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Time for an oil check: the role of essential omega-3 fatty acids in maternal and pediatric health

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Deficiency of omega-3 fatty acids (ω3FAs) is an often unrecognized determinant of clinical disease; the adequate availability of these essential nutrients may prevent affliction or facilitate health restoration in some pregnant women and developing offspring. The human organism requires specific nutrients in order to carry out the molecular processes within cells and tissues and it is well established that ω3FAs are essential lipids necessary for various physiological functions. Accordingly, to achieve optimal health for patients, care givers should be familiar with clinical aspects of nutritional science, including the assessment of nutritional status and judicious use of nutrient supplementation. In view of the mounting evidence implicating ω3FA deficiency as a determinant of various maternal and pediatric afflictions, physicians should consider recommending purified fish oil supplementation during pregnancy and lactation. Furthermore, ω3FA supplementation may be indicated in selected pediatric situations to promote optimal health among children.
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Let food be your medicine and medicine be your food.
– Hippocrates

In the enlightened age of modern medicine, some individuals are disinclined to believe that various diseases can be prevented or overcome by simply eating the right food; in the eighteenth century, this paradigm was also prevalent. Despite much evidence, it took many decades and many deaths before conventional wisdom accepted the findings of Dr James Lind, a Scottish physician with the British Navy, who discovered in about 1750 that two oranges and one lemon every day were enough to overcome scurvy, a disease that consumed more sailors than all other afflictions, naval battles and shipwrecks combined. Within contemporary medicine, the increasing recognition that myriad health afflictions can be prevented or ameliorated by addressing cellular deficits of essential molecular ingredients makes evident the primary role of nutritional assessment and therapeutic nutritional intervention in clinical medicine. This paper will explore evidence linking essential omega-3 fatty acids (ω3FAs) to maternal health as well as the correlation of these required nutrients with ongoing health and well-being of the offspring during prenatal as well as post-natal phases of development. Public health strategies for ω3FA supplementation will be discussed.

Overview of essential fatty acids

The term 'lipid' refers to fats, oils (liquid fats) and their constituent fatty acids. As required nutrients for various biochemical processes, essential fatty acids (EFAs) refer to lipids that cannot be synthesized within the body and must be ingested from dietary sources in order to meet the needs of individuals. Although the role of EFAs is not completely understood, these lipids are known to be involved in oxygen transport, energy storage, cell membrane integrity, intercellular communication and the control of inflammation, cell proliferation as well as blood clotting.[1–4] The relative absence of EFAs, usually the result of dietary deprivation, may give way to suboptimal functioning and overt clinical illness.

Biochemically, fatty acids are straight chains of carbon atoms with attached hydrogen atoms; the presence and position of a double bond in the chain is denoted by the Greek letter 'ω' (omega) followed by the site on the chain of the double bond. There are two groups of EFAs: ω3FAs and omega-6 fatty acids (ω6FAs), which are both derived from ingested lipids. Dietary alpha-linolenic acid (ALA) is the precursor to the family of ω3Fas, whereas linoleic acid provides substrate necessary to yield various ω6FAs. Whereas ω6FAs are plentiful in most diets (e.g. foods including cereal grains, most processed foods, meat, milk, eggs and some vegetable oils such as corn, sunflower, safflower and sesame), significant quantities of ω3FAs are commonly found only in a few foods including selected seeds and nuts as well as fish.

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The relative concentration of ω3FAs and ω6FAs consumed in the diet is a matter of major importance to the biochemical and clinical functioning of the individual.[5] For example, both families of fatty acids provide necessary substrate for the production of various hormone-like substances called eicanosoids, including prostaglandins, leukotrienes and thromboxanes, which regulate many physiological processes. Eicanosoids originating from ω6FAs act biochemically to promote cell proliferation, inflammation and blood clotting, whereas eicanosoids originating from ω3FAs oppose these effects and facilitate anti-inflammatory action, inhibitory effects on cell growth and blood thinning.[1,6] Both groups of EFAs compete for the same limited supply of enzymes in the biochemical assembly of eicanosoids, and diets with high ω6FAs/ω3FAs ratios will diminish the effectiveness of ω3FAs-dependent processes, leading to an overabundance of ω6-derived eicanosoids.

Many chronic disease states are characterized by a relative overabundance of ω-6 oils as relative deficiency in ω3FAs is a predisposing factor for unrestricted cell proliferation, blood clotting, undue inflammation and autoimmune reactions. With optimal diets, the consumption of ω3FAs and ω6FAs is balanced allowing for physiologic response to the demands of the body. The ratio of ω6 to ω3 (ω6/ω3 ratio) was about 1–2:1 as recent as 200 years ago in the North American diet and now it is estimated at 16:1.[5] The relative deficiency in ω3FAs in the Western diet and the plethora of ω6FAs is yielding a predisposition to a lack of inhibitory eicanosoids, a metabolic milieu which may predispose to certain cancers,[7] cardiovascular affliction,[8] arthritic disorders[9] and various other health challenges. The provision of supplemental amounts of ω3FAs improves the ω6/ω3 balance and may ameliorate various inflammatory diseases and may diminish the risk of numerous common illnesses.

Although not commonly utilized in mainstream clinical medicine, there are currently several molecular markers available to assess the biochemical status of the individual patient with regards to EFA deficiency.[4] These laboratory investigations involve plasma and erythrocyte fatty acid analysis through gas chromatography.[4] For patients presenting with various health complaints, a nutritional assessment of EFA status may be considered.

The health significance of EFA biochemistry is beginning to be appreciated in many areas of medicine. From development of intelligence *in utero*[10] to managing common pediatric problems such as recurrent ear infections,[11] from amelioration of hostility in young adults[12] to abating various psychiatric disorders[13] and from diminishing the risk of cardiac disease[14] to a role in preventing Alzheimer's,[15] it is evident that EFAs are necessary at all stages of life. In this paper, use of ω3FAs in the gestational period and in pediatric health will be highlighted.

Maternal health and omega-3 fatty acid

Recognizing that the physiological status of the mother as well as the biological health of developing children are dependent on the adequate availability of ingested maternal nutrients, the integral and paramount role of nutritional advice as a fundamental component of prenatal care has long been recognized.[16] Essential fatty acids such as arachadonic acid (ω6) and docosahexaenoic acid (DHA) (ω3) are critical for normal development of the placenta and the fetus early in pregnancy,[17] and it is now clear that both are also necessary for brain and retinal development in later stages of gestation.[18–20] Considerable amounts of ω3FAs, especially DHA, are transferred from mother to child particularly throughout the third trimester[21] – residual DHA in the mother may not fulfill requirements for optimal function if maternal stores are inadequate.

An important clinical consideration in maternal and pediatric health is that differing members of the ω3FA family have specific molecular functions within the body; DHA, for example, is the main ω3FA ingredient required for fetal brain development. Accordingly, the importance of receiving an adequate intake of ω3FAs during pregnancy, particularly DHA, has recently been realized. Certain dietary sources of ω3FAs, such as fish oil, contain DHA; other sources of ω3FAs such as specific plant sources do not have DHA. Conversion from plant source ω3FAs to DHA is possible but requires energy and enzymatic availability. Provision of direct DHA from fish sources is the most secure way to provide the necessary DHA required for optimal fetal neurological development.[17]

Over the last century, there has been an 80% decline in the intake of ω3FAs[22,23] and recent evidence confirms a significant diminution of ω3FA concentration in breast milk among Canadian women.[24] A relative deficiency of ω3FAs has been associated with a variety of maternal problems which may be ameliorated by the adequate availability of ω3FAs during pregnancy. Three obstetrical conditions related to ω3FAs will be highlighted.

(1) Hypertensive disorders of pregnancy: In the developed world, gestational disorders of blood pressure are very common, occurring in about 6% of pregnancies. Although the degree of hypertension and the associated complications vary, this medical condition not infrequently results in pre-eclampsia and is often associated with intrauterine growth retardation, preterm delivery, surgical intervention, prolonged hospital stays and considerable emotional distress for the patient and family members. Nutrient factors relating to EFAs appear to significantly influence the incidence of this disorder.

Inuit women with a high consumption of fish and sea mammals have a low incidence of pregnancy-induced hypertension compared to controls.[25] Pregnant women in a cross-sectional case–control study with the lowest levels of ω3FAs were shown to

be 7.6 times more likely to have pre-eclampsia than those with the highest level of ω3FAs.[26] A 15% increase of the $\omega 3/\omega 6$ ratio resulted in a 46% reduction in risk of developing pre-eclampsia.[26] Furthermore, meta-analytical reviews confirm that ω3FAs lower blood pressure in a dose-dependent manner.[27,28] The recent revelation that blood pressure control later in life is impacted negatively by low levels of specific ω3FAs in the perinatal period[29] has prompted further study into the potential long-term benefits of gestational ω3FA supplementation.

(2) Preterm birth: Preterm birth is a major obstetrical complication which often necessitates hospitalization for the mother and remains a significant cause of major morbidity and mortality in newborn children. Many potentially risky drugs are used in an effort to interrupt premature labor. A safe, inexpensive and effective agent to diminish the risk of preterm birth would be a welcome addition to current interventions.

There is now substantial evidence suggesting that adequate consumption of ω3FAs through natural dietary sources or from supplementation may significantly decrease the likelihood of early labor.[30] A prospective cohort study looking at seafood consumption and risk of preterm delivery showed that women who never consumed fish had a 7.1% chance of having a preterm baby as compared to those eating fish once weekly who had a 1.9% chance of preterm birth.[31] Furthermore, a study using 4 g of fish oil daily beginning at 30 weeks gestation was associated with a longer gestational period and increased birth weight.[32] Utilization of a low risk, readily available preparation to diminish the likelihood of preterm labor, particularly for individuals at risk for this obstetrical complication, appears prudent.

(3) Postpartum depression: Postpartum depression is a prevalent and disturbing condition that has tragically consumed the lives of many new mothers. At a time when joy and excitement are anticipated, severe depression can have a profound effect on the woman, on her adult relationships and on the emotional stability of other offspring. Increasing evidence suggests that nutrient biochemistry involving ω3FAs may be a determinant of mood in the postpartum period.

There is a strong correlation between lower seafood consumption during pregnancy and higher rates of postpartum depression.[33,34] The incidence of postpartum depression in North America, for example, is about 12%, whereas the occurrence of this mood disorder remains at about 2% in Japan where fish consumption is high.[33] Furthermore, a lower DHA content in mother's milk correlates with higher postpartum depression rates[33] and ω3FAs (especially DHA) are commonly low in breast milk and red cells of depressed postpartum women,[21] reductions that are generally associated with a low intake of EFAs in pregnancy.[35] Although further study is required, DHA has been proposed as a prophylactic therapy to prevent mood disorders, as a treatment for mild depression and as an adjunct intervention in managing established major depression in the postpartum period.[36–38]

Omega-3 fatty acids and pediatric health

An extensive literature suggests substantial potential benefit to children exposed to sufficient levels of ω3FAs during prenatal development and early post-natal life. Furthermore, ω3FA supplementation in selected pediatric situations appears to ameliorate specific medical challenges in children. A brief discussion of brain function, metabolic outcome and formula supplementation in relation to ω3FAs will be presented.

Brain function

Adequate maternal levels of ω3FAs appear to have a long-term positive impact on the central nervous system functioning of the child. As well as experiencing less risk of EFA deficiency in the early post-natal period,[17,39] offspring of mothers who consumed cod liver oil (rich in ω3FAs) in late pregnancy and early lactation have improved intelligence quotients and mental processing scores at 4 years of age.[10,40] A case–control study correlating gestational dietary patterns and risk of cerebral palsy in progeny showed that fish intake during pregnancy significantly diminished risk.[41]

Perinatal and early childhood ω3FA sufficiency may have long-term implications for neurosystem development in children. Interesting research correlating ω3FAs levels with autism and attention-deficit hyperactivity disorder have recently been published.[42–47] Levels of DHA are significantly lower and the $\omega 6/\omega 3$ ratio is significantly higher in autistic children as compared to controls;[47] similarly, fatty acid levels are also reported to be lower in children with attention-deficit hyperactivity disorder.[45] Supplementation with fish oil in 18 children with autism, however, resulted in parents reporting improvements in general health, motor and cognitive skills, sleep patterns, sociability and eye contact in the majority of patients.[42] Most children in this group also experienced reduced frequency of infections, less irritability, less aggression and less hyperactivity.[42]

It is yet unclear whether selected neurosystem disorders, which appear to be ameliorated by EFA supplementation, are etiologically associated with gestational or perinatal lipid deficiency. Research demonstrates nonetheless that various afflictions, however caused, appear to respond to EFA intervention. Several studies have shown benefit of supplementation with ω3FAs in children with learning difficulties, dyslexia and dyspraxia.[46,48,49] A randomized clinical trial conducted on British children with difficulties in learning, behavior and psychosocial adjustment was performed by giving fish oil supplementation to the intervention group over 3 months, and a one-way crossover from placebo to intervention was performed for an additional 3 months[50] – children receiving fish oil demonstrated remarkable progress in reading skills compared to the controls, and similar improvement was noted in the placebo crossover group when they received fish oil.[50] Furthermore, using Bayley Scales of infant development, a 7.3% increase in the Mental Development Index was noted for offspring receiving an early dietary supply of DHA,[51] whereas a low intake of ω3FAs predicted

poorer reading, spelling, auditory memory and general ability in males.[52] Despite potential deficiency in early life, supplementation with ω3FAs appears to subsequently confer positive health benefits in some children.

From improved intellectual functioning to amelioration of the signs and symptoms associated with various pediatric central nervous system difficulties, the results discussed suggest benefits of sufficient ω3FAs during prenatal and post-natal stages on subsequent cognitive and behavioral functioning in children.[53]

Pediatric metabolic concerns

In an era of troubling rates of pediatric diabetes, the correlation between ω3FA availability and development of blood sugar disturbances is noteworthy. The use of cod liver oil during pregnancy appears to reduce the risk of developing diabetes in offspring.[54] Furthermore, there is also evidence that ω3FA supplementation appears to be beneficial in diabetic pregnancy for the prevention of long-term metabolic abnormalities in the child.[55] In the post-natal phase, case–control studies have demonstrated that regular use of cod liver oil in the first year of life is associated with a lower risk of subsequent childhood type-1 diabetes.[56]

Over the past few decades, there has been a major qualitative transition in nutritional patterns with a dramatic increase in the relative consumption of ω6 lipids. As ω6FAs appear to be potent promoters of fetal adipogenesis during gestation and lactation,[57,58] there is increasing evidence that the high ω6/ω3 fatty acid ratio of many contemporary diets is an important determinant of childhood obesity.[57]

Formula supplementation with essential fatty acids

With the recognition that visual acuity for both preterm and full-term infants appears to be positively impacted by adequate availability of ω3FAs,[59–61] there has been a move to supplement some formula preparations with essential lipids. Increasing research has suggested that non-breast-fed infants require EFAs in their feeding[62] and that infants supplemented with EFAs in formula have similar fatty acid profiles to those seen in breast-fed infants.[60]

Recent work investigating the safety and benefits of feeding preterm infants formulas containing DHA has been encouraging. For example, a recent study published in the *Journal of Pediatrics* reported that DHA supplemented groups had higher Bayley mental and psychomotor development scores at 118 weeks post-menstrual age without any increase in morbidity or adverse events compared to the control group with unsupplemented formulas.[63] Furthermore, with the recognition that non-breast-fed healthy term infants may also need EFAs in their feeding,[62] recent work has studied the impact of formula supplementation on this group. Term infants receiving EFA-containing formulas during the first year of life appear to realize clear benefit in terms of visual function,[64,65] but further study is required to determine the outcome on a range of indices.

Public health considerations

Recent medical literature has emphasized the importance of beneficial nutrition as a primary determinant in health outcomes, a determinant that is potentially modifiable by proactive interventions. Although learning about nutrients and skills for nutritional promotion have not secured a prominent place in medical education,[66,67] the World Health Organization's new Global Strategy on Diet,[68] the recently published Dietary Guidelines for Americans[69] and increasing numbers of publications in the medical literature[70,71] draw attention to the need for physicians to acquire amplified knowledge relating to nutrition. In order to disseminate important research findings to physicians and patients, 'what is needed is scientific consensus, education of professionals and the public, … and willingness of governments to institute changes.'[72]

According to much contemporary evidence, increased consumption of selected EFAs in pregnancy and during the post-natal period appears to be an innovation that might benefit the health and well-being of numerous individuals. To facilitate the diffusion of innovation and the provision of optimal care for women and children, two questions are important to address in considering public health recommendations regarding ω3FAs: (1) Why are pregnant women and children deficient in ω3FAs? and (2) What is the best means to address the deficiency of ω3FAs?

In the absence of an intestinal absorption disorder, maternal and pediatric ω3FA deficiency is usually a reflection of inadequate consumption of source foods. Western diets have become increasingly deficient in ω3Fas as many people have the perception that 'fat is bad' and that any fat ingestion contributes to obesity, dyslipidemia and cardiovascular disease. Furthermore, dietary intake of fish, a premium source of ω3FAs, has declined substantially over the last few years because of public awareness of widespread seafood contamination. Increasing scientific literature has confirmed escalating aquatic contamination from toxicants such as heavy metals, dioxins, polychlorinated biphenyls (PCBs) and estrogens[23,73–77] that have potential to harm the developing child as well as the mother. The increasing scare regarding mercury (Hg) intoxication from seafood has followed the realization that this element is very toxic to the fetal brain and that most fetal Hg exposure occurs through maternal seafood intake.[78] As 'maternal fish consumption brings both risks and benefits to the fetus,'[78] there are now warnings to limit the consumption of seafood in pregnancy because of teratogenic potential.

With apparent health benefits associated with adequate ω3FA intake in pregnancy, four recommendations are provided for consideration:

1. It is recommended that ω3FA intake be considered as a supplement during pregnancy and lactation. As it is recognized, the DHA is required for optimal fetal and infant brain development and as plant source ω3FAs such as ALA 'may not

be converted to DHA in sufficient amounts to meet an infant's needs,'[17] it is recommended that fish oil supplementation containing abundant DHA be discussed with parturient and lactating women.

2. It is recommended that only supplemental preparations that have been purified (through such processes as molecular distillation and then independently tested to verify untainted status) be consumed. As toxic contamination of many fish oils is evident,[21] 'the quality of the ω3FA preparation is important'[21] and contamination with heavy metals, dioxins, hormones, PCBs, and any other contaminant should be absent.
3. It is recommended that non-breast-fed preterm infants receive formulas supplemented with DHA to optimize neurodevelopment. Non-breast-fed term infants may also benefit from supplemented formulations.
4. It is recommended that clinical practice guidelines (CPGs) on the subject of nutritional guidance in prenatal care be considered as a means to facilitate the diffusion of information relating to maternal and infant health. 'The average time from conception to realization of an innovation is 20 years;'[79] the dissemination of CPGs will hopefully expedite this process.

Conclusion

There is increasing medical literature emphasizing the need for good nutrition as a means to prevent major health difficulties and to effect optimal health in patients. In 1976, for example, an important paper published in the *Archives of Diseases in Childhood* provided credible evidence that deficiency of important nutrients might increase the incidence of open neural tube defects in offspring.[80] The declining incidence of this congenital anomaly as a result of routine folate supplementation is a testament to the public health benefits of diffusing important information regarding nutritional deficiency. Other biochemical agents, including ω3FAs, also appear to be requisite molecules necessary for optimal development of the neurological system as well as for numerous other functions throughout the body.

The health and well being of the child in the short and long term appears to be improved by the availability of adequate amounts of ω3FAs during fetal and post-natal development. Deficiency of ω3FAs is a common problem and may be a contributing factor for certain maternal and pediatric health problems; extensive evidence-based data confirm that ω3FA supplementation is associated with improved outcome for mothers and children. Accordingly, it is recommended that untainted fish oil containing abundant ω3FAs be considered as a routine supplement during pregnancy and lactation, as well as in selected pediatric situations.

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