

Carotenoids and nutrients in vision and retinal health

Pinakin G Davey OD, PhD, FAAO, FOWNS, FARVO
Professor
Director of Clinical Research
Western University of Health Sciences



1

Disclosures

Has a relevant financial relationship with Sanofi, ZeaVision, Guardion Health and Innova systems as a speaker or research / consultant

The content and format of this course is presented without commercial bias and does not claim superiority and commercial product or service.

2

Outline

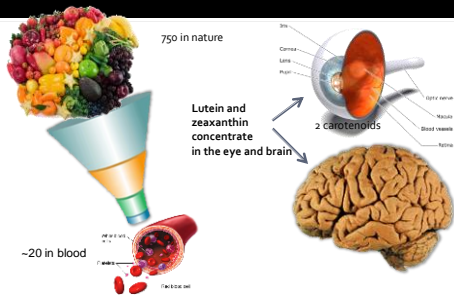
- Carotenoids MPOD basics
- MPOD and AMD
- Glaucoma and MPOD
- MPOD and sleep, stress
- Adults and Children and MPOD
- Sports vision and MPOD
- Cognition and MPOD
- Diabetes, RP and carotenoids and MPOD

3

Carotenoids- Xanthophylls the Basics

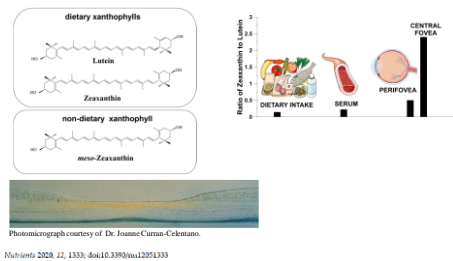
4

Carotenoids



5

Carotenoids in retina-Xanthophylls



6

Macular Xanthophylls

- Around 50 carotenoids consumed
- Around 20 or so see in serum
- Two that are obtained in diet make it to all over the body (Lutein and zeaxanthin)
- RPE65 converts lutein to meso-zeaxanthin in retina

Carotenoid ratios	L:Z:M
US Diet	5:1:0
Blood:	3:1:0
Whole retina:	2:1:0.5
Fovea:	1:1:1 (2:1)

7

Table 1 Carotenoids in fruits and vegetables

	Nonanthenes and Xanthoxanthins	Lutein and zeaxanthin	Lutein	Zeaxanthin	Cryptoxanthin	Lycopene	α-carotene	β-carotene
Egg yolk	8	89	54	35	4	0	0	0
Milk (cont)	9	86	60	25	5	0	0	0
Egg	18	54	54	0	0	0	0	0
Red seedless grapes	23	53	43	10	4	0	0	16
Zucchini squash	19	52	47	5	24	0	0	5
Tomato	30	48	48	0	0	0	0	2
Spinach	14	47	47	0	19	8	0	26
Orange pepper	4	45	46	37	22	0	8	2
Yellow squash	19	44	44	0	0	0	28	9
Cucumber	14	42	36	4	39	0	0	6
Pea	33	41	41	0	21	0	0	5
Green pepper	29	39	36	3	20	0	0	12
Red grape	27	37	33	4	29	0	1	6
Butternut squash	24	37	37	0	34	0	5	0
Orange juice	28	35	15	20	25	0	3	8
Broccoli	18	35	17	18	4	0	0	48
Celery (stalks, leaves)	12	34	25	2	40	0	13	9
Green grapes	10	32	32	0	30	0	0	0
Brussels sprouts	20	29	27	2	36	0	0	11
Scallions	32	29	27	3	35	8	0	0
Green beans	27	29	22	3	42	0	1	5
Orange	36	22	7	15	12	11	8	11
Beetroot	5	22	22	0	49	0	0	25
Apple (red delicious)	22	20	19	1	23	13	5	17
Mango	12	18	2	16	4	6	0	20
Green lettuce	33	15	15	0	36	0	16	0
Tomato juice	0	13	11	2	2	57	12	16
Peach	20	13	8	8	1	0	10	50
Yellow pepper	88	12	12	0	0	0	0	0
Nectarine	58	11	9	6	23	0	0	48
Red pepper	50	7	7	0	3	82	0	12
Junonia (fruit)	9	6	6	0	0	0	0	22
Carrot	0	2	2	0	0	0	43	55
Carrot juice	9	1	1	0	0	0	0	25
Dried apricot	2	1	1	0	0	0	0	87
Green kidney beans	2	1	0	0	28	0	0	0

By Y Oshikawal 1998;82:907-910



8

Carotenoids food sources

Foods	Serving Size	Lutein + Zeaxanthin Content (mg)
Spinach, frozen (cooked)	1 cup	29.8
Kale, frozen (cooked)	1 cup	25.6
Swiss chard (cooked)	1 cup	11.0
Collard greens, frozen (cooked)	1 cup	8.9
Summer squash (cooked)	1 cup	4.0
Peas, frozen (cooked)	1 cup	3.8
Brussel sprouts, frozen (cooked)	1 cup	2.4
Broccoli, frozen (cooked)	1 cup	2.0
Edamame, frozen	1 cup	1.6
Sweet yellow corn (boiled)	1 cup	1.5
Asparagus (boiled)	0.5 cup	0.7
Avocado, raw	1 medium-size	0.4
Egg yolk, raw	1 large	0.2

Meso-zeaxanthin is not found in common food - in shrimp shells, turtle fat, and fish skin



Lein, D.W., Gierhart, D.L., Davey, P.G. A Systemic Review of Carotenoids in the Management of Diabetic Retinopathy. *Nutrients* 2021, 13, 2644. <https://doi.org/10.3390/nu13072644>

9

Why is Zeaxanthin the Most Concentrated Xanthophyll in the Central Fovea?



Justyna Widomska ^{1,2}, John Paul SanGiovanni ^{1,2} and Witold K. Subczynski ¹

- Very potent antioxidant-particularly in region of high oxygen tension and metabolism compared to lutein
- Zeaxanthin structure more stable in the lipid bilayer membranes
- Zeaxanthin is less predisposed to destruction than lutein when counteracting oxygen singlets



Nutrients 2021, 13(10), 1611. <https://doi.org/10.3390/nu13101611>

10

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

Binxing Li¹, Evan W. George¹, Gregory T. Rognon¹, Aruna Gonsoupsud¹, Arunkumar Ranganathan¹, Fu-Yen Chang¹, Lajla Shi¹, Jeanne M. Frederik¹, and Paul S. Bernstein^{1*}

¹Department of Ophthalmology and Visual Sciences, Moran Eye Center, University of Utah School of Medicine, Salt Lake City, UT 84143

Zeaxanthin	Lutein
<ul style="list-style-type: none"> Mainly accumulates in the IPL, OPL, and ONL at the center of the human foveal pit Concentrates highly in Fovea centralis Fovea high risk of Light induced oxidative damage, singlet oxygen 	<ul style="list-style-type: none"> Distributed more diffusely across the retina at a much lower concentration relative to zeaxanthin Evenly and low concentration across macula

Take home "the current AREDS2" formula's 10 mg of lutein and 2 mg of zeaxanthin may not be enough and greater amounts may be needed.

11

Astaxanthin

ASTAXANTHIN
C40 carotenoid, with 10 times higher free radical inhibitory activity than related antioxidants

Scavenges radicals from the surface of the cell and at the center of the phospholipid membrane

Increases retinal blood flow
Increases retinal antioxidant capacity
Increases retinal antioxidant capacity

Clinical trial results: 15 weeks of treatment with 15 mg of astaxanthin daily significantly improved retinal blood flow, retinal antioxidant capacity, and retinal antioxidant capacity. No side effects reported.

Review
"Therapeutic uses of natural astaxanthin: An evidence-based review focused on human clinical trials"

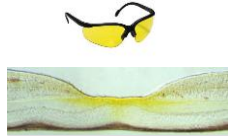
Andres Donoso¹, Javiera González-Durán², Andrés Agurto Muñoz³, Pablo A. González⁴, Cristian Agurto-Muñoz^{3,5}

Pharmacological Research 166 (2021) 1044-9

12

Carotenoids influence visual function

- Optical mechanisms
 - Glare Disability,
 - Color Contrast
 - Visual Range
 - Contrast Sensitivity
- * Biological mechanisms
 - Glare Recovery

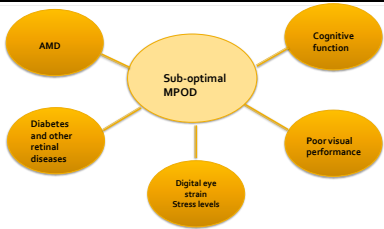


13

Macula pigment optical density- A biomarker

14

MPOD is a Biomarker



PG Davey et al, Differences in macular pigment optical density across ethnicities: A comparative study *The Advances in Ophthalmol* 2020

15

Clinical devices

QUANTIFEYE- ZEAVISION

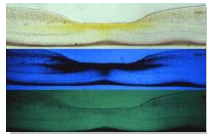
MAPCATSF- GUARDION HEALTH



16

Measurement of Macular Pigment Optical Density

- Heterochromatic flicker Photometry- principle
- Macular pigment absorbs blue light (not green light)
- More macular pigment = longer time you see flicker
- Results are quantified via software



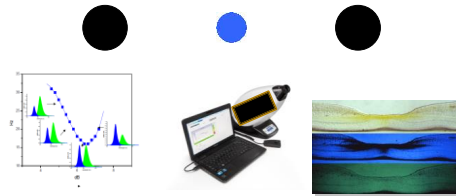
17

QuantifEye® MPS II Instrument (simple efficient, 2-3 minute test)

Left Peripheral Fixation target

Centre Flickering Target

Right Peripheral Fixation target



18

Things I wanted to know about measuring MPOD

- Is it easy? Yes
- Do I need to perform in both eyes? NO
- How long does it take? 2 minutes for testing
- Dominant eye? Any eye
- Correlation between eyes? Excellent
- Is it repeatable? Excellent
- Is it reproducible? Yes
- Can it measure changes? Yes

Davey PG et al., *Clin Ophthalmol*. 2016 Aug 29;10:1671-8. doi:10.2147/



19

Research devices not available clinically

20

Macular pigment reflectometry

- Provide quicker measurements-Objective
- Provide undilated measurements of MPOD
- Provide measures of Lutein and Zeaxanthin
- Provide lens density measures
- Provide measures in eyes with pathology

PROCEEDINGS OF SPIE

Macular pigment reflectometry: development and evaluation of a novel clinical device for rapid objective assessment of the macular carotenoids

Pinakin G. Davey, Jordan Bass, Frank Spors, Dennis L. Gierhart, Pinakin G. Davey

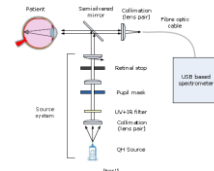
Macular pigment Reflectometry work from Davey Lab

21

nutrients

Macular Pigment Reflectometry: Developing Clinical Protocols, Comparison with Heterochromatic Flicker Photometry and Individual Carotenoid Levels

Pinakin G. Davey^{1,*}, Richard B. Rosen² and Dennis L. Gierhart³



22

Measurement of Carotenoids in Perifovea using the Macular Pigment Reflectometer

Keywords: macular pigment reflectometry, heterochromatic flicker photometer, lutein, zeaxanthin, retina, macular degeneration, macular pigment optical density

Date Published: 1/28/2020

Citation: Sanabria, J.C., Bass, J., Spors, F., Gierhart, D.L., Davey, P.G. Measurement of Carotenoids in Perifovea using the Macular Pigment Reflectometer. *J. Vis. Exp.* (1), e60429, doi:10.3791/60429 (2020).



23

Other devices

- Autofluorescence techniques
- Raman Spectroscopy
- Dual Wavelength Autofluorescence technique

24

AMD classification, hypothesis and more

25

Chronic disease- AMD

- AMD in USA 3-3.5 million 2020
- 196 million worldwide 2020; 288 million 2040
- AMD # 1 cause of legal blindness in the developed world.
- 7.1% of individuals over the age 75 years have late stage AMD

26

AMD

Dry or non exudative	Wet or exudative
Chronic visual acuity remains unchanged for long, some degree vn loss, may progress to severe blindness	10-15% of AMD Vision dramatically reduced
Advanced AMD Geographic Atrophy Or choroidal neovascular growth	

27

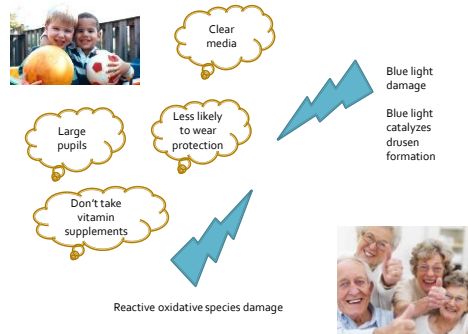
Classification and pathogenesis

- Although neat to classify as dry and wet
- There is overlap of pathogenesis
- The end stage of dry AMD continues into wet AMD
- So important to understand that wet AMD pathogenesis continues in the background of dry AMD
- Neovascular AMD-Anti VEGF
- Dry AMD- Vitamins

28

AMD a journey

29



30

Dry- AMD

PATHOGENESIS

- Exact pathogenesis unknown
- Oxidative damage due to higher oxygen levels and reactive oxidation species (ROS)
- Blue light
- Lifetime light exposure

NATURAL PROTECTION

- Antioxidants present in eye
 - Vitamin C
 - Zeaxanthin
 - Meso-zeaxanthin
 - Lutein
- Natural filter of blue light
- Pupils become smaller with age
- Yellowing of lens cuts of blue

31

Poll 1

When do you prescribe carotenoid vitamin supplement to individuals that have risk of AMD?

- A) First sign of drusen formation
- B) Early AMD
- C) Intermediate AMD
- D) Advanced AMD
- E) Never Patients just don't take them regularly enough.

32

Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration

The Age-Related Eye Disease Study 2 (AREDS2)
Randomized Clinical Trial

- No true placebo- patients got AREDS formula
- Addition of lutein (10 mg)+zeaxanthin (2mg)+ EPA (650 mg) + DHA (350 mg) did not further reduce the risk of progression to Advanced AMD
- More lung cancer was noticed in β -carotene group compared to no β -carotene

JAMA. 2013;309(19):2005-2015
Published online May 5, 2013. doi:10.1001/jama.2013.4997

33

Population of AREDS-2

- Extremely educated
- Well nourished population

34

Sub-group analysis



Specially lutein and zeaxanthin was most beneficial when the individuals were taking it had lowest level to begin with

35

Management of Dry-AMD... current practice

Is this good enough?



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).

36

AMD classification system

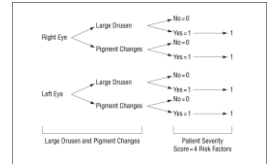
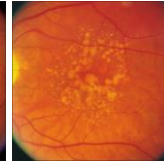


Classification	Characteristics
No abnormal findings	<ul style="list-style-type: none"> No aging changes: Absence of drusen No pigmentary abnormalities
Early AMD	<ul style="list-style-type: none"> Normal aging changes: Druselets only (small drusen $\leq 63 \mu\text{m}$) No pigmentary abnormalities
Intermediate AMD	<ul style="list-style-type: none"> Medium-sized drusen $> 63 \mu\text{m}$ and $\leq 125 \mu\text{m}$ No pigmentary abnormalities
Late AMD	<ul style="list-style-type: none"> Large drusen $> 125 \mu\text{m}$ and/or pigmentary abnormalities Neovascular AMD and/or any geographic atrophy

Abbreviation: AMD, age-related macular degeneration.

37

AMD Simplified Severity Scale- AREDS 18



38

AMD risk calculator

Risk Calculation

Risk of developing advanced AMD within years

Calculate Risk

Risk of advanced AMD %

Risk of GA %

Risk of NV %

Advanced AMD Risk Calculation

Substitutions for Use

Demographic/Environmental Factors

Age (years)

Family history of AMD in parent or sibling

Current cigarette smoker

Retinal Examination

Simple scale score

Very large drusen ($> 250 \mu\text{m}$) in either eye

Advanced AMD present in either eye

If advanced AMD is present, geographic atrophy (GA) or neovascular AMD (NV)

Genotype Information (if Available)

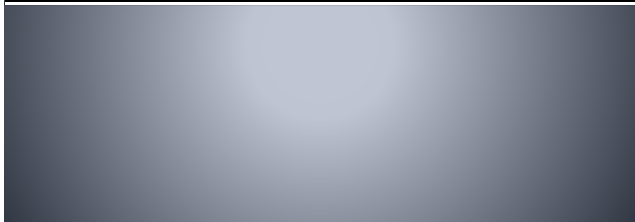
CFH (rs1061170)

ARMS2 (rs10443924)



39

Measurements performed for AMD



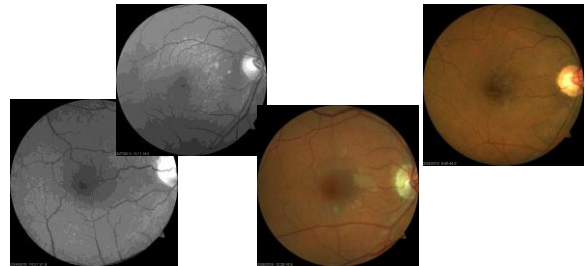
40

Bad tests bad data

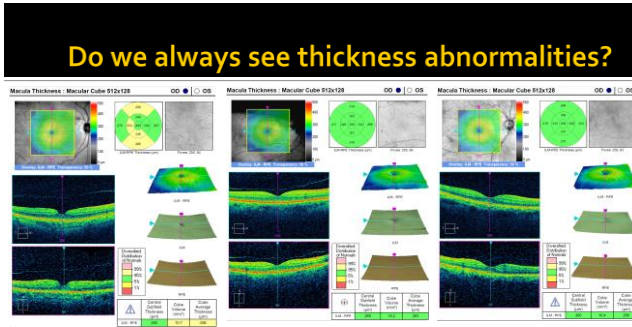
- 1) Snellen Acuity (circa 1865) -archaic-Remains stable
 - 2) Amsler Grid (circa 1895) –archaic-Insensitive
- Maybe works but definitely makes us feel better

41

Structural changes



42



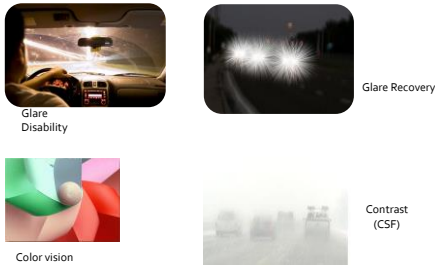
43

Bad tests bad data

- 1) Snellen Acuity (circa 1865) -archaic
 - 2) Amsler Grid (circa 1895) – archaic
- Maybe works but definitely makes us feel better

44

Functional vision is affected in Early AMD



45

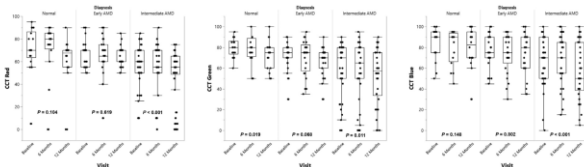
How do you monitor treatment?

- Baseline fundus photos then OCT ... then ... do all over in 6 months?
 - So you have measured structural damage...what about the function?
- Contrast sensitivity changes
 - Color contrast changes
 - Dark adaptation changes
 - Visual field changes
 - Electrodiagnostics
- } Visual function changes observed in AMD

46

Longitudinal Study of Visual Function in Dry Age-Related Macular Degeneration at 12 Months

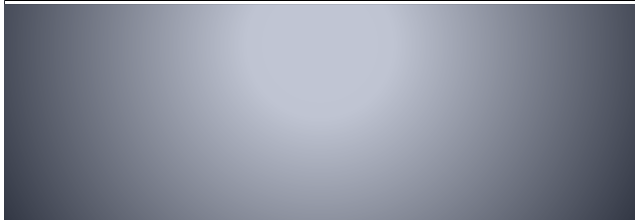
S. Tammy Hsu, BA,¹ Atilia C. Thompson, MD, MPH,¹ Sandra S. Stimmert, DrPH,¹ Ulrich F.O. Luhmann, PhD,² Lejla Vajzovic, MD,¹ Anupama Horne, MD,¹ Stefanie G. Schuman, MD,¹ Cynthia A. Toth, MD,¹ Scott W. Cousins, MD,³ Ekenora M. Lal, MD, PhD¹



Ophthalmology Retina 2019;

47

Contrast sensitivity testing



48

Distance or near contrast



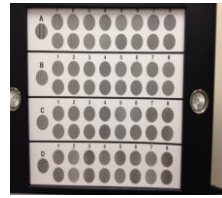
Disadvantage: Produces only one number peak contrast sensitivity...
 Cannot assess various spatial frequencies

Mars contrast testing



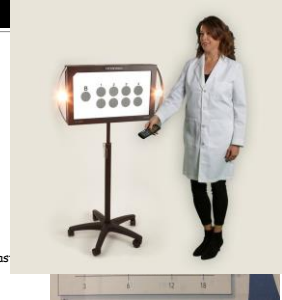
49

CSV-1000



- Varying spatial frequencies and contrast
- Without and with glare

Contrast sensitivity work from Davey Lab



CSV-2000



50

What tests do we perform?

- Visual acuity- Stable
- OCT- can see the changes but how does that relate to vision and function?
- OCT-Angiography – Research
- Do we perform contrast sensitivity???
- No
- What do we give “vitamins”...
- Do we always know if its helping?
- Do we quantify its benefits?

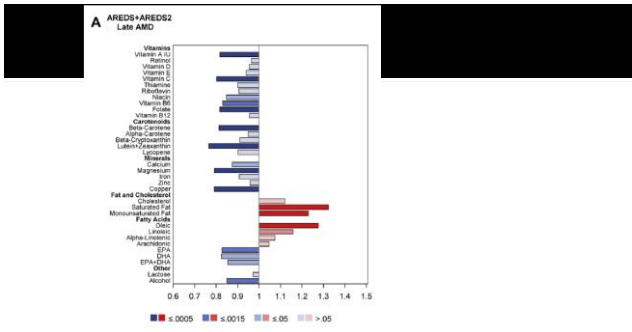
51

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

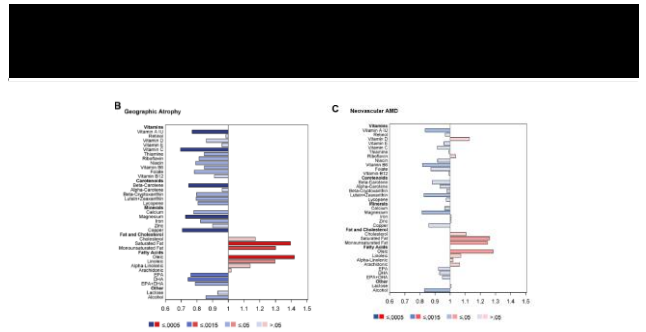
Elvira Agrón, MA,¹ Julie Mares, PhD,² Traci E. Clemons, PhD,³ Anand Swaroop, PhD,⁴ Emily Y. Chew, MD,¹ Tilmann D.L. Koenen, BM BCh, PhD,¹ for the AREDS and AREDS2 Research Groups*

Ophthalmology 2021;128:425-442

52



53



54

antioxidants

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

Drake W. Lem ¹, Pinakin Guvant Davey ¹, Dennis L. Gierhart ² and Richard B. Rosen ³

There is robust evidence all stages of AMD are helped by carotenoid vitamin therapy

Antioxidants 2021, 10, 1255. <https://doi.org/10.3390/antiox10081255>

55

Management of your patient with AMD

- Dosage does matter
- A good vitamin carotenoid supplement that you can trust.
- Ingredients certified
- NSF certification
- Measure MPOD
- Provide a real recommendation
- Assess change in MPOD 3 months and 6 months period.

56

CLINICAL TRIALS
 SECTION EDITOR: ANNE S. LINDBLAD, PhD

Clinical Trial of Lutein in Patients With Retinitis Pigmentosa Receiving Vitamin A

ARCHIVES EXPRESS

Eilat J. Benou, MD, Bernard Rosser, PhD, Michael A. Sanberg, PhD, Carol Wajgl DiFranco, MA, Robert J. Brocheaux, MD, K. C. Ripps, PhD, Elizabeth J. Johnson, PhD, Eilat J. Anderson, MD, Chen A. Johnson, PhD, Alexander E. Gaudin, MD, Walter C. Willet, MD, Ernst J. Schaefer, MD

- Randomized controlled trial
- Patients received 12 mg of lutein or a control tablet daily.
- All were given 15 000 IU/d of vitamin A palmitate.

12 mg/d of lutein to slow visual field loss among nonsmoking adults with retinitis pigmentosa taking vitamin- A

Arch Ophthalmol. 2010;128(4):403-411

57

What can we differ than AREDS?

<p>TESTING</p> <ul style="list-style-type: none"> • Measure MPOD • Measure functional tests 	<p>MANAGEMENT</p> <ul style="list-style-type: none"> • More amounts of carotenoids • Omega-3 • Measure baseline MPOD • Check Functional vision tests
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Show me the data

58

59

Summary of various RCTs in AMD

- Increase in serum levels
- Increase in MPOD
- Enhanced central retinal functions mfERG
- Slight benefits to BCVA
- Contrast improvements
- Glare improvements
- Mesopic vision improvements
- Risk reduction to progression

60

What can we do different than AREDS?

TESTING

- Measure MPOD
- Measure functional tests
 - Contrast sensitivity
 - Color Contrast
 - Glare function

MANAGEMENT

- More amounts of carotenoids
- Omega-3
 - Enhances carotenoid absorption
- Measure baseline MPOD
 - Check it every 3 months
 - Monitor compliance
 - Monitor uptake
- Check Functional vision tests
 - Monitor improvement

61

NEI Announces AREDS AMD Scale



9-Step Severity Scale

- Patients increasing 2 step within first 2 years of the study had a significantly greater risk of progressing to late AMD five years later
- Likelihood even greater for those who increased at least 3 steps
- 2 and 3 step increases were also associated with a higher chance of vision loss five years later

Excerpt from "Association of 2-year progression along the AREDS AMD scale and development of late age-related macular degeneration or loss of visual acuity." JAMA Ophthalmol. 2020

62

Glaucoma and Carotenoids

Carotenoids in the Management of Glaucoma: A Systematic Review of the Evidence *Nutrients* 2021



63

Poll 2

Do you think there is a role for adjunctive therapy with nutrition in glaucoma?

- A) Possibly
- B) Yes
- C) Probably no
- D) Definitely NO
- E) Open minded

64

Glaucoma an epidemic

- **Glaucoma in USA** 2.7 million; 50% undiagnosed
- Glaucoma suspects 4 times more than glaucoma
- 64.3 million worldwide; 76 million by 2020 ; 111.8 by 2040

65

Macular Pigment and glaucoma

- We know the advantages of multivitamins and AMD
 - Prevents oxidative damage
 - Quenches any free radical
 - Prevents photoreceptor death
 - Absorbs stray light
- Oxidative damage can also occur in glaucoma
 - Both Anterior and posterior segment

66

Where is the evidence?

- Aqueous humor has lot of vitamin-C
- Macular pigment optical density can be lower in glaucoma patients than individuals without glaucoma

67

Evidence of lower macular pigment optical density in chronic open angle glaucoma

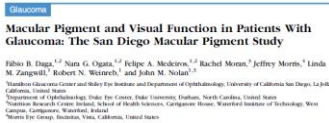
Clinical science

Macular pigment is associated with glare-affected visual function and central visual field loss in glaucoma

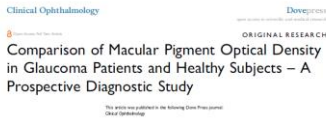
We Fong Siah,¹ Colm O'Brien,^{1,2} James J Loughman^{3,4}



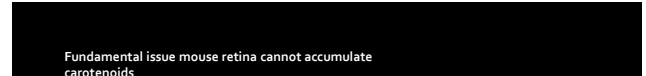
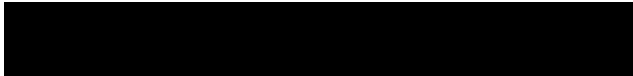
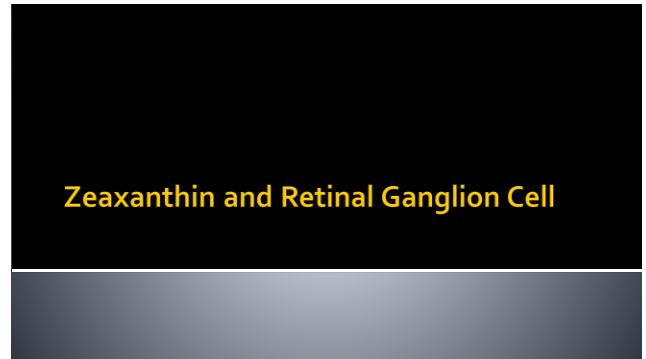
68



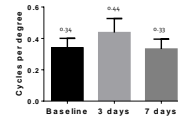
69



70



OKR Visual Acuity measurement. Visual acuity was measured by immobilizing the mouse head and restraining the mouse with a home-made OKR device. An infrared camera was used to monitor and record pupil movement and videos were analyzed with the Tracker video analysis and modeling tool. A 34.3 cm-diameter grating drum rotated around the mouse illuminated with a 200 lx white light. The grating frequency was decreased using the stair case method until eye tracking ceased, identifying the smallest grating detected by the mouse's eye.

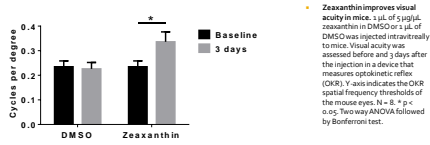


1 µl of 5 µg/µl zeaxanthin in DMSO was injected intravitreally to mice. Visual acuity was assessed before the injection and 3 and 7 days after the injection in a device that measures optokinetic reflex (OKR). Y-axis indicates the OKR spatial frequency thresholds of the mouse eyes. N = 4.

71

72

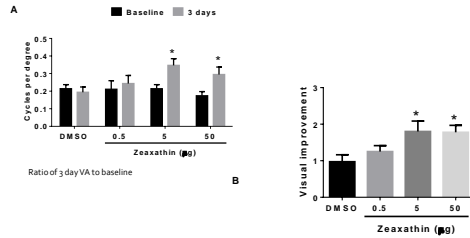
Result



Zeaxanthin improves visual acuity in mice. 1 µl of 5 µg/ml zeaxanthin in DMSO or 1 µl of DMSO was injected intravitreally 10 times. Visual acuity was assessed before and 3 days after the injection in a device that measures optokinetic reflex (OKR). Y axis indicates the OKR spatial frequency threshold of the mouse eyes. N = 8. * p < 0.05. Two-way ANOVA followed by Bonferroni test.

73

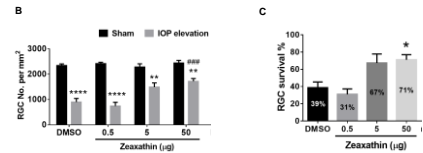
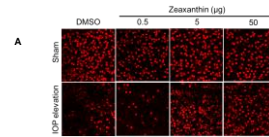
Dose response testing



74

IOP SPIKE 1 HOUR 110 MMHG

Mouse acute glaucoma model. Mice were anesthetized with isoflurane. Pupils were dilated with 1% tropicamide. The anterior chamber of the right eye was cannulated with a 30-gauge infusion needle connected to a normal saline reservoir, which was elevated to maintain an intracocular pressure of 140 mmHg for 60 min. Retinal ischemia was confirmed by whitening of the fundus. A sham procedure performed without elevating the pressure in the contralateral left eye was used as control.



75

76


Summary MPOD and Glaucoma

- Measure Macular pigment in glaucoma patients
- Measure Ganglion Cell Complex/ Analysis
- Recommend multivitamin intake with good amount of Lutein and Zeaxanthin- **Dosage matters!**
- Helps age-related diseases and may provide some benefits to glaucoma.

77

Poll 3
 Do you think there is a role for adjunctive therapy with nutrition in glaucoma?
 A) Possibly
 B) Yes
 C) Probably no
 D) Definitely No
 E) Open minded

78



Screen time stress and cognitive performance

79

Poll 4
Carotenoid and vitamins have a role to play in screen time related stress and fatigue
 A) Agree
 B) Possibly agree
 C) Disagree
 D) Definitely disagree
 E) Don't know open to ideas

80

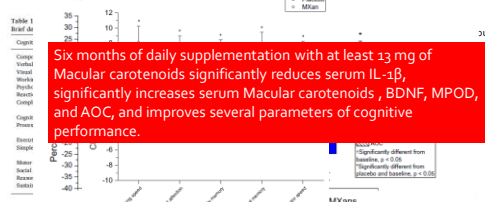
Carotenoids and health ?

- Carotenoids in macula improves vision and decreases ocular fatigue- easy sell
- But not so straightforward....
- Cortisol, stress ???

81

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

Nicole T. Stringham^{1,2*}, Philip V. Holmes^{1,2}, James M. Stringham¹



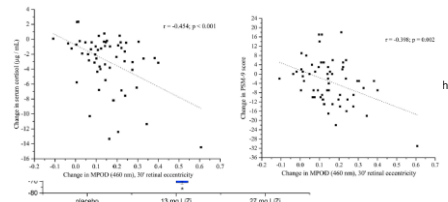
Six months of daily supplementation with at least 13 mg of Macular carotenoids significantly reduces serum IL-1β, significantly increases serum Macular carotenoids, BDNF, MPOD, and AOC, and improves several parameters of cognitive performance.

young adults given Carotenoids for 6 months and 6 Month BDNF, IL-6, IL-1β, TNF-α, cognitive function test battery

82

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. Stringham¹



Change in serum cortisol (µg/dL) vs Change in MPOD (400 nm, 30° retinal eccentricity) $r = -0.454, p = 0.001$

Change in MPOD (400 nm, 30° retinal eccentricity) vs Change in Psychological Stress $r = -0.338, p = 0.002$

Nutritional Neuroscience 2015, VOL. 21 NO. 4

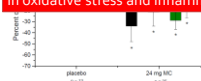
83

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

James M. Stringham^{1,2*}, Nicole T. Stringham¹ and Kevin J. O'Brien¹

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

84

Summary

- Carotenoid supplementation has a real role in decreasing stress and betterment.
- Dose matters
- Duration matters -6-12 months effects visible
- Don't turn your computers on unless you have taken your Lutein and Zeaxanthin
- Don't be Lazy; take your LZ (Lutein and Zeaxanthin)

D Lem and PG Davey Tackle Digital eye strain *Opt Management article*

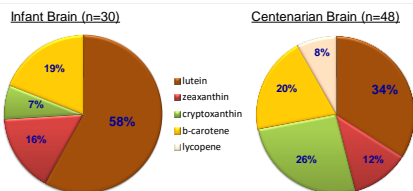


85

Cognition and MPOD Children and Adults

86

Brain carotenoid profile in infants and centenarians

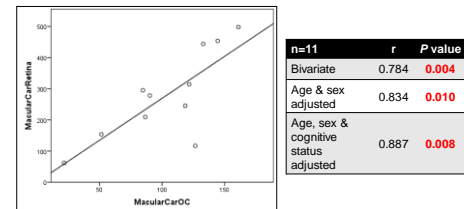


Vishwanathan et al, 2014

Johnson EJ et al. 2013

87

Correlation – Human retina and occipital cortex concentrations of lutein and zeaxanthin.
have an amazingly strong correlation



Macular pigment carotenoids = Lutein (Meso-zeaxanthin) + Zeaxanthin in the retina

Vishwanathan R, Schalch W, Johnson EJ. *Nutr Neurosci.* 2016;19(3):95-101

88

Renzi et al., The relation between serum xanthophylls, fatty acids, macular pigment and cognitive function in the Health ABC Study. *FASEB J* 2008;22:1877-5.

- n = 118 healthy older subjects in the Memphis, Tennessee area
- ages 76–85 y; equal numbers of men and women, were assessed for serum lutein and zeaxanthin, MP density, and various measures of cognitive function.

MP was related to performance on a variety of indexes designed to assess processing **speed, accuracy, and completion ability** ($P < 0.05$).

90

Hammond BR et al., Effects of lutein/zeaxanthin supplementation on the cognitive function of community dwelling older adults: A Randomized, Double-Masked, Placebo-Controlled Trial, *Front. Aging Neurosci.* 9:254, 2017.

- AREDS II carotenoid dosing (12 mg LZ) was evaluated in community dwelling older adults 73.7 +/- 8.2 yrs. of age.
- Participants receiving the active LZ dietary supplement had statistically significant increases in MP ($P < 0.03$)

Improvements in complex attention ($p < 0.02$) and cognitive flexibility domains ($p < 0.04$) relative to study participants taking the placebo.

91

Dietary carotenoids related to risk of incident Alzheimer dementia (AD) and brain AD neuropathology: a community-based cohort of older adults

Changsheng Yuan,^{1,2,3} Hai Chen,⁴ Yimin Wang,⁵ Julie A Schneider,⁶ Walter C Willett,^{2,3,6} and Martha Clare Morris⁴
¹Department of Big Data and Health Science, Zhejiang University School of Public Health, Hangzhou, Zhejiang, China; ²Department of Nutrition, Harvard TH Chan School of Public Health, Boston, MA, USA; ³Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; ⁴Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, IL, USA; ⁵Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA, and ⁶Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA, USA

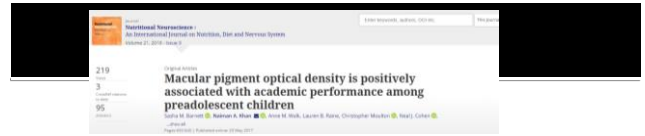
927 participants (No AD) were followed up for 7 years- Rush Memory and Ageing project AD neuropathology was assessed in 508 deceased participants

Results were controlled for Age, sex, education, cognitively stimulating activities, physical activities, Apolipoprotein

Conclusions: Our findings support a beneficial role of total carotenoid consumption, in particular lutein/zeaxanthin, on AD incidence that may be related to the inhibition of brain β -amyloid deposition and fibril formation.

Am J Clin Nutr 2021;113:200-208.

92



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

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.

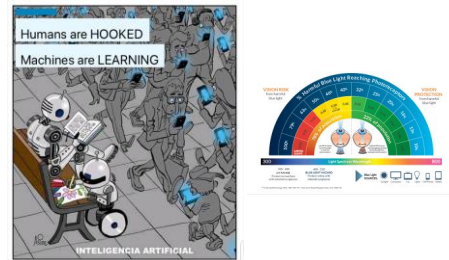
93

Renzi-Hammond LM et al, Effects of a Lutein and Zeaxanthin Intervention on Cognitive Function: A Randomized, Double-Masked, Placebo-Controlled Trial of Younger Healthy Adults, *Nutrients* 2017

Daily supplementation with LZ in healthy 18-30 year old, resulted in significant improvements in spatial memory ($p < 0.04$), reasoning ability ($p < 0.05$) and complex attention ($p < 0.04$), "above and beyond improvements due to practice effects".

94

"Children" and smart devices



95

Diabetes

Diabetes an endemic condition?

- **Diabetes** 30.3 million diabetes or 84 million prediabetes in USA
- 4.2 million adults had DR and 655,000 had vision-threatening DR.

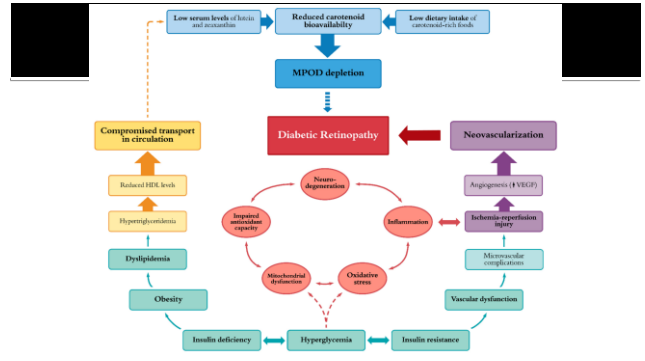
96

97

Diabetic eye disease

- Retina takes a good 10-15 years of beating
- Elevated blood glucose is the culprit
- Metabolic control is a must
- Furthermore, there is a big body of literature that MPOD is depleted in diabetics
- Can we do anything with nutritional supplements without changing A1C?

98



99

nutrients

Review
A Systematic Review of Carotenoids in the Management of Diabetic Retinopathy

Drake W. Lem ^{1,†}, Dennis L. Gierhart ² and Pinakin Guntant 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>

100

The Diabetes Visual Function Supplement Study (DiVFuSS)

The Diabetes Visual Function Supplement Study (DiVFuSS) was designed to test the effects of a novel, multi-component nutritional supplement on visual function. Participants included patients with both type 1 and type 2 diabetes.

- British Journal of Ophthalmology
- six-months
- placebo controlled

CLINICAL STUDY RESULTS WITH DVS
 Randomized, placebo-controlled study demonstrated:

- 21%** improvement in color vision**
- 19%** improvement in contrast sensitivity (easier to read link on a newspaper)**
- 12%** improvement in central and peripheral vision**

**Improvements were made without significantly affecting blood glucose levels.

101

Healthy eyes and Sports vision

102

Visual Performance Research

Billy Hammond PhD, Emily Bovier PhD, Lisa Renzi PhD, University of Georgia, Athens, GA

A Double-Blind, Placebo-Controlled Study on The Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency. (Published: PLOS One, September, 2014)

N= 64 young adults aged 18-32 years.
3 arm study: 29 subjects took 20 mg of zeaxanthin (carotenoids), 25 subjects took the Eye Promise Visual EDGE PRO supplement (26mg of zeaxanthin, 34mg of carotenoids), and 10 subjects took placebo, duration 4 months.

Purpose of the study: to determine whether improving MPOD via zeaxanthin (20 mg) or mixed carotenoid (Eye Promise Visual EDGE PRO) supplementation improved neural efficiency and visual motor performance in young, healthy, adults.

Summary: Subjects in the zeaxanthin and EyePromise visual EDGE arms experienced;

- A 20% increase in Macular Pigment Optical Density (MPOD)
- A 22% Improvement in Critical Flicker Fusion Threshold
- A 10% Improvement in Visual Motor Reaction Time

103

Night vision and Carotenoids

104


nutrients MDPI

Communication

Night Vision and Carotenoids (NVC): A Randomized Placebo Controlled Clinical Trial on Effects of Carotenoid Supplementation on Night Vision in Older Adults

Stuart Richer ^{1,2,*}, Steven Novil ¹, Taylor Gullett ², Avni Dervishi ², Sherwin Nassiri ², Co Duong ², Robert Davis ³ and Pinakin Gunvant Davey ^{4,*}

Aim:
Can carotenoid improve night vision and comfort in driving in individuals that complain of nighttime driving issues?

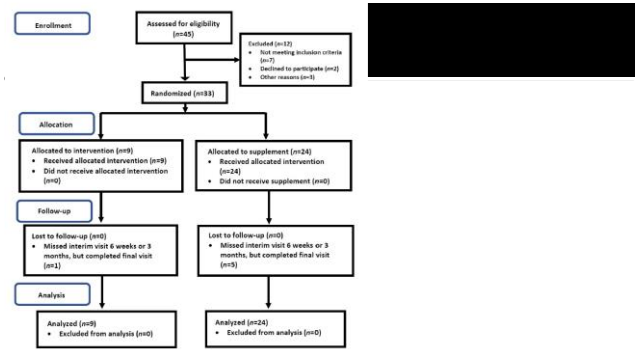


105

Table A1. Active Components of ScreenShieldPro.

Active Ingredients	Amount per Serving
Zeaxanthin	14 mg
Lutein	7 mg
Vitamin A	2500 IU
Vitamin C	60 mg
Vitamin D	1000 IU
Vitamin E	60 IU
Vitamin B6	2 mg
Folic Acid	400 mcg
Vitamin B12	6 mcg
Zinc	15 mg
Selenium	70 mcg
Manganese	2 mg
Fish Oil	150 mg
Coenzyme Q10	15 mg
Bilberry	15 mg
Berry Anthocyanin Extract	15 mg
Alpha Lipoic Acid	10 mg
Mixed Tocopherols	6 mg

106

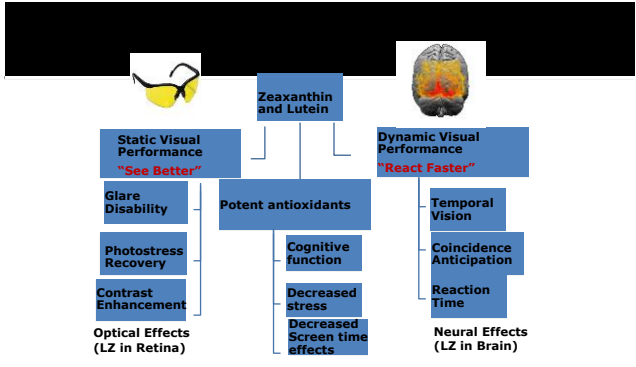


107

Results

- Improvements in contrast sensitivity with glare in both eyes
- Monocularly tested glare recovery time improved 2.76 and 2.54 s, respectively, (p = 0.008 and p = 0.02),
- decreased preferred luminance required to complete visual tasks
- Improvements in UFOV scores of divided attention (p < 0.001) and improved composite crash risk score (p = 0.004) were seen in the supplemented group.
- The placebo group remained unchanged.

108



109

Evaluating & Increasing Macula Pigment

- Better Visual Quality
- Better “Day and Night” Driving Vision
- Better Blue Light Protection
- Better Cognition
- Better Sports Vision
- Better Sleep and less stress
- “Better Eye Exam and Better Care”

110

Global summary

- It is tough to get perfect nutrition everyday.
- Nutritional supplements can be a reliable way of augmenting your diet.
- Carotenoids are important for vision
- Maybe even more for health than we thought!
- Measuring MPOD allows for a trackable measure in various health and disease states-compliance and bioavailability measure.
- An ounce of prevention...

111

Thank You!

Pinakin Davey OD, PhD, FAAO, FOWNS, FARVO
 Professor & Director of Clinical research
 Western University of Health Sciences
pdavey@westernu.edu
 909-469-8473

112