

The Role of Omega-3 Long-Chain Fatty Acids During Pregnancy

By **Arianna Carughi, Ph.D., C.N.S.**

In the past decade or so, scientists have recognized the importance of omega-3 long chain polyunsaturated fatty acids (n-3 LCFA) during pregnancy and early developmental life of the newborn child. Research shows that adequate levels of omega-3 fatty acids enhance development of the fetal and infant brain and may improve cognitive development, visual acuity, hand eye coordination and attention span. In addition, recent research indicates that maternal omega-3 fatty acid intake lowers the infant's risk of developing allergies and asthma later in life. Omega-3 fatty acids are also very important for maternal wellbeing. Not only do they protect from cardiovascular diseaseⁱ, lower triglyceride levelsⁱⁱ and may prevent inflammatory diseases like rheumatoid arthritis, they also have a specific effect on maternal health and the outcome of pregnancy: They appear to reduce incidence of preeclampsia, preterm labor and the risk for perinatal and postpartum depression.

What are Omega-3 Fatty Acids and why are they important for fetal and infant development?

Long-chain polyunsaturated fatty acids are longer versions of the essential fatty acid alpha linolenic acid (ALA, 18:3n-3). There are a total of eight (8) omega-3 fatty acids involved in human nutrition. Eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3) are the main n-3 LCFA in the diet and in tissues, though emerging evidence is drawing attention to docosapentaenoic acid (DPA, 22:5n-3) as well. Although they can be made in the body from ALA, synthesis is slow, especially for DHA. In the fetus and the newborn, synthesis is insufficient and so they depend practically entirely on the mother's supply.ⁱⁱⁱ Maternal omega-3 status is also critical during pregnancy and lactation because these nutrients are key building blocks for the brain and the nervous system. DHA is particularly concentrated in retinal and neuronal cell membranes. It is crucial for neurotransmission and neurogenesis.^{iv} The human brain has a growth spurt during the last trimester of pregnancy and the first postnatal months. At this time cerebral DHA increases dramatically, it more than triples. Studies have shown that the fetus accumulates about 65 mg DHA per day during the last trimester. During lactation, a typical mother would supply her infant about 80 mg DHA per liter of milk produced.^v Such losses to either the fetus or the infant exceed the intake of most pregnant and nursing women, and highlight a possible shortage for both the mother and the baby. Many studies have shown that maternal blood levels of omega-3 fatty acids determine both umbilical cord and milk levels of these nutrients. Therefore improving maternal omega-3 status throughout pregnancy and lactation ultimately benefits the infant.^{vi} Studies have shown that supplementing mothers' diets with omega-3 fatty acids during pregnancy improves infant's omega-3 status and attenuates depletion of maternal stores.^{vii} Finally, it is important to remember that after a woman's first pregnancy, maternal stores can become depleted and without supplementation return to pre-pregnancy levels.

Omega-3 Fatty Acids and outcome of pregnancy

Observational studies show that there is an association between high fish consumption and lower risk of preeclampsia (pregnancy-induced hypertension).^{viii} Pre-eclampsia, which complicates

approximately 5-10% of all pregnancies, is a leading contributor to maternal mortality, preterm delivery, fetal growth retardation, and perinatal mortality. Clinically, EPA and DHA have been shown to modulate inflammatory and vascular effects. Because pre-eclampsia and gestational hypertension are associated with vasoconstriction it has been postulated that omega-3 fatty acids may benefit these conditions. In addition, several observational studies show that supplementation with omega-3 fatty acids lengthen pregnancy by 4 to 6 days and lower the risk of pre-term deliveries among women with a history of premature births. ^{ix x}

Omega-3 Fatty Acids and Post-partum Depression

Higher dietary intake of n-3 LCFA during pregnancy may also be necessary to maintain both optimal physical and mental wellbeing. Mothers who rarely eat seafood or have low DHA breast milk concentration are more likely to suffer from postpartum depression. Although common in western countries, depression appears to be virtually absent in countries with high seafood intake. ^{xi} Observational data support the association between low omega-3 intake from seafood and increased risk of high levels of depressive symptoms during and after pregnancy. A prospective study showed that lower maternal intake of omega-3 from seafood was associated with high levels of depressive symptoms. Compared with women consuming more than 1.5 g omega-3 from seafood per week, those consuming none were more likely to have high levels of depressive symptoms at 32 weeks' into the pregnancy. ^{xii} A recent case-controlled study supports these findings: Women with high DHA, high total omega-3 and a low omega-6: omega-3 ratio, were associated with significantly lower risk of depression. The study results estimated that women with lower omega-3 levels as being six times more likely to be depressed compared to women who had higher omega-3 levels. ^{xiii} While this data looks promising, more controlled clinical studies are needed to establish the efficacy of omega-3 fatty acids in preventing or treating depression during or after pregnancy.

N-3 LCFA intake and cognitive development

There is a large and growing body of scientific literature which links DHA levels during pregnancy and a baby's behavioral performance. ^{xiv xv} A recent study shows that omega-3 intake during the last months of pregnancy enhances an infant's sensory, cognitive, and motor development. Researchers measured DHA concentration in the blood of the umbilical cord of 109 infants. DHA concentration in the umbilical cord is a good indicator of intra-uterine exposure to omega-3 fatty acids during the last trimester of pregnancy. Tests conducted on these infants at 6 and 11 months showed that their visual acuity as well as their cognitive and motor development was closely linked to DHA concentration in the umbilical cord blood at the time of their birth. Researchers observed that DHA concentration in the umbilical cord blood was in direct relation with the concentration found in a mother's blood, a reminder of the importance of a mother's diet in providing omega-3 fatty acids for the fetus. They also noted that DHA concentration was higher in the fetus's blood than in the mother's. ^{xvi}

In another study, researchers found that infants born to mothers with higher blood levels of DHA at delivery had greater attention span well into their second year of life. During the first six months of life, these infants were two months ahead of those babies whose mothers had lower DHA levels. The study involved about 70 mothers and infants. At the ages of 4-, 6-, and 8-months of age, the ba-

bies were tested for visual learning ability. Babies born to mothers who had higher blood levels of DHA scored better on the attention tests until 6 months of age, and they scored better on different tests designed to measure visual learning in older babies at 1 year and 18 months. ^{xvii}

A large longitudinal study of more than 11,000 pregnant women compared their children's cognitive performance from age 6 months to 8 years. Children were grouped according to the amount of seafood mothers ate during pregnancy. Maternal seafood intake during pregnancy of less than 340 g per week was associated with increased risk of their children being in the bottom 25% for verbal intelligence quotient (IQ) compared with mothers who consumed more than 340 g per week. Low maternal seafood intake was also associated with increased risk of suboptimum outcomes for pro-social behavior, fine motor, communication, and social development scores. For each measure tested, the lower the intake of seafood during pregnancy, the higher the risk of suboptimum developmental outcome. ^{xviii} In another study Helland et al ^{xix} reported that supplementing pregnant and lactating women with omega-3 fatty acids promoted higher IQ scores at 4 years of age as compared with maternal supplementation with omega-6 polyunsaturated fatty acids. In a follow-up study, the children were examined at 7 years of age. Researchers found that mother's who had higher plasma concentrations of ALA and DHA during pregnancy did better in sequential processing. ^{xx}

A recent study looked at the association between maternal fish intake during pregnancy and hyperactivity scores and verbal IQ in their children. After adjustment for potential confounding factors researchers found that children whose mothers had eaten oily fish in early pregnancy had a reduced risk of hyperactivity compared to those whose mothers did not eat oily fish. Children whose mothers had eaten fish (whether oily or non-oily) in late pregnancy had a verbal IQ that was 7.55 points higher than those whose mothers did not eat fish. ^{xxi}

Prenatal n-3 LCFA and allergic and inflammatory disorders

Over the past decades there has been an increase in childhood allergies. Some scientists have postulated that a contributing factor may be the lower maternal intake of omega-3 fatty acids in the modern, western diet. Studies show that omega-3 fatty acid supplementation during the last trimester dampen certain immune responses (e.g. PGE2 secretion) involved in allergic inflammation. ^{xxii} In a recent study of 150 pregnant women, who suffered from allergies themselves or had a husband or previous child with allergies, supplementation of omega-3 fatty acids lowered risk of allergic disorders in their infants. In this randomized placebo-controlled trial, mothers received an EPA/DHA supplement from the 25th week of pregnancy through the 3rd or 4th month of lactation. Maternal omega-3 fatty acid supplementation decreased the risk of food allergies and eczema in infants with a family history of allergic disease. ^{xxiii} This study follows a large cross-sectional study in Japan showing that DHA intake is associated with a lower prevalence of atopic eczema in pregnant women. ^{xxiv} Finally, a long-term population-based study showed that children from mothers that received an omega-3 fatty acid supplement during gestation had 63% lower risk of developing asthma and 87% lower risk of allergic asthma. ^{xxv}

Sources of n-3 FA in the diet

Fish: Fish are generally regarded as the most omega-3 rich foods. Not all fish are good sources however. The high levels of omega-3 fatty acids are found in oily fish, like salmon, mackerel,

herring, sardines, anchovies, and fresh or frozen tuna. Fresh water fish on the other hand often deliver much lower amounts. It is also important to keep in mind that fish may be contaminated with mercury, so choice of safe types of fish is essential. Farmed salmon may contain unsafe levels of the toxic chemical dioxin and polychlorinated byphenols. Other fish from high in the food chain where toxins can accumulate, like sword fish or shark are best avoided during pregnancy and lactation.

Fish oil supplements: High quality fish oil supplements offer convenience of daily intake and the assurance of consistent potency. Look for whole food sources from fish found naturally in the human food chain. Also look for “complete” fish oil supplements that deliver “standardized” amounts of all eight (8) omega-3 fatty acids just as they appear in fish naturally. Make sure the product is screened to assure the absence of potential contaminants.

Fortified foods: Fortification of some traditional foods with omega-3 fatty acids is becoming more common in some parts of the world. If the goal is to supplement the diet with omega-3 fatty acids missing as a result of low fish consumption be sure to look for products that contain more than just one or two omega-3 fatty acids in isolation.

Plant sources: A few plants, like walnuts or borage oil are relatively rich sources of omega-3 fatty acids and though their dietary contribution can be significant it is important to remember that these are in the basic alpha linolenic acid form and must be converted (elongated) by the body to the more active forms like DHA, DPA or DHA.

How much do I need? While the greatest need for omega-3 fatty acids is during the third trimester of pregnancy and throughout lactation, these nutrients should present in the diet, in adequate amounts on a regular basis. While it may be early to formulate specific recommendations for omega-3 fatty acid intakes during pregnancy and lactation, many scientists now recommend that women of reproductive age should achieve an average dietary omega-3 fatty acid intake of at least 650 mg/day.

xxvi

References

- ⁱ Kris-Etherton, PM, Harris, W.S., Appel, L.J. AHA Scientific Statement: Fish Consumption, Fish Oil, Omega-3 Fatty Acids, and Cardiovascular Disease. *Arterioscler Thromb Vasc Biol* 2003; 23:e20-e31
- ⁱⁱ von Schacky, C, Harris, WS Cardiovascular Benefits of Omega-3 Fatty Acids *Cardiovasc Res* 2007; 73:310-315
- ⁱⁱⁱ Clandinin MT, Chappell JE, Leong S et al. Intrauterine fatty acid accretion rates in human brain: implications for fatty acid requirements. *Early Human Development*. 1980; 4:121-129
- ^{iv} Innis SM. Fatty acids and early human development. *Early Human Dev* 2007; 83; 761-766
- ^v Innis SM. Perinatal biochemistry and physiology of long-chain polyunsaturated fatty acids. *J Pediatrics* 2003; 143:S1-S8
- ^{vi} Kilari AS, Mehendale SS, Dangat KD. et al Long chain polyunsaturated fatty acids in mothers and term babies. *J Perinat Med*. 2009 Jun 3. [Epub ahead of print]
- ^{vii} Krauss-Etshmann S, Shadid R, Campoy C, et al Effects of fish-oil and folate supplementation of pregnant women on maternal and fetal plasma concentrations of docosahexaenoic acid and eicosapentaenoic acid: a European randomized multicenter trial. *Am J Clin Nutr*. 2007; 85(5):1392-400
- ^{viii} Makrides M and Gibson RA. Long chain polyunsaturated fatty acid requirements during pregnancy and lactation. *Am J Clin Nutr* 2000; 71:301S-311S
- ^{ix} Olsen SF, Secher NJ, Tabor A, et al. Randomized clinical trials of fish oil supplementation in high risk pregnancies. *Br J Obstet Gynaecol* 2000; 107:382-95
- ^x Cetin I, Koletzko B. Long-chain omega-3 fatty acid supply in pregnancy and lactation. *Curr Opin Clin Nutr Metab Care*. 2008; 11(3):297-302
- ^{xi} Golding J, Steer C, Emmett P. et al. High levels of depressive symptoms in pregnancy with low omega-3 fatty acid intake from fish. *Epidemiology*. 2009; 20:598-603

- ^{xii} Golding J, Steer C, Emmett P. et al. High levels of depressive symptoms in pregnancy with low omega-3 fatty acid intake from fish Epidemiology. 2009 Jul;20(4):598-603.
- ^{xiii} Rees AM, Austin MP, Owen C, Parker G. Omega-3 deficiency associated with perinatal depression: case control study. Psychiatry Res. 2009; 166:254-9
- ^{xiv} Susan E Carlson Docosahexaenoic acid supplementation in pregnancy and lactation Am J Clin Nutr 2009; 89:678S-684S,
- ^{xv} Fleith M, Clandinin MT. Dietary PUFA for preterm and term infants: review of clinical studies. Crit Rev Food Sci Nutr. 2005; 45:205-29
- ^{xvi} Jacobson JL, Jacobson SW, Muckle G. et al. Beneficial effects of polyunsaturated fatty acids on infant Development: Evidence from the Inuit of Artic Quebec J Pediatrics 2008; 152:356-64
- ^{xvii} Colombo J, Kannass KN, Shaddy DJ, et al. Maternal DHA and the development of attention in infancy and toddlerhood. Child Development. 2004; 5:1254-67.
- ^{xviii} Hibbeln JR, Davis JM, Steer C, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. Lancet. 2007; 369(9561):578-85
- ^{xix} Helland IB, Smith L, Saaem K. et al. Maternal supplementation with very-long chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. Pediatrics 2009; 111:e39-e44
- ^{xx} Helland IB, Smith L, Blomén B, et al. Effect of supplementing pregnant and lactating mothers with n-3 very-long-chain fatty acids on children's IQ and body mass index at 7 years of age. Pediatrics 2008; 122:e472-9.
- ^{xxi} Gale CR, Robinson SM, Godfrey KM et al. Oily fish intake during pregnancy--association with lower hyperactivity but not with higher full-scale IQ in offspring. J Child Psychol Psychiatry. 2008; 49:1061-8
- ^{xxii} Warstedt K, Furuholm C, Duchén K, et al. The effects of omega-3 fatty acid supplementation in pregnancy on maternal eicosanoid, cytokine and chemokine secretion. Pediatr Res. 2009 Apr 22. [Epub ahead of print]
- ^{xxiii} Furuholm C, Warstedt K, Larsson J, et al. Fish oil supplementation in pregnancy and lactation may decrease the risk of infant allergy. Acta Paediatr. 2009 Jun 1. [Epub ahead of print]
- ^{xxiv} Miyake Y, Sasaki S, Tanaka K, et al. Relationship between dietary fat and fish intake and the prevalence of atopic eczema in pregnant Japanese females: baseline data from the Osaka Maternal and Child Health Study. Asia Pac J Clin Nutr. 2008; 17:612-9
- ^{xxv} Olsen SF, Østerdal ML, Salvig JD, et al. Fish oil intake compared with olive oil intake in late pregnancy and asthma in the offspring: 16 y of registry-based follow-up from a randomized controlled trial. Am J Clin Nutr. 2008; 88:167-75
- ^{xxvi} Simopoulos ATP, Leaf A, Salem N. Essentiality of and recommended dietary intakes for omega-6 and omega-3 fatty acids. Ann Nutr Metab. 1999; 43:127-130



Arianna Carughi, Ph.D., C.N.S.
 Nutritional Scientist
 Stanford Fellow
 Member, GNLD Scientific Advisory Board

Dr. Carughi received her B.A. in Biology/Ecology and Conservation from Vassar College, her Master of Sciences degree in Human Nutrition from Columbia University, and her Ph.D. in Nutritional Sciences from the University of California at Berkeley. Dr. Carughi also holds the title of Fellow at Stanford University for her postdoctoral research, and the title of Certified Nutrition Specialist (C.N.S.), from the American College of Nutrition. The recipient of the International Institute of Education Scholarship, Dr. Carughi has received numerous fellowships, grants, and honors, including the Neizer Fellowship from Stanford University and a National Institute of Health (NIH) research grant in experimental nutrition.

Dr. Carughi's research has been published in numerous scientific journals and presented at prestigious scientific conferences. As a researcher in nutritional biochemistry at Columbia, Berkeley, and Stanford Universities, Dr. Carughi focused on the role that nutrients play in growth and development.

Fluent in English, Spanish, and Italian, and with extensive contacts within the international scientific community, Dr. Carughi believes strongly that a fundamental purpose of scientific research is to contribute to creating new products that have the potential to literally change people's lives for the better.