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Editor: Cynthia Brock, Executive Assistant

Dietary Supplements for Macular Degeneration

The discovery of vitamins and the deficiency diseases associated with them is one of the most exciting and inspiring stories in medicine. Most will remember the Scottish surgeon James Lind, who in 1747 discovered that citrus foods helped prevent scurvy, and Christiaan Eijkman, who in 1897 discovered that feeding unpolished rice instead of polished rice to chickens helped to prevent beriberi. Sir Edward Mellanby discovered that the cause of rickets in impoverished and malnourished children in the Glasgow slums in 1920 was lack of vitamin D due to lack of sunlight, which could be prevented or remedied by ingesting food rich in vitamin D. As dramatic as these stories are, I would venture to say that none of my readers has ever seen a case of scurvy, beriberi, or rickets. The fact is, vitamin deficiency diseases are quite rare in the modern industrial world, occurring only in those few patients with unusual malabsorption syndromes or severe liver diseases. Why then, do we recommend "mega doses" – 4 times the recommended daily allowance – of vitamins and minerals to our patients with macular degeneration?

In the late 1980s and early 1990s, studies by individual investigators, and the Eye Disease Case Control Study, the Baltimore Longitudinal study and the Beaver Dam Eye study had conflicting results as to the benefit of antioxidants and mineral supplements in the prevention of cataract and macular degeneration. This led to the first Age Related Eye Disease Study, or AREDS 1, completed in the year 2001. Over 4000 patients participated in this 7 year prospective multicenter clinical trial, sponsored by the NIH. Although there was no reduction in risk for the formation of cataract, the study investigators concluded that high doses of antioxidants (500mg Vitamin C, 400mg Vitamin E, and 15mg of beta carotene) and minerals (80mg zinc and 2mg of copper) reduced the risk of visual loss from advanced macular degeneration from 28% to 20%, or about 2% per year after 5 years, when compared to placebo. Side effects were very few. Since none of the patients (or the investigators) knew whether they were taking placebo or not, almost everyone took an over-the-counter vitamin (i.e. Centrum Silver), but this had no effect on reducing visual loss.

The AREDS 1 study was controversial because the study as a whole failed to demonstrate statistical significance; only when subgroup analysis was performed – comparing those with small or no drusen to those with large drusen or advanced AMD in one eye - were the results felt to be significant. This in part led to AREDS 2, a second prospective multicenter clinical trial sponsored by the NIH, completed in 2013. Again, over 4000 patients participated over a 7 year period. This time the control group took the AREDS 1 formula plus a placebo, and 3 study groups took the AREDS 1 formula and the carotinoids Lutein and Xeaxanthin, omega-3 fatty acids, or both. In all 4 groups, there was a 30% progression to advanced AMD, and omega-3 fatty acids were of no benefit. However, the investigators concluded that Lutein and Xeaxanthin may be successfully substituted for Vitamin A (beta carotene) and that this confers a slight reduction in the risk of developing lung cancer (2% vs 1%), mostly in former smokers. This recommendation has resulted in the "AREDS 2" formula now on drug store shelves.

The controversy over supplements continued when Carl C. Awh, MD, and colleagues published study findings in **Ophthalmology** this year regarding the influence of genetic risk markers on response to nutritional supplements in patients with age-related macular degeneration, suggesting that genotype-directed nutritional therapy could result in improved outcomes for patients with moderate AMD. However, Emily Chew, MD, principle investigator in the AREDS2 study, stood by the AAO guidelines to "avoid routine genetic testing for genetically complex disorders like age-related macular degeneration". Genetic testing remains important in research, Chew said, but genetic testing of AMD for customizing AREDS supplement is not recommended. While I believe that genetic testing will ultimately be of benefit, I don't recommend it at the present time for patients with AMD or their relatives.

At the present time, vitamin and minerals contained in AREDS 2 preparations are considered "dietary supplements" by the FDA, but in 2012 an estimated 70% of manufacturers were considered noncompliant with "good manufacturing practices". We recently tested by gas chromatography mass spectrometry the concentration of vitamins C and E and minerals zinc and copper in National and Local brands of dietary supplements recommended for patients at risk for macular degeneration in the chemistry department at U of L. We found that all the dietary supplements we analyzed had relatively accurate labeling of the concentrations of Vitamin C, E, Zinc and Copper, and manufacturers of these products seem to be following "good manufacturing practices". Physicians may recommend generic brands of these supplements with some confidence. While there is a great deal of variation from store to store, both generic and national brands of AREDS 1 and AREDS 2 cost about the same -- $15 a month – at various stores in the Louisville area.

In conclusion, I have ambivalent feelings about recommending dietary supplements for patients at risk for AMD. The science is a little shaky – why would "mega doses" for vitamins and minerals work better that the recommended daily allowance?" Why was subgroup analysis needed to demonstrate a benefit in the AREDS studies? Nonetheless, patients want to do something about their disease, and I believe that recommending AREDS supplements is of significant psychological benefit, and perhaps of some physiological benefit to patients at risk for visual loss from macular degeneration.

By: Charles C. Barr, MD

To schedule an appointment at the Kentucky Lions Eye Center, please call 502-852-5466.

Physicians
EYE SPECIALISTS

Kentucky Lions Eye Center
301 East Muhammed Ali Blvd.
Louisville, KY 40202-1594

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Office Locations:

Kentucky Lions Eye Center
University of Louisville
301 E. Muhammad Ali Blvd.
Louisville, KY 40202
Adult Clinic (502) 852-5466
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The Springs Medical Center
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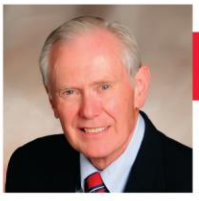

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