Thursday, 
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Objectives
After this program, you will have increased your ability to:
• Describe the role of key nutrients for eye health
  in age-related macular degeneration (AMD)
• Determine the appropriate nutrients for different stages of AMD
• Differentiate the various nutritional
  supplements available
• Educate your patients on lifestyle factors and proper nutritional supplementation for AMD
  prevention and progression management

Agenda
6:00 pm – 6:30 pm Pre-test
6:30 pm – 8:30 pm CE Presentation
Q&A Session
Post-test

This Program is Interactive
We encourage you to participate in the case discussions.

While there is a Q&A session at the end, if you have questions please ask. There are Question Cards on the table you can hand to the staff person; or just raise your hand.

**AMD and Nutritional Supplements: Sorting Fact From Fiction**
Counseling Strategies for Your Patients

**Fact or Fiction?**
- Nutritional supplements don't really work
- Only selected patients with dry AMD benefit from taking AREDS formula supplements
- All supplements are essentially the same
- The evidence on macular pigment is weak
- Vitamins are completely safe
- Meso-zeaxanthin is a crucial carotenoid
- Taking Centrum Silver is generally enough for our AMD patients
- AREDS2 is better than AREDS1
- Only AMD patients benefit from nutritional supplements
- Omega-3 lowers coagulation factors
- Mega-doses of vitamin E are harmless and have significant health benefits

**Can we eat a healthy, natural diet that provides appropriate levels of all necessary vitamins, minerals, and other nutrients?**

How many of us in modern day America can do this for
A day?
A week?
A month?
A lifetime?
Where would we even start?

**Multivitamins in the News**

**AMD Overview**

**What Is AMD?**
- Degenerative retinal disease that can cause central vision loss and blindness
- The leading cause of severe vision loss in people older than 50 years in the western world...
  and is becoming more prevalent with aging of baby-boomers
- 2 forms of AMD
  - Non-neovascular (Dry)
    - Affects 80%-90% of patients
  - Neovascular (Wet)
    - Affects 10%-20% of patients
    - Responsible for 90% of vision loss

**The Stages of Dry AMD**

**ARED5 Staging**

**ARED5 Staging**

**Wet AMD**
The patho of Dry, plus development of either:
- subretinal choroidal neovascular membranes
• subretinal hemorrhage
• RPE detachment

19 **Natural Course of Wet AMD**
Without treatment, chance of severe vision loss and legal blindness is high. Significant chance of 2nd eye becoming affected
– Annual rate of 4%-12%
– Unilateral neovascular AMD becomes bilateral in >40% at 5 yrs
As population ages, more people will have wet AMD; approximately 7.5 million in developed countries by 2020

20 **Treatment**
• Most treatment research has focused on neovascular AMD
• Anti-VEGF therapy has driven a paradigm shift in neovascular AMD therapy
  – Pegaptanib (Macugen)
  – Ranibizumab (Lucentis)
  – Bevacizumab (Avastin)
  – Aflibercept (Eylea) [VEGF Trap-Eye]

22 **Secondary End Point:**
**Mean Change in Visual Acuity Over Time**

23 **Letter Gains From Baseline**

24 **Secondary End Point:**
**Mean Change in Visual Acuity Over Time**

25 **Letter Gains From Baseline at Month 12**

26 **Lucentis Studies**
ANCHOR: Predom. classic
MARINA: Min. classic
Similar results in both

28 **Comparison on AMD**
**Treatments Trial (CATT)**
Lucentis monthly vs Lucentis PRN vs Avastin monthly vs Avastin PRN
• Results: Monthly Lucentis and monthly Avastin equivalent. PRN Lucentis equal to PRN Avastin. PRN Lucentis equal to monthly Lucentis. PRN Avastin vs monthly Avastin inconclusive.
• Lucentis essentially equal to Avastin in outcome measures
• FA and OCT – may be signal that Lucentis slightly better—need year 2 data
• PRN: Lucentis slightly fewer injections needed vs Avastin (6.9 vs 7.7)
• Lucentis essentially equal to Avastin in adverse events: both relatively low
• Avastin
  • not FDA approved or manufactured for ocular use
  • has significant economic benefits

29 **Statistics From CATT 1 Year Results**

30 **Eylea (aflibercept)**
• VEGF Trap-Eye
• Mimics the VEGF receptor, traps VEGF
• Recently FDA approved for q8wk dosing
• Q8wk dosing = q4wk Lucentis dosing

31 **Reactive vs Proactive Approach**
**AMD Risk Factors**

1. **Non-Modifiable**
   - Age (chronological)
   - Gender
   - Hereditary: Genetics
   - Race/Pigmentation

2. **Modifiable**
   - Smoking
   - Cardiovascular disease
   - Alcohol intake
   - Light exposure
   - Nutrition
   - MPOD

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**The Importance of Genetics and Macular Pigment**

**Genetic Tests Commercially Available**
- Macula Risk from ArcticDx
- RetnaGene from Sequenom (not yet available for ODs)
- AMD Risk Assessment from Asper Ophthalmics
- University laboratories

**The Genetic Components of AMD**
Naturally Occurring Variations Conferring AMD Risk

**Macula Risk Macula Risk Score**

**Sample Patient Report, Macula Risk Category 1**

**3 Human Macular Pigments**
- Lutein, Zeaxanthin, and Meso-zeaxanthin
  - Lutein is 5x more common in the US diet.
    - Carotenoid ratios: L:Z:M
      - Blood: 3:1:0
      - Whole retina: 2:1:0.5
      - Fovea: 1:2:1

**Macular Pigment Optical Density**
- The 2 macular pigments are from yellow and orange carotenoids (L&Z), + MesoZ
  - L&Z unable to be synthesized by humans
  - Accumulation can protect RPE and photoreceptors
- Lower MPOD associated with lower carotenoid intake/serum levels, females, smoking, diabetes, increased BMI...AMD
- Measurable

**Techniques for Measuring Macular Pigment Optical Density**
- HFP- Heterochromatic flicker photometry – (gold standard)*
– Macuscope®
– QuantifEye®

• SLO-based methods - HRA
• Reflectometry
• Raman Spectroscopy – (absorbance re-emission)
• Fluorescence attenuation

The Science

Atrophic AMD Nutrition/Visual Function Trials
(w carotenoids Lutein and Zeaxanthin)
• Falsini Study – 2003
• LAST – April 2004 (1-year data)
• TOZAL – February 2007 – open case control
• LUXEA – February 2007 and April 2006 (1-year data)
• LUNA – April 2007
• LAST II – May 2007
• CARMIS – Feb 2008 (2-year data)
• Lutein in normal subjects July 09 Brit J Nutr
• ZVF – S. Richer: November 2011

Case Discussion: Diagnosing AMD

73 W/M 1/16/2007
• Followed for 2+ years for dry AMD
• Taking 6 mg Lutein/day + Centrum Silver
  – And a host of medications

Your Diagnosis/AREDS Category?

What Else Would You Evaluate?
• MPOD?
• Genetic risk?

Overview of AREDS1 and AREDS2

AREDS
• AREDS 1 constituents:
  – 500 mg vitamin C
  – 400 IU vitamin E
  – 15 mg beta-carotene (25,000 IU)
  – 80 mg zinc
  – 2 mg copper

  • 25% decrease risk reduction in developing advanced AMD (groups 3 and 4) with antioxidants plus zinc

AREDS: Progression to Exudative AMD
• Risk at 5 years depending on formulation
  – Placebo: 28%
  – Antioxidants: 22%
  – Zinc: 21%
  – Antioxidants + Zinc: 20%
• Vision outcome: 3 or more line vision loss at 5 years
  – Placebo: 29%
  – Antioxidants: 26%
Statistical Analysis of AREDS

Is AREDS Formula Ideal?

Beta-carotene:
- Numerous studies have demonstrated little or no effect from beta-carotene alone
- Smokers most at risk for AMD, but cannot take vitamin A (beta-carotene)

Xanthophyll carotenoids:
- Lutein and zeaxanthin missing and evidence for benefit exists

Omega-3:
- Numerous articles pointing to benefits
- Benefits of fatty acids through diet

Zinc:
- Amounts may be excessive

AREDS 2 Study Objectives
1. Effects of high supplemental doses of lutein and zeaxanthin and omega-3 LCPUFAs (DHA and EPA).
2. Effects of these supplements on advanced AMD, moderate vision loss (doubling of the visual angle or the loss of 15 or more letters on the ETDRS chart).
3. Effects of these supplements on cataract.
4. Effects of eliminating beta-carotene on the development and progression of AMD.
5. Effects of reducing zinc on the development and progression of AMD.
6. Validate the fundus photographic AMD scale developed from AREDS.

AREDS2

Will AREDS2 give us the answers we need?
- YES – Is AREDS1 adequate or does it need modification?
- NO – Still not truly preventing

Nutrients
Zeaxanthin
- Relatively minor component of higher green plants
- Very limited data for zeaxanthin content of foods
- Zeaxanthin has an extra conjugated double bond, compared with lutein, which may make it a better antioxidant

- Found in most fruits and vegetables
- Role of lutein well known in plants
- Beta-carotene and lutein are predominant carotenoids found in higher green plants
- Three chiral centers; 8 possible isomers, only 1 is found naturally

Lutein
- Western diets low in lutein\(^1,2\)
  - NHANES adults: .6-1 mg/day
- How much lutein is thought to be an adequate level?
  - No current RDA or RDI amount
  - 10 mg are being studied in AREDS2
- How much lutein is in Centrum Silver?
  - 250 micrograms
- How much lutein is safe?
  - Water soluble
  - No toxicity or side effects observed in elderly on 10 mg for 6 months\(^3\)

Effect of Lutein + Zeaxanthin

Advanced AMD:

Effect of Lutein and Zeaxanthin:

Early AMD
ZVF Study (builds on LAST study)
- 60 older adults (57 men, 3 women) with mild-to-moderate AMD
- randomized to zeaxanthin 8 mg, lutein 9 mg, or zeaxanthin 8 mg plus lutein 9 mg
- Results: central foveal 1° macular pigment optical density increased in all 3 groups from low-normal to normal density
  - Zeaxanthin: high contrast central visual acuity improvements
  - Lutein: low contrast visual acuity improvements, glare recovery
  - Benefit: Improved driving performance

The Third Carotenoid: Meso-Zeaxanthin (MZ)
MZ key carotenoid in the macula
- Proven to increase MP via supplements
- Enzyme conversion of lutein
- Strong antioxidant

Found in small amounts in some shrimp exoskeleton, fish skin, turtle fat
- Not in American diet...hence, some believe supplementation is needed
Still controversial

Omega-3 Fatty Acids

Essential, not synthesized by body
Role in AMD
- Constituent of photoreceptors and helps promote survival
  - Precursor for Neuroprotectin D1 - delays apoptosis
- Antioxidants
- Anti-inflammatory and anti-angiogenic properties
  - Protection for the more advanced stage of the disease

Forms
- ALA: from vegetables
- DHA/EPA: converted from ALA but not efficient. From fish oil.

Studies Show \( \Omega-3 \) Is Associated With Reduced Risk of AMD

**Omega-3s**
- How much DHA/EPA does the average American consume on a daily basis? ~100 mg
- How much Omega-3 is thought to be an adequate level?
  - 350 mg DHA and 650 mg EPA in AREDS2
- Really no guidance for the eye
- Cardio recommendations: at least 250 mg/day of long-chain n-3 PUFA or at least 2 servings/week of oily fish¹

Zinc, Omega-3, L + Z: Early AMD-Rotterdam Study
- Study with 2167 participants
- Higher intakes of zinc, omega-3 fatty acids, and lutein/zeaxanthin beneficial in attenuating incidence of early AMD
- Benefits achieved with high but not excessive amounts of nutrients

The Proof That People Do Not Eat Recommended Amounts F/V
- Food ideal, but may be difficult to achieve
  - NHANES: below average fruits and vegetables intake US adults below recommended level
- Recent study shows that achieving and sustaining a F/V intake at RDI amounts cannot be done with only behavioral interventions (reminders, setting goals, etc)
  - Added on average only 1.1 serving/day more with behavior change
- Supplements have a role

A Few Cautions on Vitamin Supplements...

Recommendations on Beta-Carotene and Smoking History
- Current smokers –
  - Advise not to take beta-carotene
- Past smokers –
  - Caution those who recently quit (within 5 years)
- Passive smokers –
  - Caution those exposed to heavy smokers

Careful With MEGA-doses of a SINGLE Nutrient
- Caution with Vitamin E
  - There may be an increased mortality rate (but studies inconsistent)
  - Vitamin E and Coumadin – cumulative blood thinners
  - SELECT Study (400IU/d) – increased risk of prostate cancer
High Dosages of Zinc: The Paradox

Benefits
− Zinc alone decreases the progression of AMD by 21%

Side Effects
− Association with Alzheimer disease?
− Increase in genitourinary (UTI) hospitalizations
  • 7.5% of zinc-treated AREDS patients had UTI
  − ? prostate cancer
− Associated with copper deficiency anemia
− Inhibits absorption of other drugs?
  • Oral tetracycline

Sorting Through It All

Available Supplements

Which Vitamin for Treatment or Prevention?
Treatment: technically for AREDS-defined intermediate/advanced
• Easiest to treat based on science: AREDS formula
• What about lutein?
• Omega-3?

Prevention of progression at any stage
• Even “pre-AMD”
• Lutein, zeaxanthin

The AREDS formulas
Most products contained all constituents present in AREDS
− But few contained the dosages recommend by AREDS

The AREDS2 Products
Non-AREDS Supplements
Lutein and Zeaxanthin
• Look for ratio as in AREDS2:
  − Lutein 10 mg/Zeaxanthin 2 mg
• Water soluble

Omega-3
• Look for ratio of EPA/DHA of 650 mg/350 mg
• Drawbacks:
  − Fishy taste
  − Gas/Nausea
  − Increased bleeding

Considerations

Patient Counseling Strategies
Where Do We Fit In as Optometrists?
• Not likely to be administering injections or other treatments, unless topical
• Even with potential topical treatments, our emphasis must be on prevention
• How can we help our patients?
  − Ask questions
  − Open-ended
– Disseminate accurate information
– Recommend proper nutrition, whether via diet or supplements, or both

82 **Query Patient’s Lifestyle**
How is your diet?
Do you smoke?
How often do you eat fish?
What is your family history of AMD?
How often do you drink wine?
Describe your lifestyle, activity, exercise, meals
How well do you think you see?

83 **Patient Education Brochure**
• To help answer patient questions about AMD and Nutritional Supplements
• 50 brochures in packet
• PDF available after the program on [www.mededicus.com](http://www.mededicus.com)

84 **Vitamins are not ONE type fits ALL**

BE SPECIFIC and encourage proper dosing (don’t fairy-dust) depending on:
• Age
• Sex
• Nutrition status
• Systemic health/Social behavior
• Current supplements and medications
• Stage of the disease or the “at-risk patient”

85 **Practice Management Pearls**

86 **Reimbursement**
Reimbursement:
ICD-9 Codes
• 362.50 – non-specific AMD
• 362.51 – nonexudative senile macular degeneration
• 362.52 – exudative senile macular degeneration
• 362.57 – drusen

No Reimbursement:
• No insurance
• No diagnosis of AMD

87 **Frequency of Visits**
• Drusen 362.57
  – With RPE changes?
  – Coalescing?
• Dry AMD 362.50
• Wet AMD 362.52
• + F H

88 **Additional Testing**
• OCT Retina 92134
• PHP 92082
• Photos 92250
• MPOD ?
• Genetic testing?
• LCD – Local Carrier Determination

Supplement Distribution
• Prescription to patient for local acquisition
• Stock and sell directly to patient
• Guide patient to specific Web site/source

Profitability on Supplements
• Prescription to patient – none
• Direct distribution – wholesale vs retail difference
• Rebate from referral methodology

Case Discussions
Case 1
45 yo single male truck driver
– Diet consists of all meals at fast-food restaurants and truck stops
– Grandmother (deceased) blind in 1 eye and poor vision in the other from AMD
– c/o some
– Night driving
difficulty
– And glare

Case 1
• Smokes 2 packs per day unfiltered cigarettes
• Genetic testing predicts higher probability of AMD (MR3-MaculaRisk)
• 20/25 BVA OD and 20/20 OS with plano distance correction

Case 1
• LEE 10 years ago, now having near acuity problems
• Moderate drusen formation OD macula with no RPE breaks
• PHP basically WNL
• MPOD : .18
• Ranges for MPOD *
  <.35 low
  .36-.45 mod
  >.46 high
  •

Management Discussion
Diagnosis/Impressions:
– AREDS Category?
How would you manage?
– Which supplements to prescribe?
– How would you counsel on dietary/lifestyle changes?
– What follow-up would you do?
How would you code?

Follow-up
Patient given Lutein/Zeaxanthin
3 months later, RTC: MPOD: .26
Subjective report: improved visual quality

Case 1
What if patient has genetic testing done and is now Risk Category MR 5? Does this change your management plan? — Follow-up plan? — Supplements?

Case 2
75 yo Hispanic male
Unknown family history
Well-nourished, normal weight
Hypertensive, T2DM
POAG

75 yo Hispanic Male
20/30 OU, POAG OU

Management Discussion
Diagnosis/Impressions:
— AREDS Category?
How would you manage?
Would you do OCT?
Would you recommend supplements? If so, what would you prescribe?
What if the patient was a smoker?

Case 3
58 yo white female
No family history
MPOD: .21
BMI: 30.4
Retinal examination: Normal
Diet: f/v: 2/d fish: 1/mo
Medications: none
Supplements: 1-a-day multivitamin
Social drinker and smoker

Management Discussion
Diagnosis/Impressions:
— AREDS Category?
How would you manage?
How would you counsel when asked:
— “Am I at risk for developing AMD”
— “I have heard about macular degeneration. What should I do to prevent it?”

Case 4
Revisiting our patient from earlier
73 yo White Male 1/16/2007
Followed for 2+ years for
dry AMD
• Taking 6 mg Lutein/day + Centrum Silver
  – And a host of medications
• BCVA  20/40+, 20/40+
• Drusen and pigment changes in each macula

What would you do now?

Case 5

• 76 yo white male presents for routine examination
  – Distance vision is good, needs reading glasses, uses OTC readers
  – HIGH BMI
• OH: unremarkable
• Medical history: type 2 DM, HTN, hyperlipidemia
• Medications: glipizide, metformin, atenolol

Management Discussion

Diagnosis/Impressions:
  – AREDS Category?
How would you manage?
  – Any supplements?
  – How would you counsel on dietary/lifestyle changes?
  – What follow-up would you do?
How would you code?

Fact or Fiction?
• Nutritional supplements don't really work
• Only selected patients with dry AMD benefit from taking AREDS formula supplements
• All supplements are essentially the same
• The evidence on macular pigment is weak
• Vitamins are completely safe
• Meso-zeaxanthin is a crucial carotenoid
• Taking Centrum Silver is generally enough for our AMD patients
• AREDS2 is better than AREDS1
• Only AMD patients benefit from nutritional supplements
• Omega-3 lowers coagulation factors
• Mega-doses of vitamin E are harmless and have significant health benefits

Post Test

Question-and-Answer Session

Thank you for participating
Please have your Certificate stamped as you exit and turn in the top copy