WHITE PAPER:

LUTEIN FOR EVERY AGE

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The idea that a single nutrient could serve functions as varied as normal brain development, eye protection, skin protection, cardiovascular health, reaction time improvement, cognitive function enhancement and warding off age-related disease at first seems preposterous. Indeed, any reasonable person approached with such a claim should be highly skeptical, and ask for the evidence. In the following couple of pages, I will lay out the evidence for lutein as the nutrient described above, and characterize how lutein plays a role in normal development, enhanced function and health for every age group.

Lutein is a naturally-occurring carotenoid pigment found primarily in leafy-green vegetables, such as spinach and kale (Sommerburg et al. 1998). Lutein is not synthesized by the body, and so must be obtained from dietary sources, or supplements. Those who have diets rich in leafy greens, or supplement with sufficient lutein, tend to have higher blood and tissue concentrations of lutein (Ciulla et al. 2001; Bone et al. 2003). In terms of functions in the body, lutein has some very special qualities; namely it is an extremely potent antioxidant and high-energy light absorber. Lutein's antioxidant capability enables it to protect bodily tissues against damaging free-radical oxygen (Krinsky et al. 2003). This is an extremely important function, because if free-radical reactions continue unabated they can lead ultimately to DNA damage, which manifests as tissue degeneration or cancer. We often fail to appreciate the high-energy, somewhat violent nature of the chemistry of our body; for this reason the body builds a defense against oxidation in key areas, such as the retina and brain, where it is most needed. With regard to lutein, this preferential placement in vulnerable tissues starts very early.

Lutein in the Womb / Infancy / Childhood

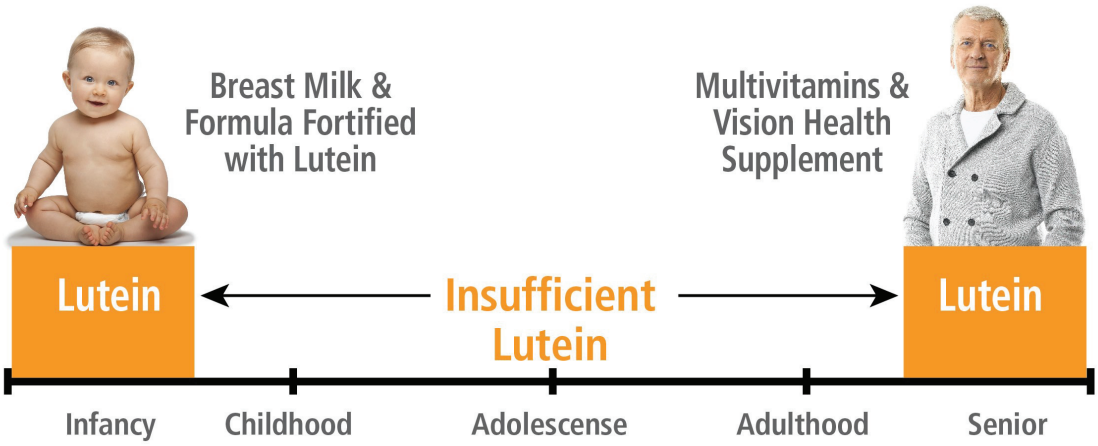
Until fairly recently, lutein's role in health was thought to be limited to helping guard against the development of age-related macular degeneration (AMD; e.g. Seddon et al. 1994). Over the last 6-7 years, however, solid evidence from prenatal and neonatal research indicates an important role for lutein in the *very beginning* of life. For example, it has been shown that lutein plays a major role in the early development of neural tissue in utero: At about 6 weeks of gestation (before the

ABOUT THE AUTHOR

James M. Stringham, Ph.D. is currently a Research Professor at the University of Georgia, where he studies the potential benefits of lutein for infant neural and ocular development. Additionally (because children do not generally consume an adequate quantity of vegetables), he is interested in studying how this population would respond, in the eye and systemically, to lutein supplements. Dr. Stringham has held appointments at the Schepens Eye Research Institute (Harvard Medical School), the Medical College of Georgia, and the Air Force Research Laboratory and is considered one of the leading research experts in lutein.

"At 20 weeks gestation, as the retina begins to be 'built,' lutein is diverted from the vitreous humor into the now-forming retinal tissue, where it serves as an antioxidant during the volatile, extremely high metabolic environment of neurogenesis"

retina starts to develop), lutein is transferred via the umbilical cord (Rubin et al. 2012) from the mother to the fetus, and **starts** to accumulate in an ocular reservoir called the vitreous humor. At 20 weeks gestation, as the retina begins to be "built," lutein is diverted from the vitreous humor into the now-forming retinal tissue, where it serves as an antioxidant during the volatile, extremely high metabolic environment of neurogenesis (Panova et al. 2007). Because oxygen is one of the major building blocks of neural tissue, the potential for free-radical oxidative stress and damage is high; based on the conspicuous timing of passage from the vitreous humor to the retina, coupled with the antioxidant capability of lutein, it is not unreasonable to suggest that lutein plays a crucial, early role in the development of neural tissues. Lutein is also found in high concentrations in the infant brain (Vishwanathan et al. 2011). This is true of no other carotenoid. The development of the brain occurs so rapidly and with such metabolic intensity that it makes sense the body would put lutein (a potent antioxidant) in an area of such high oxidative stress. Additionally, because much neurodevelopment in the brain and retina occurs after birth, lutein no doubt maintains this role well into childhood. In fact, an argument could be made that children, despite their relatively small stature, actually need as much or more daily lutein as adults. This is for two reasons: 1) Children are still developing, and are thus using more oxygen to build tissues. More oxygen leads to increased potential for oxidative stress, and lutein can help to reduce it. 2) Tissue stores of lutein, such as the retina, brain, and adipose tissue, are relatively empty. By ensuring that a meaningful amount of lutein is included in a child's diet, accumulation of lutein in these critical areas of the body is promoted. This would ultimately lead to enhanced protection into adulthood and beyond.



Lutein in Adulthood / Old Age

In adults, lutein in the retina has been shown to be positively associated with a number of important functions related to both health and performance. There are several visual performance advantages, including increasing visual processing speed (Hammond & Wooten, 2005), and many parameters of visual performance in bright light environments. On average, subjects with higher concentrations of retinal lutein are able to maintain visibility of a flickering light at higher frequencies than those with lower retinal lutein (who see the light as a stable, solid disc of light). In other words, those subjects with higher concentrations of lutein in their retinas have faster visual systems; this presumably leads to faster reaction time performance. Visual performance benefits of high retinal lutein in bright light environments include reduced visual discomfort (Stringham et al. 2003; 2004; 2011), increased ability to see through glare (Stringham and Hammond, 2007; 2008), and decreased photostress recovery time (recovering a visual target after exposure to an extremely bright light; Stringham and Hammond, 2007; 2008; Stringham et al. 2011). More recently, lutein has been shown to be associated with better cognitive function in people over 50 – subjects with higher retinal lutein (which has been shown to be correlated to brain levels of lutein) perform better on cognitive tasks related long-term memory and decision-making (Feeney et al. 2013). Additionally, in a recent study of deceased centenarians—those who had lived to over 100 years of age (Johnson et al. 2013)—found that brain concentrations of lutein were significantly higher than any other carotenoid, especially in areas that serve cognitive function, such as the frontal and temporal lobes. This suggests not only that lutein appears to be very important to brain function well into old age, but also (based on the areas into which it is deposited) that lutein is important in preserving high-level cognitive function. Lutein also appears to play a protective role in cardiovascular health, in that it appears lutein inhibits vascular cell adhesion molecules from accumulating atherosclerotic plaques (Kailora et al. 2006). Over time, this function leads to a greatly reduced risk for developing atherosclerosis, and cardiovascular disease. Interestingly, lutein (by virtue of its deposition throughout the layers of the skin) also appears to provide protection from UVB-induced erythema (i.e. sunburn; Heinrich et al. 2003).

"Visual performance benefits of high retinal lutein in bright light environments include reduced visual discomfort, increased ability to see through glare, and decreased photostress recovery time…"

Moreover, lutein was shown to help manage and limit damage already caused by UVB light. Lastly, as noted earlier, there is a well-established relationship between high retinal lutein and a reduced risk for developing AMD, the leading cause of blindness in people over 60 in the United States (National Eye Institute). Importantly, there is evidence that even after the onset of AMD symptoms (e.g. mild distortions of central vision), lutein supplementation can slow down, or even perhaps stop the progression of the disease (Richer et al. 2004). It appears therefore that lutein has not only long-term protective effects on tissues, but also can have acute beneficial effects as well.

In summary, lutein appears to play a significant, positive role throughout the lifespan. The more we learn about lutein, the more it becomes apparent that it is crucial to development, health, and performance. From its involvement very early in protecting developing neural tissues, to reducing cumulative damage that results in age-related disease, lutein appears to have significant, positive benefits.

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REFERENCES

1. Bone RA, Landrum JT, Guerra LH, Ruiz CA. Lutein and zeaxanthin dietary supplements raise macular pigment density and serum concentrations of these carotenoids in humans J Nutr. 2003 ;133(4):992-8.
2. Ciulla, T. A., Curran-Celantano, J., Cooper, D. A., Hammond, B. R., Jr., Danis, R. P., Pratt, L. M., Riccardi, K. A., & Filloon, T. G. Macular pigment optical density in a midwestern sample. Ophthalmology. 2001;108(4):730-7.
3. Feeney J, Finucane C, Savva GM, Cronin H, Beatty S, Nolan JM, Kenny RA. Low macular pigment optical density is associated with lower cognitive performance in a large, population-based sample of older adults. Neurobiol Aging. 2013;34(11):2449-56
4. Seddon, J. M., Ajani, U. A., Sperduto, R. D., Hiller, R., Blair, N., Burton, T. C., Farber, M. D., Gragoudas, E. S., Haller, J., Miller, D. T., & et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. JAMA. 1994;272(18):1413-20.
5. Rubin LP, Chan GM, Barrett-Reis BM, Fulton AB, Hansen RM, Ashmeade TL, Oliver JS, Mackey AD, Dimmit RA, Hartmann EE, Adamkin DH. Effect of carotenoid supplementation on plasma carotenoids, inflammation and visual development in preterm infants. J Perinatol. 2012 ;32(6):418-24.
6. Krinsky NI, Landrum JT, Bone RA. Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. Annu Rev Nutr. 2003;23:171-201.
7. Panova I, Iakovleva MA, Fel'dman TB, Zak PP, Tatikolov AS, Sukhikh GT, Ostrovskiĭ MA. Detection of carotenoids in the vitreous body of the human eye during prenatal development. Ontogenez. 2007;38(5):380-5.
8. Vishwanathan R, Neuringer M, Schalch W, and Johnson E (2011). Lutein (L) and zeaxanthin (Z) levels in retina are related to levels in the brain. FASEB 2011.344.1 (abstr.).
9. Hammond, B. R., Jr., & Wooten, B. R. (2005). CFF thresholds: relation to macular pigment optical density. Ophthalmic & physiological optics. Ophthalmic Physiol Opt. 2005;25(4):315-9.
10. National Eye Institute: Fact sheet, leading causes of blindness in the U.S. Webpage: http://www.nei.nih.gov/health/fact_sheet.asp [accessed on 02/03/2014].
11. González S, Astner S, An W, Goukassian D, Pathak MA. Dietary lutein/zeaxanthin decreases ultraviolet B-induced light epidermal hyperproliferation and acute inflammation in hairless mice. J Invest Dermatol. 2003;121(2):399-405.
12. Richer S, Stiles W, Statkute L, Pulido J, Frankowski J, Rudy D, Pei K, Tsipursky M, Nyland J. Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial). Optometry. 2004;75(4):216-30.
13. Heinrich U, Gärtner C, Wiebusch M, Eichler O, Sies H, Tronnier H, Stahl W. Supplementation with beta-carotene or a similar amount of mixed carotenoids protects humans from UV-induced erythema. J Nutr. 2003;133(1):98-101.
14. Kaliora AC, Dedoussis GV, Schmidt H. Dietary antioxidants in preventing atherogenesis. Atherosclerosis. 2006 ;187(1):1-17
15. Sommerburg O, Keunen JE, Bird AC, van Kuijk FJ (1998). Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes. Br J Ophthalmol. 1998;82(8):907-10.
16. Stringham JM, Fuld K, Wenzel AJ. Action spectrum for photophobia. J Opt Soc Am A Opt Image Sci Vis. 2003;20(10):1852-8.
17. Stringham JM, Fuld K, Wenzel AJ. Spatial properties of photophobia. Invest Ophthalmol Vis Sci. 2004;45(10):3838-48.
18. Stringham JM, Hammond BR, Jr. The glare hypothesis of macular pigment function. Optom Vis Sci. 2007;84(9):859-64.
19. Stringham JM, Hammond BR. (2008). Macular pigment and visual performance under glare conditions. Optom Vis Sci. 2008;85(2):82-8.
20. Stringham JM, Garcia PV, Smith PA, McLin LN, Foutch BK. Macular Pigment and Visual Performance in Glare: Benefits for Photostress Recovery, Disability Glare, and Visual Discomfort. Invest Ophthalmol Vis Sci. 2011;52(10):7406-15.