Ocular Nutrition Controversies: From A to Z (Astaxanthin to Zeaxanthin)

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Disclosure

I havebeen a speaker/consultant/advisor to:

Alcon, Allergan, AstaReal, Bausch & Lomb, Genentech, Luneau, Kemin, Maculogix, Notal Vision, Optos, Regeneron, VSP & Zeavison

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Before we start….

- Diana and I like interaction (with you better than with ourselves)
- Any questions/suggestions or topics before we start?

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How much can diet affect vision?

- Junk food can cause blindness!
  - French fries, potato chips, white bread, processed ham and sausage
- Complaints at age 14 of tiredness
  - Normal BMI, no signs of malnutrition
    - Low B12 and anemia treated and given dietary advice
- Age 15: hearing and vision loss
- Age 17: Blindness
  - Low B12, Vit D, bone density and high Zinc
- Optic neuropathy caused by junk food diet!
  - Some controversy as to possibility of other cause…..
  - BMI isn't everything (as seen in this case)

Harrison et al. Blindness by Junk Food. Annals of Int Med. 9/19

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"Let Thy Food Be Thy Medicine" Hippocrates

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Why do we need to discuss?

- What is the leading source of Antioxidants in the average American's diet?[1]
  - Coffee (2nd and 3rd are black tea and bananas)
- What percentage of Americans follow the 4 healthy lifestyle habits?
  - 3%
- What percentage of vege intake in the US is potato + ketchup
  - >50%
    - 2010-2015 F/V consumption down 7% compared to prior period measured
    - Leading "fruit" is OJ and leading "vege" is potato
    - 15% of tomato consumption is ketchup

Vinson et al. Polyphenols and US consumption. American Chem. Society 8/2005.

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Where is the best place to find nutrition?

- But what's the reality?
- What foods are good for Xanthophyll?
  - Kale (40mg/serving), Spinach (12mg), Romaine lettuce (2.3mg), Broccoli (1.7mg)
- Do you ever ask your patients about f/v consumption?
- What about Mediterranean diet?
  - Approx 47% less Adv AMD
    - More L/Z the better! Hogg. Ophthalmology 11/16.
- An apple a day keeps AMD away!
  - 15% decrease Ophthalmologica 2015: Coimbra Eye Study
- An Orange a day keeps away AMD
  - 60% decrease with daily orange vs never oranges Gopinath et al. Dietary flavonoids & AMD. *American Journal of Clinical Nutrition,* 2018

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BMI

What is BMI and how is it calculated?

HOW DO YOU TALK TO PTS ABOUT BMI?

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How do you talk to your pts about exercising?

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When does nutrition become important?

- Should everybody pay attention to it?
- Is nutrition preventative or should discussion be reserved for "active" disease?
- At point in AMD do you start to discuss nutrition?
- At what point in DM does nutrition become important?
- Is nutrition relevant to computer vision syndrome?
- When do you discuss nutrition in OSD?

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SAFETY of VITAMINS: In the NEWS

Dietary Supplements and Mortality Rate in Older Women 2011

The Iowa Women's Health Study

Jaakko Mursu, PhD; Kim Robien, PhD; Lisa J. Harnack, DrPH, MPH; Kyong Park, PhD; David R. Jacobs Jr, PhD

N=>30K women

MV, Vit B6, folic acid, Mg, **zinc**, **iron** & copper may be associated with increase mortality rate

Background: Although dietary supplements are commonly taken to prevent chronic disease, the long-term health consequences of many compounds are unknown.

Methods: We assessed the use of vitamin and mineral supplements in relation to total mortality in 38 772 older women in the Iowa Women's Health Study; mean age was 61.6 years at baseline in 1986. Supplement use was self-reported in 1986, 1997, and 2004. Through December 31, 2008, a total of 15 594 deaths (40.2%) were identified through the State Health Registry of Iowa and the National Death Index.

Results: In multivariable adjusted proportional hazards regression models, the use of multivitamins (hazard ratio, 1.06; 95% CI, 1.02-1.10; absolute risk increase, 2.4%), vitamin B_6 (1.10; 1.01-1.21; 4.1%), folic acid (1.15; 1.00-1.32; 5.9%), iron (1.10; 1.03-1.17; 3.9%), magnesium (1.08; 1.01-1.15; 3.6%), zinc (1.08; 1.01-1.15; 3.0%), and copper (1.45; 1.20-1.75; 18.0%) were associated with increased risk of total mortality when compared with corresponding nonuse. Use of calcium was inversely related (hazard ratio, 0.91; 95% confidence interval, 0.88-0.94; absolute risk reduction, 3.8%). Findings for iron and calcium were replicated in separate, shorter-term analyses (10-year, 6-year, and 4-year follow-up), each with approximately 15% of the original participants having died, starting in 1986, 1997, and 2004.

Conclusions: In older women, several commonly used dietary vitamin and mineral supplements may be associated with increased total mortality risk; this association is strongest with supplemental iron. In contrast to the findings of many studies, calcium is associated with decreased risk.

Arch Intern Med. 2011;171(18):1625-1633

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Multi-vitamins

- Are multivitamins worthwhile?
- Are they just a fairy-dust formulation?
- Are they true to label?
  - NY AG investigation of major retailers
- Frame of reference as to AREDS2…

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"True to label"

- You can't take for granted that things are what they say..
- NYT article in Nov. 2013 looking at 44 bottles from 12 companies of supplements
  - Bottles from 2 companies had 100% and 2 had 0% accuracy to label
    - 2 bottles of St John's wort contained NONE of the actual herb
  - 1/3 showed substitution (no trace of advertised)

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NY Attorney's General gets involved

- In Feb 2015 NYAG did sting with GNC, Target, Walgreens and Walmart
  - Ex: Walgreens Ginseng was only powdered garlic and rice
  - Walmart Ginko biloba was radish, houseplants and wheat (Despite being labeled gluten/wheat free)
  - 3/6 tested at Target had 0% of labeled claim
  - GNC: unlisted ingredients including legumes as fillers

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So…

- Use only brands you can trust
- **PRESCRIBE** to your patient as you would anything else
- Look for independent lab testing, production in NSF, follow BMP (best manufacturing practices) facilities and a company that will be there when you need them!
- Do patients ask you: "Is this over the counter or prescription?"

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Think about screens

No silly……not that kind…..

Think this kind…

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Think about screens

No silly……not that kind…..

Think this kind…

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Symptoms of Digital Eye Strain

- **65%** of Americans reported symptoms of digital eye strain[1]
- The average American spends **7.5** hours in front of a screen or digital device every day[1].
- **53%** of Americans are using **2** digital devices at the same time. [1]
- More than **83%** of Americans use digital devices for more than 2 hours per day. [1] It's a family affair affecting the entire family[1]
  - 72% ages 0-18 - 88% ages 18-29
  - 83% ages 40-59 - 76% ages 60 and up

TOO MUCH Screen Time

- Headaches
- Eye Strain/Fatigue
- Dry Eyes
- Irritated Eyes
- Blurred Vison
- Reduced Attention Span
- Poor Behavior
- Irritability

Do you use EHR??

1. 2015 The Vision Council US Report. 10,000 Americans in Survey

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What is Asataxanthin

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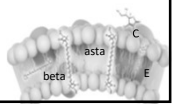
How Astaxanthin reduces eye strain..

- ✓ Eye Strain and fatigue often associated with CVS as well as prolonged exposure to blue light .
- ✓HE blue light reduces contrast and overworks ciliary muscles.
- ✓Tired ciliary muscles directly cause eyes to feel strained and fatigued.
- ✓Astaxanthin has been shown to improve ciliary muscle endurance and recovery.
- ✓Astaxanthin is strongest natural antioxidant on ORAC scale and is pure antioxidant
  - ✓ Penetrates cell membranes without disrupting structure
  - ✓ Crosses blood-retina and blood-brain barrier



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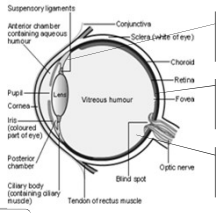
Astaxanthin Mechanism of Action Summary



Cause of Eye Fatigue	Astaxanthin's Efficacy
The ciliary muscle fatigue causes asthenopia or accommodation failure	1 Increase Ciliary Muscle Recovery and Endurance
Poor blood flow cannot support highly metabolically active organ	2 Improve Capillary Blood Flow and Blood Rheology
Eye inflammation e.g. visible swelling, sensations of heat and pain and redness	3 Inhibit Inflammation via NF-kB pathway

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Summary of Clinical Body of Evidence by Dose

***In vivo/vitro* study**

Anti-oxidant effects
- ✓ Scavenges reactive oxygen, especially singlet oxygen (Nishida 2007)
- ✓ Inhibits lipid peroxidation (Miki 1991)
- ✓ Protects cell membrane from oxidative stress comprehensively (Goto 2001)

Protection of retinal damage
- ✓ Protected retinal ganglion cell (RGC) from oxidative stress, glutamate stress, hypoxia, and UV (Nakajima 2004, Dong 2013, and Yamagishi 2016, and Iannikov 2012)
- ✓ Inhibited light-induced retinal dysfunction (Otsuka 2013)

Anti-inflammatory effects
- ✓ Inhibited NF-κB-dependent signaling pathway in inflamed eyes (Suzuki 2006, and Ohgami 2003)

Vasodilating action
- ✓ Extended vascular via a vascular relaxing factor NO (Hussein 2005a)
- ✓ Shortened the blood microchannel transit time (Hussein 2005b)

Dosage of Astaxanthin — **Clinical study**

- **1 mg** — **Anti-oxidant effects blue light**
- **2 mg** — Decreases plasma oxidative stress marker (Kim 2004 and Park 2010)
- **4 mg** — **Improves accommodation and visual acuity** (Nakamura 2004)
- **5 mg** — **Improves accommodation and, attenuates symptom of digital eye strain** (Nagaki 2002)
- **6 mg** — **Improves accommodation and attenuates symptom of eye strain** (Nagaki 2006, Nitta 2005, Shiratori 2005, Iwasaki 2006, Kajita 2009, and Takahashi 2005)
  - ➢ **Shows anti-oxidative and anti-inflammatory effects in aqueous humor** (Hashimoto 2007;2009)
  - ➢ **Promotes circulation around optic papilla** (Nagaki 2005)

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Front to Back Eye Protection

Lutein/Zeaxanthin
Back of the Eye Protection
Filters Blue Light

- ✓ Crosses blood retinal & blood brain barrier
- ✓ Localized to the retina
- ✓ Antioxidant
- ✓ Anti-inflammatory
- ✓ Filters blue light
- ✓ Improves visual acuity and contrast sensitivity
- ✓ Helps reduce risk of dry AMD
- ✓ Improved glare tolerance
- ✓ Improved macular pigment optical density

Astaxanthin
Front of the Eye Protection
Reduces Eye Fatigue

- ✓ Crosses blood retinal & blood brain barrier
- ✓ Localized to the ciliary body
- ✓ Antioxidant
- ✓ Anti-inflammatory
- ✓ Improves circulation
- ✓ Improves accommodation/focus
- ✓ Reduces oxidative stress in aqueous humor

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Available products

- Blue Light Defender Plus
  - – Vitamin Health/VitEyes
- Guardion
  - – Lumega-Z
  - – GlaukoCetin
- Fortifeye
  - – Fortifeye focus
- Note: numerous "general" supplements have astaxanthin

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A quick comparison

- Astaxanthin is:
  - 6000x stronger than Vitamin C
  - 770x stronger than Coenzyme Q10
  - 100x stronger than Vitamin E

    When it comes to combatting reactive oxygen species (ROS)

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What about blue light specifically

- Which is better Inside or Outside protection?
- Why pick one…choose both

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Beta Carotene

- What's up doc?
- Is it helpful?
- Is it harmful?

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What about Fish Oil

- What did AREDS2 say?
- What have European studies said?
- What about other potential worries with fish oil?
  - What about DR specifically?

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MPOD

- Does MPOD only relate to AMD risk?
- Are carotenoids important beyond AMD?

  Remember what I said earlier about how to easily discuss with patients?

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Can we improve visual function

- ZVF, LAST, LAST2
  - What do we mean by visual function?

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Which is better….2 or 3

- Carotenoids found in macula
  - Lutein
  - Zeaxanthin
  - Mesozeaxanthin
- Does something need to be dietary to be important?
  - Can you make a case either way
- Does it need to be able to "perform" on it's own?
  - Again…can you make a case either way
- We may not know the final answer yet…..

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True or False

- Nutritional supplementation at any stage of AMD is important?
- What about Sub-clinical AMD???

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AREDS2

- What did the abstract from AREDS2 tell us?
- What did AREDS2 really tell us?

National Eye Institute Recommended Formula:

Nutrient	Amount (per day)	Percent Daily Value*
Vitamin C	500 mg	840%
Vitamin E	400 IU	1340%
Zinc	80 mg	840%
Copper	2 mg	100%
Lutein	10 mg	--
Zeaxanthin	2 mg	--

*Percent Daily Values (DV) based on a 2,000-calorie diet
**Daily Value (DV) not established
Speak with your doctor to determine if the updated AREDS 2 formula is right for you.

AREDS 2
Age-Related Eye Disease Study 2
Funded by the National Institutes of Health

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OK…what to think about Zinc?

- Is it friend or foe?
- It is necessary for general body function?
- What did AREDS1 say?
- What did AREDS2 say?
- What do we know about the genetics of zinc?

Zinc Rich Foods

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The Accumulation of Zinc studies..

- Several by the Awh group: all same conclusion of efficacy of genetic testing and importance
- Several by the Chew group: All same conclusion of lack of efficacy and unimportant
- Seddon et al. 12/16 BJO: Some importance in genetics driving response
- Vavvas et al. 1/18 PNAS: Genetics drives response to nutraceuticals
- Assel et al. 3/18 Ophth: Genetics don't matter

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CREST

Central Retinal Enrichment Supplementation Trials

- Impact of Supplemental AO on VF in non-advanced ARMD: Head-to-head randomized trial by Akuffo et al.
- 98 of 121 completed trial of AREDS2 low Z vs AREDS2 low Z w 10mg MZ
- Improvements in MPOD, CS, glare disability and reading speed statistically significant in both groups

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Ca in AMD

- Previously thought that Calcium may have negative affect
- AREDS1 data showed:
  - Highest vs lowest tertial of Ca has .73 HR of advanced AMD
  - GA HR .80
  - Central GA HR .64
  - NV AMD HR .70
  - *Unable to control for other confounding factors

Jama Ophth 2019

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Good Carb: Bad Carb

Do particular dietary sources of carbohydrate influence glucose homeostasis, inflammation and risk of eye disease?

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Are GI and GL Useful?

- Low GI food delay hunger, reduce caloric intake *(Lipids. 2003;38(2): 117-21)*
- Low dGI/dGL diets reduce fasting blood glucose, glycated protein and insulin resistance *(Am J Clin Nutr. 2008 Jan;87(1):258S-268S)*
- *High dGL and CHO intake increased mortality risk almost 50% in EPIC* (PLoS One. 2012;7(8):e43127. Epub 2012 Aug 23)
- **High dGI increases the risk of developing T2DM** *(Diab Technol Ther 2006;8(1): 45-54)* **& AMD (large drusen, GA, CNVM)** *(Am J Clin Nutr. 2007;86(1): 180-8)*

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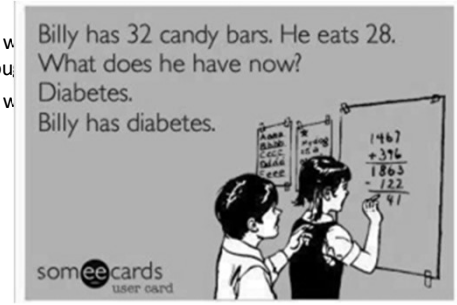
There is more to Diabetes than sugar!

- Can w
- Can w



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Fish Oil for DR

- New study showing benefit to 1:5 EPA:DHA
- Nuretin by PRN: A medical food

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Summary

- Nutrition IS a part of primary care optometry
- Nutrition can be easy (and doesn't have to be controversial)
- Prevention and early treatment are better than needing Diana's partners!

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Thank You

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