An Overview of Why Lutein Matters During the Prenatal Period

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INTRODUCTION

Healthful nutrition during pregnancy is vital to support maternal health, pregnancy outcomes, fetus development, and infant health, as well as guide later life outcomes (ref 1). Perinatal development and infancy are characterized by the development of several organ systems and represent a critical window of opportunity for eye and brain development (ref 2).

The role of protein, carbohydrates, fats, vitamins and minerals in influencing fetal development and maternal health is well established and now research has shifted focus on the functional relevance other nutritional bioactives such as docosahexanoic acid (DHA), choline and lutein. Lutein in particular has caught the attention of the scientific community given its role in both eye and brain health through the life stages.

Lutein a non-provitamin A dietary carotenoid, along with zeaxanthin isomers, are typically referred to as macular carotenoids since they are exclusively deposited in the macula of the eye, and preferentially accumulated in the brain during fetal development, infancy, childhood, and through adulthood. The body cannot make lutein, but it can be obtained from foods such as dark green, leafy vegetables, corn, eggs, and avocados. There is a solid body of evidence linking lutein to visual function as well as being protective against age-related eye diseases, particularly age-related macular degeneration (AMD) and cataracts (ref 3).

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Lutein and zeaxanthin have been shown to be present in maternal plasma throughout the course of pregnancy, in the placenta, and additionally transferred to the developing fetus via the cord blood. In the placenta, Thoene and colleagues reported that lutein and zeaxanthin are the most abundant carotenoids in umbilical cord blood (ref 4).

This overview is a synthesis of the research to date supporting the nutritional and functional relevance of lutein and zeaxanthin mainly in the context of retinal and brain development during pregnancy.

RETINAL AND BRAIN DEVELOPMENT

That the eye is an extension of the brain is not surprising as they both originate from the neural tube during fetal development. The retinal blood supply is present around 16 weeks gestation, the foveal pit forms at 25 weeks of gestation, and photoreceptor cone density increases around 22 weeks of gestation. While the peripheral retina is fully developed at birth, the fovea is still immature and matures over the next several years of early childhood. The fovea is extremely important to visual performance because it mediates central vision and maintains the highest performance in terms of color discrimination, motion detection, contrast sensitivity, and acuity (ref 5). Foveal cone density continues to increase until about four years of age. Along with this, there is maturation of the visual circuits and together with the cones, they contribute to visual function in the postnatal period (ref 6,7).

The size of the eye is ~50% that of adults at six months of gestation and by nine months, is ~66% the size of adult eyes (ref 8). The visual system continues to develop during the first few years of life.

Similar to the retina, the brain also grows rapidly starting from around mid-pregnancy and most of the brain's rapid growth is completed postnatally around 4-6 years of age. This maturation is associated with an increase in brain volume accompanied by an increase in lipid content (ref 9).

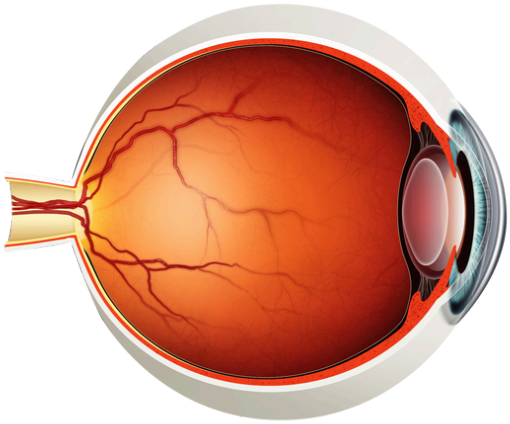
The eye and the brain are highly metabolic organs, and given the time spent in their development and maturation periods, along with their high oxygen

consumption and exposure, and the presence of polyunsaturated fatty acids in neuronal membranes, both organs are vulnerable to environmental stressors that may result in oxidative stress. Oxidative stress is not the only threat to the fovea—light energy incident on the retina can itself be damaging (ref 10). This is especially true of short-wave high-energy blue light. While this may be less of a concern during the prenatal period, this becomes more relevant in the postnatal years of life.

Herein, the light filtering system of the eyes is less functional in children due to the more crystalline eye lens, especially those younger than nine years of age, resulting in transmission up to ~5% UVA light (ref 11,12). In infants and children, more blue light in the 460-480 nm range reaches the retina (ref 11) further increasing oxidative stress conditions.

Additionally, immaturity of endogenous antioxidant mechanisms such as antioxidant enzymes further increases susceptibility to cellular damage by free radicals (ref 13,14). This underscores the importance of adequate nutrition including lutein and zeaxanthin to help facilitate optimal growth and development during pregnancy.

The next few sections will briefly describe how lutein and zeaxanthin accumulation in specific regions of the eye and brain appear to coincide with key milestone developments within these highly metabolic organs.



LUTEIN AND RETINAL DEVELOPMENT

Due to their yellow-orange coloration and location in the retina, lutein and zeaxanthin filter an appreciable amount of incident short-wave light before it reaches the photoreceptors of the sensory retina (ref 15). Given their physical (light filtration) and biochemical (antioxidant) properties, lutein and zeaxanthin are ideally suited to protect the central retina, protect the lipid-dense retina from oxidation, and thereby facilitate visual performance.

At around 14-16 weeks of gestation, lutein and zeaxanthin begin to accumulate in the vitreous humor, and peaks around 20–22 weeks of gestation (ref 16). Subsequently, lutein is diverted to the retinal space at a time when the key layers of the retina are developing, e.g. Bruch's membrane, the plexiform layer, ganglion cell layer, nuclear layer, and photoreceptor layer (ref 17). These observations of the early and very specific accumulation of lutein in the retina along with favorable evidence from preterm infants (born < 33 weeks of gestation) fed lutein-supplemented infant formula, support a role for lutein retinal development (ref 18).

LUTEIN AND VISUAL PERFORMANCE

Owing to their selective deposition in the macula, lutein and zeaxanthin makes up the macular pigment (MP), the yellow pigmentation at the back of the retina. MP is typically measured as macular pigment optical density (MPOD) and can range among individuals from 0 to values as high as 1.60 (ref 19).

Accumulating evidence points to a pivotal role of MPOD in determining the ability of the retina to block

out blue light (and hence photooxidative damage), as well as other aspects of visual performance such as glare discomfort and photostress recovery under bright light conditions, visual processing speed, and contrast sensitivity. Finally, MPOD levels have been associated with brain cognitive outcomes in children, and, other later life outcomes, e.g., risk to age-related macular degeneration (ref 20).

In 2013, research by Henriksen and colleagues reported a relationship between mother and infant serum and MPOD levels (ref 21). The GUSTO study (Growing Up in Singapore Towards healthy Outcomes), an observational study, revealed that higher maternal lutein and zeaxanthin plasma concentrations during pregnancy were associated with lower likelihood of poor distance-visual acuity in children supporting a role for lutein and zeaxanthin in the infant's visual development (ref 22).

More recently, Paul Bernstein's lab demonstrated that infants whose mothers received lutein and zeaxanthin supplementation during the last trimester of pregnancy, had a significant 5-fold increase in cord blood serum lutein and zeaxanthin concentrations, over a 3-fold increase in cord blood total carotenoids, and a 38% increase in skin carotenoid status compared to the control group. Although not statistically significant, infants whose mothers were in the Carotenoid Group had a 20% increase in macular pigment compared to those in the Control Group ($p = 0.242$) (ref 23).

LUTEIN, BRAIN DEVELOPMENT, AND COGNITION

As discussed earlier, most of the brain maturation and growth occurs postnatally with the physical structure of the brain completed by six years of age. However, it is important to note that modification of that structure continues until early adulthood. For instance, a second wave of synaptogenesis occurs near puberty (11–12 years of age) with 1% of grey matter being lost every year between 13–18 years (ref 24).

Lutein crosses the blood-brain barrier as well as the placenta and through these means makes it way to the brain. Lutein is the predominant carotenoid in the infant brain making close to 60% of the carotenoids

and reaching about 75% of the total carotenoids when combined with zeaxanthin. It appears to be mainly distributed in the frontal cortex, hippocampus, and occipital cortex (ref 25, 26).

Since the brain is highly lipid in nature, lutein is well positioned in membranes to limit oxidation of these vulnerable brain lipids. Inhibition of DHA oxidation not only helps to maintain membrane structure and fluidity but also preserves docosahexanoic acid (DHA) so it remains available for cleavage and conversion into anti-inflammatory molecules (ref 26). Although this potential lipid-protective action by lutein may, in part, explain the relation between lutein and neural function, it is possible that lutein may function through other independent mechanisms, including modulation of membrane stability and function, as well as communications between neurons (ref 20).

The academic community agrees that MPOD levels not only reflects lutein and zeaxanthin levels in the eyes, but can also be used as a biomarker of lutein and zeaxanthin levels in the brain (ref 27). On this basis, cross-sectional studies have assessed the relation between MPOD and cognitive function in preadolescent children between 7-13 years of age. Collectively, these studies revealed that: 1] MPOD levels were negatively associated with relational memory errors (ref 28), 2] MPOD was significantly related to executive processes and brief intellectual ability (ref 29), and 3] children with higher MPOD had lower brain activation when conducting the same cognitive tasks as children with lower MPOD. In other words, matched on a range of personal variables, children with lower MPOD had to use more brain to do the same task (decreased neural efficiency) and they made significantly more errors (ref 30). Intervention studies to confirm the cause-effect relationship between lutein and zeaxanthin intake and

cognitive outcomes in children 5-12 year of age are now available, (e.g., the Lutemax Children's study [ref 31]). Specific to the prenatal stage, the Project Viva Study, which comprised 1,580 mother-child pairs, reported that higher maternal intakes of lutein were associated with better verbal intelligence in children (ref 32).

DIETARY SOURCES AND INTAKES OF LUTEIN (AND ZEAXANTHIN)

Foods rich in lutein and zeaxanthin include green leafy vegetables (spinach and kale), squash, broccoli, and corn (Table 1). Although eggs and avocados have relatively lower concentrations of lutein, both are considered highly bioavailable food sources of lutein, owing to their favorable fat profiles, and have been shown to increase MPOD and cognitive function in older adults (ref 20).

Food	Serving	L+Z (mg)
Spinch: frozen, cooked	1 cup	29.8
Kale: frozen, cooked	1 cup	25.6
Summer squash: cooked	1 cup	4.0
Peas: frozen, cooked	1 cup	3.8
Pumpkin: cooked	1 cup	2.5
Brussel sprouts: frozen, cooked	1 cup	2.4
Broccoli: frozen, cooked	1 cup	2.0
Sweet yellow corn: boiled	1 cup	1.5
Avocado: raw	1 medium	0.4
Egg yolk: raw	1 large	0.2

Table 1. Lutein and zeaxanthin content in food

In addition to being present in the diet, lutein has been found in breast milk throughout the breastfeeding period. Of the carotenoids found in breast milk, lutein and zeaxanthin has been reported to be the most abundant carotenoid (ref 33-35).

Bettler and colleagues showed that breastfed infants had approximately six-times more serum lutein concentration than infants fed unfortified milk formula (ref 36).

Additionally, lutein supplementation of mothers during breastfeeding increased lutein levels in maternal plasma, breast milk, and infant plasma (ref 34,37).

Estimates of lutein and zeaxanthin intakes by the average American population are low since most Americans are not achieving their recommended servings of fruit and vegetable intakes per day. Data from the NHANES 2003–2004 showed that the intake of lutein and zeaxanthin was less than 0.6 mg/day in children and adolescents (1–18 years of age) and less than 2 mg/day in women of childbearing age (ref 38). More recent data from pregnant women between 19–43 years old showed that maternal lutein and zeaxanthin intakes averaged 2.48 mg/day (ref 39).

IN CONCLUSION

Collectively, the available scientific evidence, along with dietary intake data, reiterates the role of adequate lutein and zeaxanthin intakes to help support brain and eye development during pregnancy, and, in the first few years of life, when the brain and eye are still rapidly developing. This review also highlights the value of educating consumers at all life stages, especially during pregnancy, on the importance of achieving their recommended fruit and vegetable intakes per day, both for the mother and her baby. Healthcare professionals can also play an essential role in raising awareness of these important nutrients, and their intakes through healthful food choices, along with the possible role of lutein and zeaxanthin supplementation when moms are not able to get adequate amounts through diet alone.

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LUTEIN FOR EVERY AGE

Lutein for Every Age is an educational initiative, which focuses on raising awareness with patients and healthcare practitioners of early and consistent lutein and zeaxanthin intake to help support eye, cognitive, and general health throughout life.

Help empower your patients
Learn more about the importance of lutein and zeaxanthin at every age.

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