

Maternal Health and Omega-3 Fats

With a look at postpartum depression

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The need for essential fats for a healthy pregnancy has been under investigation for more than 30 years. Investigators are becoming aware of the critical importance of functional omega-3 fatty acids, such as those found in fish oil, in optimal fetal development. And recently, researchers have begun to look at the importance of omega-3 levels in the pregnant woman and in postnatal maternal health, including postpartum depression.

Omega-3 fats are essential for human health and development, yet they are not synthesized in the body and must be obtained through diet. Most Americans under-consume omega-3s (found in cold water fish, flax) while over-consuming omega-6 fats (found in meats, vegetable and seed oils). This imbalance in fatty acid intake has many health complications^{1,2}, not the least of which concern pregnant women who may not be getting enough omega-3 fats. Inadequate intake of omega-3s may have extensive implications for both mother and infant.

Importance of DHA in fetal development

Development of the central nervous system, brain, eyes, and immune system, including reduced risk for chronic disease, has all been related to adequate intake of DHA during fetal development. In fact, DHA has been shown to rapidly accumulate during the last

trimester of pregnancy (beginning around week 26) and to continue for the first two years of life³.

DHA is a prominent component of phospholipids in the central nervous system and is also found in high concentration in the retina. For example, in infants, 15–20% of the fatty acids in the grey matter of the cortex and brain stem is DHA and about 25% of the fatty acids in the retina is DHA^{4,5}. Specifically, DHA is found in the membranes of neuronal synapses and photoreceptor outer segments⁶. Animal studies performed in the 1970s and 1980s, including several with rhesus monkeys, showed that deficiencies in omega-3 intake caused a rapid drop in the levels of DHA in neural and visual tissue, resulting in compromised function². Abnormal effects on vision, electroretinogram results, cognition function, and behavior related to DHA deficiency have been also reported^{7,8,9}.

Role of DHA in neonates

Adequate intake of DHA during pregnancy appears to influence development of attention and focus in infancy. Infants born of mothers with low DHA levels were shown to be more distractible while mothers with higher DHA levels at the time of birth had babies who could attend longer (measured as “peak look duration”) and were less distractible¹⁰. The authors of that study concluded that DHA levels at time of birth could have long-term cognitive effects, including higher child development and performance.

A Scandinavian study found that children born to mothers who had taken cod liver oil (10ml/day) during pregnancy and lactation had higher IQs at age 4 than those born to mothers who had taken the corn oil placebo¹¹. Recruited in week 18 of their pregnancy, 48 women were randomly assigned to fish oil or placebo until 3 months after delivery (levels of vitamin A and D were the same in both oils). All women breast-fed their infants until the end of the study period. When the children reached 4 years of age, they were administered the Mental Processing component of the Kaufman Assessment Battery for Children, which measures intelligence and achievement. The children (n=41) from mothers in the cod liver oil group scored significantly higher than those (n=35) in the corn oil group. In a multiple regression model, maternal intake of cod liver oil was the only variable of statistical significance.

And in a recent preliminary study¹² of umbilical fatty acids and neurological status at postnatal day 10–14, the infants who demonstrated neurological abnormalities had lower levels of fetal DHA and essential fatty acids (EFA). The authors also noted that linoleic acid and trans fatty acids may have a negative impact on intrauterine neurological development because they impair EFA status.

Why DHA?

DHA works to:

- Support normal fetal development of the central nervous system, brain, eyes, and immune system.
- Improve gestational length and help prevent premature delivery.

Fish oil supplementation during pregnancy has been shown to:

- Improve DHA levels in pregnant women and their infants.
- Increase infant weight at birth.
- Supply recommended levels of essential omega-3 fats.
- Reduce the risk of allergies in infants.
- Improve immunomodulatory factors in breast milk.
- Increase IQ levels in children.
- Improve attention and focus in infants and young children.

Dependence of the fetus on maternal omega-3 intake

As with all nutrients, the fetus is dependent on the mother for essential fatty acid intake, which must be sufficient to maintain the mother's own healthy levels and meet fetal demands¹³. During pregnancy, DHA is preferentially transferred to the fetus, and the higher the mother's level of DHA, the more is carried to the fetus for its use in development.

Alpha-linolenic acid (ALA), the plant form of omega-3, is found in flax and walnuts. It has been believed that through conversion, ALA consumption could meet the nutritional needs for omega-3 fats in adults and children. However, it has become evident that ALA does not effectively convert to EPA and DHA in humans and is, therefore, not a reliable source for these important nutrients^{14,15}.

Pre-formed DHA is the preferred form of DHA in infant development⁵. Isotope studies have confirmed that dietary intake of DHA is preferred over DHA from metabolic synthesis⁵. It has been shown that plant-source ALA is not a reliable source of DHA in pregnancy. Investigators who have looked at plant sources of omega-3 (ALA) determined that the fetus and neonate have little ability to metabolize DHA from ALA, and some infants have no ability at all to convert ALA⁵. This has also been shown in animals: Animals fed diets with ALA were unable to achieve the tissue DHA concentrations achieved by those fed pre-formed DHA⁶.

Fish oil supplementation improves DHA status

Fish oil supplementation has been shown to improve the DHA status of infants at birth and in mothers, too¹⁶. In one study, 23 healthy pregnant women were given fish oil (2.7g/day of omega-3) from week 30 to delivery. Control subjects took olive oil. More omega-3 fatty acids were found in the maternal plasma phospholipids in the fish oil group. Further, higher amounts of omega-3 fats, particularly DHA, were found in the phospholipids of umbilical plasma and vessel walls.

Fish oil supplementation as an effective means of improving omega-3 status in healthy pregnant women has been confirmed in other clinical research¹⁷. Ninety-eight healthy women were given 4g/day of fish oil (56% DHA / 28% EPA) or olive oil placebo from 20 weeks until delivery. Results showed that the maternal levels of EPA and DHA were higher in the supplemented group at 30 and 37 weeks gestation and then remained

so for 6 weeks postpartum. EPA and DHA levels were also higher in the neonates. The authors concluded that omega-3 supplementation could prevent DHA depletion in pregnancy.

Fish oil supplementation has also been shown to improve DHA status in breast milk¹⁸. Finally, it's also been shown that plant sources of omega-3s, such as flax seed oil, do not improve DHA status in breast milk¹⁹.

Fish oil supplementation in pregnancy outcomes

Omega-3 trials in pregnant women have shown a significant reduction in the incidence of premature delivery²⁰. One such study reported that fish oil supplementation improves gestational length. Infants born of mothers who had supplemented with cod liver oil had higher levels of DHA in their umbilical cord phospholipids, longer gestational length, and more mature electroencephalography measures on the second day of life²¹. This double-blind randomized study involved 590 healthy pregnant women who received 10ml/day of cod liver oil or corn oil until 3 months after delivery. Conversely, other studies have reported associations with preterm delivery and low birth weight in infants born of women with little to no intake of omega-3 fats from fish or fish oil²².

A recent Icelandic study²³ showed that healthy women consuming liquid cod liver oil in the first 15 weeks of pregnancy delivered babies with higher birth weight, yet the women themselves did not gain more weight, compared to controls. A larger size at birth is related to a lower prevalence of common adult diseases, such as cardiac disease, hypertension, and glucose intolerance^{24,25}. In addition, DHA's crucial role in the development of the central nervous system may well begin during the early weeks of gestation²⁶. In this observational study, 435 women were given a semi-quantitative food frequency questionnaire between 11 and 15 weeks of gestation and again between 34 and 37 weeks. The daily intake of marine food and cod liver oil was estimated. Results showed that the 63 women who took liquid cod liver oil (average dose of 10ml/day) early in their pregnancy gave birth to infants with mean weights that were 139 g heavier. These correlations were not seen in those who consumed fish or common cod liver oil capsules. The women supplementing with liquid cod liver oil consumed an average of 1.8 g of long chain omega-3s, whereas those taking capsules consumed an average of 0.18 g of omega-3s (10x less).

Fish oil provides eicosapentaenoic (EPA) and docosahexaenoic (DHA), two dietary essential long-chain omega-3 fatty acids. Standard fish oils contain about 30% omega-3, and more concentrated forms are available. Cod liver oil, traditionally considered "nature's brain food," delivers proportionately more DHA than EPA.

The authors suggested the difference in dose as the most probable reason for the difference in findings. Furthermore, they noted “Healthy women are 11 times more likely to give birth to an infant of 4500 g or more after a healthy pregnancy if they used liquid cod liver oil during the first trimester.”

Fish oil supplementation during pregnancy has been shown to reduce the risk of allergies in infants²⁷, and it has been shown to measurably improve immunomodulatory factors in breast milk, which are thought to positively influence infant immune development²⁸.

Finally, supplementing infants with cod liver oil during the first year of life has been associated with lower risk of childhood-onset type 1 diabetes. A Norwegian nationwide case-control study²⁹ examined 545 cases of childhood-onset type 1 diabetes and 1668 control subjects. Their results showed that supplementation with cod liver oil during the first year of life significantly reduced the risk of childhood-onset diabetes, even after controlling for duration of breastfeeding, maternal age, maternal education, and age of onset of solid foods. The researchers suggested that the omega-3 fatty acids in cod liver oil have anti-inflammatory properties that may be the mechanism of action in the reduction in risk.

DHA recommendations and intake

Recommendations for effective amounts of DHA during pregnancy have not been established in the United States. However, the *International Society for the Study of Fatty Acids and Lipids* (ISSFAL) recommends 2.87g/day of omega-3 fatty acids for adults (1.3% total energy), with a minimal intake of 300mg of DHA for pregnant and nursing women³⁰. For infants from 12 to 18 months, ISSFAL recommends 32mg EPA + DHA per pound of body weight. And the Acceptable Macronutrient Distribution Range (AMDR) established as part of the Canadian Dietary Reference Intakes recommends that 0.6–1.2% of energy for pregnant women be comprised of omega-3 fats¹³.

How much DHA are pregnant women ingesting? Very recently, dietary intake of DHA was carefully measured during the second and third trimester in 20 pregnant Canadian women. The researchers reported a mean intake of 82mg +/- 33mg day of DHA and a remarkable 90% consumed less than the ISSFAL minimum recommendation¹¹. In another group, mean dietary intake of DHA was estimated to be 68mg +/- 75mg of DHA per day in pregnant African American women³¹. This is consistent with the average intake of DHA among Americans in general. In fact, according to the most recent national nutrition survey (NHANES III), the median intake of DHA (and EPA) among Americans is zero with a mean intake of 70mg/day of DHA and 40mg/day of EPA³². It has been reported³³ that women

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Safety considerations concerning seafood contaminants

Because of environmental contamination, the US Food and Drug Administration and Environmental Protection Agency advise women who may become pregnant, nursing mothers, and young children to avoid certain types of fish and shellfish, and to limit others³⁴. Many fish contain high levels of a form of mercury called methylmercury, a known damaging neurotoxin.

In all people, including pregnant women and small children, choosing to supplement with fish oil may have far reaching benefits. Substituting purified fish oil supplements for fish can reduce or virtually eliminate exposure to mercury and other environmental toxins, e.g., PCBs, dioxins, pesticides. Toxicological examination shows that high-quality fish oil supplements may be a safer alternative to dietary fish and provide the benefits of omega-3s without risk of toxicity^{35,36}.

Conclusion

Clinical research suggests a beneficial role for fish oil supplementation both in pregnancy and postpartum. And high-quality fish oil supplements that adhere to established standards, such as the European Pharmacopoeia and Norwegian Medicinal Standards, which aggressively limit the amount of heavy metals, dioxins, and PCBs in such supplements, can help alleviate concerns about toxicity.

Given the preponderance of evidence indicating developmental benefit to the infant from increased maternal intake of omega-3 fatty acids as well as the correlation between low maternal DHA levels and postpartum depression, fish oil supplementation rich in functional omega-3s during pregnancy and lactation seems reasonable and prudent. ■

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OMEGA-3 FATTY ACIDS AND POSTPARTUM DEPRESSION

Interest in the role of essential fatty acids in depression started in the late 1990s when associations with alterations in fatty-acid composition in both serum and red blood cell membranes were observed with major depression^{37,38,39}. Human controlled studies have shown that fish oil also shows promise for reducing major depression and bi-polar disorder in the non-pregnant^{40,41}. Now, a link between increased prevalence of depression and decreased omega-3 fatty acid consumption has been observed⁴².

The prevalence of postpartum depression varies between 10–15% in the general population and typically arises within 4 weeks of delivery and lasts for up to 12 months; lactating women do not appear more predisposed than non-lactating women to develop depressive symptoms⁴³. Postpartum depression can have a negative impact on the infant's development, including attachment and behavior⁴⁴. Maternal serum levels of DHA steadily decline after delivery, and some investigators have begun to hypothesize a relationship between maternal DHA depletion and postpartum depression^{45,46,47}.

An international cross-analysis⁴⁸ showed that higher levels of DHA in breast milk and greater seafood consumption predicted a lower prevalence of postpartum depression; further, those who consumed little or no seafood suffered nearly twice the rate of depression. While the findings are not causal, they do suggest a beneficial role for marine-derived omega-3 fats in helping postpartum depression.

Low levels of DHA at delivery may increase depression risk. One study compared fatty acid levels in 48 women post-delivery. Ten of the women developed postpartum depression and they were shown to have significantly lower levels of DHA after delivery than those who did not develop depression⁴⁹. The authors suggested that women at risk for postpartum depression may benefit from prophylactic treatment with a combination of EPA and DHA.

A randomized dose-finding 2005 trial⁵⁰ of American women showed that supplementation with omega-3 in a dose as low as 0.5 g/day (EPA:DHA ratio 1.5:1) had significant benefits against postpartum depression. During the 8-week intervention, 16 women were randomized to groups receiving 0.5, 1.4, or 2.8 g/day of omega-3 from fish oil or placebo (corn oil). Participants were 15–45 years of age and had had at least one major depressive episode with onset within 1 month of live childbirth. Each woman was assessed with the Edinburgh Postnatal Depression Scale (EPDS) and the Hamilton Rating Scale for Depression (HRSD) at entry and then again at 1, 2, 4, 6, and 8 weeks. Mean scores on the EPDS and HRSD were 18.1 and 19.1, respectively, at baseline. At the end of 8 weeks, they were 9.3 and 10.0, respectively, with decreases of 51.5% and 48.8%. No significant differences between dosage groups were noted. The authors noted the health benefits of omega-3 supplementation and the low risk of the modest doses.

One small, open-label pilot trial in pregnant women, however, failed to show a benefit of fish oil for postpartum depression, although it is likely that intervention began too late; supplementation did not begin until the 34th to 36th weeks⁵¹. An animal study recently found that regular intake of fish oil was able to induce an antidepressant effect in female rats⁵². The authors concluded that this finding was related to increases in EPA and DHA concentration in the cerebral cortex and hippocampus.

Another group observed that women who became depressed postpartum had a slower rate of recovery of their plasma DHA status when compared to the non-depressed³⁴.

Finally, a case study⁵³ reported successful treatment of a pregnant woman who had suffered for five years from major depressive episodes. The 34-year-old woman was treated with 4g EPA and 2g DHA daily beginning in the 25th week. She evidenced significant improvement in depressive symptoms four weeks later (the 29th week of gestation) and her condition remained stable throughout the pregnancy. After delivery, the baby appeared normal in all physical and neurobehavioral aspects.

Fetal Health and SSRIs

What little is known about the effects of antidepressant medications, such as selective serotonin reuptake inhibitors (SSRIs), on the offspring of women who use them during pregnancy or breastfeeding is not encouraging. A 2004 publication was one of the first to compare the effect on newborns of maternal use of SSRIs during pregnancy with newborns not exposed to SSRIs. The study found that the newborns exposed to SSRIs had full birth weight and were healthy but showed disruptions in various neuro-behaviors⁵⁴. Another group reported that infants exposed to SSRIs in late pregnancy are at an increased risk for adverse serotonergic central nervous system effects⁵⁵.

References

1. Simopoulos, AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr* 2002;21(6):495–505.
2. Cordain L. Origins and evolution of the Western diet: Health implications for the 21st century. *Am J Clin Nutr* 2005 Feb;81(2):341–354.
3. Carlson, SE. Overview of n-3 fatty acids in maternal and infant nutrition. Presented at the American Dietetics Association Food and Nutrition Conference, Anaheim, CA. October 4, 2004.
4. Brenna, JT. *Infant Formulas Containing DHA and ARA*. Cornell Cooperative Extension. Cornell University: Ithaca, NY, April 4, 2003.
5. Salem, N. The relative importance of dietary alpha-linolenic acid vs. preformed docosahexaenoic acid in supporting brain lipid composition. Presented at the American Dietetics Association Food and Nutrition Conference, Anaheim, CA. October 4, 2004.
6. Al M, van Houwelingen A, Hornstra G. Long-chain polyunsaturated fatty acids, pregnancy, and pregnancy outcome. *Am J Clin Nutr* Jan 2000;71:285–291.
7. Connor WE, Neuringer M, Reisbick S. Essential fatty acids: The importance of n-3 fatty acids in the retina and brain. *Nutr Rev* 1992;50:21–29.
8. Neuringer M, Connor WE, Van Petten C, Barstad L. Dietary omega-3 fatty acid deficiency and visual loss in infant rhesus monkeys. *J Clin Invest* 1984;73:272–276.
9. Neuringer M, Connor WE, Lin DS, Barstad L, Luck S. Biochemical and functional effects of prenatal and postnatal omega-3 fatty acid deficiency on retina and brain in rhesus monkeys. *Proc Natl Acad Sci USA* 1986;83:4021–4025.
10. Colombo J, Kannass KN, Shaddy DJ, et al. Maternal DHA and the development of attention in infancy and toddlerhood. *Child Dev* 2004;75:1254–1267.
11. 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 Jan;111(1):e39.
12. Dijk-Brouwer DA, Hadders-Algra M, Bouwstra H, et al. Lower fetal status of docosahexaenoic acid, arachidonic acid and essential fatty acids is associated with less favorable neonatal neurological condition. *Prostaglandins, Leukot Essent Fatty Acids* 2005;72:21–28.
13. Denomme J, Stark KD, Holub BJ. Directly quantitated dietary (n-3) fatty acid intakes of pregnant Canadian women are lower than current dietary recommendations. *J Nutr* 2005;135:206–211.
14. Pawlosky RJ, Hibbeln JR, et al. Effects of beef- and fish-based diets on the kinetics of n-3 fatty acid metabolism in human subjects. *Am J Clin Nutr* 2003;77:565–572.
15. Davis BC, Kris-Etherton PM. Achieving optimal essential fatty acid status in vegetarians: Current knowledge and practical implications. *Am J Clin Nutr* 2003;78:640–646.
16. van Houwelingen AC, Sorensen JD. Essential fatty acid status in neonates after fish-oil supplementation during late pregnancy. *Br J Nutr* 1995;74(5):723–731.
17. Dunstan JA, Mori TA, Barden A, et al. Effects of n-3 polyunsaturated fatty acid supplementation in pregnancy on maternal and fetal erythrocyte fatty acid composition. *Eur J Clin Nutr* 2004;58(3):429–437.
18. Helland IB, Saarem K, et al. Fatty acid composition in maternal milk and plasma during supplementation with cod liver oil. *Eur J Clin Nutr* 1998 Nov;52(11):839–845.
19. Francois CA, Connor SL, Bolewicz LC, Connor WE. Supplementing lactating women with flaxseed oil does not increase docosahexaenoic acid in their milk. *Am J Clin Nutr* 2003;77:226–233.
20. Allen KG, Harris MA. The role of n-3 fatty acids in gestation and parturition. *Exp Biol Med* 2001;226(6):498–506.
21. Helland IB, Saugstad OD, Smith L, et al. Similar effects on infants of n-3 and n-6 fatty acids supplementation in pregnant and lactating women. *Pediatrics* 2001;108(5):E82.
22. Olsen SR, Slicher NJ, et al. Randomized clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials in Pregnancy Team (FOTIP). *BJOG* 2000;107(3):382–395.
23. Olafsdottir AS, Magnusardottir AR, Thorgeirsdottir H, et al. Relationship between dietary intake of cod liver oil in early pregnancy and birth weight. *BJOG* 2005 Apr;111:424–429.
24. Birgisdottir BE, Gunnarsdottir I, Thorsdottir I, Gudnason V, Benediktsson R. Size at birth and glucose intolerance in a relatively genetically homogenous high-birth weight population. *Am J Clin Nutr* 2002;76:399–403.
25. Gunnarsdottir I, Birgisdottir BE, Benediktsson R, Gudnason V, Thorsdottir I. Relationship between size at birth and hypertension in a genetically homogenous population of high birth weight. *J Hypertens* 2002;20:623–628.
26. Malcolm, CA, Hamilton R, McCulloch DL, et al. Scotopic electroretinogram in term infants born of mothers supplemented with docosahexaenoic acid during pregnancy. *Invest Ophthalmol Vis Sci* 2003;44:3685–3691.
27. Dunstan JA, Mori TA, Barden A, et al. Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: A randomized, controlled trial. *J Allergy Clin Immunol* 2003;112:1178–1184.
28. Dunstan JA, Roper J, Mitoulas L, et al. The effect of supplementation with fish oil during pregnancy on breast milk immunoglobulin A, soluble CD14, cytokine levels and fatty acid composition. *Clin Exp Allergy* 2004;34:1237–1242.
29. Stene LC, Joner G. Norwegian Childhood Diabetes Study Group. Use of cod liver oil during the first year of life is associated with lower risk of childhood-onset type 1 diabetes: A large, population-based, case-control study. *Am J Clin Nutr* 2003;78:1128–1134.
30. Simopoulos AP, Leaf A, Salem N. Workshop statement on the essentiality of and recommended dietary intakes for omega-6 and omega-3 fatty acids. *Prostaglandins Leukot Essent Fatty Acids* 2000;63:119–121.
31. Stark KD, Beblo S, et al. Comparison of bloodstream fatty acid composition from African-American women at gestation, delivery, and postpartum. *J Lipid Res Mar* 2005;46:516–525.
32. Third National Health and Nutrition Examination Survey, NIH. Source: National Library of Medicine, Agency for Healthcare Research and Quality Evidence. Report No. 93 (AHRQ, 2004). Accessed March 29, 2006. <http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hsta1a.table.35383>.
33. Carlson S. Behavioral and molecular effects of a modest reduction in brain DHA. Presented at the International Conference on Fatty Acid and Utilization of Fatty Acids, Lipids & Lipoproteins, Bethesda, MD. October 8, 2004.
34. <http://www.cfsan.fda.gov/~dms/admehg3b.html>. Accessed March 30, 2006.
35. Melanson SF, Lewandrowski EL, Flood JG, Lewandrowski KB. Measurement of organochlorines in commercial over-the-counter fish oil preparations: Implications for dietary and therapeutic recommendations for omega-3 fatty acids and a review of the literature. *Arch Pathol Lab Med* 2005;129(1):74–77.
36. Foran SE, Flood JG, Lewandrowski KB. Measurement of mercury levels in concentrated over-the-counter fish oil preparations: Is fish oil healthier than fish? *Arch Pathol Lab Med* 2003;127(12):1603–1605.
37. Maes M, Christophe A, et al. Lowered omega-3 polyunsaturated fatty acids in serum phospholipids and cholesteryl esters of depressed patients. *Psychiatry Res* 1999;85(3):275–291.
38. Maes M, Smith R, et al. Fatty acid composition in major depression: Decreased omega-3 fractions in cholesteryl esters and increased C20:4 omega-6/C20:5 omega-3 ratio in cholesteryl esters and phospholipids. *J Affect Disord* 1996;38(1):35–46.
39. Edwards R, Peet M, et al. Omega-3 polyunsaturated fatty acid levels in the diet and in red blood cell membranes of depressed patients. *J Affect Disord* 1998;48(2–3):149–155.
40. Su K-P, Huang S-Y, Chiu C-C, et al. Omega-3 fatty acids in major depressive disorder: A preliminary double-blind placebo-controlled trial. *Eur Neuropsychopharmacol* 2003;13:267–271.
41. Stoll AL, Severus WE, Freeman MP, et al. Omega 3 fatty acids in bipolar disorder: A preliminary double-blind, placebo-controlled trial. *Arch Gen Psychiatry* 1999;56(5):407–412.
42. Hibbeln, JR. Fish consumption and major depression. *Lancet* 1998;351(9110):1213.
43. Otto SJ, de Groot RH, Hornstra G. Increased risk of postpartum depressive symptoms is associated with slower normalization after pregnancy of the functional docosahexaenoic acid status. *Prostaglandins Leukot Essent Fatty Acids* Oct 2003;69(4):237–243.
44. Cicchetti D, Rogosch FA, Toth SL. Maternal depressive disorder and contextual risk: Contributions to the development of attachment insecurity and behavioral problems in toddlerhood. *Dev Psychopathol* 1988;10:283–300.
45. Holman RT, Johnson SB, Ogburn PL. Deficiency of essential fatty acids and membrane fluidity during pregnancy and lactation. *PNAS* 1991;88:4835–4839.
46. Freeman, MP. Omega-3 fatty acids: An ideal treatment for depression in pregnancy? *Evidence-Based Integrative Med* 2003;1(1):43–49.
47. Al MD, van Houwelingen AC, et al. Maternal essential fatty acid patterns during normal pregnancy and their relationship to the neonatal essential fatty acid status. *Br J Nutr* 1995;74(1):55–68.
48. Hibbeln JR. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: A cross-national, ecological analysis. *J Affect Disord* May 2002;69(1–3):15–29.
49. De Vriese SR, Christophe AB, Maes M. Lowered serum n-3 polyunsaturated fatty acid (PUFA) levels predict the occurrence of postpartum depression: Further evidence that lowered n-PUFAs are related to major depression. *Life Sci* Nov 2003;73(25):3181–3187.
50. Freeman MP, Hibbeln JR, Wisner KL, et al. Randomized dose-ranging pilot trial of omega-3 fatty acids for postpartum depression. *Acta Psychiatr Scand* 2001:1–5.
51. Marangell LB, Martinez JM, Zboyan HA, Chong H, Puryear LJ. Omega-3 fatty acids for the prevention of postpartum depression: Negative data from a preliminary, open-label pilot study. *Depress Anxiety* 2004;19(1):20–23.
52. Naliwaiko K, Araujo RL, da Fonseca RV, et al. Effects of fish oil on the central nervous system: A new potential antidepressant? *Nutr Neurosci* 2004;7(2):91–99.
53. Chiu C-C, Huang S-Y, Shen WW, Su K-P. Omega-3 fatty acids for depression in pregnancy. *Am J Psychiatry* 2003;160:385.
54. Zeskind PS, Stephens LE. Maternal selective serotonin reuptake inhibitor use during pregnancy and newborn neurobehavior. *Pediatrics* 2004;113:368–375.
55. Laine K, Heikkinen T, Ekblad U, Kero P. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. *Arch Gen Psychiatry* 2003;60:720–726.

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