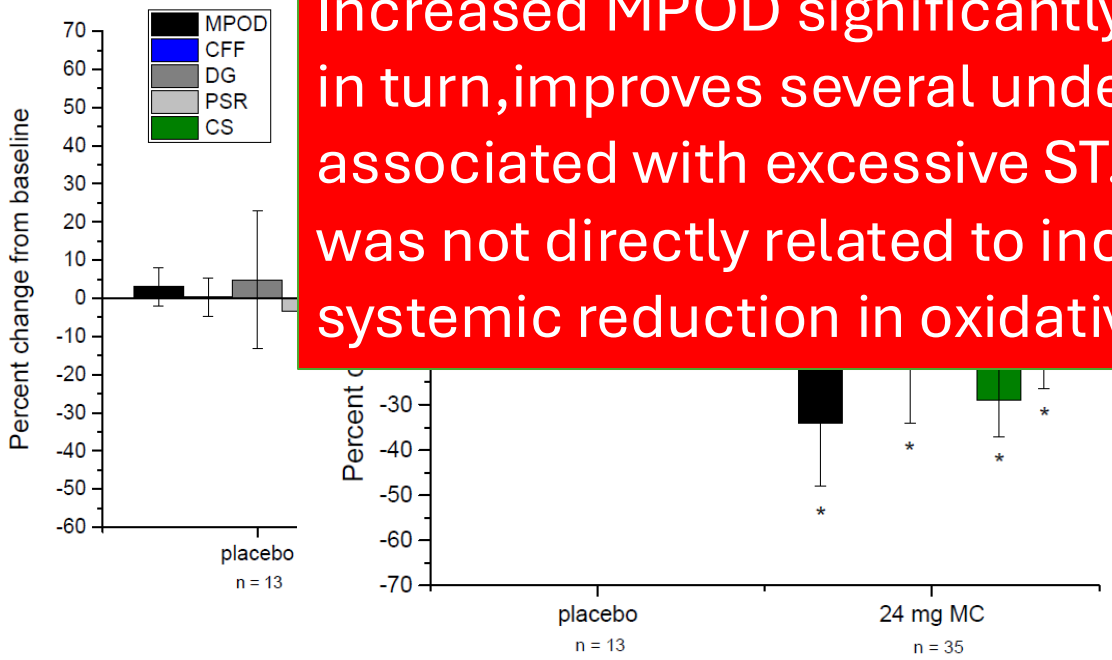
Article

Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure

James M. Stringham [1,*], Nicole T. Stringham [2] and Kevin J. O'Brien [3]

48 healthy young adults

Increased MPOD significantly improves visual performance and, in turn,improves several undesirable physical outcomes associated with excessive ST. The improvement in sleep quality was not directly related to increases in MPOD, and may be due to systemic reduction in oxidative stress and inflammation.



Foods **2017**, *6*, 47; doi:10.3390/foods6070047

nutrients

Review

A Systematic Review of Carotenoids in the Management of Diabetic Retinopathy

Drake W. Lem [1,†], Dennis L. Gierhart [2] and Pinakin Gunvant Davey [1,*,†]

of DR, specifically in patients with type 2 or poorly managed type 1 diabetes. Meanwhile, early interventional trials with dietary carotenoid supplementation show promise in improving their levels in serum and macular pigments concomitant with benefits in visual performance. These findings provide a strong molecular basis and a line of evidence that suggests carotenoid vitamin therapy may offer enhanced neuroprotective effects with therapeutic potential to function as an adjunct nutraceutical strategy for management of diabetic retinopathy.

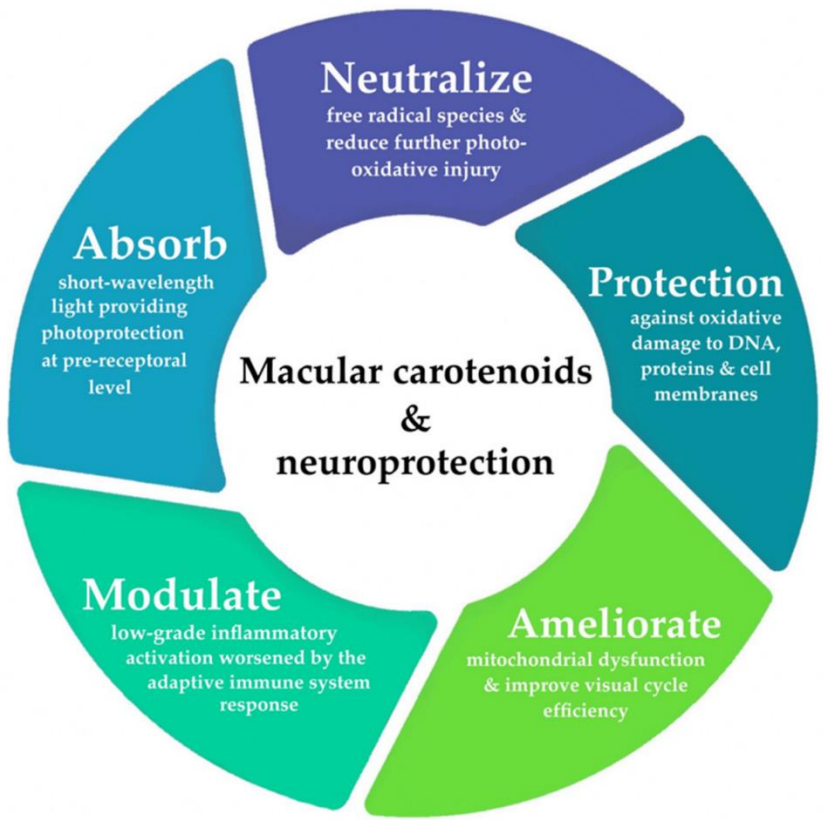
Nutrients **2021**, *13*, 2441. https://doi.org/10.3390/nu13072441

antioxidants

Systematic Review

A Systematic Review of Carotenoids in the Management of Age-Related Macular Degeneration

Drake W. Lem [1], Pinakin Gunvant Davey [1,*], Dennis L. Gierhart [2] and Richard B. Rosen [3]



nutrients

Review

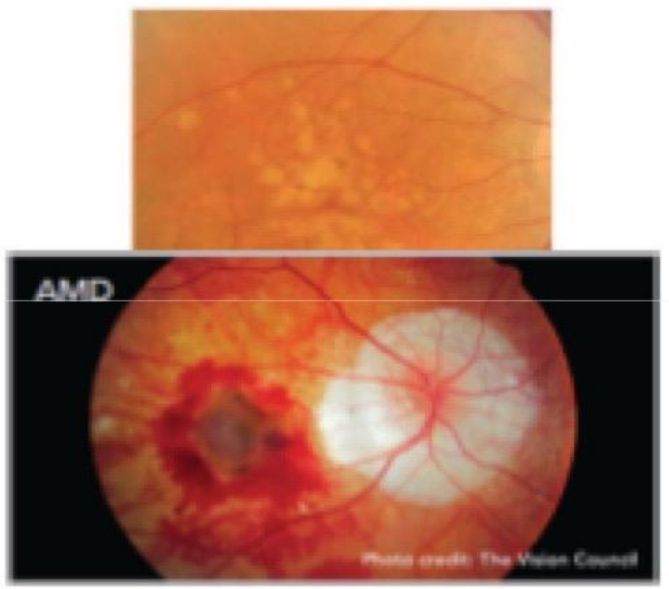
Carotenoids in the Management of Glaucoma: A Systematic Review of the Evidence

Drake W. Lem [1], Dennis L. Gierhart [2] and Pinakin Gunvant Davey [1,*]

In clinical studies, a protective trend was seen with greater dietary consumption of carotenoids and risk of glaucoma, while greater carotenoid levels in macular pigment were largely associated with improved visual performance in glaucomatous eyes. The data suggest that carotenoid vitamin therapy exerts synergic neuroprotective benefits and has the capacity to serve adjunctive therapy in the management of glaucoma

Nutrients **2021**, *13*, 1949. https://doi.org/10.3390/nu13061949

Lutein plays a role in prevention of Long term UV / blue - ocular radiation damage



Courtesy of Stuart Richer, OD, PhD, FAAO

Nutritional Manipulation of Primate Retinas, V: Effects of Lutein, Zeaxanthin, and *n*–3 Fatty Acids on Retinal Sensitivity to Blue-Light–Induced Damage

- Blue-light photooxidative damage has been implicated in the etiology of age-related macular degeneration (AMD). The macular pigments lutein and zeaxanthin and omega 3 fatty acids are shown to reduce this damage and lower the risk.
- This study investigated the effects of the lifelong absence of xanthophylls followed by Lutein or Zeaxanthin supplementation, combined with the effects of omega fatty acid deficiency, on acute blue-light photochemical damage.

Invest Ophthalmol Vis Sci. 2011;52: 3934-3942

Supplementation with Lutein, Zeaxanthin, and Omega 3's protected against blue light damage

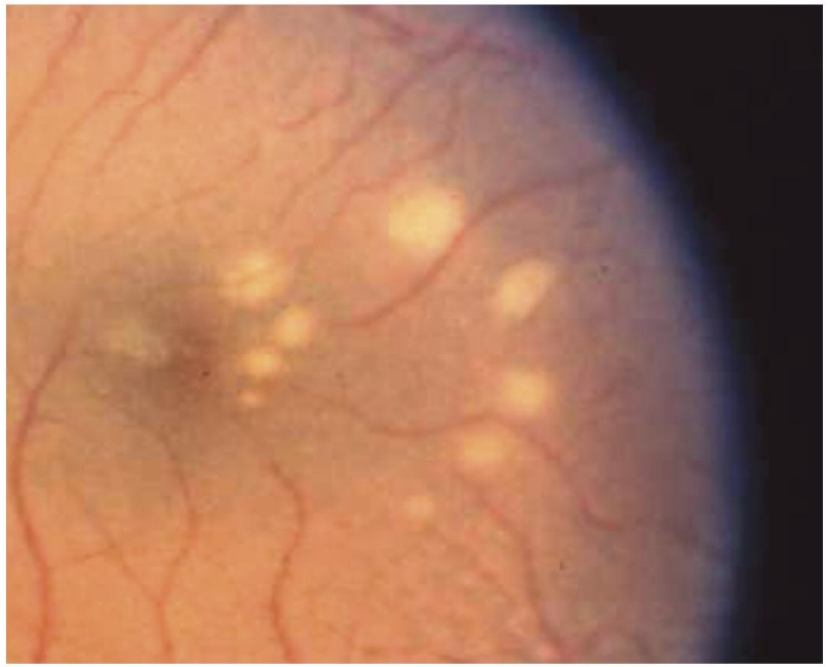
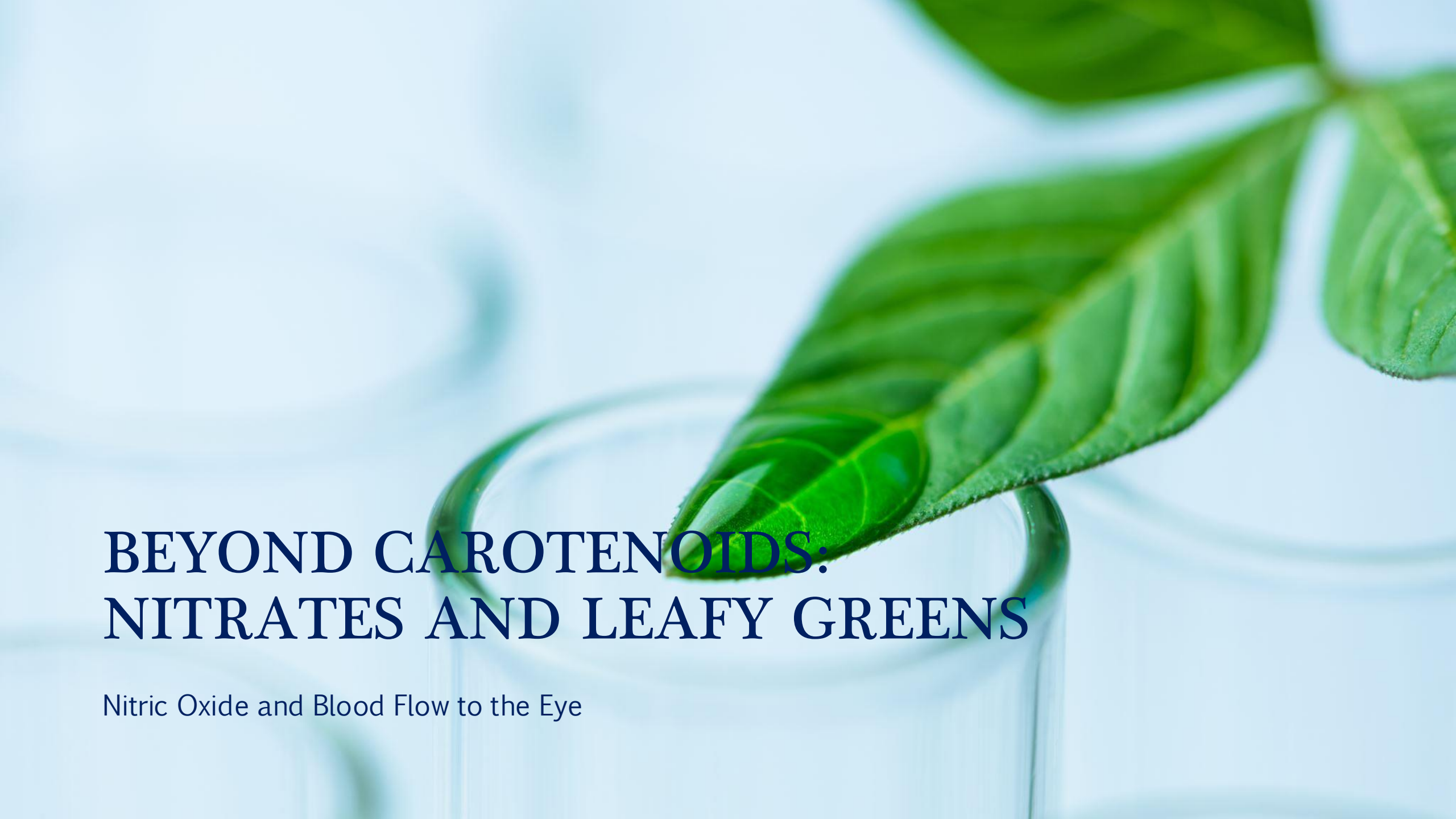


FIGURE 1. Color photograph of the ocular fundus showing lesions (white spots) induced by blue-light exposures. There were two series

RESULTS. In control animals, the fovea was less sensitive to blue-light–induced damage than the parafovea. Foveal protection was absent in xanthophyll-free animals but was evident after supplementation. In the parafovea, animals low in *n*-3 fatty acids showed greater sensitivity to damage than animals with adequate levels.

CONCLUSIONS. After long-term xanthophyll deficiency, L or Z supplementation protected the fovea from blue light–induced damage, whereas adequate *n*-3 fatty acid levels reduced the damage in the parafovea. (*Invest Ophthalmol Vis Sci.* 2011;52: 3934–3942) DOI:10.1167/iovs.10-5898

Invest Ophthalmol Vis Sci. 2011;52: 3934-3942



BEYOND CAROTENOIDS: NITRATES AND LEAFY GREENS

Nitric Oxide and Blood Flow to the Eye

According to research, eating green leafy vegetables, high in nitrates, may be associated with a reduced risk of developing glaucoma, particularly primary open-angle glaucoma (POAG), due to the body's conversion of nitrates into nitric oxide which helps maintain healthy blood flow to the optic nerve and regulate eye pressure; studies have shown a 20-30% lower risk of glaucoma in individuals with higher dietary nitrate intake from leafy greens like spinach, kale, and lettuce.

- **Nitrates in leafy greens:**

- Green leafy vegetables are a primary source of dietary nitrates.

- **Nitric oxide production:**

- When consumed, the body converts nitrates into nitric oxide, a molecule important for blood vessel health.

- **Improved blood flow:**

- Nitric oxide helps maintain optimal blood flow to the optic nerve, which is crucial for eye health.

- **Glaucoma risk reduction:**

- Studies have linked higher dietary nitrate intake from leafy greens with a significantly lower risk of developing glaucoma.

Association of dietary nitrate intake with primary open-angle glaucoma: a prospective analysis from the Nurses' Health Study and Health Professionals Follow-up Study

Jae H Kang [1], Walter C Willett [1,2,3], Bernard Rosner [1,4], Emmanuel Buys [5], Janey L Wiggs [6], Louis R Pasquale [1,6]

•PMCID: PMC4966649 NIHMSID: NIHMS801754 PMID: 26767881

Higher dietary nitrate and green leafy vegetable intake was associated with a lower POAG risk, particularly POAG with early paracentral VF loss at diagnosis.

OPHTHALMIC MANIFESTATIONS OF NUTRITIONAL DEFICIENCIES

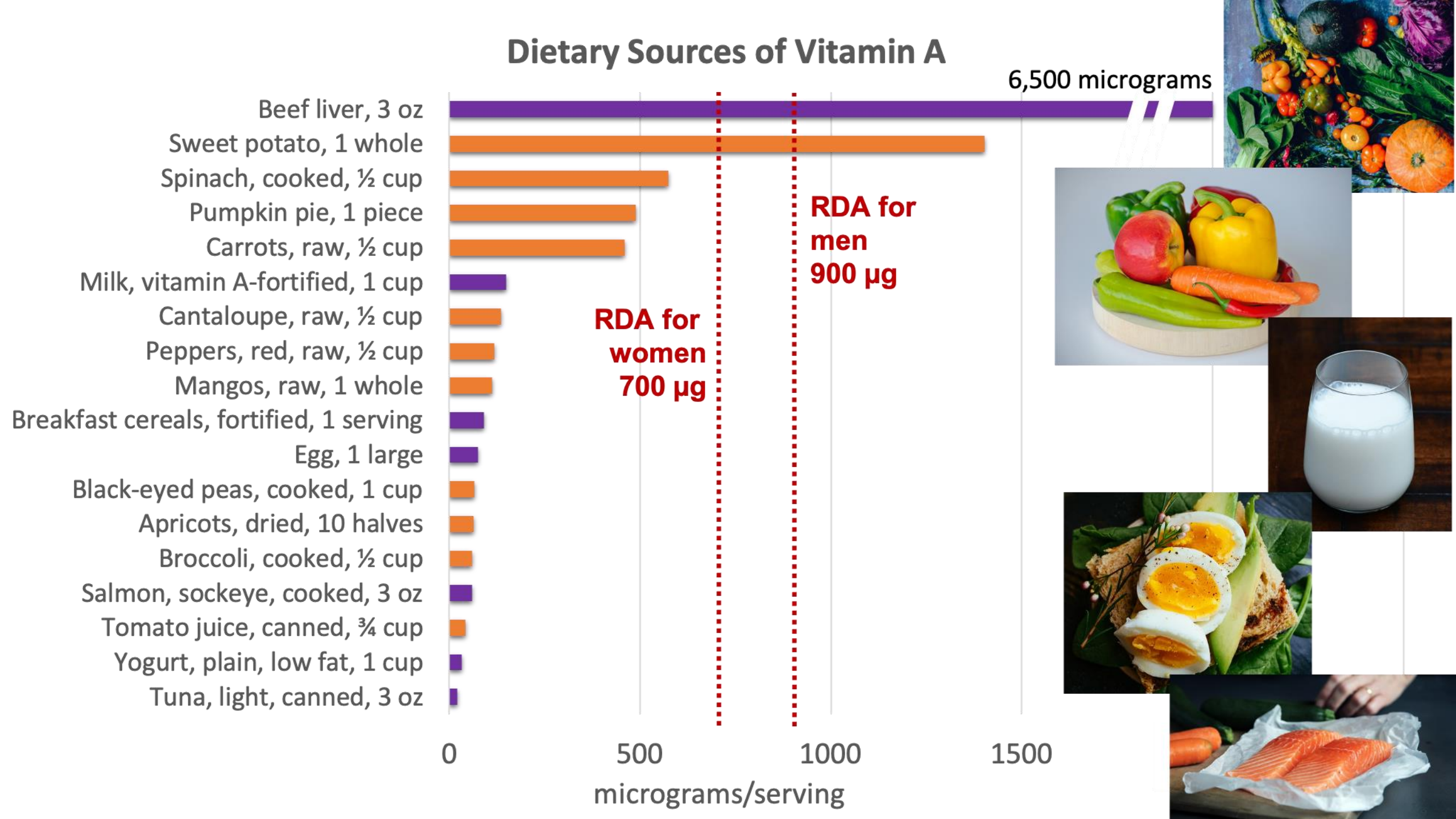
Introduction

- Nutritional deficiencies significantly impact ocular health.
- Key vitamins, minerals, and fatty acids are essential for visual function.
- Causes, risk factors, and ophthalmic effects of deficiencies in Vitamins A, B, C, D, E, zinc, folate, and Omega-3s will be discussed
- As Americans are suffering more and more from diet-related illnesses and nutrient deficiencies, practitioners on the frontlines of caring for sight should be familiar with these potentially sight-threatening deficiencies

Vitamin A Deficiency

- · Role: Essential for rhodopsin production, corneal health, and tear secretion.
- · Causes:
- - Malnutrition, fat malabsorption (e.g., celiac disease, Crohn's disease)
- - Chronic liver disease, alcoholism
- · Risk Factors:
- - Children in developing countries, pregnant women, elderly
- - Low dietary intake of animal-based foods and vegetables
- · Deficiency Effects:
- - Night blindness, xerophthalmia, corneal ulcers, keratomalacia
- · Sources: Liver, dairy, eggs, leafy greens, orange-colored vegetables.

Dietary Sources of Vitamin A



Vitamin B Complex Deficiencies

- Role: Essential for optic nerve function, metabolism, and neurotransmission.
- · Causes:
- - Poor diet, chronic alcohol use, malabsorption disorders
- - Bariatric surgery, pernicious anemia (B12)
- · Risk Factors:
- - Elderly, vegans (B12), individuals with gastrointestinal diseases
- · Deficiency Effects:
- - B1 (Thiamine): Optic neuropathy, visual disturbances
- - B2 (Riboflavin): Cataract formation, photophobia
- - B6 (Pyridoxine): Retinal dysfunction, visual fatigue
- - B12 (Cobalamin): Optic atrophy, loss of central vision

B Vitamin Sources

- : Meat, fish, dairy, eggs, legumes, whole grains.
- B1 (Thiamine): whole grains, legumes, nuts, meat, enriched flour
- B2 (Riboflavin): dairy products, eggs, legumes, meat, fish, poultry, green leafy vegetables, fruits, and whole grains
- B6 (Pyridoxine): potatoes, bananas, meat, poultry, fish, and whole grains
- B12 (Cobalamin): present almost exclusively in animal foods which include meat, poultry, fish, dairy, and eggs. Vegans and some vegetarians should take a B12 supplement

Vitamin C Deficiency & Ocular Impact

- · Role: Antioxidant, collagen synthesis, maintains ocular vascular integrity.
- · Causes:
- - Poor intake of fruits and vegetables, smoking, alcoholism
- - Chronic illness, poor wound healing
- · Risk Factors:
- - Elderly, smokers, individuals with limited diets
- · Deficiency Effects:
- - Increased cataract risk, delayed corneal wound healing
- - Scurvy-related retinal hemorrhages

Food Sources of Vitamin C

- Citrus fruits, cantaloupe, broccoli, Brussel sprouts, cauliflower, and potatoes
- Substantial amounts of vitamin C are lost during high-temperature cooking and during prolonged warming

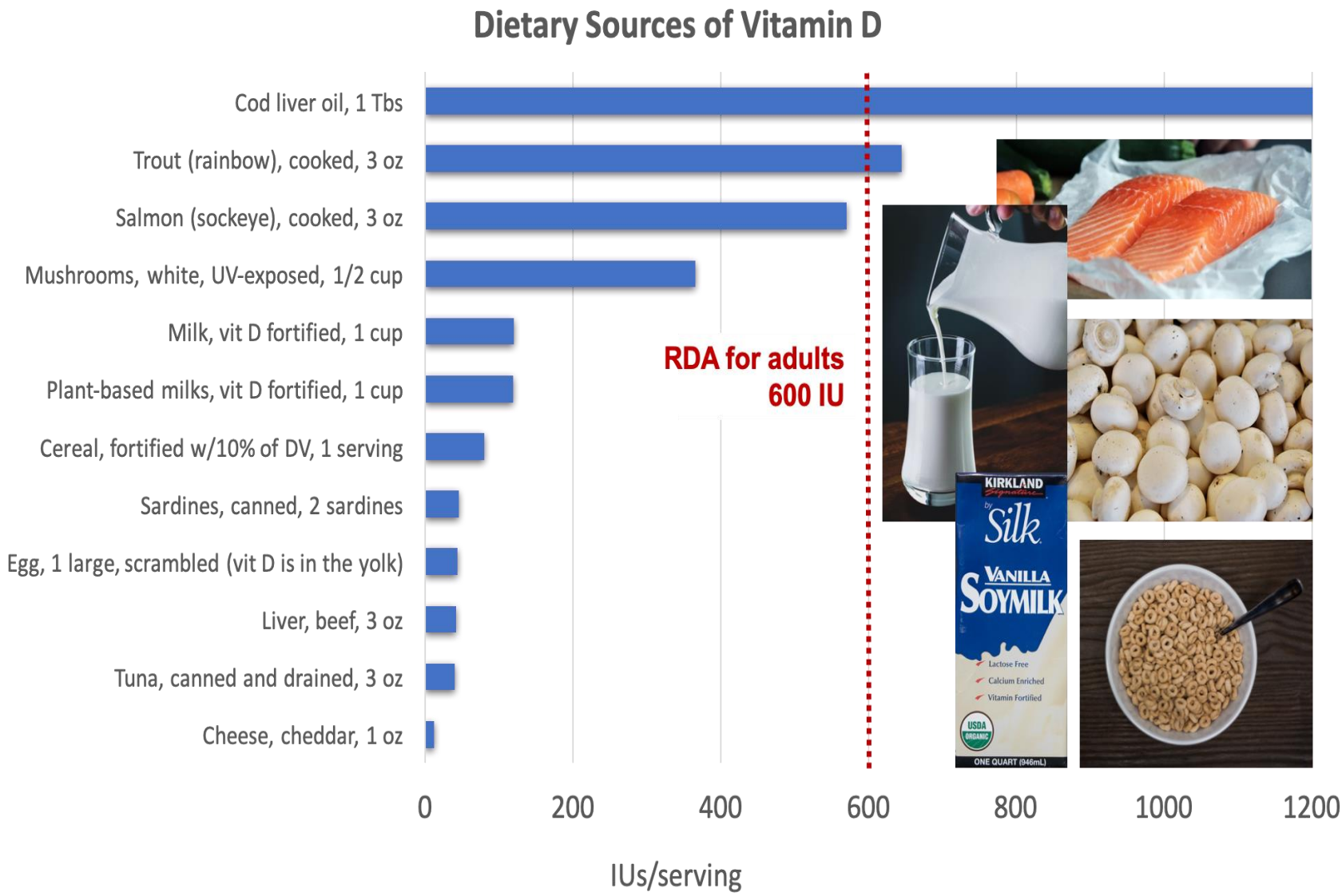
Vitamin D Deficiency & Eye Disorders

- · Role: Immune function, anti-inflammatory, protects retinal neurons.
- · Causes:
- - Limited sun exposure, dark skin pigmentation, kidney disease
- - Fat malabsorption (celiac disease, Crohn's disease)
- · Risk Factors:
- - Older adults, people living in northern latitudes, obesity
- · Deficiency Effects:
- - Dry eye syndrome, age-related macular degeneration (AMD)
- - Increased risk of diabetic retinopathy

.

Sources of Vitamin D

- The sun, cod liver oil, oily fish, vitamin D-fortified foods

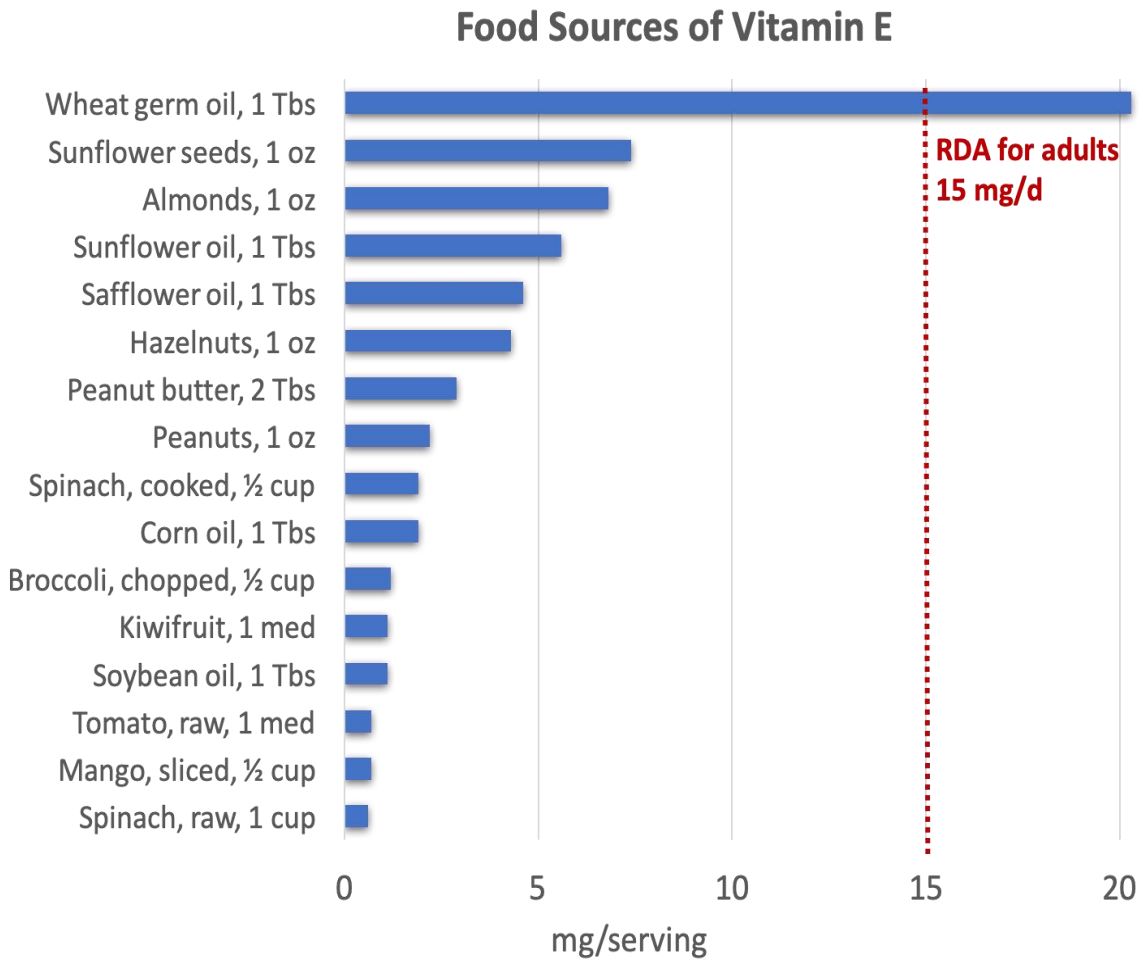


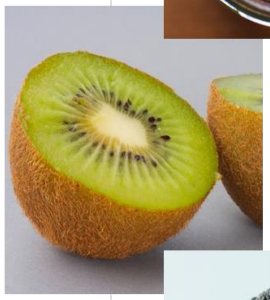
Vitamin E Deficiency

- **- Role: Antioxidant, prevents oxidative retinal damage.**
- - Causes: Fat malabsorption, genetic disorders (abetalipoproteinemia)
- - Risk Factors: Premature infants, individuals with liver disease
- - Deficiency Effects: Macular degeneration, retinal damage

Foods Sources of Vitamin E

Nuts, seeds, unprocessed vegetable oils, whole grains, egg yolks, leafy green vegetables,





Zinc Deficiencies

- **Role: Essential for retinal function and night vision.**
- - Causes: Inadequate dietary intake, alcoholism, chronic illness
- - Risk Factors: Vegetarians, elderly, digestive disorders
- - Deficiency Effects: Poor night vision, retinal degeneration

Food Sources of Zinc

- Seafood, meats, whole grains, wheat germ, wheat bran, dairy products, legumes, peanuts, egg yolk, nuts, and seeds

Omega-3 Fatty Acids & Eye Health

- · Role: Maintains retinal function, reduces inflammation, enhances tear film stability.
- · Causes of Deficiency:
- - Low seafood intake, high consumption of processed foods
- · Risk Factors:
- - Individuals with dry eye disease, AMD risk, high inflammatory states
- · Deficiency Effects:
- - Increased risk of AMD, diabetic retinopathy, dry eye syndrome

Sources of Omega 3's

- **Fish is the main dietary source of EPA and DHA.**
- Fish oils that contain more than 40% by weight of omega 3's include cod, haddock, mackerel, sardines, ocean trout, and whiting.
- Fish oils that contain 28-40% by weight include tuna, pink salmon, coho salmon, halibut, flounder, grouper, red snapper, sole, and rainbow trout.
- The omega 3 content of farmed fish is lower than wild
- Eggs, dairy products, meat and poultry also contain EPA and DHA, although in lesser amounts than fish.
- Feeding animals grass and other omega-3-rich foods increases the EPA and DHA content of their eggs, milk, and meat.

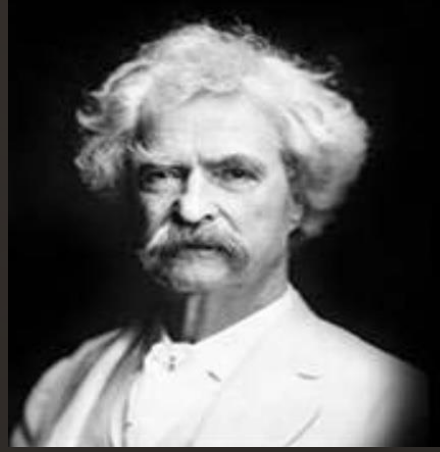
Prevention & Public Health Strategies

- · Balanced diet rich in essential nutrients.
- · Public health interventions:
- - Vitamin A supplementation programs
- - Fortified foods (Vitamin D, B12, Omega-3s)
- - Nutritional education campaigns
- · Regular screening for nutritional deficiencies in at-risk populations.
- · Collaboration between optometrists, ophthalmologists, and nutritionists.

Nutrients Act Synergistically

"When we try to pick out anything by itself,
We find it hitched to everything else in the universe." John Muir

It ain't what you don't know that gets you into trouble. It's what you know for sure that just ain't so.



Mark Twain

American Author and Humorist

(1835-1910)