

- Topics:** Omega-3 fatty acids, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), long chain polyunsaturated fatty acids (LC-PUFAs), pregnancy, infant morbidity
- Background:** The beneficial effects of DHA intake during pregnancy through either maternal diet or supplement use on cognitive development during infancy has been well known for over a decade. This knowledge has resulted in an official recommendation for women to consume at least 200 mg/DHA daily during pregnancy. However, intake of LC-PUFAs also influences immune cell function, but few studies have investigated the extent to which DHA supplementation during pregnancy can benefit infant morbidity.
- Objective:** To determine the impact of DHA supplementation during pregnancy on infant morbidity.
- Method:** This randomized, double-blind, placebo-controlled clinical trial included 1094 pregnant women who took either 400 mg of algal sourced DHA or a placebo daily from 18-22 weeks' gestation through parturition.  
**Inclusion criteria:** gestation week 18-22, aged 18-35 years, planned to deliver at the IMSS General Hospital Inn Cuernavaca, planned to breast feed after delivery, and planned to live in the area for 2 years.  
**Exclusion criteria:** high risk pregnancy, lipid metabolism/absorption disorders, regular intake of fish oil or DHA supplements, chronic use of certain medications
- The infants were assessed at ages 1 (n=849), 3 (n=834) and 6 (n= 834) months for the occurrence and duration of the following common illness symptoms in the preceding 15 days:
- Colds, Cough
  - Phlegm, Nasal congestion
  - Wheezing
  - Rash
  - Vomiting, Diarrhoea
  - Fever
  - Nasal secretion, Difficulty breathing
  - Other illness
- Findings:**
- 1) The occurrence of specific illness symptoms was not different between groups. However, the occurrence of combined cold symptoms was lower in the DHA group at 1 month (OR:0.76; 95% CI:0.58-1.00)
  - 2) At 1 month, the DHA group experienced a 26%, 15% and 30% shorter duration of cough, phlegm and wheezing, respectively, but 22% longer duration of rash (all  $p < 0.01$ ).
  - 3) At month 3, infants in the DHA group were ill 14% less of the time ( $p < 0.0001$ )
  - 4) At 6 months, infants in the DHA group experienced 20%, 13%, 54%, 23% and 25% shorter duration of fever, nasal secretion, difficulty breathing, rash and other illness respectively, but 74% longer duration of vomiting (all  $p < 0.05$ )
- Conclusion:** DHA supplementation during pregnancy decreased the occurrence of colds in children at 1 month and reduced illness symptom duration at 1, 3 and 6 months.
- Relevance to** Efanatal, Efalex Mother & Baby, Efamol Mother & Baby
- Reference:** Imhoff-Kunsch B, Stein AD, Martorell R, Parra-Cabrera S, Romieu I et al. Prenatal Docosahexaenoic acid supplementation and infant morbidity: Randomized Controlled Trial. *Pediatrics* 2001;Aug 1 [Epub ahead of print]. Doi:10.1542/peds. 2010-1386.

**PRESS RELEASE****Docosahexaenoic acid (DHA) during pregnancy improves infant health<sup>1</sup>.**

A recent study completed at Emory University and funded by the National Institute of Health, USA and the March of Dimes Foundation charity, has confirmed a preliminary finding that DHA supplementation during pregnancy improves infant's immune function as measured by frequency and intensity of illness symptoms.

The randomized, double-blind, placebo-controlled clinical trial included 1094 pregnant women who took either 400 mg of algal sourced DHA or a placebo daily from 18-22 weeks' gestation through parturition. Their infants were assessed at ages 1 (n=849), 3 (n=834) and 6 (n= 834) months for the occurrence and duration of a variety of common illness symptoms in the preceding 15 days including colds, cough, phlegm, nasal congestion, wheezing, rash, vomiting, diarrhoea, fever, nasal secretion, difficulty breathing, and other illness.

While both groups had similar numbers of illnesses, the infants whose mothers had taken DHA had reduced symptom duration at 1 month compared to the placebo group. At 1 month, the DHA group experienced a 26%, 15% and 30% significantly shorter duration of cough, phlegm and wheezing, respectively, but 22% longer duration of rash. At month 3, infants in the DHA group were ill 14% less of the time compared to those in the placebo group. At 6 months, infants in the DHA group experienced 20%, 13%, 54%, 23% and 25% shorter duration of fever, nasal secretion, difficulty breathing, rash and other illness respectively, but 74% longer duration of vomiting.

To date, only one other randomized, placebo- controlled trial has specifically addressed the impact of Omega-3 LC-PUFA supplementation on infant immunity<sup>2,3,4</sup>. That study included atopic women provided with fish oil rather than algal sourced DHA. It showed that fish oil changed some aspects of infants immune function and lowered the risk of specific allergies as assessed by skin prick test. It also modified maternal breast milk composition such that it might enhance infant immune response. The Emory University study extended those results to show the clinical response of those alterations in infant immune function.

Previous studies have reported other benefits of omega-3 LC-PUFAs during pregnancy and/or while breast feeding on the infant and toddler. Two studies published earlier this year showed that higher dietary intake of DHA during pregnancy improved memory in 11 year old children,<sup>5</sup> while DHA supplementation during pregnancy enhanced brain function in children just entering school (approximately age 5 years).<sup>6</sup> Others have reported higher maternal DHA status at birth is associated with enhanced attentional functioning in toddlers during their first and second years of life<sup>9,10</sup> while higher DHA concentration in umbilical cord blood (a good indicator of foetal exposure to that nutrient during the last trimester of pregnancy) and higher DHA concentration in infant cord blood increases gestation, improves visual acuity and intelligence at 6 months of age, and also increases mental and psychomotor development at 11 months of age<sup>11</sup>. A trial including term infants showed the quality of movement was dependent on how high the infants DHA was at the time of birth and was independent of gender, cognitive performance, gestational age and age at measurement<sup>12</sup>. Earlier in 2007, a similarly designed study showed that low infant blood levels of DHA predict the development of internalizing problem behaviour later in life<sup>13</sup>. A 2009 study reported that babies born to mothers who took DHA during pregnancy and while breast feeding are 7.5 times less likely to develop food allergies and 3 times less likely to develop eczema.<sup>8</sup> A study published in early 2011 reported that babies born to mothers who eat the recommended quantity of DHA during pregnancy are 32 percent less likely to have excessive body fat indicative of potential obesity<sup>7</sup>. The largest clinical study ever providing DHA to 2,399 pregnant women, reported a 60% reduction in slow developing cognitive and language skills in infants, a 35% reduction in the incidence of low birth weight babies and 50% reduction in the number of very early pre-term deliveries with no serious adverse effects for either the mother or infant<sup>15</sup>.

Other clinical studies have shown that maternal fish intake during pregnancy is associated with higher IQ in offspring<sup>14</sup>, and that pregnant mothers taking DHA rich fish oil supplements during the last trimester can maintain their DHA status.<sup>16</sup> In addition, infants born to these mothers have also been shown to start life with higher DHA levels than those of mothers who were not supplemented.<sup>16</sup> Infants with higher DHA status have enhanced sleep patterns suggesting greater central nervous system maturity<sup>17</sup>, enhanced attention and mental processing<sup>10</sup>, score better in mental processing tests<sup>18</sup>, have higher IQs at four years of age<sup>19</sup> and higher scores for language comprehension, average phrase length and vocabulary<sup>20</sup>.

The Emory University study adds to the massive body of information supporting the need for and importance of DHA supplementation for the health of future generations. This study group is now turning age 4, and at age 5 the researchers plan to study their school performance and other long-term effects aimed at confirming if children grow better and are smarter following maternal supplementation during pregnancy.

## References:

1. Imhoff-Kunsch B, Stein AD, Martorell R, Parra-Cabrera S, Romieu I et al. Prenatal Docosahexaenoic acid supplementation and infant morbidity: Randomized Controlled Trial. *Pediatrics* 2001;Aug 1 [Epub ahead of print].
2. Dunstan JA, Mori TA, Barden A et al. Maternal fish oil supplementation in pregnancy reduces interleukin-13 levels in cord blood of infants at high risk of atopy *Clin Exp Allergy* 2003;33(4):442-448.
3. Dunstan J, 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(6):1178-1184.
4. Prescott SL, Barden AE, Mori TA, Dunstan JA. Maternal fish oil supplementation in pregnancy modifies neonatal leukotriene production by cord-blood-derived neutrophils *Clin Sci (Lond)* 2007;113(10):409-416.
5. Boucher O, Burden MJ, Muckle G, Saint-Amour D, Ayotte P et al. Neurophysiologic and neurobehavioral evidence of beneficial effects of prenatal omega-3 fatty acid intake on memory function at school age. *Am J Clin Nutr.* 2011 May;93(5):1025-37.
6. Escolano-Margarit MV, Ramos R, Beyer J, Csábi G, Parrilla-Roure M et al. Prenatal DHA Status and Neurological Outcome in Children at Age 5.5 Years Are Positively Associated. *J Nutr.* 2011 Jun;141(6):1216-23.
7. Donahue SM, Rifas-Shiman SL, Gold DR, Jouni ZE, Gillman MW, Oken E. Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort. *Am J Clin Nutr.* 2011 Apr;93(4):780-8. Epub 2011 Feb 10.
8. Furuhejm 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]
9. Kannass KN, Colombo J, Carlson SE. Maternal DHA levels and toddler free-play attention. *Dev Neuropsychol*2009;34(2):159-74.
10. Colombo J, Kannass KN, Shaddy DJ, et al. Maternal DHA and the development of attention in infancy and toddlerhood. *Child Dev.* 2004;75(4):1254-67.
11. Jacobson JL, Jacobson SW, Muckle G, Kaplan-Estrin M, Ayotte P, Dewailly E. Beneficial effects of a polyunsaturated fatty acid on infant development evidence from the Inuit of Arctic Quebec. *J Pediatr* 2008;152:356-64.
12. Bakker EC, Hornstra G, Blanco CE, Vles JS. Relationship between long-chain polyunsaturated fatty acids at birth and motor function at 7 years of age. *Eur J Clin Nutr.* 2007 Dec 19; doi:10.1038/sj.ejcn.1602971.
13. Krabbendam L, Bakker E, Hornstra G, vanOs J. Relationship between DHA status at birth and child problem behavior at 7 years of age. *Prostaglandins Leukot Essent Fatty Acids* 2007;76:29-34.
14. Hibbeln JR, Davis JM, Steer C, Emmett P, Rogers I, Williams C, Golding J. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. *Lancet* 2007;369:578-585.
15. Makrides M, Gibson R, McPhee A, Yelland L, Quinlivan J et al. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children. *JAMA* 2010;304(15):1675-1683.
16. Van Houwelingen AC et al. EFA status in neonates after fish oil supplementation during late pregnancy. *Br J Nutr* 1995; 74(5):723-31.
17. Cheruku et al. Higher maternal plasma DHA during pregnancy is associated with more mature neonatal sleep-state patterning. *Amer J Clin Nutr* 2002;76:608-13.
18. Decsi T and Koletzko B. N-3 fatty acids and pregnancy outcomes. *Curr Opin Clin Nutr Metab Care.* 2005;8(2)161-6.
19. Helland 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):e39-44.
20. Dunstan J, Simmer K, Dixon G, Prescott S. Cognitive assessment of children at age 2.5 years after maternal fish oil supplementation in pregnancy: a randomized controlled trial. *Archives of Disease in Childhood: published online ahead of print:* 10.1136/adc.2006.099085.