

COOL THINGS ABOUT CAROTENOIDS AND OCULAR NUTRITION



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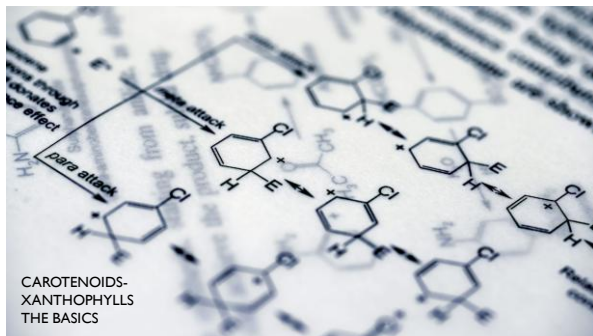
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DISCLOSURE

- Sanofi Speaker
- EyePromise Employee

The content and format of this course is presented without commercial bias and does not claim superiority and commercial product or service.
"All relevant financial relationships have been mitigated"

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Retina

Highly metabolically active tissue

Uses a lot of energy

Produces a lot of waste products as free radicals

Antioxidants in the retina are a source of protection

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WHILE ~750 CAROTENOIDS ARE FOUND IN NATURE, ONLY TWO ARE CONCENTRATED IN THE RETINA



~750
Carotenoids

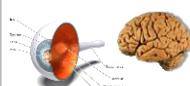


<50 Primary
Carotenoids



~20 Carotenoids

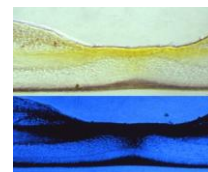
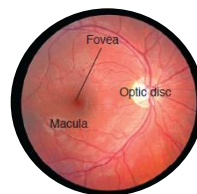
Dietary carotenoids –
Lutein and Zeaxanthin –
are concentrated in the
eye and brain



≈ 75 % of carotenoids in
infant's brain is lutein and
zeaxanthin

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ANATOMY: RETINA, MACULA, FOVEA (WHERE MACULAR PIGMENT RESIDES)



- Optical mechanisms
 - Glare Disability,
 - Color Contrast
 - Visual Range
 - Contrast Sensitivity

- Biological mechanisms
 - Glare Recovery
 - Neural Efficiency
 - Biomarker for Sleep Issues
 - Systemic Diseases

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WHAT IS MPOD?



- AKA yellow spot
- Macular pigment optical density: Pigment deposit in the macula
- Central Macula- AKA Fovea has a yellow spot visible- dense concentration of xanthophylls carotenoids are zeaxanthin and lutein

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RETINA AND CAROTENOID DISTRIBUTION

- **Common misconception that carotenoids not present in the rest of the retina**
- Centrally 2.5: 1 (zeaxanthin and isomers: Lutein ratio)
- Peripherally 1:2 (zeaxanthin and isomers: Lutein ratio)
- **Can there be an absence of yellow spot ?**

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SCARCE IN THE DIET

ZEAXANTHIN AND LUTEIN DIETARY GAP

Studies prove that consuming more of the dietary antioxidants zeaxanthin and lutein increases macular pigment levels, or your "internal sunglasses," but zeaxanthin is particularly scarce in the average U.S. diet. Our formulas contain the optimal levels of dietary zeaxanthin and lutein necessary to bridge the dietary gap and support ocular health.

• AVERAGE U.S. DAILY INTAKE

• DIETARY GAP

• AMOUNT ASSOCIATED WITH REDUCED AMD RISK

*According to the National Eye Institute's AREDS 2 study



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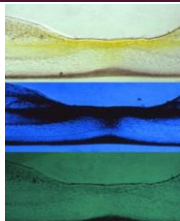
TECHNOLOGY HELPFUL IN NUTRITIONAL CLINICS



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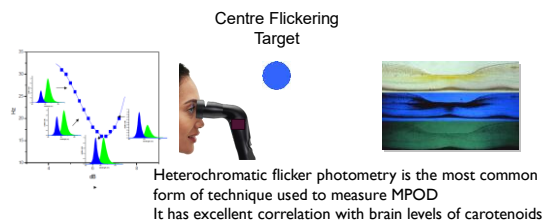
MEASUREMENT OF MACULAR PIGMENT OPTICAL DENSITY

- 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



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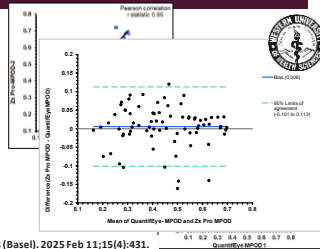
MPOD TEST SIMPLE EFFICIENT ,APPROX 2 MINUTE TEST



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ZX PRO™ RELIABILITY AND REPEATABILITY RESULTS ARE COMPELLING

- Training datasets – 600+ measurements on 150 subjects
- Testing datasets – 76 subjects
 - 23-70 YOs
 - Wide range of refractive errors performed via QuantifEye and Zx Pro™ in randomized order
 - All subjects were novice observers
- Study Performed at Western University of Health Sciences, Pomona, CA



Davey PG, et al., *Diagnostics (Basel)*. 2025 Feb 11;15(4):431.

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- Is it easy? Yes
- Do I need to perform in both eyes? No
- How long does it take? 2 minutes for testing
- Is it repeatable? Yes
- Dominant eye? Any eye
- Can it measure changes? Yes
- Is it comparable to QuantifEye



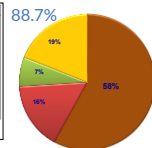
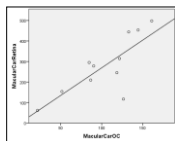
Davey PG et al., *Clin.Ophthalmol*. 2016 Aug 29;10:1671-8. doi: 10.2147

Davey PG, et al., *Diagnostics (Basel)*. 2025 Feb 11;15(4):431.

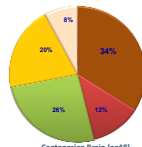


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MPOD is a neural biomarker



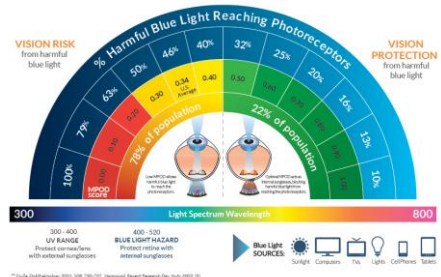
Infant Brain (n=30)



Centenarian Brain (n=48)

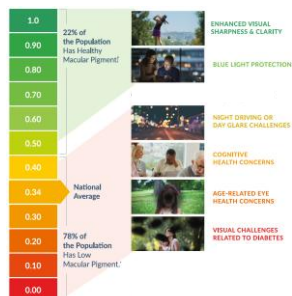
Vishwanathan R, Schach W, Johnson E. *J Neurosci*. 2016;36(3):95-101

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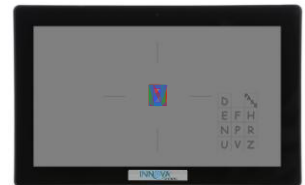
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78%
Of The US Is Below The Optimal MPOD Score of 0.50



Rabin Cone Contrast Test

- Based in science
 - Co-developed between Innova Systems and US Air Force
- Combines Cone Isolation technology and Contrast Sensitivity
- Color vision technology sensitive enough to detect subtle changes from disease
- Threshold test, similar to visual field
 - But just faster...

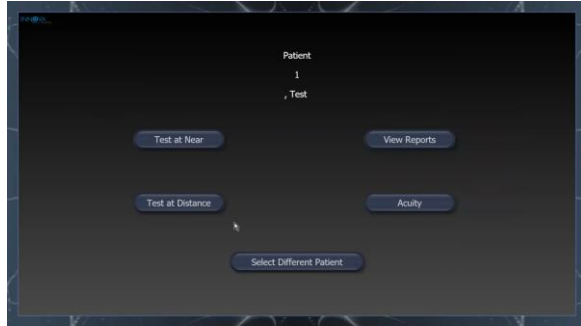


➢ Patent No. US 9,883,794

Simulation

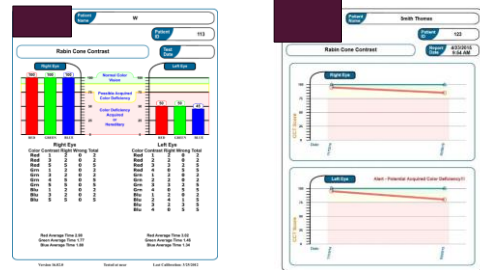
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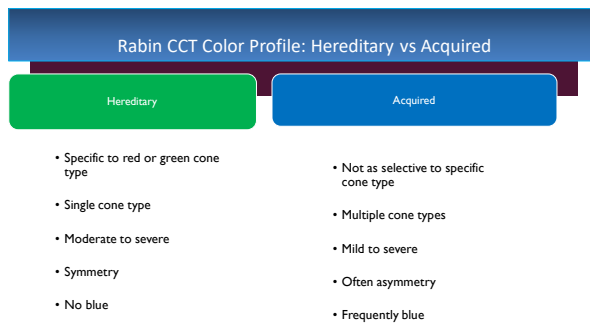


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RABIN CONE CONTRAST TESTING OUTPUT



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MPOD MODEL OF CONTROLLING INFLAMMATION IN THE EYE

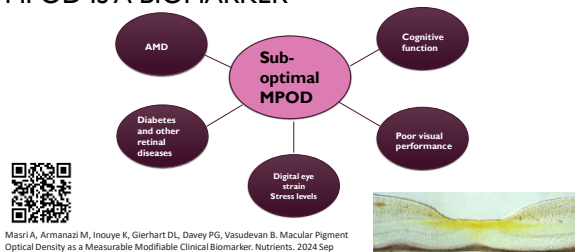


Masri A, Armanazi M, Inouye K, Gierhart DL, Davey PG, Vasudevan B. Macular Pigment Optical Density as a Measurable Modifiable Clinical Biomarker. *Nutrients*. 2024 Sep 27;16(19):3273. doi: 10.3390/nu16193273. PMID: 39408240; PMCID: PMC11478551.



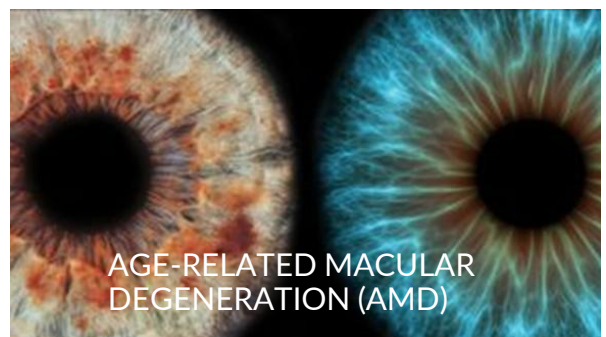
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MPOD IS A BIOMARKER



Masri A, Armanazi M, Inouye K, Gierhart DL, Davey PG, Vasudevan B. Macular Pigment Optical Density as a Measurable Modifiable Clinical Biomarker. *Nutrients*. 2024 Sep 27;16(19):3273. doi: 10.3390/nu16193273. PMID: 39408240; PMCID: PMC11478551.

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Stages of age-related macular degeneration

Category	Description
Category 1 - No AMD	A few small or no drusen
Category 2 - Early stage AMD	Many small drusen or a few medium-sized drusen in one or both eyes
Category 3 - Intermediate AMD	Many medium-sized drusen or one or more large drusen in one or both eyes
Category 4 - Advanced AMD	In one eye only, either a breakdown 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)

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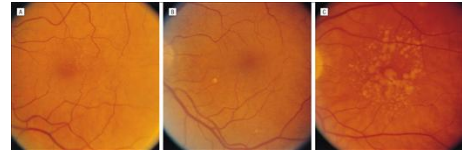
AMD	
Dry or non exudative	Wet or exudative
Chronic visual acuity remains unchanged for long, some degree vn loss, may progress to severe blindness	10-15% of AMD Vision dramatically reduced Advanced AMD Geographic Atrophy Or choroidal neovascular growth

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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

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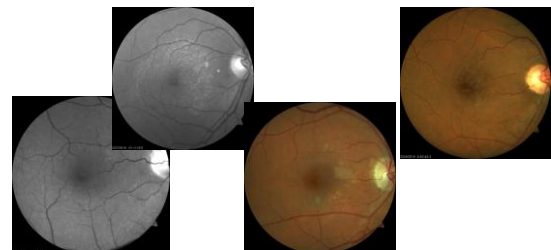
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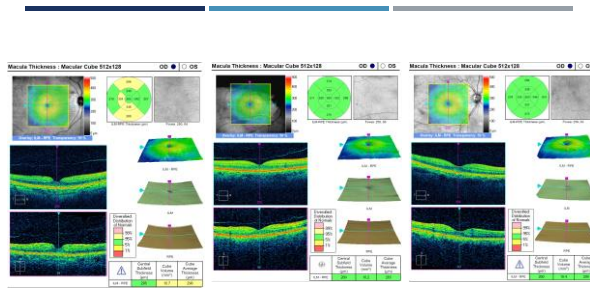
MEASUREMENTS PERFORMED FOR AMD



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FUNCTIONAL VISION IS AFFECTED IN EARLY AMD

Glare Disability

Glare Recovery

Color vision

Contrast (CSF)

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CURRENT MANAGEMENT OF AMD...AN AREDS SAGA

PRN GROUP

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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 all patients got the AREDS formula
- Extremely educated population
- Well-nourished population
- Baseline serum carotenoid levels were very high

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

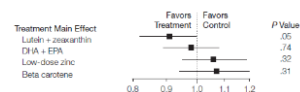
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TO TEST THE FOLLOWING

- Additional to AREDS-1 supplement
- Addition of
 - lutein (10 mg)+zeaxanthin (2mg)
 - EPA (650 mg) + DHA (350 mg)
- Will this help prevent progression?

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SUB-GROUP ANALYSIS



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

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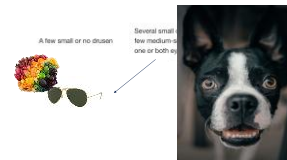
AREDS-2 FINAL FORMULA

Micronutrient Levels based on daily dosage	PreserVision AREDS 2 Formula
Zinc ¹	80 mg
Lutein ²	10 mg
Zeaxanthin ³	2 mg
Vitamin C ⁴	500 mg
Vitamin E ⁵	180 mg
Copper ⁶	2 mg
Vitamin A (500% as Beta-Carotene)	

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MANAGEMENT OF DRY-AMD... CL

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).

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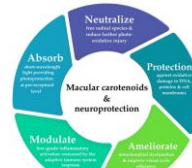
Can we do better than AREDS -2?

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antioxidants

Systematic Review

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

Drake W. Lim^{1,2}, Pinakin Gargant Davey^{1,2,3}, Dennis L. Gierhart² and Richard B. Rosen³

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



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

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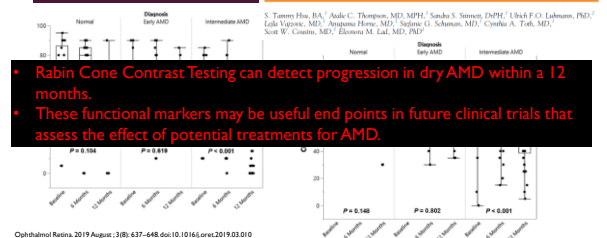
SUMMARY OF BENEFITS OF CAROTENIDS IN AMD

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

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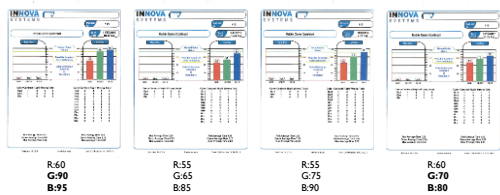
Duke University

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



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INTERMEDIATE DRY AMD: SUB-CLINICAL PROGRESSION

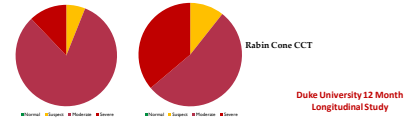


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RABIN CONE CCT EFFECTIVENESS IN STAGING DRY AMD

No AMD Early Stage AMD Intermediate AMD Advanced AMD

"All patients in Early Stage AMD had abnormal Rabin Cone CCT scores"



Duke University 12 Month Longitudinal Study

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AMD MANAGEMENT

- Monitoring vision
- Detection of progression
 - Early intervention initiatives
- Nutritional changes
- Nutritional supplements
 - Early and greater amount
- Medical management when needed



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WHAT CAN WE DO DIFFERENT THAN AREDS?

Testing

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



Management

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

MPOD values greater than 0.5 du
If baseline is already at .5 or higher increase it by 0.15 du

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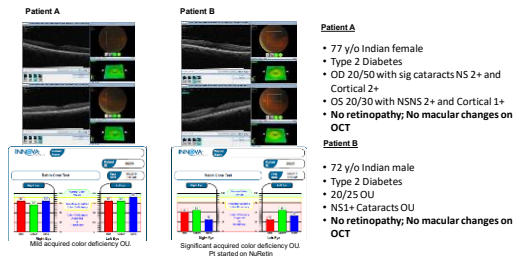
DIABETES AN ENDEMIC CONDITION?

Diabetes 30.3 million diabetes or 84 million prediabetes in USA

4.2 million adults have DR and 655,000 had vision-threatening DR.

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Subclinical Detection of Diabetes Advancement- Case Study



Case courtesy of Becky Verma, OD

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nutrients

A Systematic Review of Carotenoids in the Management of Diabetic Retinopathy

Dhruv W. Lee ^{1,4,5}, Dennis L. Gierhart ¹ and Pinakin Current Davey ^{1,4,5}



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

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.

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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.

- 2016 British Journal of Ophthalmology
- six-months
- placebo controlled



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

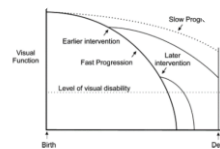
- 21% improvement in color vision**
- 19% improvement in contrast sensitivity (easier to read ink on a newspaper)**
- 12% improvement in central and peripheral vision**

**Improvements were made without significantly affecting blood glucose levels

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DIABETES AND DR: REDUCES CONE CONTRAST

- Monitoring vision
- Detection of progression
- Health initiatives
- Weight management
- Exercise
- Nutritional changes
- Nutritional supplements
- Medical management when needed



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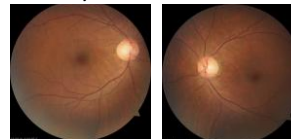
CASE: DIABETES EXAM- WHAT'S YOUR DIAGNOSIS?

Courtesy of Pinakin Davey OD, PhD

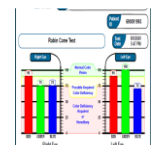
- 49 YO Asian male,
- HO DM type 2, 10 years "recently" not compliant with meds
- HO HTN x10 years
- Restarted metformin recently but has side effect of diarrhea
- Blood pressure today 168/96

What was his MPD? 0.28
Dominant eye

Diabetic Eye Exam Standard of Care



- OD and OS color vision defect
- Asymmetrical = Acquired
- Mild - Moderate degradation
- Overall, OD > OS

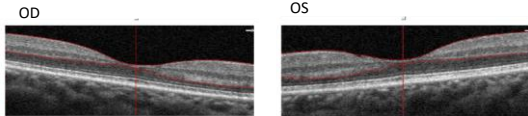


Based on RCCE, RTC in 1 month for OCT

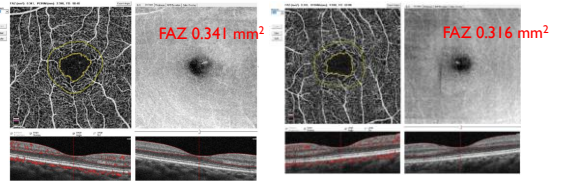
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Patient worried enough about change in vision that he returned
for 1 Month follow-up visit

Foveal Avascular Zone measurements OCT-A done 1 month later



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WHAT WOULD BE A GOOD PLAN FOR HIM

- Adding Rabin Cone Contrast and MPOD was helpful in management
- Revealed changes from early diabetic eye disease which otherwise would have been missed
- Motivated patient to follow-up with 1 month visit
- Allowed for detailed discussion about diet, lower blood pressure
- Patient began carotenoid vitamin nutritional supplements

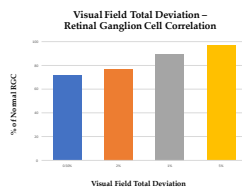
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Glaucoma

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Visual field has delays in identifying glaucomatous damage

- Visual Field Loss is correlated to retinal ganglion cell loss
- However, 27% of cell death occurs prior to SAT abnormality
- Visual Field ineffective in detecting early changes in glaucoma or glaucoma suspects

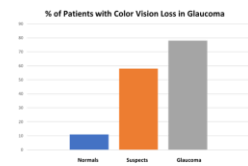


Kerrigan-Baumrind et al., Invest. Ophthalmol. Vis. Sci., Mar 2000

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Color vision changes in glaucoma suspects

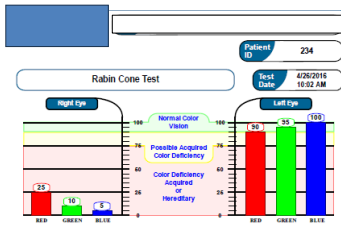
- 78% of glaucoma patients had color vision loss
- 58% of glaucoma suspects demonstrated color vision loss
 - Elevated intra ocular pressure
 - No optic nerve head changes
 - No visual field changes
- Central retinal changes may occur earlier than previously believed



Adams et al., Invest. Ophthalmol. Vis. Sci., Oct 1992

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Case: Glaucoma



- 20/20 OD
- 20/30 OS
- Patient diagnosed with glaucoma.
- Points to remember
- Glaucoma is an asymmetric disease
- Does not influence visual acuity
- Functional deficits are apparent when right functional tests are used
- Visual fields are insensitive unless
 - 50 % of RGC lost in a location
 - Or
 - 30% loss overall
- OCTs are insensitive in early glaucoma because the normal range of OCT is wide.

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Review

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

Duke W. Lee ^{1,2}, Dennis L. Gierhart ³ and Pinakin Garvankar Davey ^{1,*}

Lutein demonstrated enhanced neuroprotection on retinal ganglion cell survival and preserved synaptic activity. 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.

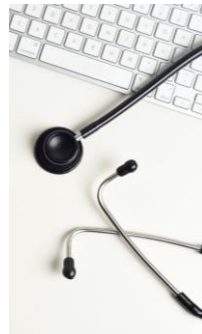
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Global summary



- 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...

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THANK YOU!

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