Functional Foods for Childhood Development

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Preventive medicine has undergone great advances, in the last decade alone demonstrating the crucial role of nutrition for preventing diseases, especially those related to diet. The philosophy that food has health-promoting effects beyond its nutritional value has gained considerable acceptance in recent years and the specific disease-preventing effects of nutrition have even led to the new science of functional foods.

Although these foods have no universally accepted definition, they are described as foods or nutritional elements that have health-promoting benefits and/or prevent diseases. In this sense, the concept of food expands beyond that which is not only necessary for sustaining life, to include the concept that foods comprise a source of mental and physical well-being that decreases risk factors and prevents disease or enhances physiologic functions.

Foods that produce a beneficial effect on specific functions of the body, beyond basic nutritional effects that are relevant to well-being, health, or reduction of disease, and risk of disease are gaining respect as a form of medicine. Nutritional foods can be utilized by increasing their concentrations or by adding or improving upon the bioavailability of particular components of these foods.

The use of functional foods as medicines is especially relevant to intrauterine and early childhood development; during pregnancy, nutrition can be thought of as functional because of influences on prenatal development. After birth, foods that are used in a functional manner may confer certain health advantages to the developing child. In light of the relatively recent findings in nutritional medicine on childhood growth and development, science is revealing even more important aspects of specific micronutrients and the prevention of diseases and other disabilities.

These findings continue to be highlighted as the micro- and macronutritional states of young children have come into question with the apparent decreased quality and relative proportions of foods consumed. Nutritional science continues to reveal more specific uses for micronutrients in medicine beyond that of basic nutrition. There is now a realization that the Western diet, with its excesses, is inadequate and may be causing some of the diseases that occur today.

Using specific foods beyond standard nutritional requirements is aimed at modifying genetic and physiologic aspects of disease prevention and treatment. Several food substances are included in this category; they exert actions on different systems acting to enhance development and differentiation by positively modulating nutrient metabolism, oxidative stress, gene expression, and mental development.

The establishment of health claims surrounding functional foods depends on the discovery of efficiency in biologic responses to treatment with these foods. The optimum intake of specific functional foods is yet to be established; much controversy surrounds this issue. Therein, the greatest challenge for the practitioner is to work with each patient's diet as a whole and ensuring that each patient consumes at least adequate amounts of known biologically active foods.

Zinc and Development

Zinc is the second most abundant trace element in the body, totaling roughly 2 g.[1] The mineral exists in more than 300 enzymes and 100 of them rely directly on zinc as a catalyst.[2] Zinc serves as a cofactor in the synthesis of DNA, RNA, and protein, and is thought to play a role in regulating gene expression, immune function, growth and development, behavior and learning, and thyroid hormone and insulin function.[3]

Insufficient zinc intake can cause growth retardation, mental lethargy, irritability, impaired thyroid function, low insulin levels, and reduced levels of insulin-like growth factor, among other symptoms.[4]

Zinc is present in the brain and plays a contributory role in its structure and function. Some evidence in the literature indicates that zinc deficiency may play a role in delaying cognitive development. The exact mechanism for this has not yet been completely elucidated. However, investigators have speculated that inadequate amounts of zinc lead to deficits in neuropsychologic functioning, activity, and motor development that interfere with cognitive development.[5] These investigators have also suggested that the relationship between zinc deficiency and cognitive development varies by age in children.

Because of the necessary role of zinc in metabolizing thyroid hormones, androgens, and growth hormones, patterns of stunted growth linked to zinc deficiency have been observed during gestation and the neonatal period and in children through adolescence.[6] During these three time periods, zinc had been deficient in the mother's diet, in breast milk, and in the child's own diet, respectively.

Frank zinc deficiency is not uncommon throughout the world, especially in developing areas. Depending on the geographic area, 5–30 percent of children suffer from moderate zinc deficiency that causes decreased stature. Although comparatively rare in the United States, zinc deficiency is still a clinical consideration when assessing the health of all children, regardless of age.[7]

A well-balanced diet with plenty of whole grains, animal products, and fresh vegetables and fruits will provide at least enough zinc to prevent stark growth developmental delays. However, children with malabsorption syndromes or other chronic, debilitating diseases are still at higher risk for inadequate zinc intake.[8]

Currently, tests for zinc status are not wholly reliable; they are neither sensitive nor specific. Measurement of zinc levels on a population basis has proved useful; however, individual measurement is difficult to perform, especially in people with chronic inflammatory diseases or infections.[9] Perhaps the most reliable method for diagnosing zinc deficiency is a positive clinical response to supplementation with the element and subsequent reduction in symptoms.

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Zinc and Attention-Deficit Hyperactivity Disorder

Several studies have revealed insufficient levels of zinc in children with attention-deficit hyperactivity disorder (ADHD),[10,*] and zinc levels were shown to be lower in children with ADHD compared to children that did not have ADHD.[11] Zinc supplementation appears to reduce hyperactivity, impaired socialization, and impulsiveness in adolescents with ADHD.

The mineral appears to be the most helpful for children who have ADHD, a high body–mass index, and low zinc and free fatty-acid levels.[12]

One study unveiled a relationship between serum-free fatty acid levels and zinc levels in children with ADHD.[13] The children with ADHD compared to children without the disorder had lower serum levels of zinc and free fatty acids; the study investigators hypothesized that low levels of free fatty acids might have been the cause of the low zinc levels and that the low amount of fatty acids was a contributor to ADHD development.

Zinc, as a cofactor in synthesis of neurotransmitters, can affect dopamine metabolism indirectly. Dopamine is believed to be involved in ADHD, because low levels of the neurotransmitter are associated with ADHD. Dopamine agonist supplementation is effective for treating ADHD symptoms.[14]

While reviewing scientific literature and clinical findings over the last decade, the principal investigator of the Zinc–Attention Deficit (ZAD) study[†] noted that low zinc levels and copper stores were clearly related to notable signs and symptoms of attention dysfunctions and cognitive deficits.

A central hypothesis of the ZAD study is that dietary intake of zinc is insufficient in relation to copper absorbed from exogenous sources such as copper plumbing. Copper is known to interfere with zinc absorption in the body.

In addition, the often highly selective and limited nature of the typical North American child's diet is lacking in ample sources of zinc. It has been proposed that, when compounded with other sources of zinc antagonism (i.e., xenobiotics with hormonal properties requiring additional zinc for metabolism), a relative deficiency of zinc can arise.

Normal biologic processes—such as the spike in the zinc-dependent enzyme alkaline phosphatase that presents during growth spurts—and the necessity of zinc for testosterone and androgen metabolism during puberty lead to a decrease in zinc stores and availability. This relative lack of zinc may predispose a young person to zinc-deficient clinical symptoms, including acne, anorexia, eczema, and ADHD.

Docosahexaenoic Acid

Docosahexaenoic acid (DHA) is a long-chain omega-3 polyunsaturated fatty acid derived from the tissues of oily fish and marine mammals. DHA is available in commercial fish-oil products. DHA is incorporated into the human brain quite rapidly during the third trimester of pregnancy and during the course of early postnatal development.[15]

DHA and other long-chain polyunsaturated fatty acids (LCPUFAs) comprise a third of all the lipids in brain grey matter,[16] and DHA is considered to be important for the development of neural and synaptic membranes. Thus, DHA plays a key role in normal neural function.[17] LCPUFAs are highly concentrated in the phospholipid bilayer of active brain and retinal neural membranes. They play a role in neuronal function and phototransduction in these areas respectively.

The primary rationale for adding LCPUFAs to infant formulas was largely because of their presence in large quantities in the retina and brain, and in human breast milk. Until recently, these fatty acids have not been included in formulas marketed in the United States.

Comparative studies of infants fed breast milk and those fed only formula have also exemplified the importance of LCPUFAs

*For information on a very recent study about the effects of both zinc and conventional medicine, see item on page 122 of this issue in "News You Can Use."

†Dr. Meletis is the principal investigator of this study.

in early human development. Formula-fed infants had lower plasma and cerebral cortex levels of DHA than infants who were fed breast milk. Infants who were fed formula containing LCPUFAs had comparable red cell-and plasma levels to those of infants who were fed breast milk.[18]

Recent evidence shows DHA as a positive effector of retinal and visual function and memory and learning.[19] However, the functional benefits (particularly for visual and neural development) from formulas containing LCPUFAs are controversial at this time as a result of conflicting study results.

One literature review revealed that LCPUFAs were associated with improved visual and cognitive development as evidenced by breastfed children with higher IQ scores compared to children who received infant formula that was devoid of LCPUFAs.[20]

Another study explored the link between several factors—DHA precursor fatty acids, alpha-linolenic acid (ALA), and the plasma and erythrocyte phospholipid contents of DHA—in early infancy and the neurodevelopmental outcome of term infants.[21] The group of infants who had the lowest amount of ALA had the lowest mean plasma and erythrocyte phospholipid DHA contents at 4 months of age. This group also had the lowest mean score on every neurodevelopmental measure. In addition, across all of the supplemental ALA groups, motor score indices were correlated positively with plasma phospholipid DHA content at 4 months of age.

Another study examined neurologic outcomes via measurement of stereoacuity in 3½-year-old children that were either breastfed (thus were exposed to adequate amounts of postnatal DHA sources) to same-age children who had not been breastfed (and not supplied with DHA-fortified formula).[22] After adjusting for economic status and maternal diet, The researchers noted that children who were breastfed for at least 4 months had better stereoscopic vision than children who were not breastfed. In addition, when mothers consumed more oily fish during pregnancy, their children also had better stereoscopic vision than the children whose mothers did not consume oily fish during gestation.

This study demonstrated the effect of breastfeeding and a maternal DHA-rich diet on positive vision outcomes at age 3½, irrespective of infant feeding beyond the brief postnatal period of 4 months.

Many study results on the link between LCPUFAs and neurodevelopment have been equivocal. Interestingly, it appears that studies that produced equivocal findings on the effects of LCPUFAs utilized younger infants for test subjects while studies that yielded positive clinical benefit were on older infants. We speculate that LCPUFA supplementation may possibly provide benefit that may be more obvious as a child ages and undergoes more complex neurologic testing techniques. LCPUFAs have been shown to be of clear benefit in preterm infants, because these children receive a nutrient normally supplied in later stages of pregnancy.

Probiotics

There is a progressive increase in frequency of atopic disease (asthma, allergies, and eczema) throughout the Western world and methods for primary prevention are much needed. According to the hygiene hypothesis, this increase in allergic-type disease results from reduced exposure to microbes early in life. Left unchallenged, so to speak, the immune system turns its attention toward other substances and reacts to them as challenges for protecting the body. The body then reacts accordingly, with symptoms of allergy and asthma.

Probiotics have been researched as potential primary inhibitors of the atopic process. Several studies have investigated the effects of probiotic supplementation on prevention and treatment of allergic disease in recent years. The results have been promising.

Despite its wide acceptance as the best source of nutrition for the infant, proof of the benefits of breastfeeding as a protection against atopic disease remains elusive. However, studies on the effects of probiotics, both in the ante- and postnatal periods, have produced fascinating results.

In a study of 62 mother–infant pairs, administration of probiotics to the mothers during pregnancy and lactation increased the immunoprotective properties of their breast milk, which was assessed by the amount of transforming growth factor–β2 (TGF-β2) in the milk.[23] Infants whose mothers took probiotics had a significantly reduced risk of developing atopic eczema in their first 2 years of life compared infants whose mothers did not take the supplement.

The risk for eczema development was 15 percent of babies of mothers who took probiotics and 47 percent in the infants whose mothers did not take the supplement. In addition, maternal atopy was a clear risk factor for eczema in the infants, and those most likely to benefit from maternal probiotic supplementation were those who had elevated umbilical cord-blood concentrations of immunoglobulin E, a primary mediator of allergy.

Based on this study, investigators extended their analysis of whether probiotics prevented atopy past 2 years in a separate study.[24] At 4 years' postsupplementation, atopic disease was diagnosed in 26 percent of children who took probiotics and in 46 percent of children who took a placebo. These results suggest a preventive effect of probiotics on atopic disease that extends past infancy.

Dosing Guide to Nutrients

Zinc
Pregnancy and lactation; 30 mg per day
Birth to 6 months; 2 mg per day
7 months to 3 years; 3 mg per day
4–8 years; 5 mg per day
9–13 years; 8 mg per day
14–18 years; 9–11 mg per day
Adults; 15 to 20 mg per day

Docosahexaenoic acid
Doses range from 72 to 312 mg per day in 5 g of fish oil; some infant formulas contain 0.32% docosahexaenoic acid

Probiotics
Several types available; *Lactobacillus*, *Bifidobacteria*, and *Saccharomyces boulardii* are the most common; studies use *Lactobacillus* GG most often at a dose of 20 billion organisms per day

Note: The number of living organisms per capsule typically quantifies strength of preparations; this ranges from 1 to 10 billion.

In another similar study, probiotics were given, during the prenatal period, to pregnant mothers who had at least one first-degree relative with atopic disease and to infants postnatally for 6 months.[25] Atopic eczema was diagnosed at half the frequency in the supplement-treated group (23 percent) compared to the placebo group (46 percent), demonstrating a protective effect of probiotics against early atopic disease in high-risk children.

What is more, no side-effects were reported in any of these probiotic studies.

Administration of probiotics during pregnancy and breastfeeding appears to be a safe and effective way to provide protection against atopic disease early in life. In the abovementioned studies, the main outcome measured in atopic disease was eczema; further studies are needed to determine the effects of probiotic supplementation against asthma and allergies.

Conclusions

Functional foods, or food-like nutrients have become a highly investigated new science in recent years. The exploration of foods as medicines, beyond their normal nutritional benefits, is providing interesting clinical results, with great promise for possibly preventing and treating certain diseases, some with well-established genetic origins. The three separate nutrients reviewed in this article provide solid evidence for their incorporation in the pre- and postnatal periods of child development for the prevention and treatment of disease and for enhancing neurodevelopmental potential. □

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