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PEDIATRIC NUTRITION RESOURCE LINE

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Nutritional Needs in Early Infancy and Older Age: Focus on Omega-3 Fatty Acids and Carotenoids

A report from a presentation during the

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London, Ontario - Adequate nutrition and the provision of specific nutrients are essential for optimal brain and visual development in infancy. Both docosahexaenoic acid (DHA) and the carotenoid lutein are highly concentrated in the brain and retina and both contribute to the development and protection of these 2 organs. If maternal intake of these nutrients is poor, infants also have low levels of these nutrients even if breast-fed. Studies show that carotenoid-supplemented formula in preterm infants improves measures of retinal health and may attenuate the risk of retinopathy of prematurity, the leading cause of blindness in young children. DHA and carotenoid supplementation have also been associated with improvements in cognitive function in older adults.

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As discussed by Dr. Lewis Rubin, Chair, Neonatology and Professor of Pediatrics, University of South Florida, Tampa and St. Petersburg, almost 75% of a newborn infant's energy intake goes towards brain metabolism compared to only about 25% of energy intake for adults. "This is because of the relatively larger mass of the brain in infancy compared to the rest of the body," he noted, "and it reflects the dramatic growth in the brain that occurs during the last part of pregnancy and the first year of life."

Attention to infant nutrition is critical at this time as it must support this accelerated growth. In addition to simple energy requirements, there are several dietary nutrients that selectively accumulate in the brain and in the retina in a greatly enhanced fashion. One of the most important of these is docosahexaenoic acid (DHA), which is derived from omega-3 long-chain polyunsaturated fatty acids. Via mechanisms that are not fully understood, DHA accumulates in the retina and brain in concentrations that are many-fold higher than elsewhere in the body—and higher DHA levels are associated with improved vision and cognitive function in adults and in infants, according to Dr. Rubin.

More recently, the importance of the carotenoid lutein in the maternal diet for visual and brain development has also been recognized. As Dr. Rubin explained, lutein is a powerful antioxidant as well as an anti-inflammatory agent. In the eye, lutein may protect cells by acting as an optical filter that absorbs potentially damaging blue light. Lutein may also protect the eyes and brain against oxidative damage caused by free radicals. It is important to remember that a newborn infant must adjust from an environment of low oxygen tension to one of high oxygen tension at a time when antioxidant reserves are more limited. Lutein is concentrated at levels up to 1000-fold higher in the retina compared to the rest of the body. It is also concentrated in brain tissue in both young children and adults.

"Lutein and DHA not only are both concentrated in the same place, but they appear to interact in an important way," Dr. Rubin told delegates. As a highly unsaturated fatty acid, DHA is capable of generating reactive oxygen species which can damage cells and tissues. Lutein, on the other hand, is capable of counteracting potential damage caused by oxygen radicals in the cells, a sort of symbiotic interaction.

Lutein and the closely related zeaxanthin are major components of the filtering function of the eye. Because the macular pigment is almost entirely composed of lutein and zeaxanthin, the xanthophylls are frequently referred to as the macular pigments in this area. It is now known that the loss of macular pigment is associated with a variety of eye disorders, notably acute macular degeneration and diabetic retinopathy.

For most individuals in western societies, intake of omega-3 fatty acids and lutein—a carotenoid found in dark green leafy vegetables such as spinach and kale as well as in eggs and corn—is well below recommended levels. Reflecting these low intake levels, "infants have very low lutein levels and tissue stores," Dr. Rubin observed—human milk being the sole source of lutein until the child is weaned unless the infant is fed a lutein-containing formula. The mother's diet, in turn, affects the degree to which infants are exposed to carotenoids *in utero* as well as from breast milk. Plasma carotenoid concentrations also decline significantly in formula-fed—not breast-fed—infants immediately following birth.

Importantly, evidence now indicates that low serum levels of lutein and zeaxanthin in preterm infants increase the risk for progressive retinopathy of prematurity. In a study of preterm infants, Rubin and colleagues (*J Perinatol* 2012;32:418-24) compared infants fed a formula supplemented with lutein, lycopene and B-carotene (all carotenoids) vs. controls fed a non-supplemented formula as well as a control group of preterm infants given human milk.

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A total of 203 preterm infants born <33 completed weeks of gestation were fed formula with and without supplemental carotenoids from birth until 40 weeks postmenstrual age. At all time points measured, plasma carotenoid levels were significantly higher in infants fed the supplemented formula and were similar to levels in the control group of preterm infants fed human milk. Perhaps most importantly, investigators found that plasma lutein concentrations correlated with response amplitude in rod photoreceptors and that the lutein-supplemented infants had greater rod photoreceptor sensitivity than controls.

"This study showed for the first time that lutein supplementation early in life can decrease the severity of the major cause of acquired blindness in children which is retinopathy of prematurity, and that it also improved measures of retinal function," Dr. Rubin stated. As he discussed, conclusions from this and other trials conducted in preterm infants showed that plasma carotenoid levels were consistently higher in supplemented neonates than in controls and that levels were closer to those of term breast-fed infants. Most trials also showed a trend towards less progression from mild to severe retinopathy of prematurity.

A study by Perrone et al. (*Neonatology* 2010;97:36-40) evaluated lutein supplementation in term infants and found that infants supplemented with lutein had higher biological antioxidant potential as well as reduced levels of oxidative stress. The authors concluded that these results support lutein's role in reinforcing the plasma antioxidant potential of newborns.

Cognitive Function in Older Adults

There is some evidence to suggest that the same dietary nutrients may enhance cognitive function in older adults as well. In a study by Renzi et al. (*FASEB J* 2008;22:877.5), investigators found that retinal levels of lutein and zeaxanthin—in other words, macular pigment density—were significantly related to performance on a variety of measures assessing processing speed, accuracy and completion ability in older subjects between 76 and 85 years of age.

Because lutein and zeaxanthin are embedded in cortical tissue, these findings suggest that the xanthophylls are capable of influencing cortical function. Johnson et al. (*FASEB J* 2011; 25:975.21) also found that after death, autopsy results on 49 centenarians showed that zeaxanthin levels in brain tissue significantly related to antemortem measures of global cognitive function, memory, retention, verbal fluency and severity of dementia, while lutein brain levels were related to recall and verbal fluency.

These findings again suggest that these xanthophylls may be important in cognition in at least the very old. In fact, a trial of DHA and lutein supplementation in older women found that after 4 months of supplementation with either DHA alone, lutein alone or the combination of the 2, verbal fluency scores improved significantly in all 3 groups; moreover, memory scores and the rate at which subjects learned improved significantly in the combined DHA/lutein group (Johnson et al. *Nutr Neurosci* 2008; 11(2):75-83).

The Role of Nutrients in Brain and Eye Development

- DHA promotes normal brain and eye development in infants
- Lutein may protect cells by:
  1) Absorbing damaging blue light
  2) Acting as an antioxidant, protecting cells against oxidative damage
- The macular pigment is almost entirely composed of lutein and zeaxanthin and the loss of these pigments is associated with important eye disorders
- Lutein can only be obtained through the diet; Western intake of DHA and lutein is well below recommended levels
- Until lutein-rich foods are included in the baby's diet, breast milk is the only source of lutein for infants unless they are fed a formula containing lutein
- Tissue stores of lutein in infants are usually low, a reflection of low levels of lutein intake in breast-feeding mothers or infants being fed formula without added lutein
- Studies of preterm infants show lutein supplementation early in life can decrease the severity of retinopathy of prematurity and improve measures of retinal function

Summary

"As pediatricians, we know the best diet for every baby is mother's milk," Dr. Rubin noted. Optimally, the best way to support infant nutrition is to improve the maternal diet—if necessary, by fortification and supplementation with key nutritional elements. On the other hand, for those infants for whom breast milk is unavailable or insufficient, "certainly, an alternative needs to be provided and alternatives optimally should include DHA and lutein, among other important nutrients," Dr. Rubin told delegates. ☐

This report is based on a presentation given during the educational Luncheon Symposium (S3) entitled "Brain and Eye Development in Infancy: The Role of Nutrition in Vision and Eye Health," Wednesday, June 6, 11:45-13:15, during the 89th Canadian Paediatric Society Annual Conference, June 6-9, 2012, in London, Ontario. Unless specifically stated otherwise, the opinions presented in this report are those of individual(s) presenting; they do not represent the opinions of the Canadian Paediatric Society nor the Society's endorsement of content in any way.

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