Emerging Role of Lutein Across the Life Span
Part 1 – Focus on the Infant
Lisa M. Renzi, Ph.D.
Principal Investigator,
Human Biofactors Laboratory
The University of Georgia

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Abbott Laboratories sponsored the following research studies, the results of which will, in part, be presented here:
 “Distribution of Carotenoids in Pediatric Brain Tissue”
 “Distribution of Lipids in Human Brain Tissue: Relationships with Cognitive Function.”

Learning Objectives
1. To define that lutein is a dietary carotenoid, present in nervous tissue
2. To illustrate the various roles of lutein in the nervous system, such as:
   • Protecting, when the nervous system is most vulnerable
   • Influencing maturation
   • Improving visual function
   • Directly impacting nervous function
3. To summarize the ways in which lutein is beneficial for the developing eye and brain
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The Carotenoid Funnel

Lutein (L)

Image courtesy of John Landrum.
Where Do We Obtain Our Lutein?

- Green, leafy vegetables
  - Spinach
  - Kale
  - Brussel sprouts
  - Broccoli
- Brightly colored fruits
- Egg yolk and egg products, including baked goods
- Corn products, including cereals
- Breast milk and supplemented formulas

Infant Diet vs. Infant Brain, Percent Total Carotenoids

Dietary Carotenoids (NHANES 1988-1994, 2-11 mo)
- Lutein
- Zeaxanthin
- Crypto
- a-caro
- b-caro
- lyco

Brain Carotenoids (0-11 mo)
- 59% No A-carotene
- 16% Other

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Retinal Fundus

Retina: most metabolically active tissue in the body

Lipofuscin, a Marker of Aging, Increases Rapidly During Infancy

Lipofuscin content in the total RPE plotted as a function of age ($p < 0.001$).
From Wing et al., 1978.
Oxidation Reactions

Light
Photosensitizer + O₂ → Lipid Peroxidation

Photosensitizer + O₂ → ¹O₂ → ³O₂

Lutein Embeds in Retinal Cell Membranes
Lutein stabilizes cellular membranes and serves as an antioxidant
Sujak et al, 2002.

Infant Retinas May be More Susceptible to Oxidative Damage
Oxidation Reactions

![Oxidation Reactions Diagram]

Blue Light Hazard

![Blue Light Hazard Diagram]

L + Z Supplementation Protects the Macula Against Blue Light Damage

In animals fed a normal diet containing xanthophylls, with a normal macula, more energy is needed to produce a lesion in the fovea. In depleted animals, the fovea has lost protection.

Barrie, Neuringer, et al., 2005, IOVS, 46, 1770.
Implications for Young Retinas:

The retinas of children accumulate lipofuscin quickly due to relatively transparent lenses.


Clinically Significant Signs of Sun Damage Manifest in Childhood.

FIGURE 1. Left: normal-inteproal eye of a 13-year-old boy with no established pathogenesis. (Left) The central photograph demonstrates the established progression. (Right) The corresponding UV-fluorescence photographs illustrate the presence of the pigments.

Subjects: 71 Australian children, 3-15 years
Results: 32% had increased fluorescence consistent with significant ocular sun damage

Ultraviolet photography to detect signs of early sun damage in the eye of school-aged children.

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Lutein and zeaxanthin are concentrated in an area of the retina that rapidly develops during the first year of life.

Maturational Events:
Development of the Foveal Pit

Maturational Events:
Elongation of the Cone Photoreceptor Outer Segments
Maturational Events:
Increasing Cone Density During Foveola Development

Birth
19,000 cone/mm²

15 Mos.
41,000 cone/mm²

45 Mos.
112,000 cone/mm²

Maturation: monkeys raised on xanthophyll-free (low n-3) diets have distinct and significant changes within the retinal pigment epithelium


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- The enhancement of contrast.
- The enhancement of detail by the absorption of ‘blue haze.’
- To promote comfort by the reduction of glare and dazzle.

Contrast Enhancement, Across the Lifespan

Relations to Lutein


Macular Pigment is Related to Disability Glare (r = 0.76)

Effect of L + Z (12 mg Daily) Supplementation on Disability Glare Thresholds


Macular Pigment is Directly Correlated ($r = 0.80$) with Faster Functional Recovery by Photoreceptors

Sample Size (N = 40): Effect of L + Z (12 mg Daily) Supplementation on Photostress Recovery Times
Five seconds, the reduction of PRT at the highest MPOD increase, is equivalent to about 440 feet, when driving at 60 mph.

<table>
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<th>Speed, MPH</th>
<th>30</th>
<th>60</th>
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<td>264</td>
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<td>528</td>
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<tr>
<td>4</td>
<td>220</td>
<td>440</td>
<td>660</td>
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Amblyopia: errors in visual input lead to changes in visual cortex
What’s in a Neuron?

- Fatty acids
  (cell membranes, myelin)
- Carotenoids and other nutritional components
  (cell membranes, microtubules)
- Electrolytes (sodium, calcium, potassium, etc.)
- Lipid soluble vitamins
  (cell membrane)
- Protein, Water, Sugars
  (cytoskeleton)
- Water soluble vitamins
  (aqueous compartments)

Lutein Influences Neural Communication

- Gap junctions: permit intercellular signaling
- Lutein enhances gap junction communication
Macular pigment is related to fixed and variable reaction time.

Renzi, et al. in preparation.

MP Density is Related to CFF

Hammond & Wooten, 2005; Renzi & Hammond, 2010

tCSF Strongly Declines When Measured at High Frequencies in the Fovea \( (r = -0.55, p < 0.0001) \)

Visible Even at Low Frequency

Younger adults

Older adults

Renzi, et al. in preparation.

The Relation Between MP and Temporal Visual Thresholds ($r = -0.31, p < 0.015$)


MP and Scotopic Noise ($n = 40, r = -0.38, p<0.01$)

Zimmer, Hammond. 2007.
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Macular pigment may influence the developing visual system (from retina to brain) by:

- Influencing maturation
- Altering visual input during a critical/sensitive period of visual development
- Protecting the retina during a period when the retina was particularly vulnerable
- Directly influencing the nervous system

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