NUTRITION IN OPHTHALMOLOGY

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BACKGROUND

- BS, NUTRITIONAL SCIENCE, BRIGHAM YOUNG UNIVERSITY 2011
- MD, UNIVERSITY OF UTAH SCHOOL OF MEDICINE, 2015
- TRANSITIONAL YEAR INTERNSHIP, INTERMOUNTAIN MEDICAL CENTER, 2016
- OPHTHALMOLOGY RESIDENT, CASEY EYE INSTITUTE, OHSU, CURRENT

- NO FINANCIAL DISCLOSURES.

BASIC NUTRITION

- MACRONUTRIENTS: SUPPLYING CALORIC NEEDS
  - PROTEIN (4 KCAL/G)
  - FAT (9 KCAL/G)
  - CARBOHYDRATES (4 KCAL/G)
  - (ALCOHOL 7 KCAL/G)

OCULAR IMPLICATIONS:

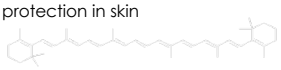
- WESTERN DIET: HIGH IN FAT, LOW IN ADDITIONAL VITAMINS AND MICRONUTRIENTS
  - OCULAR TISSUES AT HIGH OXIDATIVE RISK, COMPETE WITH ADIPOSE TISSUE FOR FAT-SOLUBLE VITAMINS AND ANTIOXIDANTS (GRUBER 2004)
  - DEVELOPMENT OF ARMD ETC.
- METABOLIC SYNDROME- OBESITY, INSULIN RESISTANCE
  - DIABETIC RETINOPATHY, NEOVASCULAR GLAUCOMA
  - CATARACTS

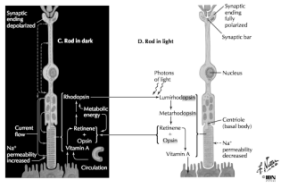
BASIC NUTRITION

- MICRONUTRIENTS:
  - FAT SOLUBLE VITAMINS:
    - **A- VISUAL CYCLE, FETAL OCULAR DEVELOPMENT, PREVENTION OF XEROPHTHALMIA**
    - D- CALCIUM HEMOSTASIS AND BONE RESORPTION, PTH PATHWAY
    - E- ANTIOXIDANT, COMPONENT OF CELLULAR MEMBRANES
    - K- ACTIVATION OF COAGULATION PATHWAY, ANTITHROMBIN PROTEINS, BONE FORMATION

CAROTENOIDS FUNCTIONS

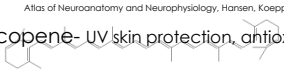
Beta Carotene- visual cycle (opsin==rhodopsin), immunity, UV protection in skin





Atlas of Neuroanatomy and Neurophysiology, Hansen, Koeppen 2002, Figure 2.32

Lycopene- UV skin protection, antioxidant effects



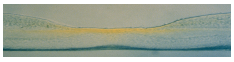
BASIC NUTRITION

- WATER SOLUBLE VITAMINS:
  - B1 (THIAMINE) – COFACTOR FOR AA AND CHO METABILISM
  - B2 (RIBOFLAVIN)- COENZYME METABOLISM (FADH2)
  - B3 (NIACIN) – COENZYME METABOLISM (NAD/NADP)
  - **B5 (PANTOTHENIC ACID) – COA, FATTY ACID AND ADEK VITAMIN SYNTHESIS**
  - B6 (PYRIDOXINE)- VARIOUS METABOLIC ACTIONS
  - BIOTIN- COFACTOR FOR METABOLISM
  - **VITAMIN C (ASCORBIC ACID)- POWERFUL ANTIOXIDANT, METABOLIC REDUCER, (CORNEAL) WOUND HEALING**
  - B12- HOMOCYSTEINE METABOLISM, NEURAL TISSUES
  - FOLATE- HOMOCYSTEINE, AA AND NUCLEIC ACID METABOLISM

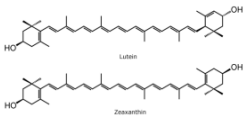
CAROTENOIDS

- Of the ~600 carotenoids in nature, 50 are found in the human diet (fruits and vegetables)

- About 10-15 types of carotenoids are found in human serum. However, only 2, lutein and zeaxanthin, are found within the macula. (Bone 1985, 1993)



Snodderly et al. 1984



AREDS AND MACULAR DEGENERATION

- Age-Related Eye Disease Study (AREDS) – 2001
  - Supplement:
    - 500mg Vit C
    - 400 IU Vit E
    - 15mg beta-carotene
    - 80mg Zinc
    - 2mg Copper
  - Decreased risk of progression to advanced AMD by 25 percent (AREDS 2001)

AREDS2

- 2013
- All groups: Original AREDS formula (Vit C, E, Beta-carotene, Zn, Cu)
  - +Lutein 10mg, Zeaxanthin 2mg (+/- beta-carotene)
  - +1000mg omega 3 FA (DHA/EPA)
  - Placebo
- Lutein/Zeaxanthin: reduction in advanced AMD
  - More pronounced without Beta-carotene supplement, low dietary L/Z
  - 20% reduction in development of neovascularization
- Beta-Carotene: double risk for lung cancer in former smokers
- Omega 3: no additional benefit for AMD
  - Ratio? Dietary sources better?
- Target population: Intermediate to advanced AMD, large drusen

RETINITIS PIGMENTOSA

- Vitamin A supplementation, slowing visual decline
  - Berson 1993- 601 adults with RP
    - Supplementation with 15,000 IU VitA decreased visual decline
    - Optimal result- patients taking supplement, +3000 IU dietary VitA
    - Vitamin E- 400 IU daily hastened visual decline
      - Competitive transport- vs. Vit A
  - Berson 2004- 221 RP patients, DHA (associated with VitA transport within the retina)
    - Vit A + DHA vs. VitA alone => No benefit from DHA
    - Subgroup analysis: VitA alone (control)
      - 200mg per day DHA from diet (3-6oz oily fish- salmon, tuna), decreased loss of central visual field sensitivity by 40-50 percent

RETINITIS PIGMENTOSA

- Berson 2010,
  - Vit A+ 12mg Lutein daily
  - Slowed mid-peripheral vision loss by approx. 10 years
- Combined analysis (Berson 2012):
  - Vit A+ high dietary DHA= 40 percent slower mean annual rate of decline in distance visual acuity
  - Potentially delaying vision loss for 20 years, depending on age of initiation of supplementation

DRY EYE SYNDROME

- Omega 3 and Omega 6 essential fatty acids (EFA)
  - Various studies showing benefit in DES (Rand 2011, Milianovic 2005)
    - Dietary (fish) consumption
    - Dietary supplementation
  - Recent study- randomized double-masked trial (Kandari 2013)
    - Supplementation with 180mg EPA + 120mg DHA BID x 30days
    - Improvements in tear breakup time, Schirmer tests, and Ocular Sruface Disease Index (OSDI)
  - Ideal supplement combination- TBD- variability between studies: DHA, EPA, gamma-linolenic acid, flax seed oil, plant oils etc.

CATARACTS

- AREDS1: antioxidant supplementation did not reduce risk of progression to cataract surgery
- AREDS2: Same results
  - Subgroup analysis- supplementation in patients with low L/Z may provide protective benefit
- Antioxidants: Lutein, zeaxanthin, Vit C, and Vit E found within the lens, preliminary studies suggest some benefit
- Italian study- OTC MV supplementation- benefited those with NSC, increased risk for PSC (Clinical Trial of Nutritional Supplements and Age-Related Cataract Study Group 2008).

GLAUCOMA

- Multiple studies have shown decreasing oxidative stress benefits glaucoma
  - One study- 584 African American women (Giaconi 2012)
    - Higher dietary Vit A, C, and carotenoids was associated with lower rates of glaucoma
  - Ginkgo biloba- some studies suggesting effectiveness

PEDIATRICS

- Retinopathy of Prematurity
  - Suggestive evidence that Lutein and Zeaxanthin supplementation may decrease oxidative damage in retinopathy of prematurity (Perrone 2010).
  - Randomized controlled trials have yet to confirm this relationship (Manzoni 2013).

MACULAR DEVELOPMENT

- Carotenoids detected by HPLC in cadaver eyes at 20 weeks gestation, although no pigment was visibly detectable (Bone 1988).
- Progressive shifts in distribution of lutein, zeaxanthin, and *meso*-zeaxanthin within the macula occur at different developmental stages.
- In 2013, Bernstein et al. reported quantification of macular pigment optical density (MPOD) by RetCam Imaging
  - Macular pigment not detected with non-invasive imaging in premature infants.
  - Macular pigment increased with age.
- Follow-up questions:
  - Macular pigment levels in term infants
  - Role of maternal nutrition on macular pigment deposition

"INTERRELATIONSHIPS BETWEEN MATERNAL CAROTENOID STATUS AND NEWBORN INFANT MACULAR PIGMENT OPTICAL DENSITY AND CAROTENOID STATUS" (HENRIKSEN 2013)

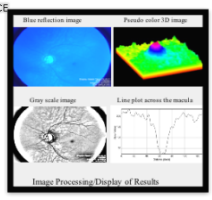
Study Purpose: Examine the relationship between infant and mother carotenoid status in newborn term infants.

Population:

- 30 healthy term (37 weeks and older) infants and their mothers
- 10 intrauterine growth restriction (IUGR) term infants and their mothers
- All infants were between 24-72 hours of age at a university hospital

METHODS

- Measurements
  - Infants: skin, serum carotenoids, MPOD (in subgroup of 14)
  - Mothers: skin, serum, breast milk carotenoids
- Quantification:
  - Serum Carotenoids: HPLC
  - Skin Carotenoids: Raman spectroscopy (non-invasive laser reflectance)
  - MPOD: RetCam imaging with blue-light reflectance



RESULTS

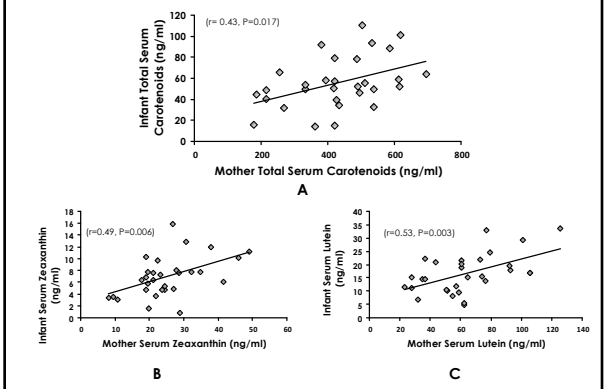


Figure 1

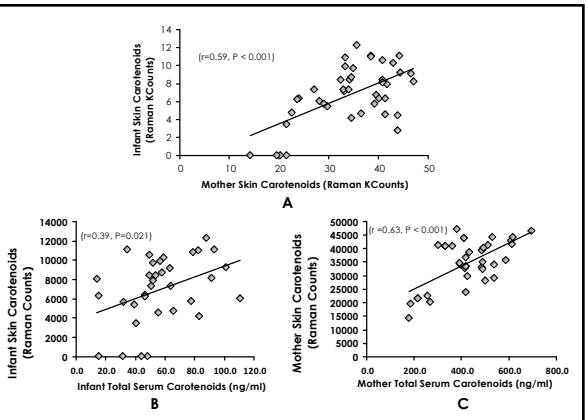


Figure 2

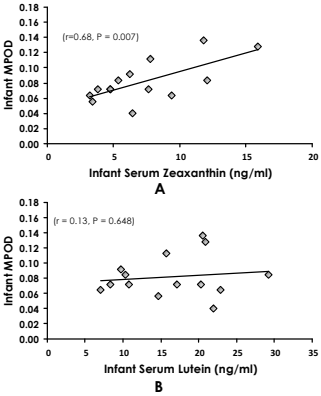


Figure 3

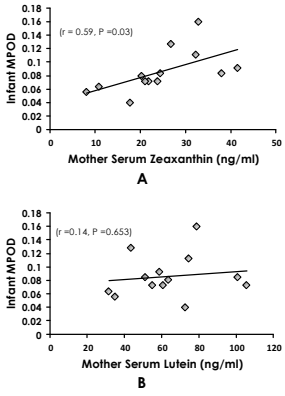


Figure 4

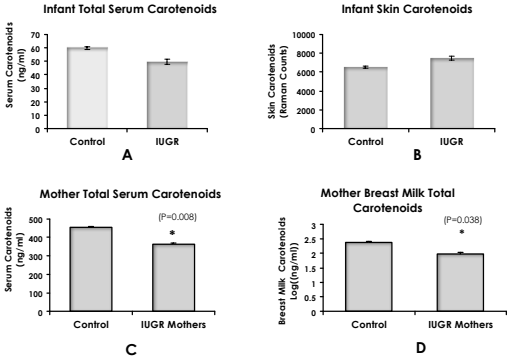


Figure 5

STUDY CONCLUSIONS

- Macular pigment is present and detectable via RetCam imaging in term infants.
  - Pigment deposition *in utero*
- Infant and Maternal zeaxanthin levels correlate with MPOD
  - Suggests role of maternal nutrition in macular development *in utero*
- Future work: prenatal supplementation trials

MAXIMIZING VISUAL HEALTH

- Various studies have examined the effects of carotenoids on visual performance on normal subjects (Bernstein 2016)
  - Evidence of positive impact on:
    - Dark adaptation
    - Light sensitivity & photophobia
    - Color discrimination (blue/yellow)
    - Contrast sensitivity
    - Visual acuity
    - Photostress recovery
    - Glare disability

CONCLUSIONS

- Nutrition plays a prominent role in disease prevention and slowing of progression
  - AREDS/AREDS2 for AMD
  - Vitamin A for RP
  - Omega 3 FA for DES
  - Others- glaucoma, ROP, etc.
- Nutrition also plays an important role in ocular development and function
  - L/Z and MP, infants and children
  - L/Z and enhanced visual function

DIETARY CONSIDERATIONS

- Better from food:
  - Thousands of phytochemicals and micronutrtients that come from fresh fruits and vegetables
  - Healthy eye habits are healthy body habits
    - Macronutrient balance, micronutrient intake
- Beware of over supplementation- toxic effects of multiple supplements
  - Beta-carotene + smokers
  - Vit A- pregancy, etc.
- Anticoagulation implications: Vit E supplements, fish oil, Ginkgo biloba

Source: USDA National Nutrient Database for Standard Reference, Release 22 (2009)

"I don't have anything against modern biochemistry, but it's a better strategy to rely on food. We're trying to fool Mother Nature, and she's had many millions of years to get it right."
--Billy Hammond Jr., PhD

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