

## Studies on Age-related Macular Degeneration

**2001 Study:** In a study published in the journal *Free Radical Biology & Medicine*, Swedish investigators determined the effect antioxidants on oxidative damage in retinal cells in culture. Cells were incubated simultaneously with high oxygen pressure (to promote oxidation) and various antioxidants, including lutein. The level of a marker of oxidative damage, lipofuscin, was then measured (1). **Results:** After combining with lutein with high oxygen treatment, lipofuscin levels were half that of oxygen alone. Similar results were obtained with zeaxanthin and  $\alpha$ -tocopherol. The results from this study support the notion that in the retina, in addition to functioning as a filter of damaging blue light, lutein also acts as a potent antioxidant by inhibiting oxidative damage.

**2001 Study:** In a study presented at the 2001 Annual Meeting for the Association for Research in Vision and Ophthalmology (ARVO) researchers maintained rhesus monkeys on a carotenoid free diet from birth to age 10 then measured macular pigment. The monkey diets were then repleted with lutein and zeaxanthin (2). **Results:** Monkeys fed a carotenoid-free diet had no macular pigment. Repletion with lutein and zeaxanthin for 6 to 12 months restored macular pigment to levels observed in monkeys fed a normal diet. This suggests that lutein is required in the diet for macular pigment.

**2001 Study:** The research group headed by Dr. Paul Bernstein from the University of Utah has identified a putative lutein-binding protein (termed XBP, for xanthophylls-binding protein), from the retina of human eyes. The XBP binds selectively and specifically to lutein and zeaxanthin, and may be part of a transport system that transports lutein from the serum to the macula (3).

**2001 Study:** Dr's John Landrum and Richard Bone and collaborators from the University of Florida conducted a study to explain the association between low macular pigment and AMD. Retinas from 56 donors and 56 controls were dissected and the amounts of lutein and zeaxanthin were measured (4). **Results:** The study showed lower lutein and zeaxanthin concentrations in retinas from AMD donors than from controls. Furthermore, the researchers reported an inverse association between the incidence of AMD and the macular pigment density, consistent with previous findings. It was also demonstrated, using a mathematical model, that the decrease of macular pigment density in AMD donors was associated with lower lutein and zeaxanthin concentrations, not with destruction of MP density due to AMD.

**2000 Study:** Researchers at the Florida International University examined the levels of lutein in people with AMD versus those without (5). **Results:** By extracting eyes from cadavers of individuals who had and who did not have the disease, the researchers found that those with the disease had lower levels of lutein in the macular region than those who did not.

**2000 Study:** Researchers from Florida International University studied the effect of 2.4-mg/day lutein (FloraGLO<sup>®</sup> Lutein) intake, in the form of a dietary supplement, on the serum levels and macular pigment (MP) densities of 24 individuals, over a six-month period (6). **Results:** The results from the study showed that all subjects responded to lutein supplementation, measured by a 130% increase of lutein in the serum. Furthermore, most of the subjects had an increase in their macular pigment density as result of the supplementation. The average increase of MP density was 14%.

**2000 Study:** Rapp and collaborators measured lutein and zeaxanthin concentrations in the rod outer segment (ROS) membranes from the perifoveal and peripheral human retinal tissues. These researchers dissected 18 eyes from donors ranging from 46 to 73 years of age (7). **Results:** High concentrations of lutein and zeaxanthin were found outside the fovea, particularly in the ROS membranes in the perifoveal region of the retina. The ROS membranes are very susceptible to oxidative damage because of their high content of polyunsaturated fatty acids and the high oxygen tension in this region. Therefore, the presence of these carotenoids in the human ROS membranes may have a protective role against AMD.

**1999 Study:** In a review article, Beatty and coworkers discussed current literature pertaining to

macular pigment and age-related macular degeneration and examined the evidence that retinal carotenoids are protective against AMD (8). **Results:** In this review, the authors presented vast evidence that supports the hypothesis that macular pigment (lutein and zeaxanthin) may protect against AMD and age related maculopathy (ARM). They also indicated the possibility that macular pigment may be protective against AMD and it should be acknowledged and further investigated. They also emphasized that people at risk of developing ARM should be encouraged to eat diets rich in fruits and vegetables.

1999 Study: Dr. Stuart Richer investigated the effect of eating a diet rich in lutein and zeaxanthin on patients with atrophic age-related macular degeneration, using a clinical protocol (9, 10). Results: Using his AMD work-up protocol, Dr. Richer was able to measure moderate vision improvements or complete resolution of scotomas metamorphosia in seven of eight patients that consumed five ounces of spinach four to seven times per week or lutein-based antioxidant (three patients).

1999 Study: In a review paper published by the Journal of the American Optometric Association, Dr. Steven Pratt discussed the link between carotenoids and age-related macular degeneration (11). Results: AMD incidence may be significantly reduced by smoking cessation, by protecting the retina from direct sunlight and by consuming green leafy vegetables rich in lutein and zeaxanthin, such as spinach and kale.

1998 Study: Dr. Billy R. Hammond and coworkers measured the macular pigment density of 27 older (aged 60 - 84 years) and 10 younger (aged 24 to 36 years) subjects and determined their visual sensitivity (12). Results: The results showed that older subjects with high levels of lutein and zeaxanthin had similar visual sensitivity as younger subjects. Conversely, older subjects with low lutein and zeaxanthin in their macula had lower visual sensitivity.

1996 Study: Dr. Stuart Richer published a study in the Journal of the American Optometric Association examining the effects of antioxidant intake upon patients who had already developed AMD (13). Results: Dr. Richer found that antioxidant supplements may have helped prevent progression of AMD among patients, providing strong evidence that AMD is a nutrition-responsive disease.

1996 Study: Two studies conducted at Harvard University examined the correlation between smoking and age-related macular degeneration (14, 15). Results suggested a lowering of antioxidant level like lutein, due to smoking may be the cause. Results: Dr. Seddon and coworkers reported data that support the hypothesis that cigarette smoking increases the risk of developing age-related macular degeneration in men and women.

1996 Study: Dr. Hammond and coworkers from the Schepens Eye Research Institute at Harvard Medical School compared macular pigment densities of smokers and non-smokers (16). Results: The smoking group had significantly lower macular pigment density, in spite of consuming similar concentrations of lutein and zeaxanthin in their diets. There seems to be more evidence that smoking lowers antioxidant protection available to tissues throughout the body.

1995 Study: Dr. Max Snodderly of The Schepens Eye Research Institute of Harvard University measured the level of lutein in the macular region of the retina in subjects at higher risk for AMD (17). Results: Subjects at higher risk for AMD, such as smokers, women, and persons with light iris color, had significantly lower levels of lutein in the macular region of the retina.

1995 Study: Dr. Fred Khachik and coworkers examined for evidence that lutein is acting as an antioxidant in the macular region of the retina (18). Results: Dr. Khachik found that lutein acts as an antioxidant in the macular region of the retina by identifying the presence of an oxidation product of lutein in the macula.

1995 Study: Dr. Joanne Curran-Celentano from the University of New Hampshire conducted a twin study to determine whether genetics or diet is the primary cause for the level of lutein in the macular region (19). Results: After dividing sets of identical twins and giving one twin a lutein-high diet, while the other received a diet low in lutein, the study found that the level of lutein was greater in the twin given the diet higher in lutein. The authors concluded diet plays the key role in the amount of lutein deposited in the macula region.

1994 Study: Dr. Johanna Seddon of Harvard University published a study in the Journal of the American Medical Association that examined the effect of consumption of specific carotenoids on AMD prevalence (20). Results: The study found that the highest correlation of disease prevention was associated with an intake of 6 mg per day of lutein, which led to a 57 percent lower risk of disease. The authors recommended a diet high in lutein to lower the risk of contracting AMD. Therefore, lutein is the key carotenoid for providing the proper amount of lutein and zeaxanthin.

1993, 1995 Studies: Two studies, by Dr. Khachik and Dr. Bone, addressed whether lutein is converted to zeaxanthin (18, 21). Lutein content is, on average, seven to 10 times higher than zeaxanthin in fruit and vegetables. Results: Dr. Khachik found that lutein can be converted to zeaxanthin in the blood serum. Dr. Bone also found that lutein can be converted to zeaxanthin. It appears that the human metabolism converts lutein to the proper amount. 1993 Study: Harvard University examined the risks associated with contracting AMD (22). Results: Researchers found a significantly lower risk of AMD associated with serum carotenoid levels. No differentiation was made between types of carotenoids.

Summary- Lutein may be required in the diet for macular pigment.

1. - Lutein inhibits the build-up of oxidative damage in retinal cells
2. - Supplementation with lutein increased serum levels and macular pigment density.
3. - Because human metabolism converts lutein to the proper amounts of zeaxanthin, lutein is the key carotenoid to obtain both lutein and zeaxanthin.
4. - A diet of 6 mg of lutein per day led to a 57 percent lower prevalence of AMD, leading authors to recommend a diet high in lutein to lower the risk of contracting AMD.
5. - Diet plays a key role in the amount of lutein deposited in the macular region.
6. - Lutein protects the retina by blocking harmful blue light.
7. - Those who have AMD have lower levels of lutein in the macular region than those who do not.
8. - Antioxidants may slow progression of AMD, and even patients who have already developed the disease are encouraged to increase their intake.
9. - Diets rich in lutein and zeaxanthin improve the visual functions of patients with AMD.

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