



Ocular Nutrition : Diagnosis, Management and Treatment of AMD with Nutritional Supplements

New Concepts in the Management of AMD

Michael A. Samuel, MD
Cell - 626-319-6464

Epidemiology: AMD Prevalence

- ◆ Beaver Dam Eye Study: 1.7%
 - ◇ (Klein R et al. Ophthalmology 99: 933-43, 1992)
- ◆ Blue Mountains Eye Study: 1.4%
 - ◇ (Mitchell P et al. Ophthalmology 102:1450-60, 1995)
- ◆ Rotterdam Study: 1.2%
 - ◇ (Vingerling JR et al. Ophthalmology 102: 205-10, 1995)

- ◆ Disclosure
 - ◇ Alcon
 - ◇ J&J
 - ◇ B&L
 - ◇ QLT
 - ◇ Novartis
 - ◇ EyeScience

AMD Public Health Impact

- ◆ #1 Cause Of Elderly Blindness In USA
- ◆ 2005: 38 Million Elderly
 - » 200,000 Blind Annually
- ◆ 2030: 88 Million Elderly
 - » 500,000 Blind Annually
- ◆ New Exudative AMD*
 - 9.4 – 11.4 per 1000 over 3 years

*Javitt J, et al. Incidence of exudative AMD among elderly Americans. Ophthal. 2003.

Epidemiology: AMD Prevalence

Staggering Statistics

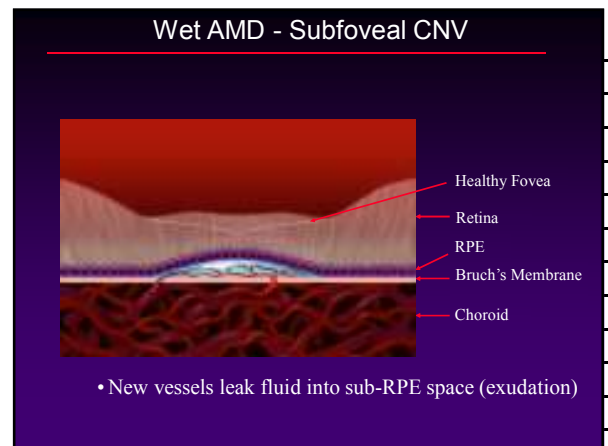
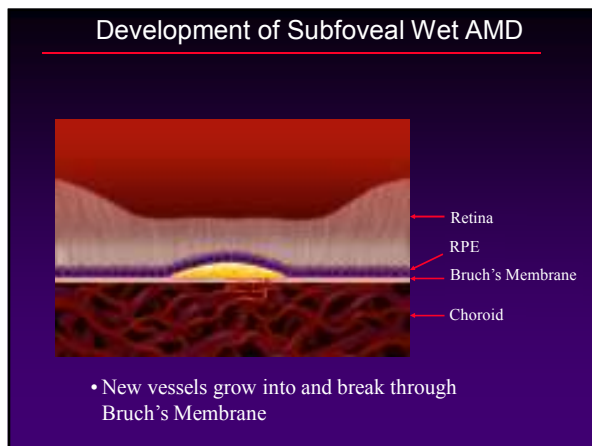
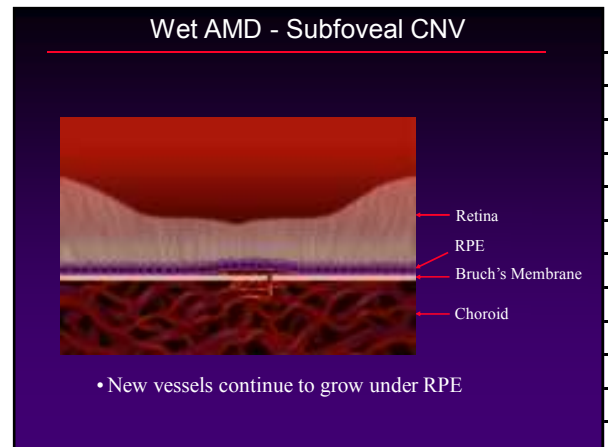
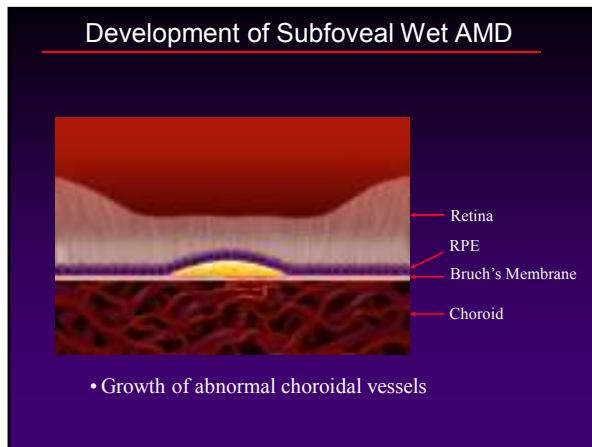
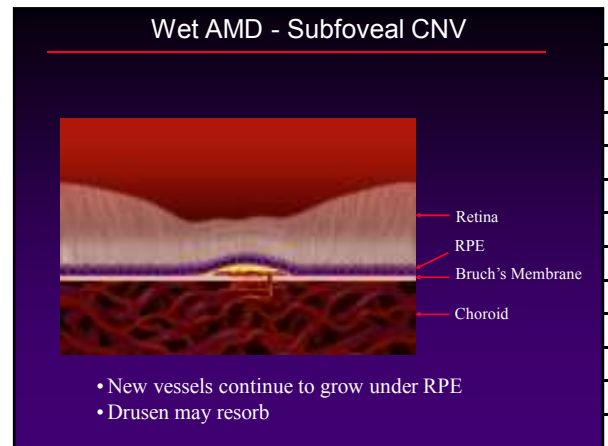
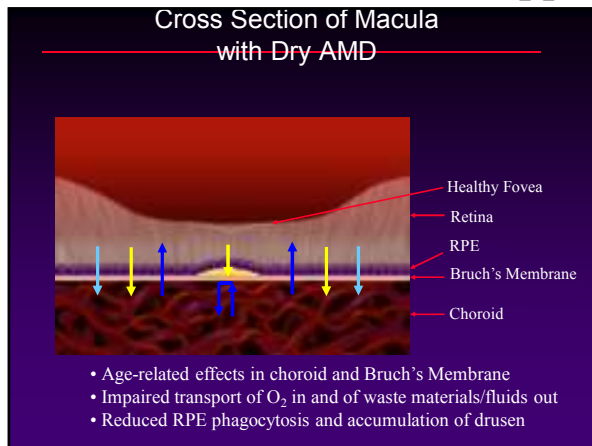
- ◆ 7.3 Million – Early Stages
- ◆ 3.6 Million – Bilateral Large Drusen
- ◆ 1 Million – Geographic Atrophy
- ◆ 1.2 Million – Wet AMD

- ◆ Reduced central vision
- ◆ Central smudge
- ◆ Distortion
- ◆ Decreased color vision

Cross Section of Healthy Macula

- Retina receives nutrients and oxygen across the RPE
- Retina disposes waste material and fluids

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Wet AMD - Subfoveal CNV

- Exudation breaks into sub-retinal space through RPE

How to Manage an AMD Patient

Am I Going Blind?

Things to Discuss:

- Family History
- Discuss Risk Factors
- Lifestyle Modification
- Amsler Grid Changes = Emergency
- Vitamin Supplements
- Reassurance

Wet AMD - Subfoveal CNV

- Type II CNV develops which typically shows classic components or remains occult to FA depending on activity of RPE cells

AMD Risk Factors

- ♦ Race
- ♦ Genetic
- ♦ Socioeconomic
- ♦ Aging
- ♦ Cardiovascular disease
- ♦ Cigarette smoking ++
- ♦ Hypertension +
- ♦ Serum lipids +
- ♦ Diabetes
- ♦ Alcohol±
- ♦ Light exposure +

Wet AMD - Disciform Scar

- Disciform scar - end-stage of wet AMD
- Severe irreversible vision loss
- Accounts for 80% of SVL in AMD

Modifiable Risk Factors for Advanced AMD

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AMD Classification

Four AMD Categories:

- Category 1 - Few if any Drusen
- Category 2 - Small to Moderate Drusen
- Category 3 - Moderate to Large Drusen or Non-central Geographic Atrophy
- Category 4 - Advanced AMD or Vision Loss Due to AMD in One Eye

Intermediate AMD

Category 3 – Clustered Intermediate & Large Drusen
N=1621

Intermediate drusen: 63-125 μm in > 360 μm circle (>656 μm if hard);
Large drusen: > 125 μm ; Non-central geographic atrophy

No AMD

Category 1- No or Few Drusen
N=1117

Small: < 63 μm drusen in a < 125 μm circle

Advanced AMD

Neovascular
N = 592

Advanced AMD in one eye:
CNV, Central GA, RPED, SRH, Fibrosis

Early AMD

Category 2 – Clustered Small & Intermediate Drusen
N=1063

Small: < 63 μm in a > 125 μm circle
OR
Intermediate: 63-125 μm drusen
OR
Pigment Abnormalities

AREDS - Results

Antioxidants – Daily Oral Dose

- Vitamin C – 500 mg
- Vitamin E – 400 IU
- Beta-carotene – 15 mg
- Zinc – 80 mg
- Copper – 2 mg

◆ Vitamins reduce CNV/visual loss

- ❖ for moderate ARMD or worse
- ❖ 20-25% by 5 years

◆ Centrum Silver in addition is ok


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AMD Trial - Summary

AREDS 1 - Showed Value of Antioxidant: 1 in 4 Protective vs. Preventative

Vitamin A - Not Good

Zinc - Too high




Question:

Who should be on an eye vitamin?

Answer: Everyone, but has to be right vitamin!

Science of AREDS 2

- Vitamin A - Beta carotene
 - CARET Study – 14,000 heavy smokers
 - 24% increase in lung cancer
 - 17% increase in mortality
 - Doesn't seem to have effect on macula in pill form
- Zinc
 - 9x higher than RDA in women
 - 6x higher in men
 - Urinary complication
 - Neurotoxicity
 - Link with beta-amyloid plaques – Alzheimer's
 - 25mg – Maximum absorption
- Omega-3
 - Essential factors in sensory process
 - Lipid in photoreceptors
 - Rhodopsin regeneration
 - Angiogenic growth factors
 - 6 studies – Role in AMD



AMD Trial - Summary

I thought it was only for Moderate and Advanced AMD.

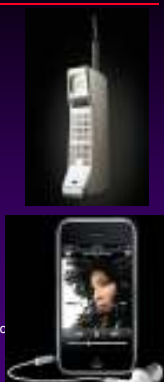
What about Early AMD (Category 1 or 2)

➤ **No Benefit** seen from supplements on Prevention of Vision Loss or the development of Advanced AMD

➤ **Rate of Progression over 5 years - 1.3%**

AREDS 1 vs. AREDS 2

- Enrollment ended June 2008
- 4000 patients / 50 –85 yo
- Goals:
 - Moderate Vision Loss
 - Cataract Progression
 - Eliminate beta carotene
 - Reduce Zinc
 - Lutein / Zeaxanthin
 - Omega -3
- AREDS 2 - 7 Subsets
 - AREDS – 15mg beta carotene
 - AREDS – no beta carotene
 - AREDS – no beta, low zinc (80mg to 25mg)
 - AREDS – low zinc
 - AREDS + Lutein 10mg / Zeaxanthin 2 mg (5:1 Ratio)
 - AREDS + Omega-3 – 1gram
 - AREDS + Lutein / Zeaxanthin / Omega-3



But what about other nutritional therapies?

- Lutein and zeaxanthin
 - carotenoids and macular pigment
 - Not Available AREDS 1
- Lower levels of lutein and zeaxanthin
 - patients with AMD
- Dietary supplements
 - may increase the density of these pigments in the macula and in serum.
- AREDS 2
 - Multicenter, Randomized
 - Designed to address the shortcomings of AREDS1



AREDS 2

- 4203 pts with moderate/advanced AMD.
- 50% were former smokers. 7% active smokers
- 59% bilateral large drusen
- 32% advanced AMD
- 5yrs
- Primary Analysis – AREDS + L/Z or O3 = failed to meet 25% reduction.

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Beta-carotene

- ◆ Removing BC – no effect on progression
- ◆ Risk of lung cancer seen, doubles risk – no risk seen with Lutein/Zeaxanthin
- ◆ Replacing BC with L/Z = 18% reduction in progression


What about other supplements?

- ◆ Vitamin B6 – Folate
 - ◇ Archives of Internal Medicine Feb 2009
 - » 5200 women over 40
 - » 41% lower risk of AMD
 - » Homocysteine ^ risk of AMD
 - » Vit B6 and Folate reduce homocysteine
 - » Role in prevention?
- ◆ Alpha-lipoic Acid
 - ◇ Protects RPE
 - ◇ Synergistic with Vit C, glutathione
 - ◇ Universal Antioxidant – lipids and water
- ◆ Selenium
 - ◇ Role in GSH – antioxidant enzyme for rpe and photoreceptors
- ◆ Grape Seed Extract
 - ◇ Powerful antioxidant
 - ◇ Strengthen vessel walls
 - ◇ Improves circulation
 - ◇ Reduces arteriosclerosis
- ◆ Glutathione
 - ◇ Studies have shown link to AMD
 - ◇ Strong Antioxidant – GSH enzyme
- ◆ Bilberry
 - ◇ French WWII – potent antioxidants
 - ◇ Strengthens capillary walls
 - ◇ Synergistic with Lutein/Zea
- Vitamin D
 - ◇ Reduces inflammation in outer retina
 - ◇ Less macrophages – sign of inflammation
 - ◇ Less – beta Amyloly

Lutein and Zeaxanthin

- ◆ Average american get 1-2mg diet
- ◆ Those study low - .7mg day
- ◆ Betacarotene – compete for absorption of L&Z.
- ◆ May have skewed impact of L&Z
- ◆ AREDS vs. AREDS plus L&Z.
 - ◇ 10% reduction in progression of advanced amd.
 - ◇ 11% reduction in progression to wet
 - ◇ 26% reduction to wet in those with low dietary L&Z.

Ocular Supplements – Be Specific



What was I supposed to get again?

Getting the Diagnosis of AMD
Overwhelmed
Scared
What about my family
Safety
Compliance

Zinc and Omega-3

- ◆ Zinc - 25mg vs. 80 mg – no statistical difference
- ◆ Trend towards higher dosage
- ◆ No difference in side effects seen
- ◆ Too low?
- ◆ Omega-3 - no benefit seen
- ◆ Role in prevention?

Reason for Confusion - 20+ products



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Supplement Facts
Serving Size: 1 soft gel
Amount per Serving

Vitamin C (ascorbic acid)	100 mg	20%
Vitamin E (d-alpha-tocopherol)	400 IU	80%
Vitamin A (all-trans-retinyl palmitate)	10,000 IU	200%
Zinc (zinc sulfate)	8 mg	160%
Copper (cupric sulfate)	2 mg	40%
Lutein	10 mg	-
Zeaxanthin	10 mg	-

Supplement Facts
Serving Size: 1 Capsule
Amount per Serving

Vitamin C (ascorbic acid)	100 mg	20%
Vitamin E (d-alpha-tocopherol acetate)	400 IU	80%
Vitamin A (all-trans-retinyl palmitate)	10,000 IU	200%
Zinc (zinc sulfate)	8 mg	160%
Copper (cupric sulfate)	2 mg	40%
Lutein	10 mg	-
Zeaxanthin	10 mg	-

PreserVision AREDS 2 Formula
120 Soft Gels

Ocuvite
Lutein and Zeaxanthin

iCaps' Lutein & Zeaxanthin
Serving Size: Two Tablets, Daily

Vitamin C (Ascorbic Acid)	600 mg
Vitamin E (DL-Alpha Tocopheryl Acetate)	100 IU
Bioflavonoid (Vitamin B3)	10 mg
Zinc (Zinc Acetate)	60 mg
Copper	4 mg
Manganese	10 mg
Selenium	60 mcg
Lutein/Zeaxanthin	4 mg
Calcium	10 mg

iCaps' MV Multivitamin
Suggested Adult Intake: Two tablets twice per day with a meal or as directed by your physician.

Supplement Facts	Amount/Serving	% Daily Value
Calcium	10 mg	<1%
Total Carbohydrates	2 g	50%
Vitamin C	500 mg	100%
Vitamin D	400 IU	100%
Vitamin E	400 IU	1425%
Vitamin K	20 mg	35%
Thiamin	1.5 mg	100%
Riboflavin	10 mg	384%
Niacin	10 mg	20%
Vitamin B6	2 mg	100%
Folic Acid	400 mcg	100%
Biotin	30 mcg	100%
Pantothenic Acid	10 mg	100%
Calcium	100 mg	20%
Phosphorus	100 mg	20%
Sodium	100 mg	100%
Magnesium	100 mg	20%
Zinc	60 mg	360%
Selenium	60 mcg	100%
Copper	4 mg	100%
Manganese	10 mg	100%
Chromium	20 mcg	50%
Molybdenum	75 mcg	100%
Copper	50 mcg	50%
Lutein	4.0 mg	1
Zeaxanthin	4.0 mg	1
Lyciene	4.0 mg	1

Supplement Facts
Serving Size: 1 soft gel, 1 to 3 times daily, 1 to 3 times daily, 1 to 3 times daily with meals

Vitamin C (ascorbic acid)	100 mg	20%
Vitamin E (d-alpha-tocopherol)	400 IU	80%
Vitamin A (all-trans-retinyl palmitate)	10,000 IU	200%
Zinc (zinc sulfate)	8 mg	160%
Copper (cupric sulfate)	2 mg	40%

Supplement Facts
Serving Size: 1 soft gel

Amount per Serving	1 Soft Gel	% of Daily Value
Vitamin C (ascorbic acid)	250 mg	50%
Vitamin E (DL-alpha-tocopheryl acetate)	200 IU	40%
Iron (Iron Sulfate)	11.4 mg	227%
Copper (Cupric Sulfate)	8.8 mg	176%
Lutein	5 mg	1

EyePromise RESTORE
Serving Size: 1 Soft Gel

Vitamin C (DL-Ascorbic Acid)	100 mg
Vitamin E (DL-Alpha Tocopheryl Acetate)	400 IU
Zinc (Zinc Oxide)	75 mg
Iron (Iron Oxide)	100 mg
Omega-3 (EPA + DHA)	100 mg
Omega-6 (Gamma-Linolenic Acid)	100 mg
Alpha Lipoic Acid	100 mg
Zeaxanthin	4 mg
Lutein	4 mg
Copper	4 mg

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CONTENT PER DAILY DOSE OF 2 TABLETS		
Blueberry Fruit Extract 5:1 equal to 1000 mg dry berries	400 mg	
Orange Peel Extract 5:1 equal to 1000 mg dry peels	200 mg	
Green Tea Extract 15:1 equal to 1000 mg dry leaves	4 mg	
Blackberry Fruit Extract 5:1 equal to 800 mg dry berries	120 mg	

Check an ingredient to view description
1 package of Blue Berry from New Herbs contains 60 tablets - equal to 1 months supply
New Herbs, Ltd. 4010 Highway 7, Unit 10, Golden and Bow for without coloring or sweeteners
Suitable for vegetarians and vegans

Conclusion:

AMD – epidemic on the rise

Supplement Facts		
Serving Size: 2 Capsules		
Amount Per Serving % DV		
Vitamin A (as retinol palmitate)	10000 IU	200%
Vitamin C (as ascorbic acid)	100 mg	200%
Vitamin E (as d-alpha-tocopherol)	100 IU	200%
Vitamin K (as menaquinone-7)	100 mcg	200%
Zinc (as zinc monomethionine)	15 mg	300%
Copper (as cupric gluconate)	2 mg	200%
Manganese (as manganese gluconate)	5 mg	100%
Selenium (as selenium yeast)	200 mcg	400%
Chromium (as chromium picolinate)	200 mcg	400%
Molybdenum (as molybdenum gluconate)	50 mcg	100%
Biotin (as d-biotin)	500 mcg	1000%
Inositol (as inositol)	100 mg	200%
Calcium (as calcium carbonate)	250 mg	500%
Iron (as ferrous fumarate)	10 mg	200%
Niacin (as niacinamide)	20 mg	400%
Thiamin (as thiamin mononitrate)	5 mg	100%
Riboflavin (as riboflavin)	5 mg	100%
Pyridoxine (as pyridoxine hydrochloride)	5 mg	100%
Cyanocobalamin (as cyanocobalamin)	500 mcg	1000%
Cholecalciferol (as cholecalciferol)	2000 IU	4000%

Supplement Facts		
Serving Size: 2 Capsules		
Amount Per Serving % DV		
Vitamin A (as retinol palmitate)	10000 IU	200%
Vitamin C (as ascorbic acid)	100 mg	200%
Vitamin E (as d-alpha-tocopherol)	100 IU	200%
Vitamin K (as menaquinone-7)	100 mcg	200%
Zinc (as zinc monomethionine)	15 mg	300%
Copper (as cupric gluconate)	2 mg	200%
Manganese (as manganese gluconate)	5 mg	100%
Selenium (as selenium yeast)	200 mcg	400%
Chromium (as chromium picolinate)	200 mcg	400%
Molybdenum (as molybdenum gluconate)	50 mcg	100%
Biotin (as d-biotin)	500 mcg	1000%
Inositol (as inositol)	100 mg	200%
Calcium (as calcium carbonate)	250 mg	500%
Iron (as ferrous fumarate)	10 mg	200%
Niacin (as niacinamide)	20 mg	400%
Thiamin (as thiamin mononitrate)	5 mg	100%
Riboflavin (as riboflavin)	5 mg	100%
Pyridoxine (as pyridoxine hydrochloride)	5 mg	100%
Cyanocobalamin (as cyanocobalamin)	500 mcg	1000%
Cholecalciferol (as cholecalciferol)	2000 IU	4000%
