Expert Discussion Forum

Exploring the importance of DHA in infant and child development

In this issue:

Proceedings from the Working Group on DHA in Canada

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Introduction

Recently, a multidisciplinary group of leading North American experts in the field of nutrition met to discuss the importance of docosahexaenoic acid (DHA) as part of a healthy diet and its role in infant nutrition as well as to consider how to advance the education of healthcare professionals regarding the topic of DHA. This group formed the Working Group (WG) on DHA. This paper presents an overview of the scientific rationale for DHA in infant nutrition, as well as some of the insights gathered from the group's discussion.

Background

The omega-3 fatty acids are a group of fats that include DHA and eicosapentaenoic acid (EPA).[1] Docosapentaenoic acid (DPA) and EPA are precursors to the synthesis of DHA from α-linolenic acid (ALA).[2] The body can use ALA, found in vegetable oils, to make EPA and DHA, but a large proportion of dietary ALA is oxidized and there is very limited conversion of this short-chain omega-3 fatty acid as ALA to DHA in humans.[1] In fact, this conversion efficiency has been found in various human trials to be very low, ranging from below 0.1% (almost undetectable) up to 9%.[3] ALA supplementation has not been found to be effective in raising levels of long-chain omega-3 fatty acids (DHA and EPA) in plasma. Supplementing the diet with EPA readily increases plasma EPA concentrations, but not DHA. In contrast, supplementing the diet with DHA increases plasma DHA concentrations in a dose-dependent manner and offers a modest increase in EPA concentrations. DHA and EPA are primarily produced by algae (plankton) in the ecosystem. As fish consume algae or crustaceans feeding on algae, they are a rich source of DHA and EPA.[1]

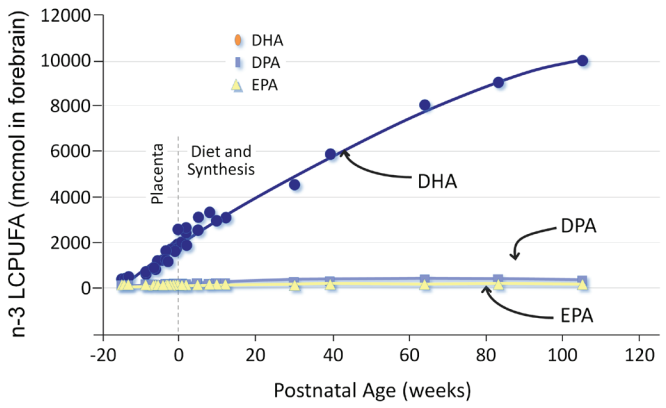
The Importance of DHA

DHA is one of the key fatty acids in the neuronal cell membranes of the brain and eye, and the most prominent omega-3 in the infant brain.[2] DHA begins accumulating in the brain early, accelerates quickly, and accumulates rapidly until about 24 months (Figure 1).[2]

Research has shown that fatty acids in the brain change from early childhood through late adulthood.[4-8] During perinatal development of the human brain, cortical concentrations of DHA increase sharply in association with active periods of neurogenesis, neuroblast migration, differentiation, and synaptogenesis.

The last 3 months of pregnancy and first 3 years of postnatal life are most crucial for brain development, and the health and nutritional status of the mother during pregnancy have significant effects on the development of the brain during fetal life.[4-8]

Figure 1: DHA accretion is rapid in the first 2 years of life: Differential accumulation of omega-3 fatty acids in the brain[2]

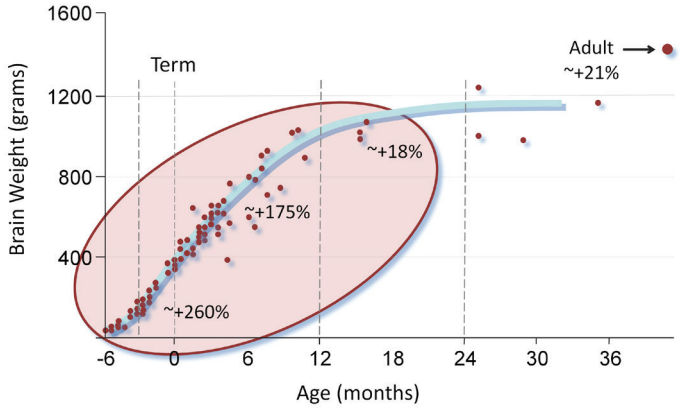


Adapted from Martinez *et al.* 1992[2]

The priority *of early human development is the brain.*

Major development takes place during a child's first year life, with the brain more than doubling in this time period. By the third year of life, 85% of a child's brain growth will have occurred. (Figure 2).[9] The prioritization of brain growth is illustrated by research showing that infants born to malnourished mothers have reduced muscle mass and abdominal circumference compared to those born to well nourished mothers, yet have comparable head circumferences.[4-8]

Figure 2: Brain growth is especially rapid in the last trimester and first 2 years of life[9]



Adapted from Dobbing *et al.* 1973[9]

The importance of DHA in neurocognitive development has been demonstrated in clinical trials comparing infant formula with the recommended levels of DHA (*e.g.*, DHA between 0.2 and 0.5 weight percent of total fat)[10] with infant formula with no DHA. The infant formula studied in these clinical trials had a DHA level of 0.32% and an arachidonic acid (ARA) level of 0.64% of weight of total fat. These studies have demonstrated improvements in sustained attention,[11] problem solving,[12] visual acuity,[13] and the mental development index[14] for infants fed the formula with the recommended DHA level compared with those fed formula with no DHA. As reviewed, 6-month old infants have much less DHA in the brain if not consuming preformed DHA, which attests to the critical importance of an incoming supply of DHA during the first 6 months of life to support normal brain accumulation of DHA.[15]

The benefits of DHA supplementation before birth have also been demonstrated in a recent Canadian study – the first study to show a DHA deficiency among pregnant Canadian women and that increasing their DHA intake during pregnancy reduces risks to their child's development. The children's vision was tested at 2 months of age and their language development at 14 and 18 months. Children of DHA-deficient mothers were more likely to have slower vision and language development.[16]

Long-term benefits of DHA supplementation

Interestingly, long-term data now suggest that the neurocognitive benefits of DHA supplementation extend beyond infancy.

A recent long-term follow-up study demonstrated that long-chain polyunsaturated fatty acid (LC-PUFA) supplementation (0.5% DHA) in preterm infants had a significant effect on cognition at 10 years of age. Girls in particular showed beneficial effects of LC-PUFAs on literacy. Supplementation in infancy was also shown to increase verbal IQ, full-scale IQ, and memory scores at 10 years of age.[17]

Other long-term follow-up of term infants randomly assigned to receive formula containing either DHA and ARA or no LC-PUFAs for 4 months showed that at 6 years of age, children who had received LC-PUFAs were faster at processing information compared with children who received unsupplemented formula.[18] Data from another trial demonstrated long-term benefits on several measures of cognitive development into early childhood after LC-PUFA provision for the first 12 months of life. Specifically, LC-PUFA supplementation in infancy was associated with improved performance on several assessments of executive function and on verbal measures derived from standardized tests at 5 and 6 years of age.[19]

Long-term data *suggest that the neurocognitive benefits of DHA supplementation extend beyond infancy.*

Dietary DHA supplementation in children

WG members suggested that the most vulnerable children may be those who benefit the most from DHA supplementation based on results from the 2012 DOLAB study. The DOLAB study was designed to determine the effects of dietary supplementation with DHA on the reading, working memory, and behaviour of healthy schoolchildren. This study showed no effect of DHA on reading in the full sample, but did show significant effects in children whose initial reading performance was at or above the 20th percentile. Parent-rated behaviour problems (attention deficit hyperactivity disorder-type symptoms) were significantly reduced in the DHA-supplemented group, but little or no effects were seen for either teacher-rated behaviour or working memory.[20]

Studies of the effects *of DHA-supplemented formula have shown:*

- Improvements in sustained attention[11]
- Improvements in problem solving[12]
- Improvements in visual acuity[13]
- Improvements in mental development index for infants[14]
- Reduced upper respiratory infections and allergies[23]
- Long-term positive effects on cognition, attention, information processing and literacy[17]

Studies of the effects *of DHA-supplemented diets have shown positive effects on:*

- Literacy in vulnerable children[20]
- Reducing the risk to vision and language development in infants born to women identified as DHA-deficient[16]

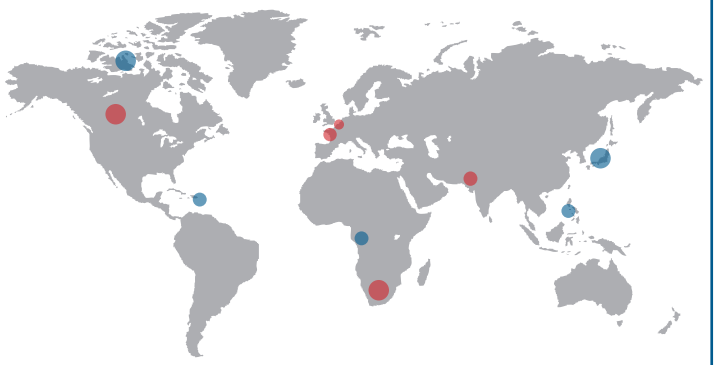
The WG commented that given that research thus far appears to support some positive or neutral effects on child development associated with adequate DHA and ARA intake, ensuring that children have appropriate dietary DHA intake should be a consideration for parents and the healthcare community as well as an area targeted for further research.

Beyond neurocognitive development

Recent research has brought to light benefits beyond neurocognitive development. A 2013 study demonstrated that supplementation with 600 mg DHA per day in the last half of gestation resulted in overall greater gestation duration and infant size. Infants from the supplemented group also had lower admissions to neonatal intensive care and shorter length of hospital stay for preterm infants, which could have important clinical and public health benefits.[21]

Breast milk DHA *content appears to be closely associated with maternal dietary DHA intake.*[25]

Figure 3: Locales with the highest and lowest concentrations of DHA in breast milk: Results of a meta-analysis[25]



DHA has also been associated with improved respiratory and allergy outcomes in preterm infants. The DINO study compared the outcomes for preterm infants <33 weeks gestation who consumed expressed breast milk from mothers taking either tuna oil (high-DHA diet) or soy oil (standard-DHA) capsules. DHA supplementation reduced the incidence of bronchopulmonary dysplasia in boys and in all low-birth weight infants (>1250 g). The incidence of hay fever at 12 or 18 months was also reduced in the infants that had the high-DHA diet breast milk. There was no effect on asthma, eczema or food allergy.[22] DHA/ARA supplementation in formula during the first year of life in term infants was also associated with delayed onset and reduced incidence of upper respiratory infections and common allergic diseases up to 3 years of age in the AIMS study.[23] In a major study of 1342 term infants, those fed formula with 0.32% of milk fat as DHA and 0.64% as ARA showed a markedly lower incidence of bronchitis/bronchiolitis at 5, 7 and 9 months relative to those on a formula lacking DHA/ARA.[24]

DHA levels in breast milk are variable

There is a broad range of DHA concentrations in human breast milk worldwide. A 2007 meta-analysis demonstrated that the mean concentration of DHA in breast milk (by weight) was 0.32% and

that of ARA was 0.47%. DHA concentration in breast milk was found to be lower and more variable than that of ARA. The highest DHA concentrations were found in the breast milk of women in the Canadian Arctic, Japan, Dominican Republic, Philippines, and Congo (1.4–0.6%). With the exception of Congo, these locations are all coastal or island with populations who have a high seafood intake. The areas with the lowest breast-milk DHA concentrations were Pakistan, rural South Africa, Canada, The Netherlands, and France (0.06–0.14%), all of which are inland or developed countries, which are usually associated with low seafood consumption (Figure 3). Breast-milk DHA content appears to be closely associated with maternal dietary DHA intake.[25]

Global and Canadian recommendations regarding DHA

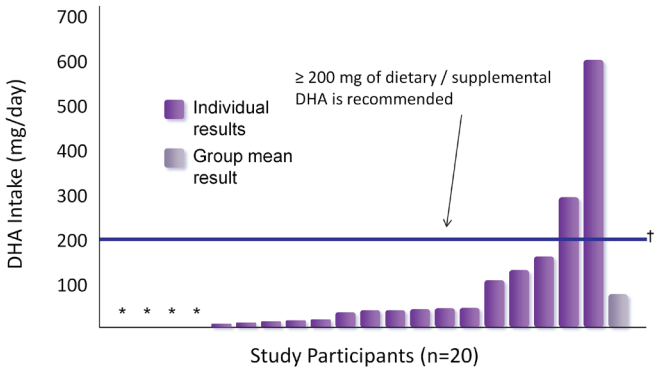
Recommendations regarding DHA vary from organization to organization and are often expressed in different terms, adding to the confusion around DHA (Table 1). Some recommendations use grams of DHA per day, while others express amounts as a percentage of daily energy intake, as a percentage of total fatty acids or even as weekly fish intake for mothers.[26-33]

In 2010, the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations recommended that adult pregnant and lactating females should have a minimum intake of 0.3 g/d EPA+DHA, of which at least 0.2 g/d should be DHA, for both optimal adult health and fetal and infant development.[26] This report also stated that many randomized controlled trials and several meta-analyses have been published on DHA and ARA supplementation and "Overwhelmingly, studies show either a neutral or positive effect on health outcomes, with negative effects rare."[26] Recommendations are supportive of the WHO statement and suggest that Canadians, particularly females of child-bearing age, consume at least 150 g (5 ounces) of cooked fish each week (including salmon, trout, herring, canned light tuna, sole) as part of a healthy pattern of eating.[32] Canadian recommendations also suggest that people vary the types of fish they consume and follow advice from Health Canada to limit their exposure to contaminants such as mercury

> **"Overwhelmingly,** ***studies show either a neutral or positive effect [of DHA and ARA supplementation] on health outcomes, with negative effects rare."***[26]
>
> **FAO, Fats and Fatty Acids in Human Nutrition**

by limiting consumption of predatory fish such as shark, swordfish, marlin, orange roughy, and fresh and frozen tuna.[32] A member of the CWG is currently working on an update of *The Dietary Guidelines for Americans* (2010), which has recommended the consumption of 8-12 ounces of seafood per week for women who are pregnant or breastfeeding.[33]

Figure 4: DHA intakes of pregnant Canadian women are very low[34]



*Trace amount (<2 mg/d)
†Recommended intake for pregnant women (Koletzko B, *et al. J Perinat Med* 2008;36:5-14.)

Adapted from Denomme *et al.* 2005[34]

The constantly emerging scientific evidence has led many expert bodies to recommend the addition of DHA to infant formula, with levels ranging from ~0.2-0.5% of fatty acids.[26-31]

Despite the facts that the WHO has established DHA recommendations and that Canada was the first country to declare an omega-3 fatty acid, ALA, as essential in 1990, at the present time, there are no Canadian recommendations specifically regarding DHA intake. The addition of DHA & ARA to infant formula is not mandatory, however they are permitted as optional ingredients and have been assessed as safe by Health Canada.†

Table 1: DHA recommendations

Organization	Recommendation for pregnant and lactating women	Recommendation for term infants
FAO/WHO[26]	EPA+DHA, 0.3 g/d of which at least 0.2 g/d should be DHA	DHA 0.1-0.18% E/0.20-0.36% fatty acids (0-6 months) DHA 10-12 mg/kg (6-24 months)
Health Canada[32]	At least 150 g (5 ounces) of cooked fish per week	
Dietary Guidelines for Americans[33]	Intake of omega-3 fatty acids, in particular DHA, from at least 8 ounces up to 12 ounces of seafood from choices that are lower in methyl mercury	

† Nutrition for Healthy Term Infants: Recommendations from Birth to Six Months.
A joint statement of Health Canada, Canadian Paediatric Society, Dietitians of Canada, and Breastfeeding Committee for Canada.
Available at: http://www.hc-sc.gc.ca/fn-an/nutrition/infant-nourisson/recom/index-eng.php#a3

WHO Guidelines *clearly recommend a DHA intake of 0.20–0.36% of total fatty acids for infants aged 0–6 months.*[26]

What is the DHA Situation in Canada?

Canadian maternal DHA intakes are low. Studies have shown that average DHA intake in pregnant Canadian women is 82 mg/d (Figure 4), well below the international recommendations of ≥200 mg/day.[28,34]

North American women have some of the lowest levels of DHA in breast milk among various countries. The average intake of DHA among Canadian breast-fed infants is only about 56 mg/day of DHA in breast milk,[25,35] leading the WG to comment that there appears to be a nutrient gap between the mother and the infant.

Despite the fact that DHA-enriched infant formulas have been available in Canada since 2003, all infants are not routinely fed DHA-enriched formula. In fact, about 50% of the infant formula purchased in Canada is non-DHA-enriched formula, which is in stark contrast to the situation in other global markets where virtually all infant formulas that are sold contain DHA.[36]

Nutrition is not a topic commonly covered by time-strapped Canadian physicians. Given the importance of proper nutrition to the prevention of many health issues, the WG strongly felt that physicians should be encouraged to speak to their patients about nutrition in general, as well counseling patients on choosing a diet rich in DHA, particularly during prenatal and well-baby visits to identify proactively a possible nutrient gap. The WG identified the lack of Canadian guidelines as a possible cause for physicians' reluctance to address nutrition and DHA with their patients. Despite the absence of Canadian guidelines, there are numerous prestigious international organizations with established recommendations; including WHO, which clearly recommends a DHA intake of 0.20-0.36% of total fatty acids for infants aged 0-6 months and 10-12 mg/kg for those aged 6-24 months.[26-32] The WG also suggested that the uncertain conclusions of the 2011 Cochrane Review "Longchain polyunsaturated fatty acid supplementation in infants born at term"[37] might have led physicians to question the importance of DHA. However, as leaders in the field of nutrition, the WG were adamant that the Cochrane Review results should be interpreted cautiously given their reliance on very heterogeneous studies, and commented that studies to date do not show negative effects of DHA supplementation but that many in fact show either a positive effect or a neutral effect. It is noteworthy that recent long-term follow-up studies in children up to age 10 (as mentioned earlier) have supported the health benefits of providing breast milk and preterm or term formula with enriched levels of DHA. While dietary DHA may not be an essential nutrient for infants, the overall literature indicates that some infants would derive various health benefits from its presence. This view was supported by the WHO recommendations, which stated; "Overwhelmingly, studies show either a neutral or positive effect [of DHA and ARA supplementation] on health outcomes, with negative effects rare."[26]

North American women *have some of the lowest levels of DHA in breast milk.*

The WG further suggested that given the recent publication of long-term follow-up data, it is possible that previous studies were simply not of long enough duration to fully demonstrate the benefits of DHA supplementation.

Recommendations of the WG on DHA*

- ***The potential benefit of DHA in infant development should be recognized and further explored***
- ***Canadian guidelines regarding DHA should be established***
- ***Healthcare practitioners should:***
  - ***encourage mothers and expectant mothers to eat at least 2 servings of fish per week or to take a DHA supplement (i.e., ensure a diet rich in DHA)***
  - ***consider recommending DHA-supplementation for non-breastfed infants***

Recommendations of the WG

To further the understanding of the importance of DHA in infant and child development, the WG suggested addressing pediatricians, family practitioners, nurses and other healthcare practitioners, as well as the public health community on the topic of DHA. This could be accomplished by engaging with various pediatric associations and organizations to lead discussion concerning DHA. In addition, the WG proposed encouraging physicians to address nutrition with their patients/parents of patients during routine visits.

* These recommendations are the opinions expressed by the WG.

Conclusions

DHA may have a positive role to play in human development and health and currently is under recognized as such. The Working Group on DHA is committed to advancing the education of healthcare professionals regarding the importance of DHA in a public health context, recognizing the potential benefits DHA may provide to some infants in regards to cognitive development, visual acuity, reduction in low-weight births, greater gestation duration, as well as immunity and respiratory health.

As evidence continues to emerge showing the importance of DHA in both infant and adult nutrition, it falls on Canadian physicians to help ensure the health of their patients with counseling regarding proper nutrition as well as by encouraging research and discussion on the topic.

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Comments from WG Members

"It's about the nutrient gap; through mom to get to baby."

"As calcium is to the bones, DHA is to the brain."

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