# Omega-3 Fatty Acids and Pregnancy

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*Omega-3 fatty acids are essential fatty acids that must be consumed in the diet. Adequate consumption of omega-3 fatty acids is vitally important during pregnancy as they are critical building blocks of fetal brain and retina. Omega-3 fatty acids may also play a role in determining the length of gestation and in preventing perinatal depression. The most biologically active forms of omega-3 fatty acids are docosahexaenoic acid and eicosapentaenoic acid, which are primarily derived from marine sources such as seafood and algae. Recent surveys, however, indicate that pregnant women in the United States and in other countries eat little fish and therefore do not consume enough omega-3 fatty acids, primarily due to concern about the adverse effects of mercury and other contaminants on the developing fetus. This review discusses the benefits of omega-3 fatty acid consumption during pregnancy and provides guidelines for obstetricians advising patients.*

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Fish and other seafood contain long-chain omega-3 polyunsaturated fatty acids (PUFA), which are essential nutrients. The most biologically active omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Both have been shown to have multiple beneficial effects, including improving childhood development when ingested during pregnancy.[1] Fetal brain growth accelerates during the second half of pregnancy, and the rate of growth remains high during the first year of life with continued growth for the next several years. It is likely that, during pregnancy, omega-3 requirements increase over normal to support fetal growth, particularly of the brain and eyes. Animal studies have demonstrated that deprivation of omega-3 fatty acids during pregnancy is associated with visual and behavioral deficits that cannot be reversed with postnatal supplementation.[2] For these reasons, it is important for omega-3 fatty acids to be supplied to the fetus in adequate amounts throughout pregnancy.[1] To optimize pregnancy outcomes and fetal health, consensus guidelines have recommended that pregnant women consume at least 200 mg of DHA per day.[3] A woman can achieve this threshold by consuming 1 to 2 servings of seafood per week, dietary intake that is consistent with the current US Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) advisory.[4]

Seafood can also contain organic mercury and other harmful toxins (eg, polychlorinated biphenyls [PCBs]), which could be harmful to the growing fetus. For this reason, the FDA/EPA recommends limiting fish consumption to 2 servings (approximately 340 g or 12 oz of seafood) per week.[4] Recent surveys have demonstrated that, despite the FDA/EPA advisory indicating that up to 2 servings of fish is safe in pregnancy, many pregnant women consume little to no fish, thereby potentially depriving the fetus of necessary nutrients.[5,6] Furthermore, some women indicated that a physician's advice played a key role in their decision whether to eat fish during pregnancy.[6] This leaves the obstetrician with the role of counseling patients on the appropriate amount of seafood intake during pregnancy to maximize benefits and minimize risk. This review provides the obstetrician and health care provider with the proper information to advise patients on how to consume an adequate amount of omega-3 fatty acids during pregnancy.

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## What Are Omega-3 Fatty Acids?

Essential fatty acids are lipids that cannot be synthesized within the body and must be ingested through the diet or from supplements.[7] Two families of essential fatty acids, omega-3 and omega-6, are required for physiologic functions including oxygen transport, energy storage, cell membrane function, and regulation of inflammation and cell proliferation. Humans can synthesize many other fatty acids, such as saturated and monounsaturated fatty acids, but are incapable of making fats with the first double bond at the omega-3 and omega-6 position. These polyunsaturated fatty acids are required for normal growth and maturation of many organ systems, most importantly the brain and eye.[8]

The parent fatty acid for omega-3s is $\alpha$-linolenic (ALA) acid and for omega-6s the parent fatty acid is linoleic acid (LA). LA is converted to the biologically active omega-6 fatty acid, arachidonic acid (AA), which is involved in cell-signaling pathways and functions as a precursor for proinflammatory eicosanoids. ALA is converted to the biologically active omega-3 fatty acid, EPA, which, in turn, is converted to the omega-3 fatty acid, DHA. DHA is the critical component of cell membranes in the brain and retina, where it is involved in visual and neural function as well as neurotransmitter metabolism.[8] The accumulation of DHA begins in utero and is derived predominantly through placental transfer. Ultimately, fetal DHA concentrations are determined by maternal diet as the human body is not efficient at converting ALA to DHA.

Diets that are balanced in both omega-6 and omega-3 may be less inflammatory and immunosuppressive.[9] Unfortunately, the American diet is lopsided with too many omega-6s and too few omega-3s, which may lead to a proinflammatory milieu. This may increase the risk of chronic diseases such as cardiovascular disease, type 2 diabetes, and osteoarthritis.[9]

## Dietary Recommendations for Omega-3 Fatty Acids

Optimal fetal neurodevelopment is dependent on many essential nutrients, including DHA and EPA, which can only be obtained from dietary sources.[3] The richest sources of these omega-3 fatty acids are marine sources, such as seafood and fish oil supplements.[10] Other sources of omega-3 fatty acids such as flax seed oil and vegetable oils, however, contain ALA that needs to be converted to longer-chain EPA and DHA to become biologically useful.

In 2004, the FDA advised all pregnant women to limit seafood consumption to 340 g (2 6-oz servings) per week to limit fetal exposure to trace amounts of neurotoxins.[4] This recommendation was later adopted by the American College of Obstetricians and Gynecologists (ACOG).[11] This amount of fish would provide approximately 200 mg of DHA per day.[12] Alternate sources of DHA include fish oil capsules, which provide variable amounts of DHA (ranging from 150-1200 mg/d), and are low in contaminants such as mercury. Many prenatal vitamins contain up to 200 to 300 mg of DHA. DHA-enriched eggs are another source of omega-3 fatty acids and may contain up to 150 mg of DHA per egg.

## Mercury Toxicity

Mercury is a reactive heavy metal emitted from both natural and human sources. It comes most commonly from waste incineration and coal burning.[13,14] Mercury cycles from rainwater into lakes and oceans where it is converted into organic methylmercury. Although inorganic mercury is poorly absorbed and does not readily cross tissue barriers, methylmercury is a known neurotoxin and accumulates in aquatic food chains with levels depending on the predatory nature and lifespan of the species. Larger, longer-living predators—swordfish, king mackerel, shark, and tilefish—have higher tissue concentrations than smaller, short-lived species (eg, salmon, pollock). Thus, pregnant women are advised to avoid consumption of these higher mercury-containing fish (Table 1). Both ACOG and the FDA/EPA recommend consuming 2 servings of fish and seafood a week, as long as they have low mercury content.[4,11] This amount does not appear to pose a toxic risk to the mother or fetus.

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Because methylmercury crosses the placenta, most data suggest that—similar to data on other heavy metals such as lead—fetal exposure correlates directly with maternal ingestion. A positive correlation between maternal seafood consumption and neurotoxicity in exposed fetuses was first noted in women exposed to the industrially polluted Minimata Bay in Japan in the 1950s.[13] As a result, public health agencies set a daily dose of methylmercury of 0.1 µg per kilogram of body weight per day as a justifiable level for the protection of the unborn fetus.[15]

More recently, 329 pregnant women who lived within 2 miles of the World Trade Center (WTC) site during the time of the collapse were identified and followed throughout their pregnancies.[16] It was known that there was an increase in the release of heavy metals, including mercury, into the surrounding environment. Hospital staff collected maternal and cord blood at delivery. Women and infants were interviewed at 6-month intervals for 4 years after birth. Mercury blood levels were significantly higher in women who ate fish/seafood during pregnancy in addition to WTC exposure ($P < .001$). Mental and psychomotor developmental evaluations and cord mercury levels were significantly negatively associated with the 36- and 48-month IQ scores. No child with a cord mercury level higher than 13 µg/L had a full IQ score greater than 100.[16]

The association between methylmercury exposure in utero and adverse developmental outcome has not been consistently reproduced. In 2006, a longitudinal analysis was made in 740 children born to mothers in the Republic of the Seychelles.[17] The investigators compared the effect of prenatal methylmercury exposure obtained from maternal hair analysis and the IQ of the child. The average mercury in the hair samples was 6.8 ppm. No association was found between levels of prenatal exposure and child IQ on repeated test

**Table 1**
**Fish Consumption During Pregnancy**

| Fish to Consume* | Fish to Avoid |
|---|---|
| Shrimp | Shark |
| Salmon | Swordfish |
| Pollock | King mackerel |
| Catfish | Tile fish |
| Scallops | |
| Sardines | Use caution for fish caught in local rivers and streams that may have high mercury content; check with local authorities before consuming fish from these waters. |
| Light tuna | |

*Have less than 0.05 ppb of mercury per 6-oz serving, except light tuna, which has < 0.12 µg/g.[15]

scores at different time points up to age 9 years.

Nonetheless, the preponderance of data indicates that methylmercury is a neurotoxin to which the developing fetal brain is particularly sensitive. Pregnant women can limit the effects of contaminants on their fetus by limiting fish intake to 2 servings per week and by avoiding larger predatory fish that tend to be higher in mercury concentration.

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## Omega-3 Fatty Acids: Effect on the Fetus and Pregnancy

Numerous benefits have been associated with omega-3 fatty acid consumption during pregnancy and the postpartum period, whether it is consumed in the diet with seafood or via supplements such as fish oil.

### *Fetal/Neonatal Development*

Data derived from observational studies have found that omega-3 fatty acid consumption during pregnancy either in the diet or via supplements is associated with improved neurodevelopmental outcomes in the child.[18-21] Investigators have used a variety of tests, such as general developmental milestones, problem solving, and language development, to assess neurodevelopmental outcomes among infants whose mothers were supplemented with fish oil compared with those who were not. A 2004 study by Oken and colleagues found that higher maternal fish consumption during pregnancy resulted in higher novelty preference on visual recognition memory and higher scores of verbal intelligence.[18]

Another group of investigators compared developmental outcomes in newborns from almost 9000 mothers consuming different amounts of fish and seafood. This observational cohort study—Avon Longitudinal Study of Parents and Children (ALSPAC)[19]—invited women to complete seafood consumption surveys and answer questions about the development and behavior of their children at ages 6, 18, 30, 42, and 81 months. Subjects were grouped according to their seafood intake: none, 1 to 340 g per week, and more than 340 g per week. Mothers who ate more than 340 g per week of seafood had children with no worse outcomes than children born to women who ate less than that amount of seafood. Children born to mothers who reported no seafood intake had the greatest risk of adverse or suboptimal outcomes, defined as testing in the lowest quartile for verbal and performance IQ at age 8 years, behavioral problems at age 7 years, and poor scores on early development tests evaluating fine motor skills, social skills, and communication skills. For those women who did consume seafood during pregnancy, the higher the maternal seafood intake was, the less likely the child was to have these suboptimal outcomes.[19]

Data from randomized, controlled trials have generally supported these findings. Similar results were seen in a randomized, double-blind study conducted in women who were supplemented with either cod liver oil or placebo during pregnancy and lactation.[20] The children born to the mothers supplemented with cod liver oil had a 4% point advantage in scores on the Kaufman Assessment Battery for Children (K-ABC). A more recent randomized, controlled trial that followed infants up to age 18 months, however, found no difference in cognitive and language scores between offspring of women supplemented with fish oil during pregnancy and those who received placebo.[21]

Omega-3 fatty acids seem to be important during lactation as well. Lactating women who received 200 mg of DHA per day for 4 months had infants who performed significantly better on the Bayley Psychomotor Development Index after 30 months compared with women who received a vegetable oil supplement.[1] Also, fish oil supplementation taken during pregnancy and lactation resulted in a decreased risk of infant allergies.[22] Women with allergies or those with a spouse or a child with allergies were randomized to 2.7 g omega-3 fatty acids or a placebo starting at the 25th week of pregnancy up until 3 to 4 months of lactation. During the first 12 months, babies born from mothers in the omega-3 group had decreased risk of developing food allergies and IgE-associated eczema.

A more recent area of investigation has been the effect of omega-3 fatty acids on the prevention and management of neonatal hypoxic ischemic brain injury. A number of studies using animal models have shown that both pretreatment with DHA and treatment with DHA reduce the degree of functional deficits after an hypoxic ischemic injury.[23-25] Because hypoxic ischemic injury complicates 2 to 9 births per thousand and may be responsible for up to 14% of all cases of cerebral palsy,[26-28] these studies and future investigation in this area may have important implications in preventing the long-term effects of hypoxic ischemic encephalopathy.

The preponderance of data suggests that omega-3 fatty acid intake during pregnancy is important for fetal brain development and the child's subsequent neurodevelopment, and that omega-3 fatty acid deprivation during pregnancy is associated with impaired developmental and behavior scores.

*Preterm Birth*

Preterm birth remains the leading cause of neonatal morbidity and mortality in the United States, with the pathophysiology largely unknown. Modifiable risk factors such as maternal diet remain an area of research. A high ratio of omega-6 to omega-3 fatty acids will result in increased proinflammatory eicosanoid production (ie, prostaglandin $E_2$ [$PGE_2$] and prostaglandin $F_{2\alpha}$ [$PGF_{2\alpha}$]). These metabolites have been associated with the initiation of labor and preterm labor. Including more EPA in the diet may lead to a reduction in the production of proinflammatory eicosanoids and increased production of prostacyclin ($PGI_2$), which may promote myometrial relaxation. Omega-3 fatty acids downregulate the production of prostaglandins $PGE_2$ and $PGF_{2\alpha}$, and may thereby inhibit the parturition process.[29,30]

The hypothesis that dietary supplementation of omega-3 fatty acids could prevent preterm birth originated from studies conducted in the Faroe Islands.[31] Compared with the diet in Denmark, the population of the Faroe Islands has a higher intake of marine foods, and babies born to these women have higher birth weights (about 200 g) at term. In fact, birth weights of babies from the Faroe Islands are higher than those in 33 other countries.[31]

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A number of randomized, controlled trials have attempted to validate these findings, but with variable results. Four randomized, controlled trials have demonstrated either a reduction in the rate of preterm birth or an increase in the average length of gestation in either primary or secondary analysis (Table 2):

- In one trial, 533 women were randomized to receive either capsules of fish oil, olive oil, or no oil from 30 weeks of gestation until delivery.[32] Compared with women receiving the other 2 treatments, those who received fish oil had a significantly longer gestational length by approximately 4 days (279.4 vs 283.3 days; $P < .006$).

**Table 2**
**Omega-3 Fatty Acid Supplementation Versus Placebo and Gestational Age at Delivery: Studies Demonstrating Pregnancy Prolongation**

| Study | No. of Patients | Intervention | Outcome |
|---|---|---|---|
| Olsen SF et al[32] | 533 | Fish oil vs olive oil vs placebo 30 weeks until delivery | Fish oil prolonged gestation (283.3 vs 279.4 days; $P < .006$) |
| Olsen SF et al[33] | 232 | Fish oil vs olive oil from 20 weeks until delivery | Fish oil decreased risk of recurrent PTB, 33% to 21% (OR 0.54; $P = .05$)<br>Fish oil increased post-term pregnancy rate (RR 2.5; $P = .01$) |
| Smuts CM et al[34] | 350 | DHA-enriched eggs vs standard eggs from 24-28 weeks until delivery | DHA enriched eggs prolonged gestation (276.5 vs 270.5 days; $P = .009$) |
| Makrides M et al[21] | 2399 | Fish oil vs vegetable oil from 19 weeks until delivery | Lower risk of PTB < 34 weeks 1.09% vs 2.25% (RR 0.49; 95% CI, 0.25-0.94); higher risk of post-term pregnancy, 17.6% vs 13.7% (adjusted RR, 1.28; 95% CI, 1.06-1.54) (both secondary outcomes) |

CI, confidence interval; DHA, docosahexanoic acid; OR, odds ratio; PTB, preterm birth; RR, relative risk.

- In one of the most compelling trials, the Fish Oil Trials in Pregnancy (FOTIP) study from Europe,[33] 232 women with a history of a prior preterm birth were randomized to fish oil or olive oil capsules from 20 weeks of gestation to delivery. Fish oil reduced the risk of recurrent preterm birth from 33% to 21% (odds ratio [OR], 0.54; 95% confidence interval [CI], 0.30-0.98; $P = .05$). Interestingly, this trial also found an increased rate of post-term pregnancies in the group supplemented with fish oil with a relative risk (RR) of 2.5 (95% CI, 1.2-4.97; $P = .01$).
- In a trial in the United States, pregnant women were randomly assigned to consume DHA-enriched eggs or standard eggs starting at 24 to 28 weeks of gestation to delivery.[34] The initial analysis did not find a statistical difference in mean gestational age at delivery between groups (271.6 vs 274.1 days, respectively). However, when the data were adjusted for confounders such as maternal body mass index at enrollment and number of prior pregnancies, there was a 6-day increase in gestational age at delivery (from 270.5 to 276.5 days; $P = .009$). This study was particularly interesting because it demonstrated that even small amounts of omega-3 fatty acids (up to 284 mg/d) could be of benefit during pregnancy.
- A recent randomized, controlled trial powered to evaluate the effect of DHA supplementation during pregnancy on maternal depression and child neurodevelopment randomized pregnant women to fish oil or vegetable oil capsules from 19 weeks of gestation to delivery.[21] Although there was no difference between the groups in depressive symptoms or neurodevelopmental outcome, the group that received fish oil had a significantly lower risk of preterm birth $<$ 34 weeks of gestation in secondary analysis: 1.09% versus 2.25% (adjusted RR, 0.49; 95% CI, 0.25-0.94). This trial also found that fish oil supplementation was associated with an increased rate of postterm births: 17.6% versus 13.7% (adjusted RR, 1.28; 95% CI, 1.06-1.54).

On the other hand, an equal number of trials have found no impact of fish oil or omega-3 fatty acid supplementation on the rate of preterm birth or length of gestation (Table 3):

- Primigravid Mexican women (n = 1094) supplemented with 400 mg of DHA from 18 weeks until delivery did not have longer gestations or a reduced risk of preterm birth compared with placebo.[35] However, women supplemented with DHA delivered babies who weighed more and had larger head circumferences. Prepregnancy DHA intake was inadequate in this population, only about 55 mg per day. Thus, small amounts of DHA may be helpful to improve fetal growth in populations with low baseline DHA intake.
- Bulstra-Ramakers and colleagues conducted a randomized, controlled trial in 68 pregnant women who received either fish oil or control capsules.[36] The study was powered to look specifically at the effects of fatty acid supplementation on intrauterine growth restriction and pregnancy-induced hypertension. A secondary analysis examined gestational age at delivery, and no significant difference was observed between the 2 groups.
- In Norway, 594 pregnant women were randomized to fish oil or corn oil supplements from 17 to 19 weeks of gestation until delivery.[37] No benefit was seen on gestational age from fish oil supplementation. Unfortunately, half of the participants

**Table 3**
**Omega-3 Fatty Acid Supplementation Versus Placebo and Gestational Age at Delivery: Studies Demonstrating No Pregnancy Prolongation**

| Study | No. of Patients | Intervention | Outcome |
|---|---|---|---|
| Ramakrishman U et al[35] | 1094 | DHA 400 mg vs placebo from 18 weeks until delivery | No difference in PTB |
| Bulstra-Ramakers MT et al[36] | 68 | Fish oil vs placebo | No difference in gestational age at delivery |
| Helland IB et al[37] | 594 | Fish oil vs corn oil from 17-19 weeks until delivery | No difference in gestational age at delivery |
| Harper M et al[38] | 852 | Fish oil + 17P vs placebo + 17P from 16-22 weeks until 36 weeks | No difference in PTB |

17P, 17-α hydroxyprogesterone caproate; DHA, docosahexaenoic acid; PTB, preterm birth.

in each group were excluded due to voluntary withdrawal from the trial.

- In another US trial, women with a history of preterm birth who were receiving 17 α-hydroxyprogesterone caproate (17P) did not achieve additional benefit from supplemental omega-3 fatty acids.[38] The women were enrolled in the study from 13 centers around the United States and were randomized to 2 g of omega-3 fatty acids per day or a matching placebo. The number of deliveries before 37, 35, and 32 weeks did not differ between the 2 groups. These data suggest that women already receiving 17P did not derive additional benefit from omega-3 fatty acid supplementation.

There are conflicting data regarding the impact of omega-3 fatty acids on the length of gestation. At present, there are not enough data to recommend omega-3 fatty acid supplementation for the sole purpose of prolonging gestation or reducing the risk of preterm birth. However, the amount of omega-3 fatty acids derived from the recommended amount of seafood intake or daily supplementation to optimize fetal brain development may have the added benefit of reducing the risk of preterm birth in high-risk populations (ie, women with a history of preterm birth or women with low baseline omega-3 fatty acid intake).

### *Depression and Pregnancy*

Major depressive disorder affects 10% to 20% of perinatal women. Pregnancy-related and postpartum depression have been shown to affect child attachment, cognitive development, and behavior. Previous research has demonstrated that increased intake of long-chain PUFA during pregnancy had reduced the risk of depressive symptoms in the postpartum period.[21] Polyunsaturated fatty acids have been shown to decrease proinflammatory cytokine production, which is elevated in depressed patients.[39] Omega-3 fatty acids are transferred from the mother to the fetus during pregnancy, thereby depleting maternal stores. Because many women remain reluctant to take antidepressant medication while they are pregnant or breastfeeding, it has been postulated that increasing intake of omega-3 fatty acids from the diet and supplements could theoretically prove beneficial and protective of maternal affect.

Epidemiologic data have shown that low seafood intake during pregnancy correlates with higher levels of depressive symptoms during pregnancy.[40] However, randomized, controlled trials have failed to demonstrate a clear benefit to omega-3 fatty acid supplementation during pregnancy and postpartum to prevent depressive symptoms.[21,41] One difficulty with randomized, controlled trials particularly in studying depression is that often the control group has lower than expected rates of depressive symptoms. This may be explained by the Hawthorn effect in which increased contact with researchers may in and of itself have decreased depressive symptoms.[21,42] As with the effect of omega-3 fatty acids on gestational length, further studies are necessary to clarify the effect of omega-3 fatty acid supplementation on perinatal depression.

## Conclusion

Omega-3 fatty acids are essential for life and must be obtained from dietary means, either from seafood or fish oil capsules. It is likely that, during pregnancy, omega-3 requirements increase over normal to support fetal growth, particularly of the brain and eyes. Two 6-ounce servings of low-mercury fish and seafood are recommended per week for pregnant women. Consuming more may pose a risk of mercury toxicity, although the absolute risk is small. Alternatively, an adequate supply of omega-3 fatty acids can be derived from supplements such as fish oil and some prenatal vitamins. Fish oil capsules are nearly devoid of mercury and other harmful compounds like PCBs and can serve to augment omega-3 fatty acids in the diet. Prospective studies in pregnant women who consumed the recommended fish intake or received supplements of fish oil generally demonstrate a beneficial effect on neurodevelopmental outcomes of offspring. At present, there are not enough data to recommend omega-3 fatty acid supplementation for the sole purpose of reducing the risk of preterm birth or preventing perinatal depression as data on the effect of omega-3 fatty acids on gestational length, risk of preterm birth, and perinatal depression are conflicting. ■

### References


1. Jensen CL. Effects of n-3 fatty acids during pregnancy and lactation. *Am J Clin Nutr.* 2006;83(6 suppl):1452S-1457S.
2. Nesheim MC, Yaktine AL, eds. *Seafood Choices: Balancing Benefits and Risks.* Washington, DC: The National Academies Press; 2007.
3. Koletzko B, Lien E, Agostoni C, et al; World Association of Perinatal Medicine Dietary Guidelines Working Group. The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. *J Perinat Med.* 2008;36:5-14.
4. What you need to know about mercury in fish and shellfish. US Food and Drug Administration Web site. http://www.fda.gov/food/foodsafety/product-specificinformation/seafood/foodbornepathogenscontaminants/methylmercury/ucm115662.htm. Updated September 17, 2009. Accessed October 23, 2010.
5. Frithsen I, Goodnight W. Awareness and implications of fish consumption advisories in a women's health setting. *J Reprod Med.* 2009;54:267-272.
6. Bloomingdale A, Guthrie LB, Price S, et al. A qualitative study of fish consumption during pregnancy. *Am J Clin Nutr.* 2010;92:1234-1240.
7. Bell SJ, Bradley D, Forse RA, Bistrian BR. The new dietary fats in health and disease. *J Am Diet Assoc.* 1997;97:280-286; quiz 287-288.
8. Innis SM, Friesen RW. Essential n-3 fatty acids in pregnant women and early visual acuity maturation in term infants. *Am J Clin Nutr.* 2008;87:548-557.
9. Simopoulos AP, Leaf A, Salem N Jr. Essentiality of and recommended dietary intakes for omega-6

and omega-3 fatty acids. *Ann Nutr Metab.* 1999;43:127-130.

10. Greenberg JA, Bell SJ, Ausdal WV. Omega-3 fatty acid supplementation during pregnancy. *Rev Obstet Gynecol.* 2008;1:162-169.
11. ACOG Updates Definitive Guide to Pregnancy: *Your Pregnancy & Birth*, Fourth Edition, Gives Women the Latest News on Genetic Disorders, Prenatal Tests, DOs and DON'Ts, and Exercise [press release]. May 10, 2005. http://www.acog.org/from_home/publications/press_releases/nr05-10-05-2.cfm. Accessed November 16, 2010.
12. Koletzko B, Cetin I, Brenna JT; Perinatal Lipid Intake Working Group; Child Health Foundation; Diabetic Pregnancy Study Group; European Association of Perinatal Medicine; European Association of Perinatal Medicine; European Society for Clinical Nutrition and Metabolism; European Society for Paediatric Gastroenterology, Hepatology and Nutrition, Committee on Nutrition; International Federation of Placenta Associations; International Society for the Study of Fatty Acids and Lipids. Dietary fat intakes for pregnant and lactating women. *Br J Nutr.* 2007;98:873-877.
13. Mozaffarian D, Rimm EB. Fish intake, contaminants and human health—evaluating the risks and the benefits. *JAMA.* 2006;296:1885-1899.
14. Mahaffey KR. Fish and shellfish as dietary sources of methylmercury and the omega-3 fatty acids, eicosapentaenoic acid and docosahexaenoic acid: risks and benefits. *Environ Res.* 2004;95:414:428.
15. US Environmental Protection Agency Office of Air. *Mercury Study Report to Congress: Volume VII: Characterization of Human Health and Wildlife Risks from Mercury Exposure in the United States.* Washington, DC: US Environmental Protection Agency Office of Air; December 1997. EPA-452/R-97-009. http://www.epa.gov/ttn/oarpg/t3/reports/volume7.pdf Accessed December 10, 2010.
16. Lederman SA, Jones RL, Caldwell KL, et al. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. *Environ Health Perspect.* 2008;116:1085-1091.
17. Strain JJ, Davidson PW, Bonham MP, et al. Associations of maternal long-chain polyunsaturated fats, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. *Neurotoxicology.* 2008;29:776-782.
18. Oken E, Bellinger DC. Fish consumption, methylmercury and child neurodevelopment. *Curr Opin Pediatr.* 2008;20:178-183.
19. 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;369:578-585.
20. Helland IB, Smith L, Saarem 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.* 2003;111:e39-e44.
21. Makrides M, Gibson RA, McPhee AJ, et al; DOMInO Investigative Team. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children: a randomized controlled trial. *JAMA.* 2010;304:1675-1683.
22. Furuhjelm C, Warstedt K, Larsson J, et al. Fish oil supplementation in pregnancy and lactation may decrease the risk of infant allergy. *Acta Paediatr.* 2009;98:1461-1467.
23. Berman DR, Liu YQ, Barks J, Mozurkewich E. Docosahexaenoic acid confers neuroprotection in a rat model of perinatal hypoxia-ischemia potentiated by *Escherichia coli* lipopolysaccharide-induced systemic inflammation. *Am J Obstet Gynecol.* 2010; 202:469.e1-e6.
24. Berman DR, Liu Y, Barks J, Mozurkewich E. Treatment with docosahexaenoic acid after hypoxia-ischemia improves forepaw placing in a rat model of perinatal hypoxia ischemia. *Am J Obstet Gynecol.* 2010;203:385.e1-e5.
25. Zhang W, Hu X, Yang W, et al. Omega-3 polyunsaturated fatty acid supplementation confers long-term neuroprotection against neonatal hypoxic-ischemic brain injury through anti-inflammatory actions. *Stroke.* 2010;41:2341-2347.
26. Graham EM, Ruis KA, Hartman AL, et al. A systematic review of the role of intrapartum hypoxia-ischemia in the causation of neonatal encephalopathy. *Am J Obstet Gynecol.* 2008;199:587-595.
27. Wu YW, Backstrand KH, Zhao S, et al. Declining diagnosis of birth asphyxia in California: 1991-2000. *Pediatrics.* 2004;114:1584-1590.
28. Thornberg E, Thiringer K, Odeback A, Milsom I. Birth asphyxia: incidence, clinical course and outcome in a Swedish population. *Acta Paediatr.* 1995;84:927-932.
29. Olsen SF. Is supplementation with marine omega-3 fatty acids during pregnancy a useful tool in the prevention of preterm birth? *Clin Obstet Gynecol.* 2004;47:768-774; discussion 881-882.
30. Roman AS, Schreher J, Mackenzie AP, Nathanielsz PW. Omega-3 fatty acids and decidual cell prostaglandin production in response to the inflammatory cytokine IL-1beta. *Am J Obstet Gynecol.* 2006;195:1693-1699.
31. Olsen SF, Joensen HD. High liveborn birth weights in the Faeroes: a comparison between birth weights in the Faroes and in Denmark. *J Epidemiol Community Health.* 1985;39:27-32.
32. Olsen SF, Sørensen JD, Secher NJ, et al. Randomized controlled trial of effect of fish-oil supplementation on pregnancy duration. *Lancet.* 1992;339:1003-1007.
33. Olsen SF, Secher NJ, Tabor A, et al. Randomized clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials in Pregnancy (FOTIP) Team. *BJOG.* 2000;107:382-395.

## Main Points

- Essential fatty acids are lipids that cannot be synthesized within the body and must be ingested through the diet or from supplements. Two families of essential fatty acids, omega-3 and omega-6, are required for physiologic functions including oxygen transport, energy storage, cell membrane function, and regulation of inflammation and cell proliferation.
- The richest sources of omega-3 fatty acids are from marine sources such as seafood and fish oil supplements. Other sources of omega-3 fatty acids include as flax seed oil and vegetable oils.
- In 2004, the FDA advised all pregnant women to limit seafood consumption to 340 g (2 6-oz servings) per week to limit fetal exposure to trace amounts of neurotoxins. This recommendation was later adopted by the American College of Obstetricians and Gynecologists.
- Data derived from observational studies have found that omega-3 fatty acid consumption during pregnancy either in the diet or via supplements is associated with improved neurodevelopmental outcomes in the child.
- At present, there is not enough data to recommend omega-3 fatty acid supplementation for the sole purpose of prolonging gestation or reducing the risk of preterm birth.
- Epidemiologic data have shown that low seafood intake during pregnancy correlates with higher levels of depressive symptoms during pregnancy. However, randomized, controlled trials have failed to demonstrate a clear benefit to omega-3 fatty acid supplementation during pregnancy and postpartum to prevent depressive symptoms.

34. Smuts CM, Huang M, Mundy D, et al. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. *Obstet Gynecol.* 2003;101:469-479.
35. Ramakrishman U, Stein AD, Parra-Cabrera S, et al. Effects of docosohexaenoic acid supplementation during pregnancy on gestational age and size at birth; randomized, double-blind, placebo-controlled trial in Mexico. *Food Nutr Bull.* 2010;31(2 suppl):S108-S116.
36. Bulstra-Ramakers MT, Huisjes HJ, Visser GH. The effects of 3g eicosapentaenoic acid daily on recurrence of intrauterine growth retardation and pregnancy induced hypertension. *Br J Obstet Gynaecol.* 1995;102:123-126.
37. Helland IB, Saugstad OD, Smith L, et al. Similar effects on infants of n-3 and n-6 fatty acids supplementation to pregnant and lactating women. *Pediatrics.* 2001;108:E82.
38. Harper M, Thom E, Klebanoff MA, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Omega-3 fatty acid supplementation to prevent recurrent preterm birth. *Obstet Gynecol.* 2010;115:234-242.
39. Owen C, Rees AM, Parker G. The role of fatty acids in the development and treatment of mood disorders. *Curr Opin Psychiatry.* 2008;21:19-24.
40. 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.
41. Freeman MP, Davis M, Sinha P, et al. Omega-3 fatty acids and supportive psychotherapy for perinatal depression: a randomized placebo-controlled study. *J Affect Disord.* 2008;110:142-148.
42. Braunholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect". *J Clin Epidemiol.* 2001;54:217-224.